RESEARCH ACTIVITY

At the Division of Ear, Nose and Throat Diseases

2025

Karolinska Institutet

KAROLINSKA UNIVERSITETSSJUKHUSET

CONTENT

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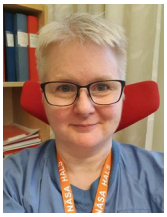	Anna Granath anna.granath@ regionstockholm.se		Sten Hellström sten.hellstrom@ki.se
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Luca Verrecchia
Jeremy Wales
Inger Uhlén

DISSERTATIONS / HALF TIME SEMINARS

Date		Name	Title
2024-06-14	Dissertation	Krzysztof Piersiala	Tumour-draining lymph nodes in head and neck cancer: immunological signatures and clinical implications
2024-10-18	Half time	Maryam Jafari	Filling the gaps in type 2 inflammation: Role of neutrophils in chronic rhinosinusitis with nasal polyps and impact of allergen-specific immunotherapy on immunoglobulin modulation and T cell glycosylation in allergic rhinitis
2024-12-18	Dissertation	Yelin Zhao	Prioritization of mechanisms and potential biomarkers in inflammatory and malignant diseases

Senior Researchers

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Sepehri, Elnaz
Skröder, Carl
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Åberg, Karin

Senior Researchers

At the Division of Ear, Nose and Throat Diseases

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Name: Babak Alinasab
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Project title:

I. Mapping of Sinonasal cancer in Sweden.

II. Isolated Orbital Floor Fractures – To operate or not to operate.

III. Zygomaticomaxillary Complex Fractures: aspects of diagnostic methods, treatment and sequelae

Supervision of PhD-student:

Samin Rahbin	Main supervisor: ☒ Co-supervisor: ☐
Oscar Solmell	Main supervisor: ☒ Co-supervisor: ☐
Sebastian Dybeck Udd	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

I. Treatment for sinonasal malignancies, like other malignancies includes surgery, radiotherapy and chemotherapy of which surgery is the most central. What combination treatment that is most effective, however, is disputed.

Recent publications of treatment combinations has found that multimodal treatment was superior, as measured by survival. Herein there is a knowledge gap that this project will attempt to address.

The aim of this ongoing project is to both map the incidence, prevalence and relative survival of patients with sinonasal cancer. Different treatment modalities will be compared and evaluated in relation to long term survival and recurrence.

II. A significant BOF needs surgical treatment otherwise it may lead to double vision and aesthetic deformities such as sunken eye. It is highly important to differentiate which patients need to be operated on or which do not.

In the on going projects below, we aim to identify which patients with BOF need an operation and which do not require an operation to prevent functional and aesthetic disorders.

1. Controlled randomized studies on patients with BOF with inferior BOF with a herniation > 1mL.

2. Prospective cohort study on isolated medial BOF.

III. In zygomaticomaxillary Complex fractures, the surgeons' individual training, experience and preference influences the treatment and not systematic evidence, even though earlier studies on surgical treatment have shown that the choice of treatment have an impact on surgical outcome. As the degree and success of the reconstruction of a fractured zygoma is assessed by evaluating the contralateral, non-fractured side, the unfractured zygoma is used as a reference when planning for surgery.

In this ongoing project we aim to:

-Evaluate the long-term results of patients with ZMC fractures.

-Detect correlations between complications and to evaluate the overall management of ZMC fractures.

-To introduce a reliable treatment algorithm based on evidence based medicine.

Ethic permit No:

2009/331-31	2018/302-31	2019-04287-1		

Publications 2022, 2023, 2024:

1. **Does more invasive surgery result in higher patient satisfaction? A long-term follow-up of 136 zygomaticomaxillary complex fractures S**amin Rahbin, M.D, Ola Sunnergren, M.D., Ph. D., Ellen Lindgren, M.D., Hatef Darabi, Ph. D., Babak Alinasab, M.D., Ph. D. Craniomaxillofacial Trauma & Reconstruction. 2024 Dec;17(4):NP271-NP280

2. **Functional and Esthetic Outcomes of Either Surgically or Conservatively Treated Anterior Frontal Sinus Wall Fractures: A Long-Term Follow-Up** Oscar Solmell MD, Babak Alinasab, M.D., Ph. D. The Journal of Craniofacial Surgery. 2024 Dec;17(4):NP68-NP76

3. **Differences Between Patient and Surgeon Perspectives: A Long-term Follow-up of 180 Patients with Zygomaticomaxillary Complex Fractures Following Either Conservative or Surgical Treatment S**amin Rahbin, M.D, Ola Sunnergren, M.D., Ph. D., Ellen Lindgren, M.D., Hatef Darabi, Ph. D., Babak Alinasab, M.D., Ph. D. Craniomaxillofac Trauma Reconstruction**.** 2024 Dec;17(4):NP121-NP130

4. **The Volume Difference Along the External Surface of the Zygomatic Bone: A Novel Method of Measuring Zygomatic Bone Asymmetry** Samin Rahbin, MD, Tina Toufani, MD, Anna-Maria Al-Khabbaz, MD, Julius Lindblom, MD,y Ola Sunnergren, MD, PhD,z Hatef Darabi, PhD,§ Abdul Rashid Qureshi, MD, PhD, and Babak Alinasab, MD, PhD. The Journal of Craniofacial Surgery 2022 Mar-Apr;33(2):463-468. doi: 10.1097/SCS.0000000000008186

Name: Julia Arebro
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Project title:
Local mapping of middle ear disease

Supervision of PhD-student:

Elnaz Sepehri	Main supervisor: ☒ Co-supervisor: ☐
Torsten Buddee Roos (awaiting admission decision)	Main supervisor: ☒ Co-supervisor: ☐

Summery of project:
- The underlying causes of middle ear disease including chronic perforations of the tympanic membrane is highly unknown. We aim to search for underlying causes through a patient based pre-clinical and clinical mapping project.

- In the recent years, cases with labyrinthitis as a complication of acute otitis media have been increased. Why an ordinary acute otitis media sometimes spread to the inner ear is however unknown, and which patients are at risk for permanent harm to the cochlea. We aim to detect risk factors for labyrinthitis to improve outcome and care.

- The cause of and presentation of acute and chronic mastoiditis needs to be better evaluated why we evaluate on all paediatric patients over 20 years to improve patient outcome.

- Oral squamous cell carcinoma (OSCC) remains an under-studied and significant global cancer killer; dismal survival rates have not changed in decades. A better understanding of the molecular basis of OSCC progression and metastasis is needed to provide new treatment/disease management options. We aim to find new strategies in diagnosing and treting this diseaes through stydying fibroblasts in the tumor microenvironment and signalling of miRNA in extracellular vesicles.

- WHO have stated COPD to be the fourth most common cause of death worldwide. In Sweden, up to 700,000 people suffer from COPD generating a yearly coast of 15 billion SEK. Todays methods for diagnosing, treating and monotoring COPD and chronic bronchitis are insufficient. It is well known that smokers with COPD and/or chronic bronchitis suffer from repeated airway infections but the underlying mechanisms are unknown. We aim to investigate IL-26, IL-17 and other markers from Th17 helper cells in the upper airway in a attempt to see if COPD and chronic bronchitis can be monitored through markers in the upper airways.

Ethic permit No:

2024-04249-01 H15-02913	2022-06851-01	2023-02989-01	2018/362-32	2022-06108-01

Publications 2022, 2023, 2024:

1. Arebro J, Pournaras N, Ramos-Ramírez P, Cardenas E, Bandeira E, Che KF, Brundin B, Bossios A, Karimi R, Nyrén S, Stjärne P, Sköld M, Lindén A. Nasal production of IL-26 involving T cells in smokers with and without COPD. Accepted for publication in The Journal of Allergy and Clinical Immunology, March 10th 2025, in press.

2. Flahat B, Bonnard Å, Arebro J. Bilateral intracochlear hemorrhage: A rare onset of chronic myelogenous leukemia. Clin Case Rep. 2024 Apr 20;12(4):e8741.

3. Jafari M, Cardenas EI, Ekstedt S, Arebro J, Petro M, Karlsson A, Hjalmarsson E, Arnarson D, Ezerskyte M, Kumlien Georén S, Cardell LO. Delayed neutrophil shedding of CD62L in patients with chronic rhinosinusitis with nasal polyps and asthma: Implications for Staphylococcus aureus colonization and corticosteroid treatment. Clin Transl Allergy. 2024 Mar;14(3):e12347.

4. Arebro J, Lee CM, Bennewith KL, Garnis C. Cancer-Associated Fibroblast Heterogeneity in Malignancy with Focus on Oral Squamous Cell Carcinoma. Int J Mol Sci. 2024 Jan 21;25(2):1300.

5. Arebro J, Towle R, Lee CM, Bennewith KL, Garnis C. Extracellular vesicles promote activation of pro-inflammatory cancer-associated fibroblasts in oral cancer. Front Cell Dev Biol. 2023 Sep 7;11:1240159.

Name: Filip Asp
Title: Docent
Email: filip.asp@ki.se

Project title:
Long-term effects of hearing loss and hearing intervention during development

Supervision of PhD-student:

Fatima Moumèn Denanto	Main supervisor: ☒ Co-supervisor: ☐
Hanna Josefsson Dahlgren	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
The goal is to alleviate the negative impact of hearing impairment, to improve hearing through cochlear implants, and increase our understanding of how impaired hearing affects humans, specifically during periods of development.

To this end, we study the long-term hearing outcomes of cochlear implantation in individuals who receive cochlear implants as young children and now are young adults. We are interested in the interplay between sensitive periods during development, hearing sensitity, technical settings of the cochlear implant system, and intracochlear electrode placement and the combined effect of these variables on functional hearing.

We have observed a high degree of experience-dependent plasticity in the auditory pathway, such that certain behaviours develop gradually as a function of time with cochlear implants. We have also found maladaptive plasticity, leading to disruption of hearing function. The findings guide clinical pratice and surgical approaches.

Ethic permit No:

2022-00863-02	2019-04696			

Publications 2022, 2023, 2024:

Moumèn-Denanto, F., Tideholm, B., Hellström S., Asp, F., (2022). Differing bilateral benefits for spatial release from masking and sound localization accuracy using bone conduction devices. Ear Hear. 2022 May 19. doi: 10.1097/AUD.0000000000001234

Eklöf, M., Asp, F., and Berninger, E. (2022). The Development of Sound Localization Latency in Infants and Young Children with Normal Hearing. *Trends in Hearing*, *26*, 23312165221088398–23312165221088398. https://doi.org/10.1177/23312165221088398

Asp, F.; Karltorp, E.; Berninger, E. Development of Sound Localization in Infants and Young Children with Cochlear Implants. J. Clin. Med. 2022, 11(22), 6758; https://doi.org/10.3390/jcm11226758. https://www.mdpi.com/2077-0383/11/22/6758

Johansson, M., Karltorp, E., Asp, F., Berninger, E. A Prospective Study of Genetic Variants in Infants with Congenital Unilateral Sensorineural Hearing Loss. J. Clin. Med. 2023, 12, 495. https://doi.org/10.3390/jcm12020495.

Josefsson Dahlgren, H., Engmer Berglin, C., Hultcrantz, M, Asp, F.. A pilot study on spatial hearing in children with congenital unilateral aural atresia. Front Pediatr. 2023 Aug 9;11:1194966.

Karpeta N., Asp F., Edholm K., Bonnard Å., Wales J., Karltorp E., Duan M & Verrecchia L. (2023) Vestibular function in children with vestibulocochlear nerve aplasia/hypoplasia, Acta Oto-Laryngologica, 143:10, 861-866, DOI: 10.1080/00016489.2023.2285453

Siegbahn, M., Jörgens, D., Asp, F., Hultcrantz, M., Moreno, R., and Engmér Berglin, C. (2024). Asymmetry in Cortical Thickness of the Heschl's Gyrus in Unilateral Ear Canal Atresia. *Otology & Neurotology*, *45*(4), e342–e350. https://doi.org/10.1097/MAO.0000000000004137

Löfkvist, U., Dahlby-Skoog, M., Persson, A., Asp, F., Verrecchia, L., Gripenberg, S., Karpeta, N., Eklöf, M., and Karltorp, E. (2025). Teenagers and Young Adults with Cochlear Implants: A Multidisciplinary Follow-Up Study Approach and Baseline Characteristics. *Audiology Research (Pavia, Italy)*, *15*(1), 16-. https://doi.org/10.3390/audiolres15010016

Name: Claus Bachert
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Email: claus.bachert@ki.se

Project title:
Chronic rhinosinusitis with nasal polyps: from cytokines to biologicals

Summery of project:

Chronic rhinosinusitis with nasal polyps (CRSwNP) is predominantly a type 2 inflammatory disease associated with type 2 (T2) cell responses and epithelial barrier, mucociliary, and olfactory dysfunction. The inflammatory cytokines interleukin (IL)-4, IL-13, and IL-5 are key mediators driving and perpetuating type 2 inflammation. The inflammatory responses driven by these cytokines include the recruitment and activation of eosinophils, basophils, mast cells, goblet cells, M2 macrophages, and B cells. The activation of these immune cells results in a range of pathologic effects including immunoglobulin E production, an increase in the number of smooth muscle cells within the nasal mucosa and a reduction in their contractility, increased deposition of fibrinogen, mucus hyperproduction, and local edema. The cytokine-driven structural changes include nasal polyp formation and nasal epithelial tissue remodeling, which perpetuate barrier dysfunction. Type 2 inflammation may also alter the availability or function of olfactory sensory neurons contributing to loss of sense of smell. Targeting these key cytokine pathways has emerged as an effective approach for the treatment of type 2 inflammatory airway diseases, and a number of biologic agents are now available or in development for CRSwNP. In this review, we provide an overview of the inflammatory pathways involved in CRSwNP and describe how targeting key drivers of type 2 inflammation is an effective therapeutic option for patients.

Publications 2022, 2023, 2024:

2022 35

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Wang X, Sima Y, Zhao Y, Zhang N, Zheng M, Du K, Wang M, Wang Y, Hao Y, Li Y, Liu M, Piao Y, Liu C, Tomassen P, Zhang L, Bachert C. Endotypes of chronic rhinosinusitis based on inflammatory and remodeling factors. J Allergy Clin Immunol. 2023 Feb;151(2):458-468.

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Delemarre T, Bachert C. Neutrophilic inflammation in chronic rhinosinusitis. Curr Opin Allergy Clin Immunol. 2023 Feb 1;23(1):14-21.

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Rubió JR, Megremis S, Pasioti M, Lakoumentas J, Constantinides B, Xepapadaki P, Bachert C, Finotto S, Jartti T, Andreakos E, Stanic B, Akdis CA, Akdis M, Papadopoulos NG. Respiratory virome profiles reflect antiviral immune responses. Allergy 2023 Jan 3.

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Hopkins C, Joseph Han, Valerie Lund, Claus Bachert, Wytske Fokkens, Zuzana Diamant, Joaquim Mullol, Ana Sousa, Steven Smith, Shibing Yang, Bhabita Mayer, Steve Yancey, Robert Chan, Stella Lee. Evaluating treatment response to mepolizumab in patients with severe CRSwNP. Rhinology 2023 Jan 20

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Bachert C, Amber U Luong, Philippe Gevaert, Joaquim Mullol, Steven G Smith, Jared Silver, Ana R Sousa, Peter H Howarth, Victoria S Benson, Bhabita Mayer, Robert Chan, William W Busse. The unified airway hypothesis: evidence from specific intervention with anti-interleukin-5 biologic therapy. J Allergy Clin Immunol Pract. 2023 Sep;11(9):2630-2641

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Siddiqui S, Claus Bachert, Leif Bjermer, Kathleen M Buchheit, Mario Castro, Yimin Qin, Hitasha Rupani, Hironori Sagara, Peter Howarth, Camille Taillé. Eosinophils and tissue remodeling: relevance to airway disease. J Allergy Clin Immunol. 2023;152:841-57

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Gevaert P, De Craemer J, Bachert C, Blauwblomme M, Chaker A, Cingi C, Hellings PW, Hopkins C, Hox V, Fokkens W, Klimek L, Lund V, Mösges R, Mullol J, Pfaar O, Scadding G, Tomazic PV, Van Zele T, Vlaminck S, Wagenmann M, Toppila-Salmi S, Alobid I. European Academy of Allergy and Clinical Immunology Position Paper on Endoscopic Scoring of Nasal Polyposis. Allergy. 2023 Jan 20. doi: 10.11

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Klimek L, Förster-Ruhrmann U, Olze H, Beule AG, Chaker AM, Hagemann J, Huppertz T, Hoffmann TK, Dazert S, Deitmer T, Strieth S, Wrede H, Schlenter W, Welkoborsky HJ, Wollenberg B, Becker S, Bärhold F, Klimek F, Casper I, Zuberbier J, Rudack C, Cuevas M, Hintschich CA, Guntinas-Lichius O, Stöver T, Bergmann C, Werminghaus P, Pfaar O, Gosepath J, Gröger M, Beutner C, Laudien M, Weber RK, Hildenbrand T, Hoffmann AS, Bachert C. Empfehlungen zur Überprüfung der Wirksamkeit und Verlaufsdokumentation von Mepolizumab bei chronischer Rhinosinusitis mit Nasenpolypen (CRSwNP) im deutschen

Gesundheitssystem – Empfehlungen des Ärzteverbandes Deutscher Allergologen (AeDA) und der AGs Klinische Immunologie, Allergologie und Umweltmedizin und Rhinologie und Rhinochirurgie der Deutschen Gesellschaft für HNO-Heilkunde, Kopf- und Halschirurgie (DGHNOKHC). Laryngorhinootologie. 2023 Feb;102(2):89-99.

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Won HK, Song WJ, Moon SD, Sohn KH, Kim JY, Kim BK, Park HW, Bachert C, Cho SH. Staphylococcal Enterotoxin-Specific IgE Sensitization: A Potential Predictor of Fixed Airflow Obstruction in Elderly Asthma. Allergy Asthma Immunol Res. 2023 Mar;15(2):160-173.

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Huang Y, Zhang N, Bachert C. Innovative treatments for severe uncontrolled chronic rhinosinusitis with nasal polyps. Expert Rev Clin Immunol. 2023; 19. 24 April 2023

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Wautlet A, Bachert C, Desrosiers M, Hellings P, Peters AT. The management of chronic rhinosinusitis with nasal polyps (CRSwNP) with biologics. J Allergy Clin Immunol Pract. 2023 May 12:S2213-2198(23)00539-1.

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Bachert C, Laidlaw, TM, Seong H. Cho, Mullol J, Swanson B, Naimi S, Naimi S, Classe M, Harel S, Jagerschmidt A, Laws E, Ruddy1M, Praestgaard A, Amin N, Mannent LP. Effect of Dupilumab on Type 2 Biomarkers in Chronic Rhinosinusitis with Nasal Polyps: SINUS-52 Study Results. Ann Otol Rhinol Laryngol. 2023;132(12):1649-1661.

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Shao S, Wang Y, Zhang N, Zhao Y, Zhang X, Sima Y, Wang P, Xu Y, Wang T, Bao S, Cao Y, Wang X, Zhang L, Bachert C. A prospective single-arm study on the efficacy and safety of short-course oral corticosteroids followed by topical corticosteroids in patients with severe chronic rhinosinusitis with nasal polyps. Expert Rev Clin Immunol. 2023 Jul-Dec;19(8):1029-1039.

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Megremis S, Constantinides B, Xepapadaki P, Yap CF, Sotiropoulos AG, Bachert C, S Finotto, T Jartti, A Tapinos, T Vuorinen, E Andreakos, DL Robertson, NG Papadopoulos. Respiratory eukaryotic virome expansion and bacteriophage deficiency characterize childhood asthma. Sci Rep. 2023 May 23;13(1):8319.

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Krysko O, Korsakova D, Teufelberger A, De Meyer A, Steels J, De Ruyck N, van Ovost J, Van Nevel S, Holtappels G, Coppieters F, Ivanchenko M, Braun H, Vedunova M, Krysko DV, Bachert C. Differential protease content of mast cells and the processing of IL-33 in Alternaria alternata induced allergic airway inflammation in mice. Front Immunol. 2023 Apr 19;14:1040493.

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Schleich F, Maury E, Bachert C, Hanon S, Michel O, Jansen M, Gurdain S, Van Schoor J; Epidemiology of sensitization to perennial aeroallergens in adults with severe asthma in Belgium. The BEIgE study. Allergy. 2023 Oct;78(10):2774-2777

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Gomes SC, Delemarre T, Holtappels G, Van Zele T, Derycke L, Bonne E, Eeckels AS, Zhang N, Voegels RL, Bachert C. Olfaction in nasal polyp patients after Reboot surgery: an endotype-based prospective study. Eur Arch Otorhinolaryngol. 2023 Jun;280(6):2821-2830.

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Wautlet A, Bachert C, Desrosiers M, Hellings P, Peters AT. The management of chronic rhinosinusitis with nasal polyps (CRSwNP) with biologics. J Allergy Clin Immunol Pract. 2023 Sep;11(9):2642-2651

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Schleich F, Moermans C, Gerday S, Ziant S, Louis G, Bougard N, Paulus V, Guissard F, Henket M, Bachert C, Louis R. Patients With Asthma Only Sensitized to Staphylococcus aureus Enterotoxins Have More Exacerbations, Airflow Limitation, and Higher Levels of Sputum IL-5 and IgE. J Allergy Clin Immunol Pract. 2023 Oct;11(10):3055-3061.

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Abdul Latiff AH, Husain S, Abdullah B, Suppiah P, Tan V, Ing Ping T, Woo K, Yap YY, Bachert C, J Schunemann H, Bedbrook A, Czarlewski W, Bousquet J. ARIA Care Pathways 2019: Next-Generation Allergic Rhinitis Care and Allergen Immunotherapy in Malaysia. J Pers Med. 2023 May 15;13(5):835.

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Lee S, Nikhil Amin, Leda Mannent, Claus Bachert, Gary Gross, Seong Cho, Amy Praestgaard, Shahid Siddiqui, Scott Nash, Siddhesh Kamat, Asif Khan, Juby Jacob-Nara. The relationship of sinus opacification, olfaction and dupilumab efficacy in patients with CRSwNP. Rhinology 2023 Dec 1;61(6):531-540

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Xu Z, Yan J, Wen W, Zhang N, Bachert C. Pathophysiology and management of Staphylococcus aureus in nasal polyp disease. Expert Rev Clin Immunol. 2023 Jul 13:1-12.

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Kolkhir P, Akdis CA, Akdis M, Bachert C, Bieber T, Canonica GW, Guttman E, Metz M, Mullol J, Palomares O, Renz H,Ständer S, Zuberbier T, Maurer M: Type 2 chronic inflammatory diseases: Promising targets, unmet treatment needs, and perspectives. Nature Review Drug Discov. 2023 Sep;22(9):743-767

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In preparation:

Tissue-resident memory IL-17-producing Th2 cells contribute to persistent inflammation in mixed endotype CRSwNP patients

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Awards & Achievements 2023
2023 - Research.com Medicine in Belgium Leader Award
2023 - Research.com Immunology in Belgium Leader Award
2022 - Research.com Immunology in Belgium Leader Award
2014 - German National Academy of Sciences Leopoldina - Deutsche Akademie der Naturforscher Leopoldina – Nationale Akademie der Wissenschaften *Ophthalmology, Oto-Rhino-Laryngology and Stomatology*

D-Index & Metrics 06.12.2023

Discipline name	D-index	Citations	Publications	World Ranking	National Ranking
Immunology	128	79,416	854	141	1
Medicine	128	80,574	1,008	1506	13

Name: Rusana Bark
Title: MD., PhD.
Email: rusana.bark@ki.se

Project title:

Advancements in Head & Neck Cancer: Diagnostic, Prognostic, and Treatment Strategies

Supervision of PhD-student:

Petronella Pettersson	Main supervisor: ☒ Co-supervisor: ☐
Evelina Jörtsö	Main supervisor: ☐ Co-supervisor: ☒
Marcus Jansson	Main supervisor: ☐ Co-supervisor: ☒

Summary of project:

The following ongoing and future research projects focus on various aspects of head and neck cancer management, aiming to improve diagnostic accuracy, treatment strategies, and patient outcomes:

1. **Ultrasound-guided Anchor in Lymph Node and Cyst Extirpation**: This prospective study explores the use of ultrasound-guided anchor for the removal of non-palpable lymph nodes and cysts in the neck, with the goal of enhancing surgical precision and improving patient outcomes.
2. **Sentinel Node-assisted Neck Dissection in Oral Cancer**: This project investigates the prevalence and localization of non-sentinel node metastases in N+ oral cancer patients. It also examines the significance of isolated tumour cells (ITCs), micro- and macrometastases in relation to regional cancer recurrence and survival.
3. **Regional Recurrence and Disease-Free Survival in Oral Cancer N+ Patients**: Focusing on oral cancer patients, this study assesses the prevalence of regional recurrence and disease-free survival following sentinel node-assisted neck dissection, with a two-year follow-up period.

4. **Pharyngocutaneous Fistulas Post-Total Laryngectomy**: This project examines the prevalence of pharyngocutaneous fistulas after total laryngectomy, identifying associated risk factors to better understand and manage post-surgical complications.
5. **Discordance Between HPV-DNA and p16 in Cancer of Unknown Primary (CUP)**: The study investigates the discordance between HPV-DNA status and p16 expression in patients with head and neck cancer of unknown primary, aiming to assess its impact on recurrence and survival outcomes.
6. **Predicting Biomarkers in Head and Neck Cancers**: This project seeks to identify tumour biomarkers associated with tumour sensitivity and aggressiveness in oropharyngeal, laryngeal, and salivary gland cancers. The goal is to reduce treatment side effects, improve patient quality of life, and provide more personalized treatment strategies based on tumour biology.
7. **Sentinel Node Technique in Salivary Gland Tumours**: In collaboration with Docent Caroline Gahm, this study investigates the sentinel node technique for predicting lymphatic drainage and detecting occult metastases in salivary gland tumours, aiming to improve diagnostic accuracy and guide targeted treatment.

Ethic permit No:

Dnr 2020–00448	Dnr 2021-00697	Dnr 2021-01265	2017/1035-31/2	2023-03476-01

Publications 2022, 2023, 2024:

1. Jörtsö E, Marklund L, Harper Hysek M, Näsman A, Hammarstedt-Nordenvall L, Von Beckerath M, Dalianis T, **Bark R**. Fine needle aspiration cytology including the analysis of human papilloma virus (HPV) DNA enhances the diagnostic workup of solitary cystic neck lesions in a population with a high incidence of HPV positive oropharyngeal cancer. Acta Oncol. 2025 Feb 17;64:276-283.

2. Nilsson O, von Beckerath M, Knutsson J, Magnuson A, Landström FJ, **Bark R**. Risk factors for local recurrence following marginal mandibulectomy in gingival cancer. Sci Rep. 2024 Nov 1;14(1):26347.

3. Piersiala K, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, **Bark R**, Elliot A, Marklund L, Margolin G, Georén SK and Cardell L-O. Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma. Front. Immunol. 2024; Oct 15:15:1455426.

4. Hjalmarsson E, Piersiala K, Lagebro, Farrajota Neves da Silva P, Petro M, Starkhammar M, Elliot A, **Bark R**, Margolin G, Kumlien Georén S, Cardell LO. High expression of PD-L1 on conventional dendritic cells in tumour-draining lymph nodes is associated with poor prognosis in oral cancer. Cancer Immunol Immunother. 2024; Jul 2;73(9):165.

5. Nordenvall L, **Bark R**, Elliot A, Von Beckerath M, Gahm C. Distribution of sentinel nodes from parotid tumors– A feasibility study. Cancer Med. 2023;12:19667-19672.

6. **Bark R**, Kolev A, Elliot A, Piersiala K, Näsman A, Grybäck P, Kumlien Georén S, Wendt M, Cardell LO, Margolin G, Marklund L. Sentinel Node-Sentinel node-assisted neck dissection in advanced oral squamous cell carcinoma—A new protocol for staging and treatment. Cancer Med. 2023; 12:12524-12534.

7. Vujasinovic M, Marsk E, Tsolakis AV, Hynning B, Nordberg M, Lindblad M, Lindqvist C, Hammarstedt- Nordenvall L, **Bark R**, Elbe P. Complications of gastrostomy tubes in patients with head and neck cancer. Laryngoscope. 2022 Sep;132(9):1778-1784.

8. Hammarstedt-Nordenvall L, Evelina J, Beckerath M, Tani E, Nordemar S, **Bark R**. Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts. Acta Otolaryngol. 2022 Jan;142(1)100-105.

Name: Mikael Benson
Title: Senior Researcher
Email: Mikael.benson@ki.se

Project title:

Supervision of PhD-student:

Yelin Zhao	Main supervisor: ☒ Co-supervisor: ☐
Martin Smelik	Main supervisor: ☒ Co-supervisor: ☐
Samuel Schäfer	Main supervisor: ☒ Co-supervisor: ☐

Summery of project:
Dynamic Digital twins for early personalised diagnostics and therapeutics

One of the greatest health care problems today is that many patients do not respond to drug treatment. This reflects the complexity of the human body, which consists of trillions of cells, each of which may ex- press thousands of genes, in different combinations, at different time points, before and during disease. There is a wide gap between this complexity and modern health care. The Swedish Digital Twin Consortium (sdtc.se) proposes that this gap can be bridged by dynamic digital twins of individual patients. The twin models show cellular and molecular evolution of malignant transformation. We focus on diseases that increase risk of colorectal cancer as proof-of-concept. The aim is to show that each twin can be computationally analysed to identify early mechanisms driving malignant transformation as well as drugs to prevent this. The twins are constructed and treated by applying network tools and artificial intelligence (AI) to multiomics data down to the spatial single cell level, and clinical data from each individual patient. We have shown clinical feasibility in mouse models and comparisons of predicted and observed treatment effects in patients (all references are found in sdtc.se). Recent case reports support the clinical applicability of scRNA-guided treatment of a patients that do not respond th that did not respond to conventional treatment. However, that treatment was based on empirical analyses of the data. By contrast, our digital twin strategy is based on systematic prioritization of drugs and computreatment of the twins with those drugs, before actually treating individual patients. We have now developed methods that are ready for clinical trials to treat digital twins of individual patients. The

ultimate aim is that each healthy individual should have her/his digital twin for predictive, preventive, personalised and participatory medicine.

Ethic permit No:

Publications 2022, 2023, 2024:

Schäfer S, Smelik M, Sysoev O, Zhao Y, Eklund D, Lilja S, Gustafsson M, Heyn H, Julia A, Kovács IA, Loscalzo J, Marsal S, Zhang H, Li X, Gawel D, Wang H, **Benson M.** scDrugPrio: A framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases. Genome Med 2024

Zhao Y, Li X, Loscalzo J, Smelik M, Sysoev O, Wang Y, Mahmud AKMF, Mansour Aly D, **Benson M.** Transcript and protein signatures derived from shared molecular interactions across cancers are associated with mortality. J Transl Med. 2024;22(1):444. doi: 10.1186/s12967-024-05268-7.

Glintborg B, Hansson M, Hammer HB, Klareskog L, Saevarsdottir S, Westerlind H, Rönnelid J, Gehring I, **Benson M**, Esbensen BA, Hetland ML, Padyukov L, Kragstrup TW, Hauge EM, AxnÄs BB, Krogh NS, Johannesson M, Askling J. Legal obstacles jeopardise research in personalised medicine - experiences from a Nordic collaboration within rheumatology. Scand J Public Health. 2024 52(8):1019-1025. doi: 10.1177/14034948231212711

Smelik M, Zhao Y, Li X, Loscalzo J, Sysoev O, Mahmud F, Mansour Aly D, **Benson M.** An interactive atlas of genomic, proteomic, and metabolomic biomarkers promotes the potential of proteins to predict complex diseases. Sci Rep. 2024;14(1):12710. doi: 10.1038/s41598-024-63399-9.

Lilja S, Li X, Lee EJ, Loscalzo J, Zhang H, Zhao Y, Gawel D, Wang H, Benson M. Multi-organ single cell analysis re- veals an on/off switch system with potential for personalized treatment of immunological diseases. Cell Reports Medicine 2023:(3):100956. doi: 10.1016/j.xcrm.2023.100956.

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Badam TV, Hellberg S, Mehta RB, Lechner-Scott J, Lea RA, Tost J, Mariette X, Svensson-Arvelund J, Nestor CE, Benson M, Berg G, Jenmalm MC, Gustafsson M, Ernerudh J. CD4+ T-cell DNA methylation changes during preg- nancy significantly correlate with disease-associated methylation changes in autoimmune diseases. Epigenetics. 2022; 17(9):1040-1055. doi: 10.1080/15592294.2021.1982510.

Name: Erik Berninger
Title: Associate Professor
Email: erik.berninger@ki.se

Project title:

Hearing impairment in newborns. New objective technologies and intervention strategies during a sensitive period of development to improve subsequent communication

Summary of project:

Our research project aims at very early diagnosis and intervention to reduce or reverse disability and thus improve the communication capacity of the hearing-impaired child. The long-term goal is to find the causes and mechanisms behind various nonsyndromic congenital sensorineural hearing losses (SNHL) and to develop future treatment options. The main research directions are:

A. Causes and mechanisms behind congenital SNHL
B. Impact of early intervention during a critical period of development
C. Sound localization as a clinical tool
D. Rapid and objective ABR technique for newborns and infants

Overall aims of the research directions are: A.) To identify and precisely diagnose various forms of congenital SNHL (e.g. nonsyndromic, bilateral, and unilateral SNHL), as determined at the level of specific anatomical structures down to the molecular level. To identify and develop future treatment options on the basis of highly specific diagnoses, as determined at birth. B.) To study the impact of relevant auditory stimulation during a sensitive period of development, and to identify the extent of that period (e.g. longitudinal studies on congenital, unilateral, SNHL). C.) To study the relationship between behavioural development and maturation of the central auditory pathways and the physiology of binaural interaction at the brainstem level. Further development of a new rapid noninvasive and objective test for e.g. central auditory processing dysfunction from 6 months of age. Evaluation of various intervention/care strategies. D.) To develop a rapid, valid, and reliable electrophysiological technique applicable in newborns and infants for diagnostics and as a basis for fine-tuning of e.g. nonlinear hearing aids.

The studies will be performed at Scientific Center for Advanced Pediatric Audiology (SCAPA), Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden.

Ethic permit No:

2018/1500-31 (Approved addendum, 2020-06-10)	2014/1162-31/1; 2015/1878-21/2	2017/293-31/4	2019-03826

Publications 2022, 2023, 2024:

Asp F, Karltorp E, Berninger E. Development of Sound Localization in Infants and Young Children with Cochlear Implants. Journal of clinical medicine. 2022;11(22).

Berninger E, Drott M, Romanitan M, Tranebjærg L, Hellström S. Congenital Nonprofound Bilateral Sensorineural Hearing Loss in Children: Comprehensive Characterization of Auditory Function and Hearing Aid Benefit. Audiology research. 2022;12(5):539-63.

Eklöf M, Asp F, Berninger E. The Development of Sound Localization Latency in Infants and Young Children with Normal Hearing. Trends in hearing. 2022;26:23312165221088398.

Johansson M, Karltorp E, Asp F, Berninger E. A Prospective Study of Genetic Variants in Infants with Congenital Unilateral Sensorineural Hearing Loss. Journal of clinical medicine. 2023;12(2).

Johansson M, Karltorp E, Edholm K, Drott M, Berninger E. A Prospective Study of Etiology and Auditory Profiles in Infants with Congenital Unilateral Sensorineural Hearing Loss. Journal of clinical medicine. 2022;11(14).

Name: Åsa Bonnard
Title: MD, PhD
Email: asa.bonnard@ki.se

Project title:
SweChole, SwedEar, Cochlear implantation and Labyrintits.

Supervision of PhD-student:

Sara Olaison	Main supervisor: ☐ Co-supervisor: ☒
Agnes Modée Borgström	Main supervisor: ☒ Co-supervisor: ☐
Mikolaj Stachurski	Main supervisor: ☒ Co-supervisor: ☐
Torsten Budde Roos	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

Ear and hearing problems are my passion, and my research involves these two subjects in different forms.

SweChole is a research group i founded together with other colleagues interested in the Cholesteatoma disease. Our main projects have epidemiological approaches where we have shown a familial trait in the Cholesteatoma disease with a higher risk for Cholesteatoma surgery in individuals with a first-degree relative surgically treated for the disease (10) and that individuals with other mucosal diseases as rhinosinositis, nasal polyposis and TE/TT and adenoidectomy in childhood also have a higher risk for Cholesteatoma surgery (5). In a cohort from Östersund, a higher risk for worse hearing outcome was seen to be associated with waiting time >3 months (8).

SwedEar is a Swedish quality register for Ear surgery where we look into different aspects regarding chronic otitis surgery, complications, and patient satisfaction (2,7,9).

Cochlear implantation is essential for improving hearing in individuals with severe hearing loss and deafness. Cochlear malformation and the impact of hearing and balance after cochlear implantation is my main interest (6, 11) but recently we have looked into patients with otosclerosis and the long-term hearing results, complications, and programming issues together with Raphaële Quatre, an otologist from Grenoble, France (1).

Finally, there appears to be an increased frequency and severity of labyrintitis since the Covid pandemic. This is the reason for a new Doctoral project with Torsten Budde Roos as a doctoral student where we are looking at this disease, the risk factors, outcome and possible new treatment methods.

Ethic permit No:

2014/2203-31/4	2019-05190, 2020-00245, 2021-05727-02	2020-05935	2022-06851-01

Publications 2022, 2023, 2024:

1. Long-Term Hearing Outcomes Following Cochlear Implantation in Far Advanced Otosclerosis. Quatre R, Eklöf M, Wales J, Bonnard Å. Otolaryngol Head Neck Surg. 2025 Mar 19. doi: 10.1002/ohn.1224. Online ahead of print. PMID: 40105439
2. Hearing Outcomes After Ossiculoplasty With Bone or Titanium Prostheses-A Nationwide Register-Based Study. Olaison S, Berglund M, Taj T, Knutsson J, Westman E, Eriksson PO, Bonnard Å. Clin Otolaryngol. 2024 Sep;49(5):660-669. doi: 10.1111/coa.14191. Epub 2024 Jun 25.PMID: 38932647
3. Clinical practice guidelines for the care of girls and women with Turner syndrome. Gravholt CH, Andersen NH, Christin-Maitre S, Davis SM, Duijnhouwer A, Gawlik A, Maciel-Guerra AT, Gutmark-Little I, Fleischer K, Hong D, Klein KO, Prakash SK, Shankar RK, Sandberg DE, Sas TCJ, Skakkebæk A, Stochholm K, van der Velden JA; International Turner Syndrome Consensus Group; Backeljauw PF.Eur J Endocrinol. 2024 Jun 5;190(6):G53-G151. doi: 10.1093/ejendo/lvae050.
4. Bilateral intracochlear hemorrhage: A rare onset of chronic myelogenous leukemia. Flahat B, Bonnard Å, Arebro J.Clin Case Rep. 2024 Apr 20;12(4):e8741. doi: 10.1002/ccr3.8741.
5. Occurrence of mucosa-affecting diseases of the upper airways in middle ear cholesteatoma patients: a nationwide case-control study. Modée Borgström A, Mogensen H, Engmér Berglin C, Knutsson J, Bonnard Å.Eur Arch Otorhinolaryngol. 2024 Aug;281(8):4081-4087. doi: 10.1007/s00405-024-08567-3.
6. Vestibular function in children with vestibulocochlear nerve aplasia/hypoplasia. Karpeta N, Asp F, Edholm K, Bonnard Å, Wales J, Karltorp E, Duan M, Verrecchia L.Acta Otolaryngol. 2023 Oct;143(10):861-866. doi: 10.1080/00016489.2023.2285453.
7. Validation of the Swedish Quality Register for Ear Surgery - SwedEar. Berglund M, Olaison S, Westman E, Eriksson PO, Steger L, Bonnard Å.BMC Med Inform Decis Mak. 2023 Oct 26;23(1):240. doi: 10.1186/s12911-023-02340-y.

8. The impact of waiting time on hearing outcome and patients' satisfaction after cholesteatoma surgery. Stachurski M, Eriksson PO, Westman E, Mogensen H, Bonnard Å. Acta Otolaryngol. 2023 Aug;143(8):662-668. doi: 10.1080/00016489.2023.2247045.
9. Prophylactic antibiotics has no benefit for outcome in clean myringoplasty-A register-based cohort study from SwedEar. Westman E, Höglund M, Nilsson FB, Bonnard Å, Englund E, Eriksson PO.Clin Otolaryngol. 2023 Nov;48(6):895-901. doi: 10.1111/coa.14089.
10. The Risk of Cholesteatoma in Individuals With First-degree Relatives Surgically Treated for the Disease. Bonnard Å, Engmér Berglin C, Wincent J, Eriksson PO, Westman E, Feychting M, Mogensen H.JAMA Otolaryngol Head Neck Surg. 2023 May 1;149(5):390-396. doi: 10.1001/jamaoto.2023.0048.
11. Vestibular Loss in Children Affected by LVAS and IP2 Malformation and Operated with Cochlear Implant. Bonnard Å, Karltorp E, Verrecchia L.Audiol Res. 2023 Feb 9;13(1):130-142. doi: 10.3390/audiolres13010013.

Name: Anders Ehnhage
Title: PhD
Email: anders.ehnhage@ki.se

Project title:

Hereditary hemorrhagic telangiektasi, HHT, in Sweden: A register-based study of mortality, morbidity, prevalenc and treatments.

Summery of project:

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant genetic disorder of aberrant blood vessel development, such as telangiectasias of skin and mucous membranes of the nose and mouth, as well as anemia, arteriovenous (AV) malformations, primarily in the gastrointestinal tract, in the brain, lung, and liver

In this study we have used data, based on the ICD-10-SE system, from The National Board of Social affairs and Health, i.e. The National Cause of Death Register, with an average degree of covering for the whole country covering 99,2 % during the period 2001-2018.

We also used the National Patient Register, that provides statistics on diseases and treatments of the in- and outpatient specialized care of Swedish patients. The great majority of Swedish caregivers, including private care, are obliged to report to this register.

To evaluate mortality and the cause of death in the HHT patient group and compare with the general Swedish population, a group of patients, Group 1, registered in The National Cause of Death Register with the diagnose of HHT in the time span 2001-2003 were included and followed until 2018. A five times as big control group, matched by age and gender, were included by Statistics, Sweden (SCB). This was the primary endpoint. Because Sweden don't have a national HHT-center our hypothesis was that mortality in HHT is higher compared to countries with a centralized care for HHT.

Another patient group, Group 2, was between 2007 and 2018 identified by the National Patient Register to evaluate prevalence, morbidity, treatment, and regional differences in the country. All registrations covering out-and inpatient data of HHT patients during that time span were evaluated. This data represented the secondary endpoints.

The statistical processes are now finished, and the results will be presented in two separate articles. We are now working with the first manuscript about mortality, death causes and prevalence, and we plan for both to be accepted throughout the end of the year.

Ethic permit No:

2020-06950	13773/2021			

Publications 2022, 2023, 2024:

-

Name: Martin Eklöf
Title: Civ.ing., PhD
Email: martin.eklof@ki.se

Project title:
Sound localization latency in bilateral cochlear implant and other interventions

Summery of project:
The first patients with early cochlear implant intervention have now become adolescent. We assess and analyze the outcomes in terms of hearing, language, and balance in a prospective study. Cochlear implant programming and mastoid morphology will be correlated to speech perception and interaural abilities. Furthermore, novel methods of the diagnostics of balance disorders is developed using inertial motion sensors and Artificial Intelligence. We are also analysing the programming difficulties in X-linked cochlear implant patients and adults with otosclerosis.

Ethic permit No:

2022-03381-01	2021-04345

Publications 2022, 2023, 2024:
Eklöf M, Asp F, Berninger E. The Development of Sound Localization Latency in Infants and Young Children with Normal Hearing. Trends Hear. 2022 Jan-Dec;26:23312165221088398. doi: 10.1177/23312165221088398. PMID: 35505627; PMCID: PMC9073128.

Name: Sandra Ekstedt
Title: Forskningsspecialist
Email: sandra.ekstedt@ki.se

Project title:
Neutrophils in airway inflammation and head and neck cancer

Summery of project:
My research focuses on characterizing distinct neutrophil subsets and their functional roles in airway inflammation and cancer. Neutrophils are essential cells of the innate immune system, and increasing evidence highlights their heterogeneity and complex interactions with surrounding tissues.

We have previously studied neutrophil subsets in airway inflammation and shown that they can influence tissue responses, including nerve-mediated airway hyperresponsiveness and structural changes. More recent work has focused on the interaction between neutrophils and epithelial cells, particularly how neutrophils may affect tissue integrity through the regulation of “eat me” and “don’t eat me” signals, mechanisms that are important for tissue homeostasis and immune regulation.

In ongoing studies, we are exploring the role of neutrophil subsets in the tumor microenvironment of head and neck cancer. We investigate how different neutrophil populations are distributed in tumor tissue and lymph nodes, and how they may influence tumor progression through immune modulation.

Together, our research aims to increase the understanding of neutrophil heterogeneity and their role in regulating inflammation, tissue remodeling, and cancer development.

Publications 2022, 2023, 2024:

Peer-reviewed papers in scientific journals

1. Jafari M, Cardenas EI, **Ekstedt S,** Arebro J, Petro M, Karlsson A, Hjalmarsson E, Arnarson D, Ezerskyte M, Georen SK, Cardell LO. Delayed neutrophil shedding of CD62L in patients with chronic rhinosinusitis with nasal polyps and asthma: Implications for Staphylococcus aureus colonization and corticosteroid treatment. CLINICAL AND TRANSLATIONAL ALLERGY 2024 14;3 e12347-

2. **Ekstedt S,** Piersiala K, Kolev A, Farrajota Neves da Silva P, Margolin G, Kumlien Georén S, Cardell LO. Phenotypical differences of neutrophils patrolling tumour-draining lymph nodes in head and neck cancer. British journal of cancer 2024 131;12 1893-1900

3. van der Burg N, Stenberg H, **Ekstedt S,** Diamant Z, Bornesund D, Ankerst J, Kumlien Georén S, Cardell LO, Bjermer L, Erjefält J, Tufvesson E. Neutrophil phenotypes in bronchial airways differentiate single from dual responding allergic asthmatics. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology 2023 53;1 65-77

4. **Ekstedt S,** Lagebro V, Kumlien Georén S, Cardell LO. Prolonged inflammatory resolution in allergic asthma relates to dysfunctional interactions between neutrophils and airway epithelium. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology 2023 131;3 349-355.e3

5. **Ekstedt S,** Piersiala K, Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO. A prolonged innate systemic immune response in COVID-19. Scientific reports 2022 12;1 9915-

6. Cardenas EI, **Ekstedt S,** Piersiala K, Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO, Lindén A. Increased IL-26 associates with markers of hyperinflammation and tissue damage in patients with acute COVID-19. Frontiers in immunology 2022 13; 1016991-

Name: Alexandra Elliot
Title: MD, PhD, Head of H&N
Email: alexandra.elliot@ki.se

Project title:
Optimizing use of sentinel node technique in head and neck cancer

Supervision of PhD-student:

Marcus Jansson	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
Head and neck cancer treatment is associated with difficult side-effects. The treatment and prevention of regional metastasis and recurrences is not always succesfull. The use of of sentinel node (SN) technique for head and neck cancers is increasing both as an investigation tool to find micro-metastasis and single tumour cells but also as a treatment to avoid more extensive surgery. Studies conducted in our group assess the benefits of the SN technique for different head and neck cancer subsites and different clinical cases and analyzes the imunological features and of the SN evaluating the predictiveness of different markers.

The overall aim of the studies is to assess tumour biology and interaction with the immune system, to asssess tumour spread-patterns for different tumour types and to individualize their treatment aiming to improve treatment effects and minimize their related complications .

Ethic permit No:

2017/1333-31/1	2012/49-31/2	2019/03518

Publications 2022, 2023, 2024:

Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma. Piersiala K, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, Bark R, Elliot A, Marklund L, Margolin G, Georén

SK, Cardell LO. Front Immunol. 2024 Oct 15;15:1455426. doi: 10.3389/fimmu.2024.1455426. eCollection 2024.PMID: 39474426

High expression of PD-L1 on conventional dendritic cells in tumour-draining lymph nodes is associated with poor prognosis in oral cancer. Eric H, Piersiala K, Lagebro V, Farrajota Neves Da Silva P, Petro M, Starkhammar M, Elliot A, Bark R, Margolin G, Kumlien Georén S, Cardell LO. Cancer Immunol Immunother. 2024 Jul 2;73(9):165. doi: 10.1007/s00262-024-03754-x.

Regulatory B cells producing IL-10 are increased in human tumor draining lymph nodes Piersiala K, Hjalmarsson E, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georén SK, Cardell LO. Int J Cancer. 2023 Aug 15;153(4):854-866. doi: 10.1002/ijc.34555. Epub 2023 May 5

Distribution of sentinel nodes from parotid tumors-A feasibility study Hammarstedt-Nordenvall L, Bark R, Elliot A, Von Beckerath M, Gahm C.Cancer Med. 2023 Oct;12(19):19667-19672. doi: 10.1002/cam4.6612. Epub 2023 Sep 30.PMID: 37776164

Sentinel node-assisted neck dissection in advanced oral squamous cell carcinoma-A new protocol for staging and treatment. Rusana Bark, Aeneas Kolev, Alexandra Elliot, Krzysztof Piersiala, Anders Näsman, Per Grybäck, Susanna Kumlien Georén, Malin Wendt, Lars Olaf Cardell, Gregori Margolin, Linda Marklund 2023 Apr 21. doi: 10.1002/cam4.5966. Cancer Med

Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells Krzysztof Piersiala , Pedro Farrajota Neves da Silva , Vilma Lagebro , Aeneas Kolev , Magnus Starkhammar , Alexandra Elliot , Linda Marklund , Eva Munck-Wikland , Gregori Margolin , Susanna Kumlien Georén , Lars-Olaf Cardell . Transl Oncol. 2022 Jun 14;23:101469. doi: 10.1016/j.tranon.2022.101469.

Name: Cecilia Engmér Berglin
Title: PhD, ENT consultant
Email: cecilia.engmer@ki.se

Project title:
Development of central auditory pathways in patients with unilateral conductive hearing loss and effects of early intervention

Supervision of PhD-student:

Hanna Josefsson Dahlgren	Main supervisor: ☒ Co-supervisor: ☐
Agnes Modée Borgström	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
The main purpose of this project is to evaluate the effect on the brain in individuals with unilateral canal atresia, which is when a child is born without a developed hearing canal causing a severe conductive hearing loss. Children with hearing habilitation and untreated adults are included in the study. An animal model will also be used for longitudinal studies to achieve information about when to expect changes in the auditory pathways of the brain. Methods used in the project are different types of audiometric testing including corneal reflection eye-tracking, questionnaires, diffusion MRI and resting state functional MRI. The heraing outcome in children with unilateral canal atresia treated with active middle ear implants and active transcutanous bone conduction devices will be evaluated regarded to directional hearing and spech in competing speech as well as assesment of quality of life through questionnaires.

Ethic permit No:

20121661-313	2018/864-31	2021-02984	2012/3:9	N191/14, N113/15

Publications 2022, 2023, 2024:
Sepehri E, Tideholm B, Hellström S, **Engmér Berglin C**. Plasminogen - safe for treatment of chronic tympanic membrane perforation: a phase 1 randomized, placebo-controlled

study. Acta Otolaryngol. 2024 Jul-Aug;144(7-8):439-445. doi: 10.1080/00016489.2024.2396488. Epub 2024 Sep 12. PMID: 39262315.

Siegbahn M, Jörgens D, Asp F, Hultcrantz M, Moreno R, **Engmér Berglin C.** Asymmetry in Cortical Thickness of the Heschl's Gyrus in Unilateral Ear Canal Atresia. Otol Neurotol. 2024 Apr 1;45(4):e342-e350. doi: 10.1097/MAO.0000000000004137. Epub 2024 Feb 15. PMID: 38361347.

Modée Borgström A, Mogensen H, **Engmér Berglin C**, Knutsson J, Bonnard Å. Occurrence of mucosa-affecting diseases of the upper airways in middle ear cholesteatoma patients: a nationwide case-control study. Eur Arch Otorhinolaryngol. 2024 Mar 22. doi: 10.1007/s00405-024-08567-3. Epub ahead of print. PMID: 38517544.

Josefsson Dahlgren H, **Engmér Berglin C**, Hultcrantz M, Asp F. A pilot study on spatial hearing in children with congenital unilateral aural atresia. Front Pediatr. 2023 Aug 9;11:1194966. doi: 10.3389/fped.2023.1194966. PMID: 37622080; PMCID: PMC10446965.

Bonnard Å, **Engmér Berglin C**, Wincent J, Eriksson PO, Westman E, Feychting M, Mogensen H. The Risk of Cholesteatoma in Individuals With First-degree Relatives Surgically Treated for the Disease. JAMA Otolaryngol Head Neck Surg. 2023 May 1;149(5):390-396. doi: 10.1001/jamaoto.2023.0048. PMID: 36929420; PMCID: PMC10020932.

Siegbahn M, **Engmér Berglin C**, Moreno R. Automatic segmentation of the core of the acoustic radiation in humans. Front Neurol. 2022 Sep 23;13:934650. doi: 10.3389/fneur.2022.934650. PMID: 36212647; PMCID: PMC9539320.

Name: Francesca Forli
Title: Associate Professor of Audiology, University of Pisa, Italy
Email: francesca.forli@unipi.it

- Associate Professor of Audiology, Department of Surgical, Medical, Molecular Pathology and Critical Care, University of Pisa.

- Medical Doctor at the Otolaryngology, Audiology and Phoniatrics Unit, Pisa University Hospital.

- Holder of a professional appointment as a HIGHLY specialized technical-professional expert in "Audiology and Cochlear Implants".

- Director of the Degree Program in Speech and Language Therapy, University of Pisa.

- Deputy Director of the Postgraduate School in Audiology and Phoniatrics, University of Pisa.

- Member of the Scientific Committee of the PhD Program in Clinical Physiopathology, University of Pisa.

- Affiliated Professor at the Karolinska Institutet in Stockholm, Sweden, Hearing Implant Section H9 Klintec (from 1/6/2024).

The scientific output consists of 160 peer-reviewed publications in national and international journals as well as in national and international conference proceedings.
H-index: 25 (SCOPUS 2025).
Papers have been published in national and international journals in the fields of audiology and otorhinolaryngology, as well as in leading journals from other medical disciplines. Research activities are primarily focused on audiology and otology, including neonatal hearing screening, pediatric and adult audiological diagnosis, the etiology of sensorineural hearing loss, cochlear implants, and implantable hearing devices. Additional topics of interest within otorhinolaryngology have also been explored, such as rhinology, laryngotracheal disorders, surgical techniques for orbital decompression, and phoniatrics.

Supervision of PhD-student:

Silvia Capobianco, MD PhD Course in Clinical and Translational Sciences, University of Pisa, Italy (Etic	Main supervisor:**X** Co-supervisor:☐

committee n. 26216_FORLI)	

Publications 2022, 2023, 2024:

1)Semeiotica clinica e strumentale del paziente otologico.

F. Forli, S. Berrettini

In: Chirurgia Specialistica 2022; 277-282, a cura di Francesco Minni

ISBN:9788808220073

Zanichellieditore.

2) Bone-Anchored Hearing Aids Fitted According to NAL and DSL

Procedures in Adults with Mixed Hearing Loss. L. Bruschini, R. Canelli, M. Guida, P. Pardini, G. Giuntini, G. Fiacchini, S. Berrettini, F. Lazzerini, F. Forli

J Int Adv Otol 2022; 18:302-307 **(I.F. 1,316)**
ISI: 000835360500005
Scopus: 2-s2.0-85134011133
DOI: 10.5152/iao.2022.21270
PubMedID: 3589452

3) Cochlear Implant in Patients with Asymmetric Hearing Loss: Reporting and

Discussing the Benefits in Speech Perception, Speech Reception Threshold, Squelch Abilities and the Patients Reported Outcomes.

F. Forli, S. Berrettini, L. Bruschini, R. Canelli, F. Lazzerini.

J LaryngolOtol 2022, 136: 964-969**(I.F. 2,187)**

ISI: 000838411700001

Scopus 2-s2.0-85122866748

DOI: 10.1017/S0022215121004333

PubMedID: 34991760

4) Battery Lifespan of an Implantable Middle Ear Device. L. Bruschini, F. Forli, G. Fiacchini, R. Canelli, S. Berrettini, F. Lazzerini .

Audiology Research 2022; 12:485-492. **(I.F. 2,1)**

ISI: 000872196700001

Scopus: 2-s2.0-85140407213

DOI: 10.3390/audiolres12050049

PubMedID: 36136856

5) Sequential bilateral cochlear implant: long-term speech perception results in

children first implanted at an early age.
F. Forli, L. Bruschini, B. Franciosi, **S.** Berrettini, F. Lazzerini.
Eur Arch Oto-rhino-laryngol, 2023 Mar;280(3):1073-1080. doi: 10.1007/s00405-022-07568-4. Epub 2022 Aug 3.**(I.F. 3,236)**
ISI: 000835610900002
Scopus: 2-s2.0-85135311489
DOI: 10.1007/s00405-022-07568-4
PubMedID: 35920894

6) Extended-hearing targeted screening for congenital cytomegalovirus

infection.

F. Forli, F. Lazzerini, R. Canelli, F. Lorenzoni, B. Franciosi, S. Berrettini, L. Bruschini.
Minerva Pediatr (Torino). 2021 May 31. **(I.F. 1,312)**

doi: 10.23736/S2724-5276.21.06287-X.

PubMedID: 34056891

7) Cochlear Implant in inner ear malformations: the experience of the ENT
clinic of University of Pisa

F. Lazzerini, F. Forli, L. Bruschini, S. Berrettini
Otorhinolaringology (Italy) 2022, 72(3), pp. 123–129
DOI: 10.23736/S2724-6302.22.02449-5

8) Sequential bilateral cochlear implant: long-term speech perception results in children first implanted at an early age.

Forli F, Bruschini L, Franciosi B, Berrettini S, Lazzerini F.

Eur Arch Otorhinolaryngol. 2023 Mar;280(3):1073-1080. **(IF 3,236)**

doi: 10.1007/s00405-022-07568-4. Epub 2022 Aug 3.

9) Temperature-Sensitive Auditory Neuropathy: Report of a Novel Variant of OTOF Gene and Review of Current Literature.

Forli F, Capobianco S, Berrettini S, Bruschini L, Romano S, Fogli A, Bertini V, Lazzerini F.

Medicina (Kaunas). 2023 Feb 13;59(2):352. **(I.F. 2.948)**

doi: 10.3390/medicina59020352.

10) The Audiological Follow-Up of Children with Symptomatic Congenital

Cytomegalovirus Infection: An Experience in Two Italian Centers.

S. Palma, F. Forli, C. Rossi, R. Filice, C. D'adamo, M.F. Roversi, D.

Monzani, F. Lorenzoni, C. Botti, S. Berrettini, L. Bruschini, A. Berardi, E. Genovese, R. Canelli

Children (Basel) 2023; 10:1136 **(I.F. 2,4)**

ISI: 001035057300001

Scopus: 2-s2.0-85166323168

DOI: 10.3390/children10071136

PubMedID: 37508638

11) Surgical Treatment of an Endolymphatic Sac Tumor.

L. Bruschini, F. Forli, G.A. Lazzarotti, A. Borraccino, M. Cosottini, S.

Berrettini, F. Lazzerini.

J Vis Exp 2023;26. **(I.F. 1,2)**

Scopus: 2-s2.0-85161841988

DOI: 10.3791/65079

PubMedID: 37306419

12) Current trends on subtotal petrosectomy with cochlear implantation in

recalcitrant chronic middle ear disorders.

P. Canzi, S. Berrettini, A. Albera, M. Barbara, L. Bruschini, A. Canale, E. arlotto, E. Covelli, D. Cuda, F. Dispenza, M. Falcioni, F. Forli, S. Franchella, L. Gaini, S. Gallina, A. Laborai, R. Lapenna, F. Lazzerini, S. Malpede, M. Mandalà, D. Minervini, E. Pasanisi, G. Ricci, F. Viberti, D. Zanetti, E. Zanoletti, M. Benazzo

Acta OtorhinolaryngolItal 2023;43: S67-S75 **(I.F. 2)**

ISI: :000993959900010

Scopus: 2-s2.0-85159318585

DOI: 10.14639/0392-100X-suppl.1-43-2023-09.

PubMedID: 37698103

13) Extrusion and Dislocation in Titanium Middle Ear Prostheses: A Literature Review.
P. Canzi, E. Carlotto, L. Bruschini, D. Minervini, M. Mosconi, L. Caliogna, I. Ottoboni, C. Chiapperini, F. Lazzerini, F. Forli, S. Berrettini, M.
Benazzo
Brain Sci 2023;13:1476**(I.F. 2,7)**
ISI:001094222700001
Scopus: 2-s2.0-85175187734
DOI: 10.3390/brainsci13101476
PubMedID: 37891843

14) The Role of Bone-Anchored Hearing Devices and Remote Microphones in Children with Congenital Unilateral Hearing Loss
F. Lazzerini, L. Bruschini, G. Fiacchini, P. Canzi, S. Berrettini, F. Forli
Brain Sci 2023;13:1379**(I.F. 2,7)**
ISI: 001094090000001
Scopus: 2-s2.0-85175169152
DOI: 10.3390/brainsci13101379
PubMedID: 37891748

15) Does the Remote Microphone Still Outperform the Pre-Processing Algorithms? A Group Study in Adult Nucleus Recipients
F. Lazzerini, L. Baldassari, L. Bruschini, S. Berrettini, F. Forli
J Otorhinolaryngol Hear Balance Med2023; 42:9
DOI: 10.3390/ohbm4020009

16) Patologia Flogistica dell'Orecchio Medio e Reflusso Faringo-Laringeo. In La Malattia da ReussoFaringo-Laringeo: Tra Falsi Miti ed EvidenceBased Medicine.
Forli F., Capobianco S., Nacci A., Lazzerini F., Berrettini S.
Relazione Ufficiale 54° Congresso Nazionale della Società Italiana di Foniatria e Logopedia. 2023. Pisa.

17) 3D Printed Piezoelectric BaTiO3/Polyhydroxybutyrate Nanocomposite Scaffolds for Bone Tissue Engineering.
Strangis G, Labardi M, Gallone G, Milazzo M, Capaccioli S, Forli F, Cinelli P, Berrettini S, Seggiani M, Danti S, Parchi P.
Bioengineering (Basel). 2024 Feb 17;11(2):193. **(I.F. 3,8)**

doi: 10.3390/bioengineering11020193.PMID: 38391679

18) Extended-hearing targeted screening for congenital cytomegalovirus infection.
F. Forli, F. Lazzerini, R. Canelli, F. Lorenzoni, B. Franciosi, S. Berrettini, L. Bruschini.
Minerva Pediat 2024; 76:590-598 **(I.F. 1,312)**
Scopus: 2-s2.0-85203880048
DOI: 10.23736/S2724-5276.21.06287-X
PubMedID: 34056891

19) Long-term outcomes of congenital cytomegalovirus infection in children early identified by extended hearing-targeted screening.
F. Forli, S. Capobianco, S. Berrettini, L. Bruschini, F. Lorenzoni, S. Fiori, F. Lazzerini.
Int J PediatrOtorhinolaryngol 2024; 184 **(I.F. 1,2)**
ISI: 001301880200001
Scopus: 2-s2.0-85202026743
DOI: 10.1016/j.ijporl.2024.112070
PubMedID: 39191004

20) Italian Fast Speech Reception Threshold Test: A New Method to investigate Adult Auditory Impairment in Noise.
I. Cantore, R. Lapenna, W. Di Nardo, F. Forli, R. Grassia, A. Murri, A. Scorpecci, E. Muzzi, A. De Lucia, F. De Paolis, G. Ricci, R. Rolesi, S. Berrettini, S. Sicignano, N. Quaranta, P. Marsella, E. Orzan, A. Della Volpe, P. Ruscito.
AudiolNeurotol 2024; 29:450-456 **(I.F. 1,6)**
ISI:001252737100001
Scopus 2-s2.0-85196861747
DOI: 10.1159/000538556
PMID: 38631316

21) L'infezione congenita da CMV: follow-up a lungo termine in bambini con diagnosi precoce tramite screening neonatale.
F. Forli, F. Lazzerini, S. Berrettini, L. Bruschini, D. Bernacca, F. Lorenzoni, S. Fiori, S. Capobianco
Audiologia&Foniatria-Italian Journal of Audiology and Phoniatrics 2024; 9:79-97
DOI: 10.25430/pupj-IJAP-2024-3-13

Name: Caroline Gahm
Title: Docent
Email: caroline.gahm@ki.se

Project title:
Studies on radiotherapy induced tissue inflammation, salivary gland cancer and reconstructive laryngotracheal airway surgery

Supervision of PhD-student:

Björn Eriksson	Main supervisor: ☒ Co-supervisor: ☐
Marcus Jansson	Main supervisor: ☒ Co-supervisor: ☐
Ida Enquist	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
I) Studies on patients treated for salivary gland cancer

- To validate the sentinel node technique in salivary gland cancer

II) Studies on radiotherapy-induced tissue inflammation. The project is a multidisciplinary collaboration between surgeons, dermatologists, pathologists and oncologists. The main area of interest is clinical outcome in patients treated for head and neck malignancies.

- The impact of irradiation on acute and long-term changes i tissues (blood vessels, fat, bone and skin) following radiotherapy treatment.

- Underlying mechanisms in human tissue and in an experimental mouse model

III) Studies on laryngotracheal airway diseases.

- Long-term outcome of reconstrutive airway surgery in pediatric and adult patients

Ethic permit No:

2025-00812-02	2024-08213-02	2024-07493-02

Publications 2022, 2023, 2024:

1) Medin G, Wendt M, Ekborn A, Andersson A, Gahm C. Supraglottoplasty for severe laryngomalacia can be effective and safe also in children with high-risk comorbidities – experience from a tertiary center. International Journal of Pediatric Otothinolaryngology 2023 171; 111632- PMID: 37352590

2) Hammarstedt-Nordenvall L, Bark R, Elliot A, Von Beckerath M, Gahm C Distribution of sentinel nodes from parotid tumors- a feasibility study – Cancer Med 2023 Sept 30. PMID: 37776164

3) Holmqvist A, Wendt M, Papatziamos G, Svensson J, Wester T, Mesas-Burgos C, Gahm C. Endoscopic chemocauterization with trichloroacetic acid for congenital or recurrent tracheoesophageal fistula in children with esophageal atresia – experience from a tertiary center. J Pediatric Surgery, 2023 oct 28:S0022-3468(23)00659-0 PMID: 37978000

4) Gahm C, Näsman A, Papatziamos G. Segmental congenital deficiency of tracheal rings in cervical trachea managed by tracheal resection: A case report and literature review. Int J Pediatr Otorhinolaryngol. 2021 Sep;148:110844.

Name: Anna Granath
Title: MD, PhD, Senior Consultant
Email: anna.granath@ki.se

Project title:

1) Acute Labyrinthitis – risk factors and outcome predictors

2) Acute and chronic mastoiditis

3) Effects of ageing in treatment with cochlear implants

Supervision of PhD-student:

Torsten Buddee-Roos	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

1)There has been a recent surge in complications to acute otitis media in the aftermath to the Covid-pandemic. Streptococcus pyogenes are especially in focus. The planned project is on acute (bacterial) labyrinthitis, prospective and retrospective. The main aim to survey clinical course, outcomes and possible risk factors.

2) The project contains two recently published studies on acute mastoiditis in children in Stockholm, retrospective data. A reduced incidence in children < 2 years of age followed the introduction of the conjugated anti-pneumococcal vaccine in the Swedish childrens vaccination program. A third study on atypical, subacute, cases of mastoiditis in children is under review.

3) A study on the outcomes of balance function after cochlear implant surgery in patients > 70 years old has recently been finished. Plans for further studies in the project include cognitive testing, simple dual-task testing and testing of sensory functions other than hearing.

Ethic permit No:

Dnr 2024-04249-01	2011/44-31/1, 2020-05332	2018/3:6		

Publications 2022, 2023, 2024:

1. Arebro J, Bennet R, Eriksson M, **Granath A.** The complexity of acute mastoiditis in Swedish children. International journal of pediatric otorhinolaryngology 2025 193; 112346-

2. Alfven T, Bennet R, **Granath A,** Dennison SH, Eriksson M. The pneumococcal conjugate vaccine had a sustained effect on Swedish children 8 years after its introduction. ACTA PAEDIATRICA 2024 113;4 764-770

3. Hultman Dennison S, **Granath A,** Holmstrom M, Stjarne P, Hertting O. Complications to acute bacterial rhinosinusitis in children - a prospective study; bacterial cultures, virus detection, allergy sensitization and immunoglobulins. Rhinology 2023 61;5 412-420

4. Westerberg J, **Granath A,** Drakskog C, Tideholm E, Kumlien Georén S, Weitzberg E, Cardell LO. Nitric Oxide Is Locally Produced in the Human Middle Ear and Is Reduced by Acquired Cholesteatoma. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2022 43;2 e198-e204

Name: Lalle Hammarstedt Nordenvall
Title: Docent, Överläkare
Email: lalle.hammarstedt@ki.se

Project title:
Kliniska studier vid huvud hals cancer

Supervision of PhD-student:

Evelina Gille	Main supervisor: ☒ Co-supervisor: ☐
Björn Eriksson, Rasmus Blomkvist	Main supervisor: ☐ Co-supervisor: ☒
Anahita Mobarga	Main supervisor: ☐ Co-supervisor: ☒
Clara Svenberg-Lind	Main supervisor: ☐ Co-supervisor: ☒
Caroline de Flon	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
1. Kliniska studier, bl.a prognostiska stidier baserat på ACCROBAT data och studier på tungcancer.

2 Registerbaserade studier ur SweHNCR, Svenskt register för huvud-hals cancer.

3. Studier på sinonasala tumörer, bl.a registerstudier men även molekylära PAD studier.

Publications 2022, 2023, 2024:
[Catch-up vaccination prevents HPV infection and related precancers when given up to age 26].
Carlander C, Borgfeldt C, Hammarstedt Nordenvall L.Lakartidningen. 2025 Mar 10;122:24097.PMID: 40070302

Fine needle aspiration cytology including the analysis of human papilloma virus (HPV) DNA enhances the diagnostic workup of solitary cystic neck lesions in a population with a high incidence of HPV positive oropharyngeal cancer.
Jörtsö E, Marklund L, Harper Hysek M, Näsman A, Hammarstedt-Nordenvall L, Von Beckerath M, Dalianis T, Bark R.Acta Oncol. 2025 Feb 17;64:276-283. doi: 10.2340/1651-226X.2025.42078.PMID: 39962709

Endoscopic management of sinonasal tumours in the Nordic university hospitals: a survey.
Korsström C, Lilja M, Hammarstedt-Nordenvall L, Mäkitie A, Haapaniemi A.
Eur Arch Otorhinolaryngol 2024:281(2):785-794.

Distribution of sentinel nodes from parotid tumors - A feasibility study.

Hammarstedt-Nordenvall L, Bark R, Elliot A, Von Beckerath M, Gahm C.

2023

Diagnosis of locally recurrent head and neck squamous cell carcinoma in the Nordic HNC centers and feasibility of the Odense-Birmingham definition.

Rohde M, Eriksen JG, Pareek M, Bratland Å, Mäkitie A, Hammarstedt-Nordenvall L, Wessel I, Lybeck JS, Mäenpää H, Gebre-Medhin M, Godballe C.

Acta Oncol 2023:62(9):1102-1105

Radiotherapy-Dose Escalated for Large Volume Primary Tumors-And Cetuximab with or without Induction Chemotherapy for HPV Associated Squamous Cell Carcinoma of the Head and Neck-A Randomized Phase II Trial.

Mercke C, Wickart-Johansson G, Sjödin H, Farrajota Neves da Silva P, Alexandersson von Döbeln G, Margolin G, Jonmarker Jaraj S, Carstens H, Berglund A, Lax I, Hellström M, Hammarstedt-Nordenvall L, Friesland S.

Cancers (Basel) 2023:15(9)

Treatment and outcome among patients with laryngeal squamous cell carcinoma in Stockholm-A population-based study.

Blomkvist R, Marklund L, Hammarstedt-Nordenvall L, Gottlieb-Vedi E, Mäkitie A, Palmgren B.

Laryngoscope Investig Otolaryngol 2023:8(2):441-449.

Occupational risk variation of nasopharyngeal cancer in the Nordic countries.

Carpén T, Gille E, Hammarstedt-Nordenvall L, Hansen J, Heikkinen S, Lynge E, Selander J, Mehlum IS, Torfadottir JE, Mäkitie A, Pukkala E.

BMC Cancer 2022:22(1):1130.

Post-treatment neck dissection of tonsillar and base of tongue squamous cell carcinoma in the era of PET-CT, HPV, and p16.

Landin D, Näsman A, Jonmarker Jaraj S, Hammarstedt Nordenvall L, Munck-Wikland E, Dalianis T, Marklund L.

Viruses 2022:14(8):1693.

Base of tongue squamous cell carcinomas, outcome depending on treatment strategy and p16 status. A population-based study from the Swedish Head and Neck Cancer Register.

Högmo A, Holmberg E, Haugen Cange H, Reizenstein J, Wennerberg J, Beran M, Söderkvist K, Hammerlid E, Sjödin H, Farnebo L, Sandström K, Hammarstedt-Nordenvall L, Zborayova K, Brun E.

Acta Oncol 2022:61(4):433-440.

Complications of Gastrostomy Tubes in Patients With Head and Neck Cancer.

Vujasinovic V, Marsk E, Tsolakis A, Nordberg, Lindblad M, Lindqvist C, Hammarstedt Nordenvall L, Bark R, Elbe P, Elbe P.

Laryngoscope 2022:132(9):1778-1784.

Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts.

Hammarstedt Nordenvall L, Jörtsö E, von Beckerath M, Tani E, Nordemar S, Bark R.

Acta Otolaryngol 2022:142(1):100-105.

Results from a prospective, randomised study on (accelerated) preoperative versus (conventional) postoperative radiotherapy in treatment of patients with resectable squamous cell carcinoma of the oral cavity - The ARTSCAN 2 study.

Wennerberg J, Gebre-Medhin M, Nilsson P, Brun E, Kjellén E, Carlwig K, Reizenstein J, Kristiansson S, Söderkvist K, Wahlgren M, Zackrisson B;

ARTSCAN study group.

Radiother Oncol 2022:166:26-32.

Long-Term Survival and Recurrence in Oropharyngeal Squamous Cell Carcinoma in Relation to Subsites, HPV, and p16-Status.

Friesland S, Zupancic M, Friesland S, Landin D, Munck-Wikland E, Dalianis T, Näsman A, Marklund L.

Cancers (Basel) 2021:13(11)

Tonsillar Microbiota: a Cross-Sectional Study of Patients with Chronic Tonsillitis or Tonsillar Hypertrophy.

Wu S, Hammarstedt-Nordenvall L, Jangard M, Cheng L, Radu S, Angelidou P, Zha Y, Hamsten M, Engstrand L, Du J, Ternhag A.

mSystems 2021:6(2)

Enteral tube feeding of head and neck cancer patients undergoing definitive chemoradiotherapy in the Nordic Countries: Survey of the Scandinavian Society for Head and Neck Oncology.

Illmarinen T, Bäck L, Hammarstedt-Nordenvall L, Mäkitie A.

Eur Arch Otorhinolaryngol 2021:278(9):3489-3496.

ARTSCAN III: A Randomized Phase III Study Comparing Chemoradiotherapy With Cisplatin Versus Cetuximab in Patients With Locoregionally Advanced Head and Neck Squamous Cell Cancer.

Gebre-Medhin M, Brun E, Engström P, Haugen H, Hammarstedt-Nordenvall L, Reizenstein J, Nyman J, Abel E, Friesland S, Sjödin H, Carlsson H, Söderkvist K, Thomasson M, Zackrisson B, Nilsson P.

J Clin Oncol 2021:39(1):38-47.

The value of HPV and p16 in non-tonsillar, non-base of tongue cancer oropharyngeal cancer.

Hammarstedt L, Holzhauser S, Zupancic M, Kapoulitsa F, Ursu R, Ramqvist T, Näsman A, Dalianis T, Marklund L.

Acta Otolaryngol 2021:141(1):89-94.

Name: Christina Hederstierna
Title: MD, Ph D
Email: christina.forshell-hederstierna@regionstockholm.se

Project title:

Hearing in the elderly and cognition, noise and, diet. Epidemiological studies where the influence of various factors on hearing function is assessed in patients, and in population databases such as H70.

Hearing in vestibular schwannoma - Gamma knife surgery vs initial conservative treatment for vestibular schwannoma patients with preserved hearing, a prospective randomized study. PI Ass Prof Förander, Department of Neurosurgery, Karolinska.

Supervision of PhD-student:

Jenny Häggström	Main supervisor: ☒ Co-supervisor: ☐

Name: Barbro Hedin Skogman
Title: MD, PhD, associated professor professor
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Project title:
The FACE study - a randomized double-blinded placebo-controlled multicenter trial for evaluation of cortisone treatment in children with acute facial nerve palsy

Supervision of PhD-student:

Sofia Karlsson	Main supervisor: ☒ Co-supervisor: ☐
Sigurdur Arnason	Main supervisor: ☒ Co-supervisor: ☐

Summery of project:
Background: Acute facial nerve palsy occur in 15-20/100 000 children/year in Sweden. The facial nerve palsy may be associated to Borrelia infection or idiopathic. About 20 % of these children get a persistent impairment of the facial nerve with problems with excesive tear secretion, pronounication, drooling on top of social/cosmetic problems due to assymmetry in the face. Studies on cortisone treatment to adult patients with acute facial nerve palsy have shown beneficial effects, but no studies with strong quality have been performed in children.

The overall purpose is to assess the utility of cortisone treatment to children with acute facial nerve palsy in a well-designed RCT.

Material/methods: We now perform a double-blind randomized doulbe blinded placebo-controlled multicenter trial on children with acute facial nerve palsy. Patients are being recruited consecutively at pediatric centers in Sweden and a total of 500 patients will be included. Prednisolone 1 mg/kg x 1 perorally in 10 days will be evaluated vs placebo. Clinical data, including clincial outcome (House-Brackmann, Sunnybrook, FaCE scale and FDI) will be documented up until the 12-months follow-up.

The primary outcome is defined as total recovery of the facial nerve palsy, measured with the House-Brackmann scale (grade 1) at 12-months follow-up.

Clincal relevance: If the total recovery rate is significantly improved in the prednisolone group as compared to the placebo group, prednisolone treatment will be introduced in clinical practice for children with acute facial nerve palsy in order to reduce the risk of

persistent impairement and disability. Guidelines will be pubished for evidens-based treatment of children with acute facial nerve palsy.

The study protocol is published in 2020 and at ClincialTrials.gov NCT03781700

305 patients are included so far, at 16 swedish centers and the inclusion continues until July 2025.

2 PhD students in the project have done half-time seminar at CLINTEC.

Ethic permit No:

Dnr 2017/554	Dnr 2019-01546	Dnr 2021-01926	Dnr 2023-02323-02	

Publications 2022, 2023, 2024:

1. Borgstrom M, Hjelm K, Skogman BH, Neveus T, Tunebjer M. Experiences of labor-intensive procedures in the management of nocturnal enuresis—An explorative interview study in children and parents. PLoS ONE. **2024**;19(12): e0314623 (doi.org/10.1371/journal. pone.0314623)
2. Fredriksson T, Brudin L, Henningsson, AH, **Skogman BH**, Tjernberg I. Diagnostic patterns of serum inflammatory protein markers in children with Lyme neuroborreliosis. Ticks Tick Borne Dis. **2024**;15(4):102349 (Epub 2024 May 8) (doi.org/10.1016/j.ttbdis.2024.102349)
3. Bruinsma1 RA, Zomer TP, **Skogman BH**, Boele van Hensbroek M, Hovius JW. Clinical manifestations of Lyme neuroborreliosis in children: a review. Eur J Pediatr. **2023**;182(5):1965-1976. (doi.org/10.1007/s00431-023-04811-w)
4. Borgstrom M, Bergsten A, Tunebjer M, **Skogman BH**, Nevéus T. Fecal disimpaction in children with enuresis and constipation does not make them dry at night. J Pediatr Urol. **2022**;18(4):446.e1-446.e7; (doi: 10.1016/j.jpurol.2022.05.008)
5. Arnason S, Molewijk K, Henningsson AJ, Tjernberg I, **Skogman BH**. Brain damage markers neuron-specific enolase (NSE) and S100B in serum in children with Lyme neuroborreliosis—detection and evaluation as prognostic biomarkers for clinical outcome. Eur J Clin Microbiol Infect Dis. **2022**;41(7):1051-1057 (doi: 10.1007/s10096-022-04460-1)
6. Arnason S, **Skogman BH**. Effectiveness of antibiotic treatment in children with Lyme neuroborreliosis - a retrospective study. BMC Pediatr. **2022**; 22:332 (doi: 10.1186/s12887-022-03335-w)
7. Nilsson T. Leijon A, Sillen U, Hellström AL, **Skogman BH**. Bowel and bladder function in infant toilet training (BABITT) – protocol for a randomized, two-armed intervention study. BMC Pediatr. **2022**;22:294 (doi:10.1186/s12887-022-03355-6)
8. Borgström M, Bergsten A, Turbjer M, **Skogman BH**, Nevéus T. Daytime urotherapy in nocturnal enuresis: a randomizsed, controlled trial. Arch Dis Child. **2022**; 0: 1-5 (doi: 10.1136/archdischild-2021-323488)
9. Lindstrom BE, **Skogman BH**, Lindstrom AK, Nilsson K, Tallstedt L. Borrelia ocular infection–a case report and a systematic review of published cases. Ophthalmic Res. **2022;** 65(2):121-130 (doi: 10.1159/000521307)

Name: Stellan Hertegård
Title: Adj Professor
Email: stellan.Hertegard@ki.se

Project title:
Reconstruction of vocal fold scarring with mesenchymal stem cells

Supervision of PhD-student:

Emma Malmström	Main supervisor: ☒ Co-supervisor: ☐
Erika Bergström Börlin	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
This projects aims to find a treatment for severe voice disorders caused by vocal fold scar. This may be the result of surgery cancer treatment severe inflammation of congenital disorders affecting voice. At present effective treatment is lacking. In a series of animal experiments since 2004 we have shown positive effects, regeneration and prevention of scar formation after injection of human mesenchymal stem cells, MSC (and embryonic stem cells).

From 2012 an ongoin study in cooperation with Professor Katarina LeBlanc at KI is including and treating patients with severe hoaseness and scarring of the vocal folds.The patients are recruited from Karolinska and other parts of Sweden. Vocal folds are dissected and scar tissue is reduced/removed followed by a local injection of autologous MSCs. Sixteen patients were treated. Results at 1 year follow up for the patients shown clearly improved vocal fold function without side effedts.

At present a clinical trial approved by EPM and Swedish Product Agency (Läkemedelsverket) is ongoing, We have treated 8 patients with severe dysphonia and voca fold scarring which are treated with an autologous MSC product injected into the operated scarred vocal folds. Preliminary results show no related side effects and

clinical relevant improvements in around two thirds depending on evaluated vocie parameter

Ethic permit No:

DNR EPN 2019-06160 and 2020-04565, 2021-00933, 2021-03904

Publications 2022, 2023, 2024:

1. Björck G., **Hertegård** S.,Ekelund J., Marsk E. Voice rest after vocal fold polyp surgery: a study of 588 patients in the Swedish National Register for Phonosurgery. *Laryngoscope Investigative Otolaryngology.*Open Access. First published: 16 March 2022. https://doi.org/10.1002/lio2.775. 2022 Mar 16;7(2):486-493. doi: 10.1002/lio2.775. eCollection 2022 Apr.

2. Paucar M., Wincent J, Rubin C., Peikert K., Kyhle J. **Hertegård** S., Möller R., Beshara S, Svenningsson P. Case report: Neuroacanthocytosis associated with novel variants in the *VPS13A* gene with concomitant nucleotide expansion for CANVAS and assessment with osmotic gradient ektacytometry. ISSN: 1662-4548, 1662-453X; DOI: 10.3389/fnins.2024.1409366; PMID: 39416949

Frontiers in neuroscience. , 2024, Vol.18, p.1409366

Name: Mats Holmström
Title: Senior professor
Email: k.mats.holmstrom@gmail.com

Project title:
Hereditary hemorrhagic telangiectasia (HHT) in Sweden – a register based study of mortality, morbidity, prevalence and treatment.

Supervision of PhD-student:

Karin Åberg	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

The National Cause of Death Register, and the National Patient Register are used to evaluate survival probability, prevalence and the morbidity among Swedish Hereditary hemorrhagic telangiectasia (HHT) patients. We will also evaluate consumption of health care and pharmaceutical use in this group of patients

In a PhD-study of chronic rhinosinusitis in adolescence, the prevalence, clinical characteristics and inflammatory markers are analyzed

Ethic permit No:

2020-06950				

Publications 2022, 2023, 2024:

1. Sunnergren O, Ahonen H, Holmström M, Broström A.Laryngoscope Investig Otolaryngol. 2023 Sep 29;8(5):1136-1145
2. Hultman Dennison S, Granath A, Holmstrom M, Stjarne P, Hertting O. Complications to acute bacterial rhinosinusitis in children - a prospective study; bacterial cultures, virus detection, allergy sensitization and immunoglobulins. Rhinology. 2023 Oct 1;61(5):412-420.

3. Morén S, Lindestad PÅ, Stålhammar L, Holmström M, Mani M. Speech in adults treated for unilateral cleft lip and palate as rated by naïve listeners, speech-language pathologists, and patients. J Plast Reconstr Aesthet Surg. 2022 Oct;75(10):3804-3812.
4. Aberg K, Asarnoj A, Georen SK, Cardell LO, Kull I, Bergstrom A, Melén E, Holmstrom M, van Hage M, Westman M. The prevalence of primary chronic rhinosinusitis in young adults from a Swedish birth cohort.. Rhinology. 2025 Apr 1;63(2):180-189.

Name: Sofia Hultman Dennison
Title: MD, PhD
Email: sofia.hultman-dennison@regionstockholm.se

Project title:
Complications to acute rhinosinusitis in children.
Pneumococcal vaccine.
Mastoiditis.

Supervision of PhD-student:

	Main supervisor: ☐ Co-supervisor: ☐

Summery of project:
PhD june 2021: Complications to acute rhinosinusitis in children. 2024: Co-author of article regarding pneumococcal vaccine.

Ethic permit No:

Publications 2022, 2023, 2024:
”The pneumococcal conjugate vaccine had a sustained effect on Swedish children 8 years after its introduction”. Acta Paediatr. 2024 Jan 12. doi: 10.1111/apa.17108. Online ahead of print.PMID: 38217260

“Complications to acute bacterial rhinosinusitis in children - a prospective study; bacterial cultures, virus detection, allergy sensitization and immunoglobulins”. Rhinology. 2023 Oct 1;61(5):412-420. doi: 10.4193/Rhin22.168. PMID: 37338824

Name: Marlin Johansson
Title: MMsc Aud, PhD
Email: marlin.johansson@ki.se

Project title:
Early Diagnosis, Development, and Intervention in Pediatric Hearing Loss: Emphasis on Unilateral Sensorineural Impairment

Summery of project:
My research focuses on hearing development, diagnostics, and intervention for newborns, infants, and young children. I have a particular interest in congenital unilateral hearing loss. My doctoral thesis was dedicated to understanding congenital unilateral sensorineural hearing loss (uSNHL).

Currently, I lead several prospective longitudinal projects on children with congenital uSNHL. These studies evaluate hearing, speech, and language development as well as hearing aid use during the first 2.5 years of life. This work was initiated together with my former supervisors, Associate Professor Erik Berninger and Associate Professor Filip Asp. The first two articles from this project, describing genetic variants, etiology, and audiological profiles of 20 infants, were published in the *Journal of Clinical Medicine* (2022, 2023). I now also plan follow-up assessments at 6–7 years of age.

In addition, I am working on a project together with Dr. Allison Mackey in which we use surveys and interviews to explore the challenges of hearing assessments in children with autism. The ethics application and data collection are set to begin in spring 2025. For this group, we are exploring alternative early diagnostic methods to improve hearing care and intervention outcomes. Dr. Allison Mackey and I also supervise/collaborate with PhD student Kristin Grindborg from Luleå University on a review article regarding OAEs and hyperacusis.

Ethic permit No:

2018/1500-31	2019–03826

Publications 2022, 2023, 2024:

Johansson, M. (2023). Children with congenital unilateral sensorineural hearing loss: Etiology, newborn diagnostics, and hearing aid amplification (Doctoral dissertation). Karolinska Institutet. hdl.handle.net/10616/48489

Johansson, M., Karltorp, E., Asp, F., & Berninger, E. (2023). A Prospective Study of Genetic Variants in Infants with Congenital Unilateral Sensorineural Hearing Loss. Journal of Clinical Medicine, 12(2), 495. DOI: 10.3390/jcm12020495

Johansson M, Karltorp E, Edholm K, Drott M & Berninger E (2022). A Prospective Study of Etiology and Auditory Profiles in Infants with Congenital Unilateral Sensorineural Hearing Loss. Journal of Clinical Medicine, 11(14), 3966. DOI: 10.3390/jcm11143966

Name: Karin Jonstam
Title: MD, PhD
Email: karin.jonstam@ki.se

Project title:

Airway complications, Nutrition and Quality of Life in Children with Tracheostomy

Supervision of PhD-student:

Ida Engqvist	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

The Long-term Intensive Care Units (LIVA) primary task is to care for children with tracheostomies. Between 1998 and 2023, 180 children have undergone follow-up from tracheostomy to decannulation at LIVA. Currently, about 80 children with tracheostomies are being monitored at LIVA.

We are evaluating this surveillance program for children with tracheostomy, characterize types of complications and risk factors in order to improve and possibly individualize follow-up with the aim to avoid unnecessary endoscopies and anaesthesia.

In a prospective study we also investigate the anaesthesiologic risks associated with the current surveillance program for children with tracheostomy, identify risk factors and weight risk versus benefit with regards to surveillance endoscopies of asymptomatic patients.

Furthermore, we are conducting two prospective studies on quality of life in patients with tracheal cannula and their care givers and investigating the prevalence of feeding difficulties within this cohort in order to develop targeted interventions for early feeding training with the aim to improve nutrition and quality of life.

Ethic permit No:

2018/1972-31	2021-06074-02	2023-07493-01

Name: Susanna Kumlien Georén
Title: Senior Research Infrastructure Specialist
Email: susanna.georen@ki.se

Project title:
Immune response in head- and neck cancer and airway inflammatory diseases.

Supervision of PhD-student:

Vilma Lagebro	Main supervisor: ☐ Co-supervisor: ☒
Maryam Jafari	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

The Role of Tumour-Draining Lymph Nodes in Cancer Immunotherapy

Cancer immunotherapies (CPI) have transformed oncology, significantly improving survival across various malignancies. However, tumour-draining lymph nodes (TDLNs) have largely been overlooked in early immunotherapy research. Our projects aim to characterise the cellular architecture and immune function of key immune cells, such as lymphocytes (B and T) and neutrophils, within TDLNs in head and neck squamous cell carcinoma (HNSCC). Additionally, we will investigate how CPI alters the immunological landscape of TDLNs using both an in vitro model based on human TDLNs and a clinical trial. The trial will assess the effects of neoadjuvant anti-PD-1 treatment in patients with locally advanced HNSCC, providing novel insights into the role of TDLNs in cancer immunotherapy

Neutrophils, Extracellular Traps, and the Resolution of Inflammation in Allergic Asthma

This project aims to elucidate the role of neutrophils in the resolution of inflammation and how this process differs between patients with allergic asthma and healthy individuals. A key focus will be on the formation and function of neutrophil extracellular traps (NETs) and their potential contribution to defective inflammation resolution. We will investigate the mechanisms underlying these differences and identify key targets for future therapeutic development. By highlighting neutrophils as a heterogeneous cell

population, we seek to demonstrate how imbalances within its subgroups, including excessive or dysregulated NET formation, may drive persistent airway inflammation. Our findings could pave the way for novel treatment strategies aimed at restoring immune balance in allergic asthma.

Ethic permit No:

2021-01265	2021-00325

Publications 2022, 2023, 2024:

1. Jafari M, Cardenas EI, Ekstedt S, Arebro J, Petro M, Karlsson A, Hjalmarsson E, Arnarson D, Ezerskyte M, **Kumlien Georén S,** Cardell LO. Delayed neutrophil shedding of CD62L in patients with chronic rhinosinusitis with nasal polyps and asthma: Implications for Staphylococcus aureus colonization and corticosteroid treatment. Clinical and translational allergy 2024 14;3 e12347-
2. Eric H, Piersiala K, Lagebro V, Farrajota Neves Da Silva P, Petro M, Starkhammar M, Elliot A, Bark R, Margolin G, **Kumlien Georén S,** Cardell LO. High expression of PD-L1 on conventional dendritic cells in tumour-draining lymph nodes is associated with poor prognosis in oral cancer. Cancer immunology, immunotherapy : CII 2024 73;9 165-
3. Ekstedt S, Piersiala K, Kolev A, Farrajota Neves da Silva P, Margolin G, **Kumlien Georén S,** Cardell LO. Phenotypical differences of neutrophils patrolling tumour-draining lymph nodes in head and neck cancer. British journal of cancer 2024 131;12 1893-1900
4. Piersiala K, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, Bark R, Elliot A, Marklund L, Margolin G, **Georén SK,** Cardell LO. Prognostic value of T regulatory cells and immune checkpoints expression in tumour-draining lymph nodes for oral squamous cell carcinoma. Frontiers in immunology 2024 15; 1455426-
5. Hjalmarsson E, Hellkvist L, Karlsson A, Winquist O, **Kumlien Georén S,** Westin U, Cardell LO. A 5-Year Open-Label Follow-up of a Randomized Double-Blind Placebo-Controlled Trial of Intralymphatic Immunotherapy for Birch and Grass Allergy Reveals Long-term Beneficial Effects. Journal of investigational allergology & clinical immunology 2023 33;5 362-372
6. Kakabas L, Piersiala K, Kolev A, **Kumlien Georén S,** Cardell LO. Allergic sensitization does not influence advancement or survival in oral cancer. Scientific reports 2023 13;1 21696-
7. Lagebro V, Piersiala K, Petro M, Lapins J, Gryback P, Margolin G, **Georen SK,** Cardell LO. A Novel Method Using Fine Needle Aspiration from Tumour-Draining Lymph Nodes Could Enable the Discovery of New Prognostic Markers in Patients with Cutaneous Squamous Cell Carcinoma. CANCERS 2023 15;13
8. van der Burg N, Stenberg H, Ekstedt S, Diamant Z, Bornesund D, Ankerst J, **Kumlien Georén S,** Cardell LO, Bjermer L, Erjefält J, Tufvesson E. Neutrophil phenotypes in bronchial airways differentiate single from dual responding allergic asthmatics. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology 2023 53;1 65-77
9. Ekstedt S, Lagebro V, **Kumlien Georén S,** Cardell LO. Prolonged inflammatory resolution in allergic asthma relates to dysfunctional interactions between neutrophils and airway epithelium. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology 2023 131;3 349-355.e3
10. Piersiala K, Hjalmarsson E, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, **Georén SK,** Cardell LO. Regulatory B cells producing IL-10 are increased in human tumour draining lymph nodes. International journal of cancer 2023 153;4 854-866
11. Bark R, Kolev A, Elliot A, Piersiala K, Näsman A, Grybäck P, **Georén SK,** Wendt M, Cardell LO, Margolin G, Marklund L. Sentinel node-assisted neck dissection in advanced oral squamous cell carcinoma-A new protocol for staging and treatment. Cancer medicine 2023 12;11 12524-12534

12. Hjalmarsson E, Petro M, **Georén SK,** Winqvist O, Cardell LO. Upregulated expression of Notch1/4 - JAG-1/DLL-1 detected in allergic rhinitis. Allergy, asthma, and clinical immunology : official journal of the Canadian Society of Allergy and Clinical Immunology 2023 19;1 41-
13. Ekstedt S, Piersiala K, Petro M, Karlsson A, Kågedal Å, **Kumlien Georén S,** Cardell LO. A prolonged innate systemic immune response in COVID-19. Scientific reports 2022 12;1 9915-
14. Hellkvist L, Hjalmarsson E, Weinfeld D, Dahl Å, Karlsson A, Westman M, Lundkvist K, Winqvist O, **Georén SK,** Westin U, Cardell LO. High-dose pollen intralymphatic immunotherapy: Two RDBPC trials question the benefit of dose increase. Allergy 2022 77;3 883-896
15. Cardenas EI, Ekstedt S, Piersiala K, Petro M, Karlsson A, Kågedal Å, **Kumlien Georén S,** Cardell LO, Lindén A. Increased IL-26 associates with markers of hyperinflammation and tissue damage in patients with acute COVID-19. Frontiers in immunology 2022 13; 1016991-
16. Westerberg J, Granath A, Drakskog C, Tideholm E, **Kumlien Georén S,** Weitzberg E, Cardell LO. Nitric Oxide Is Locally Produced in the Human Middle Ear and Is Reduced by Acquired Cholesteatoma. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2022 43;2 e198-e204
17. Piersiala K, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, **Georén SK,** Cardell LO. Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells. Translational oncology 2022 23; 101469-

Name: Åsa Kågedal
Title: MD, PhD, Senior Consultant
Email: asa.kagedal@regionstockholm.se

Project title:
Sentinel node detection and Immune response in patients with sinonasal tumors and oral cancer

Loss of smell in patients with nasal polyps

Supervision of PhD-student:

Oscar Solmell	Main supervisor: ☐ Co-supervisor: ☒
Karl Johan Borstedt	Main supervisor: ☐ Co-supervisor: ☒

Summery of project (max 2 000)**:**

Sinonasal malignancies are rare but have a high mortality and the post treatment morbidity is severe with mutilating surgery and radiotherapy. The lymphatic drainage from the nasal cavity and the paranasal sinuses are not well studied. With sentinel node procedure and flow cytometry technique for early detection of metastases and immunological biomarkers we hope to gain knowledge for better treatment both in terms of limiting the field of radiotherapy and improve the possibilities for immune therapy.

Metastases in lymph nodes are an important factor for outcome in oral cancer patients. The development of the new immune therapies has changed the field of cancer medicine and it is important to define the selection of patients for these new treatments. The overall goal of this research is to study the immune response in tumour tissue, lymph nodes and blood in patients with oral cancer. We use sentinel node technique to find the draining lymph node where we detect tumour cells with flow cytometry and identify immunological biomarkers.

Smell and taste in patients with history of nasal polyp surgery

Ethic permit No:

2018/811- 32	2015/1650-31-2	2013/1943-3-4	2011/717-31-1	

Publications 2022, 2023, 2024:

A prolonged innate systemic immune response in COVID-19.

Ekstedt S, Piersiala K, Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO.Sci Rep. 2022 Jun 15;12(1):9915. doi: 10.1038/s41598-022-13986-5.PMID: 35705573

Increased IL-26 associates with markers of hyperinflammation and tissue damage in patients with acute COVID-19.

Cardenas EI, Ekstedt S, Piersiala K, Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO, Lindén A.Front Immunol. 2022 Nov 17;13:1016991. doi: 10.3389/fimmu.2022.1016991. eCollection 2022.PMID: 36466824

Name: David Landin
Title: MD, PhD
Email: david.landin@regionstockholm.se

Project title:
Prognostic markers i head- and neck cancer

Summery of project:
Head- and neck cancer is a heterogenous group of cancers. Therefore individual treatment is crucial. Togehther with University of Linköping we do studies of biomarkers in tissue microarrays. By this we hope that we in the long rung personalize treatment.

Ethic permit No:

2009/4:8				

Publications 2022, 2023, 2024:
Landin D, Näsman A, Jaraj SJ, Hammarstedt-Nordenvall L, Munck-Wikland E, Dalianis T, Marklund L. Post-Treatment Neck Dissection of Tonsillar and Base of Tongue Squamous Cell Carcinoma in the Era of PET-CT, HPV, and p16. Viruses. 2022 Jul 30;14(8):1693. doi: 10.3390/v14081693. PMID: 36016315; PMCID: PMC9413897.

Wendt M, Hammarstedt-Nordenvall L, Zupancic M, Friesland S, Landin D, Munck-Wikland E, Dalianis T, Näsman A, Marklund L. Long-Term Survival and Recurrence in Oropharyngeal Squamous Cell Carcinoma in Relation to Subsites, HPV, and p16-Status. Cancers (Basel). 2021 May 23;13(11):2553. doi: 10.3390/cancers13112553. PMID: 34070952; PMCID: PMC8196945.

Zupancic M, Haeggblom L, Landin D, Marklund L, Dalianis T, Näsman A. Psoriasin expression is associated with survival in patients with human papillomavirus-positive base of tongue squamous cell carcinoma. Oncol Lett. 2021 Apr;21(4):277. doi: 10.3892/ol.2021.12538. Epub 2021 Feb 10. PMID: 33732353; PMCID: PMC7905654.

Name: Xinxiu Li
Title: Research specialist, PhD
Email: xinxiu.li@ki.se

Project title:

Digital Twins and Multiomics Integration for Early Biomarker Discovery of Malignant Transformation

Supervision of PhD-student:

Yelin Zhao	Main supervisor: ☐ Co-supervisor: ☒
Martin Smelik	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

arly detection of malignant transformation is critical to improving cancer prognosis and treatment outcomes. Despite advances in multiomics technologies, recent studies suggest that pan-cancer screening using peripheral blood biomarkers has limited utility, while specific biomarkers for individual cancers show promise. Building upon these findings and leveraging the digital twin framework, this project aims to systematically identify and validate early biomarkers for malignant transformation.

We propose to integrate single-cell RNA sequencing (scRNA-seq), proteomics and clinical data to construct digital twins of individuals at risk of cancer. These computational replicas will simulate cellular and molecular changes under various conditions to identify early indicators of oncogenesis. Using machine learning and network analysis, we will prioritize and validate key protein or transcriptomic signatures predictive of malignancy at the earliest stages.

This project will further develop and test an interactive platform to visualize individual disease trajectories and simulate preventive or therapeutic interventions. The ultimate goal is to enable predictive and personalized cancer prevention through early detection, guided by patient-specific digital twins.

Ethic permit No:

6798/18	202012A162	M75-08/2008		

Publications 2022, 2023, 2024:

1. Smelik M, Zhao Y, Mansour Aly D, Mahmud AF, Sysoev O, Li X, Benson M. Multiomics

biomarkers were not superior to clinical variables for pan-cancer screening. Commun Med (Lond). 2024.

2. Smelik M, Zhao Y, Li X, Loscalzo J, Sysoev O, Mahmud F, Mansour Aly D, Benson M. An interactive atlas of genomic, proteomic, and metabolomic biomarkers promotes the potential of proteins to predict complex diseases. Sci Rep. 2024.

3. Zhao Y, Li X, Loscalzo J, Smelik M, Sysoev O, Wang Y, Mahmud AF, Mansour Aly D, Benson M. Transcript and protein signatures derived from shared molecular interactions across cancers are associated with mortality. Journal of Translational Medicine. 2024.

4. Schäfer S, Smelik M, Sysoev O, Zhao, Eklund D, Lilja S, Gustafsson M, Heyn H, Julia A, Kovács I, Loscalzo J, Marsal S, Zhang H, Li X, Gawel D#, Wang H#, Benson M#. scDrugPrio: A framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases. Genome Med 2024.

5. Lilja S#, Li X#, Smelik M, Lee EJ, Loscalzo J, Marthanda PB, et al. Multi-organ single-cell analysis reveals an on/off switch system with potential for personalized treatment of immunological diseases. Cell Rep Med. 2023.

6. Li X, Lee EJ, Lilja S, Loscalzo J, Schäfer S, Smelik M, et al. A dynamic single cell-based framework for digital twins to prioritize disease genes and drug targets. Genome Med. 2022.

Name: Ulrika Löfkvist
Title: Associate professor
Email: ulrika.lofkvist@ki.se

Project titles:
Long-term follow-up of adolescents and young adults who have undergone surgery with cochlear implants during early childhood

Supervision of PhD-student:

Malin Dahlby-Skoog	Main supervisor: ☒ Co-supervisor: ☐
Jonas Fogels	Main supervisor: ☐ Co-supervisor: ☒
Karolina Falkenius Schmidt	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
Long-term outcomes in deaf youth who have received cochlear implants (CIs) early in life is rare so far in the literature. For example outcome related to higher-levels of language competence like figurative understanding, psychosocial well-being, and listening skills in more complex listening conditions reflecting everyday life. In addition, it is yet unclear whether the chronic electrical stimulation in the inner ear and the CI procedure itself affects vestibular function. The multi-disciplinary research program aimed to investigate possible effects of early age at 1st cochlear implantation (CI) in a larger cohort of adolescents and young adults who received their 1st CI before 30 months of age, and in relation to typical hearing controls.

The overall two PICO-questions motivating the multi-disciplinary research program (including five study projects):

1.How do adolescents with mono- or multilingual background implanted before 30 months with cochlear implant(s), perform long-term in linguistics, cognition, hearing,

balance, self-efficacy and health-related quality of life (HRQoL), and in comparison to age-, socioeconomic and language-matched controls with typical hearing?

2.How do adolescents and young adults with CIs perceive their listening and communication experiences with CIs in different everyday life situations and activities (school, work, leisure), and in relation to controls with typical hearing?

The project have finished the data collection. I am responbile for two parts of the project (Mental health respectively Language and cognition). We are currently analysing the data material and have so far published two articles (Löfkvist et al., 2025; Dahlby-Skoog et al., 2025).

Ethic permit No:

2015/992-31	2022-01159-01			

Publications 2022, 2023, 2024:

Löfkvist, U., Karltorp, E., Dunn, J., Teagle, H., Park, A. (2024). Congenital Cytomegalovirus (CMV) Infection: A Common Yet Overlooked Cause of Hearing Loss and Neurodevelopmental Disorders. *The Volta Review,* Vol 124 (1).

Jakhelln Laugen, N., Midtli, H., Löfkvist, U., Stensen, K. Psychometric properties of the Norwegian version of the Strength and Difficulties Questionnaire in a preschool sample. *Nord J Psychiatry.*Aug;78(6):482-488, https://doi.org/10.1080/08039488.2024.2351046

Ching, TY., Fitzpatrick, E., Huttunen, K., Löfkvist, U., Sung, V. (2024). Editorial: Early Detection and Intervention for Unilateral Hearing Loss and Mild Bilateral Hearing Loss in Children: Clinical Practices and Outcomes. Frontiers in Pediatrics, 12, https://doi.org/10.3389/fped.2024.1400074

Säfström, M., Löfkvist, U. (2024). Employees' experiences of a large-scale implementation in a public care setting: a novel mixed-method approach to content analysis. *BMC Health Serv Res.* Jan 18;24(1):107. https://doi.org/10.1186/s12913-024-10560-9

Falkenius-Schmidt, K., Nyström, A., Karltorp, E., Magnusson, M., Löfkvist, U. (2024). Long-term Linguistic Outcome in Adults with Congenital Cytomegalovirus Infection. *Infectious Diseases.* Jan;56 (1):32-41. https://doi.org/10.1080/23744235.2023.2263567

Johansen, L., Gray, T., Haukedal, C.L., Jakhelln Laugen, N., Diamanti, V., Löfkvist, U. (2023). Validation of the Norwegian version of the Parents' Evaluation of Aural/Oral Performance of Children (PEACH+) for children with typical hearing aged 12-72 months. *PLoS One*. Aug 17;18(8):e0289898. https://doi.org/10.1371/journal.pone.0289898.

Bonati, M., Levy, C., Löfkvist, U. (2022). Home language environment in relation to language outcome in Brazilian toddlers who are hard of hearing and controls with typical hearing – a pilot study including reliability analyses of the LENA recording system. *CoDAS.* 35(1). https://doi.org/10.1590/2317-1782/20212021250

de Melo, M.E., Soman, U., Voss, J., Hinojosa Valencia, M.F., Noll, D., Clark, F., Hutsell Guignard, G., Löfkvist. U. (2022). Listening and Spoken Language Specialist (LSLS) Auditory-Verbal Certification: Self-perceived Benefits and Barriers to Inform Change. *Perspectives SIG 9*. 7(6): 1828-1852. https://doi.org/10.1044/2022_PERSP-22-00060

Socher, M., Löfkvist, U., Wass, M. (2022). Comparing the semantic networks of children with cochlear implants and children with typical hearing: Effects of length of language access. *J Commun Disord*. 99(2): 106247. https://doi.org/10.1016/j.jcomdis.2022.106247

Löfkvist, U., Nilsson, S., Thalen, Y., Östlund, E., Mared, H., Johansson, C., Anmyr, L., Karltorp, E. (2022). Gender differences in Caregiver's Use of Spoken Language close to young children who are Hard-of-Hearing. *Int J Pediatr Otorhinolaryngol.* May;156:111103. https://doi.org/10.1016/j.ijporl.2022.111103

Name: Maoli Duan
Title: Assoc Prof Senior Consultant
Email: maoli.duan@ki.se

Project title:
Disorders affecting hearing and balance in children - the importance of early diagnosis and early intervention

Supervision of PhD-student:

Niki Karpeta	Main supervisor: ☒ Co-supervisor: ☐
Andra Lazar	Main supervisor: ☒ Co-supervisor: ☐
Anna Karin Strömberg	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
Early diagnosis and intervention of hearing impairment (HI) and vestibularis dysfunction/disorders (VD) in infants and young children is a still hot topic in audiology and neurotology. There are needs for an increasing knowledge on how to optimize the care for as well as to improve development of the children. The majority of HI and VD infants still do not get a specific genetic diagnosis of their illness despite 50% being genetic. NGS methods will dramatically improve the possibilities to identify different genetic causes of HI and VD. Furthermore, despite quite high prevalence of VD in HI children this has not been paid too high attention. We will investigate the HI/VD children using physiological and genetic methods to study etiology, and further develop the means for the diagnosis for clinical routine in the near future. We will develop the screening program for HI/VD children and write international consensus/guidline for gene therapy and VD screening. In addition, we will develop the therapitic means like AAV-OTOF, AAV-GJB2 gene therapy to restore hearing of the patients.

Ethic permit No:

2013/1177-31	2015/1296-31/2	2019-02019

Publications 2022, 2023, 2024:

1. Dai Q , Dai W , Wang D , Liu X, Zou L, Chen J, Zheng H, **Duan M**. Molecular screening of patients with profound hearing loss from Chengdu, China. Acta Otolaryngol. 2022 Jan;142(1): 57-60.doi: 10.1080/00016489.2021.2014564.

2. **Duan M**, Xie W, Persson L, Hellstrom S, Uhlén I. Postnatal hearing loss: a study of children who passed neonatal TEOAE hearing screening bilaterally. Acta Otolaryngol. 2022 Jan;142(1):61-66. doi: 10.1080/00016489.2021.2017476.

3. Diao T, **Duan M**, Ma X, Liu J, Yu L, Jing Y, Wang M. The impairment of speech perception in noise following pure tone hearing recovery in patients with sudden sensorineural hearing loss. Sci Rep. 2022 Jan 17;12(1):866. doi: 10.1038/s41598-021-03847-y.PMID: 35039548

4. Yao W, Gao L, Su J, Karpeta N, Xie W, **Duan M.** Effects of lesions of the organ of corti on hearing. Acta Otolaryngol 2022 Jan 29;1-9 doi: 10.1080/00016489.2022.2027517.

5. Zheng G, Liu Y, He J, Li S, Zhang Q, **Duan M**, Yang J, Jin Y. A Comparison of Local Endolymphatic Sac Decompression, Endolymphatic Mastoid Shunt, and Wide Endolymphatic Sac Decompression in the Treatment of Intractable Meniere's Disease: A Short-Term Follow-Up Investigation. Front Neurol 2022 Feb10; 13:810352.doi:10.3389/fneur.2022.810352.

6. Yupeng Liu, Ilmari Pyykkö , Shinji Naganawa , Pedro Marques , Robert Gürkov JunYang, **Maoli Duan**. Consensus on MR Imaging of Endolymphatic Hydrops in Patients with suspected Hydropic Ear Disease (Meniere). Frontiers in Surgery 2022. In press

7. Li S, Pyykkö I, Zhang Q, Yang J, **Duan M.** Consensus on Intratympanic drug delivery for Meniere`s disease. Eur Arch Otorhinolaryngol. 2022 Aug;279(8):3795-3799. doi: 10.1007/s00405-022-07374-y. Epub 2022 Apr 26.PMID: 35469039

8. Yu T, Yu H, **Duan M**. Case Report of Non-Organic Hearing Loss: Literature Review Insights in Biomedicine. Volume 07 • Issue 02 • 63.

9. Shen J, Wang L, Ma X , Chen Z , Chen J, Wang X , He K , Wang W, Sun J , Zhang Q , Shen M , Chen X , Zhang Q , Kaga K , **Duan M** , Yang J, Jin Y. Cervical vestibular evoked myogenic potentials in 3-month-old infants: Comparative characteristics and feasibility for infant vestibular screening. Front Neurol 2022 Sep 29;13:992392.doi: 10.3389/fneur.2022.992392. eCollection 2022.

10. Li S , Pyykkö I, Zhang Q, Yang J, **Duan M**. Consensus on intratympanic drug delivery for Menière's disease. Eur Arch Otorhinolaryngol. 2022 Aug;279(8):3795-3799. doi: 10.1007/s00405-022-07374-y. Epub 2022 Apr 26.

11. Liu Y, Pyykkö I, Naganawa S, Marques P, Gürkov R, Yang J, **Duan M.** Consensus on MR Imaging of Endolymphatic Hydrops in Patients With Suspected Hydropic Ear Disease (Meniere). Front Surg. 2022 Apr 28;9:874971. doi: 0.3389/fsurg.2022.874971. eCollection 2022.

12. Chen D, **Duan M.** Clinical effect of CO_2 laser resection of the epiglottic cyst under micro-laryngoscope suspension. Acta Otolaryngol. 2022 May;142(5):443-447. doi: 10.1080/00016489.2022.2079717. Epub 2022 Jun 2.PMID: 35654408.

13. Chen D, **Duan M.** The study of otoendoscopic tympanoplasty (type I). Acta Otolaryngol. 2022 Jul-Aug;142(7-8):575-578. doi: 10.1080/00016489.2022.2104923. Epub 2022 Aug 19.PMID: 35984434

14. Niu X, Han P, **Duan M**, Chen Z, Hu J, Chen Y, Xu M, Ren P, Zhang Q. Bilateral Dysfunction of Otolith Pathway in Patients With Unilateral Idiopathic BPPV Detected by ACS-VEMPs. Front Neurol. 2022 Aug 26;13:921133. doi: 10.3389/fneur.2022.921133. eCollection 2022.PMID: 36090849

15. Zhang F, Shen J, Zhu Q, Wang L, Ma X, He B, Yang Y, Wang W, Chen X, Zhang Q, Jin Y, **Duan M**, Chen J, Yang J. Evaluating children with vestibular migraine through vestibular test battery: A cross-sectional investigation. Front Neurol. 2022 Oct 31;13:997217. doi: 10.3389/fneur.2022.997217. eCollection 2022.PMID: 36388219

16. Shen J, Wang L, Ma X, Chen Z, Chen J, Wang X, He K, Wang W, Sun J, Zhang Q, Shen M, Chen X, Zhang Q, Kaga K, **Duan M**, Yang J, Jin Y. Cervical vestibular evoked myogenic potentials in 3-month-old infants: Comparative characteristics and feasibility for infant vestibular screening. Front Neurol. 2022 Sep 29;13:992392. doi: 10.3389/fneur.2022.992392. eCollection 2022.PMID: 36247765

17. Liang M, Wu H, Chen J, Zhang Q, Li S, Zheng G, He J, Chen X, **Duan M**, Yang J, Jin Y. Vestibular evoked myogenic potential may predict the hearing recovery in patients with unilateral idiopathic sudden sensorineural hearing loss. Front Neurol. 2022 Nov 2;13:1017608. doi: 10.3389/fneur.2022.1017608. eCollection 2022.PMID: 36408508

18 Yang J, Liu Y, **Duan M.** Editorial: Intratympanic and surgical treatment for Meniere's disease. Front Neurol. 2022 Dec 21;13:1072659. doi: 10.3389/fneur.2022.1072659. eCollection 2022.PMID: 36619914

19. Yang Y, Gao D, Ma X, Shen J, Zhang Q, Chen X, Zhang Q, Jin Y, Chen J, **Duan M**, Yang J. Abnormal posterior semicircular canal function may predict poor prognosis in patients with severe and profound ISSNHL. **January 2023. Frontiers in Neurology 14:1123165 DOI:10.3389/fneur.2023.1123165.**

20. Chen et al. Diagnosis, differential diagnosis, and treatment for sudden sensorineural hearing loss: Current otolaryngology practices in China. **February 2023. Frontiers in Neurology 14:1121324. DOI:10.3389/fneur.2023.1121324**

21. Xie W, Karpeta N, Tong B, Liu J, Peng H, Li C, Hellstrom S, Li Y, **Duan M. Frontiers in Neurology.** Etiological analysis of patients with sudden sensorineural hearing loss: a prospective case-control study**.** February 2023 DOI:10.21203/rs.3.rs-2559264/v1

22. Yang J, Liu Y, Zhang Q, Yu L, Murofushi T, Jahn K, **Duan M.** Editorial: Vestibular disorders in children. **February 2023. Frontiers in Neurology 14** DOI:10.3389/fneur.2023.1142504.

23. Dai Q, Long L, Zhao H, Wang R, Zheng H, **Duan M.** Genetic advances in Meniere Disease. Mol Biol Rep. 2023 Mar;50(3):2901-2908. doi: 10.1007/s11033-022-08149-8. Epub 2022 Dec 24.PMID: 36565421

24. Liang J, Xie W, Yao W, **Duan M.** Effects of basilar-membrane lesions on dynamic responses of the middle ear. Acta Otolaryngol. 2023 Apr;143(4):255-261. doi: 10.1080/00016489.2023.2187451. Epub 2023 Mar 20.PMID: 36939118

25. Chen N, Karpeta N, Ma X, Ning X, Liu X, Song J, Jiang Z, Ma X, Liu X, Zhong S, Sun Q, Liu J, Chen G, **Duan M**, Yu L. Diagnosis, differential diagnosis, and treatment for sudden sensorineural hearing loss: Current otolaryngology practices in China. Front Neurol. 2023 Feb 23;14:1121324. doi: 10.3389/fneur.2023.1121324. eCollection 2023.PMID: 36908605

26. Zhang J, Zhu Q, Shen J, Chen J, Jin Y, Zhang Q, **Duan M**, Yang J. Etiological classification and management of dizziness in children: A systematic review and meta-analysis. Front Neurol. 2023 Mar 2;14:1125488. doi: 10.3389/fneur.2023.1125488. eCollection 2023.PMID: 36937528

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52. AAV-OTOF gene therapy for autosomal recessive deafness 9: a multicenter, open-label, single-arm, investigator-initiated intervention study

Jieyu Qi, Liyan Zhang, Ling Lu, Fangzhi Tan1, Cheng Cheng, WenXiu Dong, Yinyi Zhou, Lulu Jiang, Chang Tan, Shanzhong Zhang, Sijie Sun, Huaien Song, M.D., **Maoli Duan**, Xia Gao4, Dingjun Zha, Yu Sun, Lei Xu, Fan-Gang Zeng, Renjie Chai. Accepted for publishing in Nature Medicine, 2025

Name: Linda Marklund
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Project title:

Supervision of PhD-student:

Rasmus Blomkvist	Main supervisor: ☒ Co-supervisor: ☐
Evelina Jörtsjö	Main supervisor: ☒ Co-supervisor: ☐
Aeneas Kolev	Main supervisor: ☐ Co-supervisor: ☒
Petronella Pettersson	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

Ett flertal projekt inom huvud och halscancer som syftar till förbättrad diagnostik och behandling.

Ethic permit No:

2023-00134-01	2023-03476-01	2023-04595-01	2024-02635-01	

Publications 2022, 2023, 2024:

1.Jörtsö E, Marklund L, Harper Hysek M, Näsman A, Hammarstedt-Nordenvall L, Von Beckerath M, Dalianis T, Bark R . Fine needle aspiration cytology including the analysis of human papilloma virus (HPV) DNA enhances the diagnostic workup of solitary cystic neck lesions in a population with a high incidence of HPV positive oropharyngeal cancer. Acta Oncol. 2025 Feb 17;64:276-283. doi: 10.2340/1651-226X.2025.42078.

2.Piersiala K, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, Bark R, Elliot A, Marklund L, Margolin G, Georén SK, Cardell LO. Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous

cell carcinoma. Front Immunol. 2024 Oct 15:15:1455426. doi: 10.3389/fimmu.2024.1455426.

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4. Zupancic M, Kostopoulou O, Holzhauser S, Lukoseviciute M, Jylha C, Marklund L, Nasman A, Sivars L, Dalianis T. Human papillomavirus (HPV) load is higher in HPVDNA/p16 positive than in HPVDNA positive/p16 negative oropharyngeal squamous cell carcinoma but does not differ significantly between various subsites or correlate to survival. ORAL ONCOLOGY. 2024;151:106749. PMID: 38461771, DOI: 10.1016/j.oraloncology.2024.106749

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6. Piersiala K, Hjalmarsson E, da Silva P, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georen S, Cardell L-O. Regulatory B cells producing IL-10 are increased in human tumor draining lymph nodes. INTERNATIONAL JOURNAL OF CANCER. 2023;153(4):854-866. PMID: 37144812, DOI: 10.1002/ijc.34555

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8. Blomkvist R, Marklund L, Hammarstedt-Nordenvall L, Gottlieb-Vedi E, Maekitie A, Palmgren B. Treatment and outcome among patients with laryngeal squamous cell carcinoma in Stockholm-A population-based study. LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY. 2023;8(2):441-449. PMID: 37090883, DOI: 10.1002/lio2.1034

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12. Gallus R, Nauta I, Marklund L, Rizzo D, Crescio C, Mureddu L, Tropiano P, Delogu G, Bussu F. Accuracy of p16 IHC in Classifying HPV-Driven OPSCC in Different Populations. CANCERS. 2023;15(3):656. PMID: 36765613, DOI: 10.3390/cancers15030656

13. Piersiala K, da Silva P, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georen S, Cardell L-O. Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells. TRANSLATIONAL ONCOLOGY. 2022;23:101469. PMID: 35714487, DOI: 10.1016/j.tranon.2022.101469

14. Landin D, Nasman A, Jara S, Hammarstedt-Nordenvall L, Munck-Wikland E, Dalianis T, Marklund L. Post-Treatment Neck Dissection of Tonsillar and Base of Tongue Squamous Cell Carcinoma in the Era of PET-CT, HPV, and p16. Viruses. 2022 Jul 30;14(8):1693. doi: 10.3390/v14081693.

Name: Elin Marsk
Title: Överläkare
Email: elin.marsk@regionstockholm.se

Project title:
Different aspects of peripheral facial palsy

Supervision of PhD-student:

Rebecka Ohm	Main supervisor: ☐ Co-supervisor: ☒
Siggi Arnarson	Main supervisor: ☐ Co-supervisor: ☒
Sofia Karlsson	Main supervisor: ☐ Co-supervisor: ☒
Adrianna Opalko	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

Bell's palsy is an acute peripheral facial nerve palsy with unknown etiology that can affect both adults and children. There is a higher incidence among pregnant women and in the puerperium. The disease can cause severe disfigurement of the face, impair the ability to eat, drink and speak, and seriously affect the patient's quality of life. It is important to protect the eye in the acute fase since corneal damage can occur as a complication to the inability to close the upper eylid. Many patients with defect healed palsy need surgical interventions or botox injections.

In our work, we study different aspects of Bell's palsy in both adults (especially among pregnant women) and children. Surgical interventions with nerve transfers and neurotomy on adults with severe facial plays is studied and a project in collaboration with the ophthalmological department is ongoing where eye problems among patients with inflammatory caused peripheral facial palsy is analyzed. A multi-center randomised, clinical trial is performed on children with acute facial palsy to study the effect of prednisolone on the facial outcome.

Ethic permit No:

Publications 2022, 2023, 2024:

-Complications of Gastrostomy Tubes in Patients with Head and Neck Cancer. Vujasinovic M, **Marsk E**, Tsolakis Apostolos V, Hynning Boel, Nordberg Martin, Lindblad Mats, Lindqvist Catarina, Nordenvall Lalle Hammarstedt, Bark Rusana, Elbe Peter. *Laryngoscope.* 2022 Sep;132(9):1778-1784. Epub 2022 Jan 18. doi: 10.1002/lary.30017.

-Voice rest after vocal fold polyp surgery: a study of 588 patients in the Swedish National Register for Voice improving vocal fold surgery Björck G, Hertegård S, **Marsk E** *Laryngoscope, Investigative Otolaryngology* 2022 Mar 16;7(2):486-493

-Bell's palsy in pregnancy and postpartum: a retrospective case control study of 182 patients. Lansing L, Brismar Wendel S, Hultcrantz M, **Marsk E** Otolaryngol Head Neck Surg. 2023 May;168(5):1025-1033. doi: 10.1002/ohn.188. Epub 2023 Jan 22.

-Sequelae treatment needs following peripheral facial palsy: retrospective analysis of 525 patients. Rebecka Ohm, Fredrik Brännström, Birgit Stark**, Elin Marsk**, Otology & Neurotology. 2024 Jun 1;45(5):e450-e456

-A longitudinal study of facial function, quality of life, and depression in Bell's palsy during pregnancy and puerperium. Lovisa Lansing, Sophia Brismar Wendel, Ellen Wejde Westlund, **Elin Marsk**. Sci Rep. 2024 Oct 22;14(1):24890. doi: 10.1038/s41598-024-75552-5.

Name: Eva Munck-Wikland
Title: Prof em
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Project title:

Sentinel node B-cells and their role in antitumor immune response in head and neck cancer.

Supervision of PhD-student:

Vilma Liljeström	Main supervisor: ☐ Co-supervisor: ☒

Ethic permit No:

Publications 2022, 2023, 2024:

Regulatory B cells producing IL-10 are increased in human tumor draining lymph nodes.
Piersiala K, Hjalmarsson E, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, **Munck-Wikland E**, Margolin G, Georén SK, Cardell LO. Int J Cancer. 2023 Aug 15;153(4):854-866. doi: 10.1002/ijc.34555. Epub 2023 May 5. PMID: 37144812

High Levels of FGF11 Correlate with Poor Survival in Patients with Human Papillomavirus (HPV)-Positive Oropharyngeal Squamous Cell Carcinoma.
Flon CH, Haeggblom L, Holzhauser S, Kostopoulou ON, Zupancic M, Dalianis T, **Munck-Wikland E**, Marklund L, Näsman A. Cancers (Basel). 2023 Mar 24;15(7):1954. doi: 10.3390/cancers15071954. PMID: 37046615 Free PMC article.

Brachytherapy and osteoradionecrosis in patients with base of tongue cancer.
Danielsson D, Hagel E, Dybeck-Udd S, Sjöström M, Kjeller G, Bengtsson M, Abtahi J, von Beckerath M, Thor A, Halle M, Friesland S, Mercke C, Westermark A, Högmo A, **Munck-Wikland E.** Acta Otolaryngol. 2023 Jan;143(1):77-84. doi: 10.1080/00016489.2022.2161627. Epub 2023 Jan 3. PMID: 36595465 Free article.

Post-Treatment Neck Dissection of Tonsillar and Base of Tongue Squamous Cell Carcinoma in the Era of PET-CT, HPV, and p16.
Landin D, Näsman A, Jara SJ, Hammarstedt-Nordenvall L, **Munck-Wikland E**, Dalianis T, Marklund L. Viruses. 2022 Jul 30;14(8):1693. doi: 10.3390/v14081693. PMID: 36016315 Free PMC article.

Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells.
Piersiala K, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, **Munck-Wikland E**, Margolin G, Georén SK, Cardell LO. Transl Oncol. 2022 Sep;23:101469. doi: 10.1016/j.tranon.2022.101469. Epub 2022 Jun 14. PMID: 35714487 Free PMC article.

Mandibular resection in patients with head and neck cancer: acute and long-term complications after reconstruction.
Sjöström M, Danielsson D, **Munck-Wikland E**, Nyberg J, Sandström K, Thor A, Johansson H, Ceghafi P, Dybeck Udd S, Emanuelsson J, Forsberg Pettersson L, Halle M, Laurell G. Acta Otolaryngol. 2022 Jan;142(1):78-83. doi: 10.1080/00016489.2021.2021283. Epub 2022 Jan 13. PMID: 35023428 Free article.

Name: Antti Mäkitie
Title: Professor, Visiting Scientist
Email: antti.makitie@ki.se

Project title:

Supervision of PhD-student:

Evelina Gille	Main supervisor: ☐ Co-supervisor: ☒
Rasmus Blomkvist	Main supervisor: ☐ Co-supervisor: ☒

Summary of project:

1. Identification of early diagnostic and prognostic markers (both clinical and biomarkers) that predict HNSCC treatment outcome. This collaborative project aims to identify markers that predict treatment response and can be analyzed in a tissue biopsy from a suspected tumor and/or in the patient's blood sample or saliva. The ultimate goal is to find combinations of markers, which could guide clinicians to provide cancer patients with a more adequate, individualized, and effective treatment. We also apply Machine Learning models and Radiomics to better overcome challenges encountered in the management of HNSCC.

2. The Nordic Head and Neck Cancer (HNC) Study: management and outcome of various subsites of HNC in the Nordic countries. Our aim is to evaluate current treatment outcome of HNC in the Nordic countries and to form a recommendation for a unified treatment protocol for this entity to be used in this area. The secondary aim is to find prognostic markers for clinical use by using multi-institutional series of HNC patients and available samples.

Ethic permit No:

Selected publications from 2022, 2023, 2024:

Alabi RO, Elmusrati M, Leivo I, Almangush A, **Mäkitie AA**. Collaborative machine learning-guided overall survival prediction of oral squamous cell carcinoma. Acta Otolaryngol. 2024 Dec 31:1-8.

Nikkilä R, Hirvonen E, Haapaniemi A, Pitkäniemi J, Malila N, **Mäkitie A**. Second primary cancers in patients with a pharyngeal index tumour: a register-based cohort study. BMC Cancer. 2024 Nov 11;24(1):1380.

Punovuori K, Bertillot F, Miroshnikova YA, Binner MI, Myllymäki SM, Follain G, Kruse K, Routila J, Huusko T, Pellinen T, Hagström J, Kedei N, Ventelä S, **Mäkitie A**, Ivaska J, Wickström SA. Multiparameter imaging reveals clinically relevant cancer cell-stroma interaction dynamics in head and neck cancer. Cell. 2024 Dec 12;187(25):7267-7284.e20.

Nikkilä R, Haapaniemi A, Carpén T, Pukkala E, **Mäkitie A**. Laryngeal cancer relative survival trends from 1972 to 2021 in the Nordic countries. Acta Oncol. 2024 Aug 4;63:612-619.

Nikkilä R, Hirvonen E, Pitkäniemi J, Räsänen JV, Malila NK, **Mäkitie A**. Risk of Second Primary Cancer Among Patients with Cardio-Esophageal Cancer in Finland: A Nationwide Population-Based Study. Clin Epidemiol. 2024 Jul 22;16:475-485.

Talani C, Högmo A, Laurell G, **Mäkitie A**, Farnebo L. Six-month mortality has decreased for patients with curative treatment intent for head and neck cancer in Sweden. PLoS One. 2024 Apr 16;19(4):e0296534.

Blomkvist R, Marklund L, Hammarstedt-Nordenvall L, Gottlieb-Vedi E, **Mäkitie A**, Palmgren B. Treatment and outcome among patients with laryngeal squamous cell carcinoma in Stockholm - A population-based study. Laryngoscope Investig Otolaryngol. 2023 Mar 6;8(2):441-449.

Saarentaus EC, Karjalainen J, Rämö JT, Kiiskinen T, Havulinna AS, Mehtonen J, Hautakangas H, Ruotsalainen S, Tamlander M, Mars N; FINNGEN; Toppila-Salmi S, Pirinen M, Kurki M, Ripatti S, Daly M, Palotie T, **Mäkitie A**, Palotie A. Inflammatory and infectious upper respiratory diseases associate with 41 genomic loci and type 2 inflammation. Nat Commun. 2023 Jan 18;14(1):83.

Rämö JT, Kiiskinen T, Seist R, Krebs K, Kanai M, Karjalainen J, Kurki M, Hämäläinen E, Häppölä P, Havulinna AS, Hautakangas H; FinnGen; Mägi R, Palta P, Esko T, Metspalu A, Pirinen M, Karczewski KJ, Ripatti S, Milani L, Stankovic KM, **Mäkitie A**,

Daly MJ, Palotie A. Genome-wide screen of otosclerosis in population biobanks: 27 loci and shared associations with skeletal structure. Nat Commun. 2023 Jan 18;14(1):157.

Carpén T, Gille E, Hammarstedt-Nordenvall L, Hansen J, Heikkinen S, Lynge E, Selander J, Mehlum IS, Torfadottir JE, **Mäkitie A**, Pukkala E. Occupational risk variation of nasopharyngeal cancer in the Nordic countries. BMC Cancer. 2022 Nov 4;22(1):1130.

Omobolaji Alabi R, Almangush A, Elmusrati M, Leivo I, **Mäkitie AA**. An interpretable machine learning prognostic system for risk stratification in oropharyngeal cancer. Int J Med Inform. 2022 Dec;168:104896.

Nieminen T, Tolvi M, Lassus P, Wilkman T, Lehtonen L, **Mäkitie A**. Risk factors for evaluating early mortality after microvascular reconstruction of head and neck cancers. Scand J Surg. 2022 Dec;111(4):83-91.

For the complete list of publications, please see:
https://pubmed.ncbi.nlm.nih.gov/?term=Makitie+a

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Project title:
Obstructive Sleep Apnea in children and adults; a surgical therapeutic perspective. Subglottic stenosis in adults; measurements and treatment efficiency.

Summery of project:
Within surgical treatment for obstructive sleep apnea (OSA), the group has performed five randomized controlled trials. The main focus for adult sleep apnea is on uvulopalatopharyngoplasty including tonsillectomy, which we have compared to expectancy and to plain tonsillectomy. In children, the main focus is on different techniques and additions to tonsill surgery. We compare expectancy, tonsillotomy, tonsillectomy and tonsillectomy with additional suturing of the pillars. Patients are evaluated with both objective and subjective parameters such as polysomnography findings (the gold standard sleep registration), vigilans, daytime sleepiness, quality of life, blood pressure, inflammatory markers etc.

Further the Swedish Quality Register for Tonsil Surgery is another field of research were we evaluate incidence, morbitidy and symtom relief etc using the registra as source of epidemiology research and possibility to evaluate rare concequenses etc.

Within the field of subglottic stenosis we have a project evaluating intralesional steroid injections, as well as retrospecitve and prospective evaluations of other treatment forms, for the adult population with subglottic stenosis. We are investigating the diagnosic method of a handheld peak inspiratory flow meter (PIF-meter) gathering a healthy population besides our subglottic stenosis patients.

Ethic permit No:

2021-02110	2015/755-31/2	2013/2274-32	2021-00716	2014/1000-31/1

Publications 2022, 2023, 2024:

1. A validation study of data in the National Tonsil Surgery Register in Sweden: High agreement with medical records ensures that data can be used to monitor clinical practices and outcomes

Filip Lundström, Erik Odhagen, Fredrik Alm, Claes Hemlin, Pia Nerfeldt, Ola Sunnergren.

BMC Med Res Methodol. 2022 Jan 7;22(1):3. doi: 10.1186/s12874-021-01467-8

2. Adenotonsillotomy versus adenotonsillectomy in pediatric obstructive sleep apnea: a 5-year RCT

Isabella Sjölander, Anna Borgström, Pia Nerfeldt, Danielle Friberg.

Sleep Med X. 2022 Sep 8;4:100055. doi:0.1016/j.sleepx.2022.100055.

3. Tonsillectomy vs Modified Uvulopalatopharyngoplasty in Patients with Tonsillar Hypertrophy and Obstructive Sleep Apnea -

The TEAMUP Randomized Controlled Trial.

Joar Sundman, MD, PhD1; Pia Nerfeldt, MD, PhD1; Johan Fehrm, MD, PhD1; Johan Bring, PhD2 Nanna Browaldh, MD, PhD1; Danielle Friberg, MD, PhD3

JAMA ORL 2022 Dec 1;148(12):1173-1181. doi: 10.1001/jamaoto.2022.3432.

4. Correlations between objective and subjective outcomes after adenotonsillar surgery in children with OSA.

Sjölander I, Borgström A, Nerfeldt P, Fehrm J, Friberg D.

Laryngoscope Investigative Otolaryngology 2022 Nov 4;7(6):2161-2170. doi.org/10.1002/lio2.967

5. Long-term complications after tonsil surgery – an analysis of 54 462 patients from the Swedish Quality Register for Tonsil Surgery.

Erik Odhagen, Fredrik Alm, Sara Axelsson, Claes Hemlin, Pia Nerfeldt, Joacim Stalfors, Ola Sunnergren.

Front Surg 2023 Dec 12:10:1304471. doi: 10.3389/fsurg.2023.1304471.

6. Pain management after tonsil surgery in children and adults - a national survey related to pain outcome measures from the Swedish Quality Register for Tonsil Surgery

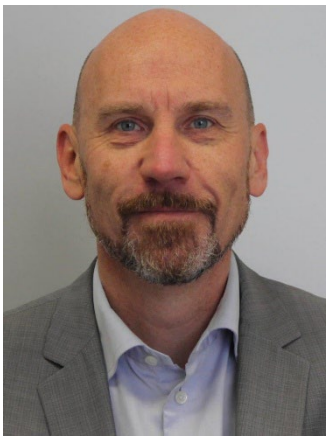
Roskvist M, Alm F, Nerfeldt P, Ericsson E.

PLoS One 2024 Mar 7;19(3):e0298011. doi: 10.1371/journal.pone.0298011

7. Postoperative Analgesic Regimens and Their Satisfaction Rates-Data from the Swedish Quality Register for Tonsil Surgery.

Alm F, Odhagen E, Sunnergren O, Nerfeldt P.

Laryngoscope. 2024 Aug 14. doi: 10.1002/lary.31691.



Name: Petter Olsson
Title: MD, PhD
Email: petter.olsson@ki.se

Project title:
Upper airway disease; treatments and health economy

Summery of project:
Research interests include the epidemiology of rhinitis and nasal polyposis, the medical and surgical management of nasal polyposis as well as immunotherapy and biologic treatments of upper airway disease, inluding health economy.

Ethic permit No:

2021-05918-01

Publications 2022, 2023, 2024:
1. Luong AU, Chua A, Alim BM, Olsson P, Javer A. Allergic Fungal Rhinosinusitis: The Role and Expectations of Biologics. The journal of allergy and clinical immunology. In practice 2022 10;12 3156-3162

2. Taniguchi M, Heffler E, Olze H, White A, Côrte-Real J, Olsson P, Lazarewicz S. The Role of Omalizumab in NSAID-Exacerbated Respiratory Disease: A Narrative Review. The journal of allergy and clinical immunology. In practice 2022 10;10 2570-2578

Name: Björn Palmgren

Title: MD,PhD

Email: Bjorn.palmgren@regionstockholm.se

Project title:
Sentinel Node technique in laryngeal and hypopharyngeal squamous cell carcinoma.

Supervision of PhD-student:

Rasmus Blomkvist	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
The sentinel node (SN) technique is a method used to identify and assess the first lymph node to which cancer cells are likely to spread from a primary tumor. This technique has been applied to cancers in various regions of the ENT (ear, nose, and throat) anatomy. However, there are relatively few published studies on the use of SN in tumors of the larynx and hypopharynx. Despite this, both sites are subject to treatment modalities that carry a high risk of morbidity. Due to the varying metastatic potential based on tumor location—low in glottic LSCC and high in supraglottic LSCC—precise mapping of lymphatic spread is important. This prospective study aims to explore the SN technique and drainage patterns in patients with laryngeal squamous cell carcinoma (LSCC). The study's objective is to assess the SN technique, with the long-term goal of enhancing neck staging accuracy, reducing overtreatment, and ultimately optimizing surgical and radiotherapy planning to minimize treatment-related side effects.

Patients with suspected T2–T4 glottic or T1–T4 supraglottic LSCC will be invited to participate, with a target sample size of 50 patients over approximately two years. The study involves peritumoral tracer injections followed by SPECT-CT imaging, and for surgical cases, perioperative SN identification and histological assessment. Sentinel node locations will be analyzed in relation to tumor site, T-classification, and planned

radiation fields. For surgical cases, SN histology will be compared with the full neck dissection specimen to evaluate the technique's accuracy.

Ethic permit No:

2024-07341-02				

Publications 2022, 2023, 2024:

1. Treatment and outcome among patients with laryngeal squamous cell carcinoma in Stockholm—A population-based study

Rasmus Blomkvist, Linda Marklund, Lalle Hammarstedt-Nordenvall, Eivind Gottlieb-Vedi, Antti Mäkitie, Björn Palmgren Laryngoscope Investig Otolaryngol. 2023 Mar 6;8(2):441-449. doi: 10.1002/lio2.1034. eCollection 2023 Apr.

2. A descriptive study highlighting the differences in the treatment protocol for oral tongue cancer in Sweden and Finland.

Mäkitie A, Kamali A, Mroueh R, Lindford A, Koivunen P, Autio T, Lassus P, Halle M, Bäck L, Palmgren B, HammarstedtNordenvall L.Mäkitie A, et al. Acta Otolaryngol. 2020 Feb;140(2):188-194. doi: 10.1080/00016489.2019.1699663. Epub 2019 Dec 18.Acta Otolaryngol. 2020. PMID: 3185234 3. Current aspects of the quality of head and neck cancer care - survey of the Scandinavian Society for Head and Neck Oncology.

Ilmarinen T, Bratland Å, Tøndel H, Guðjónsson A, Gebre-Medhin M, Palmgren B, Mäenpää H, Bjørndal K, Grau Eriksen J.Acta Otolaryngol. 2024 May-Jun;144(5-6):404-408. doi: 10.1080/00016489.2024.2386097. Epub 2024 Aug 7.PMID: 39109489

Name: Anna Persson
Title: PhD, MEd., LSLS Cert.AVEd.
Email: anna.persson.3@ki.se

Project title (completed 2022-2024):

- Auditory, speech and language development in children born with sensorineural, bilateral moderate hearing loss
- Longitudinal follow-up of auditory, speech and language development in children born with sensorineural, bilateral moderate hearing loss
- Preschool screening after the newborn period

Supervision of PhD-student:

Andra Lazar	Main supervisor: ☐ Co-supervisor: ☒

Summary of finalized and current projects:

During 2022-2024 I have performed studies on the early hearing, speech and language development in children with sensorineural bilateral moderate hearing loss as well as a longitudinal follow-up study of the same target group. We found that hours of hearing aid use the first year after hearing aid fitting showed strong correlations that are significant to numbers of established consonants and expressive vocabulary. In the follow-up study, participating children showed large variation in hours of intervention during preschool years, which also correlated to speech and language outcomes at later ages. This motivates careful monitoring of children with moderate hearing loss the first three years in life, focusing on early consonant development, expressive vocabulary and to make sure the parents attend intervention that stimulates spoken language and full-time use of the hearing technology.

My other publication targeted the importance of preschool hearing screening after the newborn hearing screening, highlighting gaps in the current screening system and providing examples of improvements.

Current ongoing projects include: Mental health in teenagers and young adults who received cochlear implants before the age of 30 months; Children with bimodal hearing – do they need a second cochlear implant?; Validation of the LittlEARS Early Expressive Speech Questionnaire; Evaluation and validation of the National Registry for children with permanent hearing loss; Equity in hearing health care.

Ethic permit No (current projects):

2021-04345	2022-02763-01	2024-05243-02	2023-02694-01	2024-03405-01

Publications 2022, 2023, 2024:

Persson A, Marklund U, Lohmander A, Flynn T. Expressive vocabulary development in children with moderate hearing loss - the impact of auditory variables and early consonant production. Clin Linguist Phon. 2022 Jun 3;36(6):547-564. doi: 10.1080/02699206.2021.1944321.

Persson A, Flynn T, Miniscalco C, Lohmander A. Impact of auditory variables on consonant production in babbling and early speech in children with moderate hearing loss - a longitudinal study. Clin Linguist Phon. 2022 Oct 3;36(10):833-848. doi: 10.1080/02699206.2021.1958260.

Mackey AR, **Persson A**, Uhlén I. Pre-school hearing screening is necessary to detect childhood hearing loss after the newborn period: a study exploring risk factors, additional disabilities, and referral pathways. Int J Audiol. 2025 Jan;64(1):80-88. doi: 10.1080/14992027.2024.2368571. Epub 2024 Jun 24. PMID: 38913507.

Nyman A, Lieberman M, Snickars M, **Persson A**. Longitudinal follow-up of hearing, speech, and language skills in 6-year-old children with congenital moderate hearing loss. Int J Pediatr Otorhinolaryngol. 2024 Nov;186:112148. doi: 10.1016/j.ijporl.2024.112148.

Name: Jianhong Shi
Title: Guest Researcher
Email: Jianhong.shi@ki.se

Project title:
Digital twin strategy for personnalized trajectroy prediction and prevention of digestive tract tumors

Summery of project:
This research proposes an innovative digital twin framework to enable personalized prediction and prevention of digestive tract tumors (e.g., colorectal, liver, pancreatic cancers) by integrating multi-modal patient data with advanced computational modeling. Leveraging artificial intelligence, longitudinal clinical data, genomic profiles, lifestyle factors, and real-time biomarker monitoring, the project aims to construct dynamic digital replicas of individual patients' gastrointestinal systems. These patient-specific twins will simulate disease progression trajectories, identify high-risk molecular and physiological patterns, and predict tumor susceptibility with spatiotemporal precision. Machine learning algorithms will analyze the digital twins to recommend tailored prevention strategies, such as optimized screening schedules, precision chemoprevention, or microbiome modulation interventions. By bridging systems biology with clinical oncology, this strategy seeks to transform cancer care from reactive treatment to proactive, individualized prevention, ultimately reducing the global burden of digestive cancers through early interception of malignant trajectories.

Ethic permit No:

Publications 2022, 2023, 2024:

1. Zhang, R.[#], Cui, N.P.[#*], He, Y.[#], Wang, T., Feng, D., Wang, Y., Bao, T., Su, C., Qin, Y., **Shi, J.H.**[*], Li, J.H.[*]. (2024). Pirarubicin combined with TLR3 or TLR4 agonists enhances anti-tumor efffciency. ***Int Immunopharmacol*** 142, 113068.

2. Zheng, N.[#], Long, Y.[#], Bai, Z., Li, J., Wang, H., Song, D.D., Liu, H.L.[*], **Shi, J.H.**[*], Zhao, S[*]. (2024). Melatonin as an immunomodulatory in CD19-targeting CAR-T cell therapy: managing cytokine release syndrome. ***J Transl Med***, 2024, 22:58.

3. Pei, S.[#], Deng, X.[#], Yang, R.[#], Wang, H.[#], **Shi, J.H.**[#], Wang, X., Huang, J., Tian, Y., Wang, R., Zhang, S., Xu, J., Zhu, Q., Huang, H., Ye, J., Wang, C. Y., Lu, W., Luo, Q.[*], Ni, Z.Y.[*], Zheng, M.[*], Xiao, Y[*]. (2024). Age-related decline in CD8(+) tissue resident memory T cells compromises antitumor immunity. ***Nat Aging*** 4, 1828-1844.

4. **Shi, J.H.**[*], Liu, L.N., Song, D.D., Liu, W.W., Ling, C., Wu, F.X., Wang, T.T., Liu, B., Cui, N.P., Qin, Y.[*], Ni, Z.Y.[*]. (2023). TRAF3/STAT6 axis regulates macrophage polarization and tumor progression. ***Cell Death Differ*** 30, 2005-2016.

5. Wan, J.[#], Cheng, C.[#], Hu, J.[#], Huang, H., Han, Q., Jie, Z., Zou, Q.[*], **Shi, J.H.**[*], Yu, X*. (2023). De novo NAD+ synthesis contributes to CD8+ T cell metabolic fitness and antitumor function. ***Cell Rep*** 42, 113518.

6. **Shi, J.H.**[*], Ling, C., Wang, T.T., Zhang, L.N., Liu, W.W., Qin, Y., Tan, Y.H., Cui, N.P., Ni, Z.Y.[*]. (2022). TRK-fused gene (TFG) regulates ULK1 stability via TRAF3-mediated ubiquitination and protects macrophages from LPS-induced pyroptosis. ***Cell Death Dis*** 13, 93.

Name: Malin Siegbahn
Title: MD, PhD
Email: malin.siegbahn@ki.se

Project title:
Growing up with one ear: central auditory structure and function in unilateral ear canal atresia

Summery of project:
I defended my thesis entitled "Growing up with one ear: central auditory structure and function in unilateral ear canal atresia" in november, 2023. The thesis included studies on human participants with unilateral ear atresia, and a rat model with unilateral surgically created atresia. We studied the effects of unilateral severe conductive hearing loss on central auditory perception, as well as imaging of central auditory structures of the brain. Human participants had worse speech perception in a cocktail party setting and sound localization. We also observed a shift in asymmetry pattern of the grey matter thickness of the Heschl's gyrus, the primary auditory cortex of the brain in atresia. Rats with atresia had differences in the auditory white matter tracts of the brain.

I am also involved in a project on localization in unilateral deafness together with Filip Asp and Martin Eklöf, CLINTEC, that is ongoing.

Ethic permit No:

Dnr113/15	Dnr 191/4	Dnr 2012/3:9	Dnr 2017/4:3

Publications 2022, 2023, 2024:
2.Siegbahn M, Engmér Berglin C, Moreno R. Automated segmentation of the core of the acoustic radiation in humans. Front Neurolog. 2022 sept 23. doi: 10.3389/fneur.2022.934650

3. Siegbahn M, Jörgens D, Asp F, Hultcrantz M, Engmér Berglin C, Moreno R. Asymmetry in cortical thickness of the Heschl's gyrus in unilateral ear canal atresia. Otol. Neurotology. 2024 feb. 16. doi: 10.1097/MAO.0000000000004137

Name: Joar Sundman

Date for Dissertation: 2020-11-13

Project title:

Longterm Effectiveness of Tonsillectomy vs Modified Uvulopalatopharyngoplasty in Patients With Tonsillar Hypertrophy and Obstructive Sleep Apnea: Follow-up Study in The TEAMUP Randomized Clinical Trial

Conclusion of the project:

Objective: To investigate whether mUPPP is more effective in the long-term than TE alone in treating adult patients with tonsillar hypertrophy and moderate to severe OSA.

Summery of project:

Modified uvulopalatopharyngoplasty (mUPPP) is a surgical treatment for selected adults with obstructive sleep apnea (OSA). Tonsillectomy (TE) alone is a less extensive alternative treatment. A previous randomized clinical trial demonstrated that mUPPP was not more effective than TE alone in treating patients with tonsillar hypertrophy and moderate to severe OSA. However, there was a small difference in favor of TE. The long term effectiveness is not clear. The patients in the RCT are currently undergoing a 5 year follow-up to evaluate if there is a long-term difference between the methods.

Ethic permit No:

2015/755-31/2

Publications/manuscript 2022, 2023, 2024:

Effectiveness of Tonsillectomy vs Modified Uvulopalatopharyngyplasty in Patients With Tonsillar Hypertrophy and Obstructive Sleep Apnea - The TEAMUP Randomized Clinical Trial. Sundman, Nerfeldt, Fehrm, Bring, Browaldh, Friberg. JAMA ORL Oct 2022

Name: Bo Tideholm
Title: MD, PhD
Email: bo.tideholm@ki.se

Project title:
Hearing and speech with bilateral implants

Supervision of PhD-student:

Fatima Moumén Denanto	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
The research focus on language development in children who have undergone surgery with hearing implants, on the development of both language and other development in these subjects. There is new material, non-analyzed subgroups and other aspects to use to deepen the research field and knowledge.

The research will also elucidate binaural hearing and the language development in subjects operated with cochlear implants and bone anchored hearing aids. Language understanding and development, localization of sound is focus.

Ethic permit No:

2013/104-31/	2013/1127-31/2	2013/104-31/4

Publications 2022, 2023, 2024:
Differing Bilateral Benefits for Spatial Release From Masking and Sound Localization Accuracy Using Bone Conduction Devices. Denanto FM, Wales J, Tideholm B, Asp F. Ear Hear. 2022 Nov-Dec 01;43(6):1708-1720.

Plasminogen - safe for treatment of chronic tympanic membrane perforation: a phase 1 randomized, placebo-controlled study. Sepehri E, Tideholm B, Hellström S, Berglin CE. Acta Otolaryngol. 2024 Jul-Aug;144(7-8):439-445

Name: Tatjana Tomanovic
Title: Överläkare., MDPhD
Email: Tatjana.tomanovic@ki.se

Project title:

1. **Effect of Different Treatments on Symptoms of Meniere's Disease**
2. **The Effect of the Secretory Protein-Rich Product Salovum® on Symptoms in Meniere's Disease**

Supervision of PhD-student:

	Main supervisor: ☐ Co-supervisor: ☐

Summery of project:

Meniere's disease is a chronic, most often unilateral (affecting one ear) inner ear disorder characterized by recurring attacks where tinnitus or a feeling of fullness is accompanied by hearing loss and vertigo attacks lasting between ½ to 24 hours. The project evaluates different treatments for the course of the disease. Treatment protocols for Meniere's disease are continuously adjusted. An in-house study with intratympanic steroid injections has shown good effectiveness in controlling vertigo and has been recommended as a first measure in attempts to interrupt episodes of dizziness. In collaboration with "Lantmännen" a study is testing a higher dose of "food for medical use"- Salovum - to control various symptoms in the same patient group. Data collection has recently been completed, and data analysis has begun. Previously, another substance, Latanoprost, was tested with the same goal but showed no effect on any of the disease's symptoms. The disease is treated in many different ways with varying results. Another difficulty with the disease is that there are no diagnostic markers that can objectively lead to a definitive diagnosis. Since 2020, the Hearing and Balance Department in collaboration with the Neuroradiology Department has introduced a form of inner ear imaging that can confirm the presence of inner ear hydrops. Data is currently being collected from 130 patients who have been examined with all tests for inner ear function: such as caloric testing, VEMP, vHIT, audiogram, and MRI using a hydrops protocol to be able to verify more uniform subgroups. This could potentially lead to providing the patient with an early prognosis of the disease progression or individualized treatment.

Ethic permit No:

2021-06481-02	**2021-06789-02**			

Publications

2022

Surano S, Grip H, Öhberg F, Karlsson M, Faergemann E, Bjurman M, Davidsson H, Ledin T, Lindell E, Mathé J, Tjernström F, Tomanovic T, Granåsen G, Salzer J. Internet-based vestibular rehabilitation versus standard care after acute onset vertigo: a study protocol for a randomized controlled trial. Trials. 2022 Jun 16;23(1):496. doi: 10.1186/s13063-022-06460-0. PMID: 35710448; PMCID: PMC9205069.

2023

Tomanovic T. Intratympanic dexamethasone in Manières disease and symptom control. Acta Otolaryngol. 2023 Aug;143(8):681-686. doi: 10.1080/00016489.2023.2244003. Epub 2023 Sep 8. PMID: 37682583

Name: Inger Uhlén
Title: Associate professor, MD
Email: inger.uhlen@regionstockholm.se

Project title:

Pre/retrospective, genetic studies and habilitation of hearing loss in children

Supervision of PhD-student:

Andra Lazar	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

The goal is to better understand the etiopathology and evolution of sensorineural hearing loss (SHL) in children. It will help build up better interventional methods and habilitation models for children with SHL In Sweden children undergo a newborn hearing screening as well as childhood hearing tests to detect SHL for early intervention important for the development of normal speech and language. All children diagnosed are enrolled in our Hearing and habilitation centre for children and youth, registered in a database called Audiohab, where they are followed until adulthood by a multiprofessional team covering their medical, behavioral, psychological and social needs. All children in Stockholm are gathered in a single medical unit which gives us a unique opportunity to assess and follow-up hearing loss in childhood.

Ethic permit No:

Dnr 2020-07203				

Publications 2022, 2023, 2024:

1. Hoeve HLJ, Goedegebure A, Carr G, Davis A, Mackey AR, Bussé AML, **Uhlén IM**, Qirjazi B, Kik J, Simonsz HJ, Heijnsdijk EAM. Modelling the cost-effectiveness of a newborn hearing screening programme; usability and pitfalls International journal of audiology 2024 63:4 235-241

2. Mackey A, Maeki-Torkko E, **Uhlen I**. Revisiting the transient-evoked otoacoustic emissions passing criteria used for newborn hearing screening INTERNATIONAL JOURNAL OF AUDIOLOGY 2024 : 1-10

3. Kik J, Heijnsdijk EAM, Mackey AR, Carr G, Horwood AM, Fronius M, Carlton J, Griffiths HJ, **Uhlen IM**, Simonsz HJ, Consortium CCJPOTES. Availability of data for cost-effectiveness comparison of child vision and hearing screening programmes JOURNAL OF MEDICAL SCREENING 2023 30:2 62-68

4. Edvall NK, Mehraei G, Claeson M, Lazar A, Bulla J, Leineweber C, **Uhlén I**, Canlon B, Cederroth CR. Alterations in auditory brain stem response distinguish occasional and constant tinnitus The Journal of clinical investigation 2022 132:5

5. Flynn T, **Uhlén I**, Miniscalco C. Hearing aid use in 11-year-old children with mild bilateral hearing loss: Associations between parent and child ratings and datalogging International journal of pediatric otorhinolaryngology 2022 156: 111120-

6. Duan ML, Xie W, Persson L, Hellstrom S, **Uhlen I**. Postnatal hearing loss: a study of children who passed neonatal TEOAE hearing screening bilaterally ACTA OTO-LARYNGOLOGICA 2022 142:1 61-66

7. Mackey AR, Bussé AML, Del Vecchio V, Mäki-Torkko E, **Uhlén IM**. Protocol and programme factors associated with referral and loss to follow-up from newborn hearing screening: a systematic review BMC pediatrics 2022 22:1 473-

Name: Luca Verrecchia
Title: Docent
Email: luca.verrecchia@ki.se

Project title:
Enhancing testing and intervention for vestibular and balance disorders in the life span.

Supervision of PhD-student:

Susanne Gripenberg	Main supervisor: ☒ Co-supervisor: ☐
Zheer Tawfique	Main supervisor: ☒ Co-supervisor: ☐
Niki Karpeta	Main supervisor: ☐ Co-supervisor: ☒
Andra Lazar	Main supervisor: ☐ Co-supervisor: ☒
Torsten Buddee Roos	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
As research leader of SCAPA (scientific center for advanced pediatric audiology) at KI, I supervise 5 different projects dedicated to the enhancement of both diagnostics and intervention of vestibular and balance disorders in both children and adults.

In PEDVEST we apply newly developed child-friendly vestibular testing in pediatric population, focusing on specific cohorts, namely children with hearing loss and motor delays, in which the vestibular loss is particularly represented. The project started in 2019 and continues within Karpeta´s and Tawfique´s doctoral projects.

MOVEST is a project exploring the role of pediatric physiotherapy in pediatric vestibular loss. The project is included in Gripenberg´s doctoral project. The first ongoing study is about the diagnostic precision of motor testing in identifying vestibular loss in infants. A second planned study will test the feasibility of a vestibular motor intervention in infants affected by vestibular loss.

TAYACI is a multiprofessional investigation of the functional levels shown by children reaching teen- and adult age with cochlear implant. Gripenberg and Karpeta, within their doctoral projects, deal with the analysis of vestibular and motor functional aspects.

AUDIOHAB is Lazar´s doctoral project and is the analysis of the regional registry Audiohab for pediatric hearing habilitation in Stockholm. The pediatric hearing loss is investigated in its clinical, etiopathological and psychosocial aspects.

VESTVIB is a project in collaboration with Chalmers Signal Processing, Biomedical and Electrical Engineering research group and represents Tawfique´s doctoral project. It focuses on bone conducted (BC) stimulation for the enhancement of both audiological and vestibular diagnostics. Studies will explore the BC ankle audiometry, the BC ABR, the vibration induced nystagmus test and BC VEMP in children and adults.

I´m also co-supervisor of Buddee Roos´ doctoral project.

Ethic permit No:

2022-03448-02	2023-04525-02	2023-01523-02	2024-02246-02	2025-00695-01

Publications 2022, 2023, 2024:

1: Velikoselskii A, Papatziamos G, Smeds H, Verrecchia L. Wideband tympanometry in ears with superior canal dehiscence before and after surgical correction. Int J Audiol. 2022 Aug;61(8):692-697. doi: 10.1080/14992027.2021.1964041. Epub 2021 Aug 21. PMID: 34420430.

2: Verrecchia L, Edholm K, Pekkari M. Asymptomatic superior semicircular canal dehiscence. J Laryngol Otol. 2022 Jan;136(1):87-90. doi: 10.1017/S0022215121003273. Epub 2021 Oct 27. PMID: 34702381.

3: Verrecchia L, Fredén Jansson KJ, Westin M, Velikoselskii A, Reinfeldt S, Håkansson B. Ankle Audiometry: A Clinical Test for the Enhanced Hearing Sensitivity for Body Sounds in Superior Canal Dehiscence Syndrome. Audiol Neurootol. 2023;28(3):219-229. doi: 10.1159/000528407. Epub 2023 Jan 12. PMID: 36634643; PMCID: PMC10273915.

4: Bonnard Å, Karltorp E, Verrecchia L. Vestibular Loss in Children Affected by LVAS and IP2 Malformation and Operated with Cochlear Implant. Audiol Res. 2023 Feb 9;13(1):130-142. doi: 10.3390/audiolres13010013. PMID: 36825951; PMCID: PMC9952810.

5: Verrecchia L, Jansson KF, Reinfeldt S, Håkansson B. The Validation of a Simultaneous Ocular and Cervical VEMP Recording Protocol to Unilateral AC Stimuli. Otol Neurotol. 2023 Dec 1;44(10):e739-e746. doi: 10.1097/MAO.0000000000004026. Epub 2023 Oct 10. PMID: 37832576.

6: Karpeta N, Asp F, Edholm K, Bonnard Å, Wales J, Karltorp E, Duan M, Verrecchia L. Vestibular function in children with vestibulocochlear nerve aplasia/hypoplasia. Acta Otolaryngol. 2023 Oct;143(10):861-866. doi: 10.1080/00016489.2023.2285453. Epub 2024 Jan 5. PMID: 38063358.

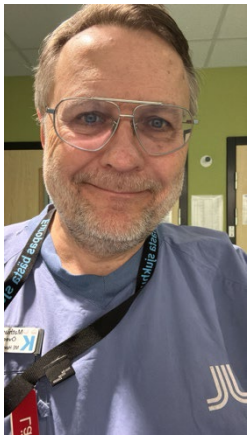
7: Fredén Jansson KJ, Håkansson B, Persson AC, Verrecchia L, Reinfeldt S. Electroacoustic evaluation of the bone conduction transducer B250 for vestibular and hearing diagnostics in comparison with Radioear B71 and B81. Int J Audiol. 2024 May 14:1-7. doi: 10.1080/14992027.2024.2352054. Epub ahead of print. Erratum in: Int J Audiol. 2025 Jan 31:1-2. doi: 10.1080/14992027.2025.2460330. PMID: 38742487.

8: Verrecchia L, Alm V, Thonberg H, Lenner F, Paivandy A, Feuk L, Lindstrand A, Nilsson D, Paucar M. Acute Vestibular Syndrome Unmasking an RFC1-Spectrum Disorder. Neurol Genet. 2025 Jan 16;11(1):e200238. doi: 10.1212/NXG.0000000000200238. PMID: 39839074; PMCID: PMC11748027.

9: Löfkvist U, Dahlby-Skoog M, Persson A, Asp F, Verrecchia L, Gripenberg S, Karpeta N, Eklöf M, Karltorp E. Teenagers and Young Adults with Cochlear Implants: A Multidisciplinary Follow-Up Study Approach and Baseline Characteristics. Audiol Res. 2025 Feb 12;15(1):16. doi: 10.3390/audiolres15010016. PMID: 39997160; PMCID: PMC11851589.

10: Ferri N, Whitney SL, Verrecchia L, Casagrande Conti L, Turolla A, Lelli T, Formisano R, Buzzi MG, Pillastrini P, Manzari L, Tramontano M. Video Head Impulse Test in Survivors From Severe Traumatic Brain Injury: New Perspectives for Implementation of Assessment in Rehabilitation. J Head Trauma Rehabil. 2025 Mar 5. doi: 10.1097/HTR.0000000000001044. Epub ahead of print. PMID: 40067959.

11: Casagrande Conti L, Ferri N, Manzari L, Lelli T, Mangeruga M, Dal Piaz M, Manzotti A, Verrecchia L, Tramontano M. Vestibulo-Oculomotor Reflex Dysfunction in Children with Cerebral Palsy Correlates with Gross Motor Function Classification System. Audiol Res. 2025 Feb 25;15(2):21. doi: 10.3390/audiolres15020021. PMID: 40126269; PMCID: PMC11932313.



Name: Mathias von Beckerath
Title: MD, PhD, Assoc Prof
Email: mathias.vonbeckerath@regionstockholm.se

Project title:
New methods in Head and Neck Surgery

Supervision of PhD-student:

Anahita Mobargha	Main supervisor: ☒ Co-supervisor: ☐
Anna Oldaeus	Main supervisor: ☐ Co-supervisor: ☒
Clara Svenberg Lind	Main supervisor: ☐ Co-supervisor: ☒
Secil Telli Erdogan	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
I am involved in the following projects as a supervisor:

* A singelblinded study of subglottic stenosis treated with dilataion and cortisone injections. With E Ntouniadakis

* Toungcancer, T1 and T2. With Anahita Mobargha

* Ultrasound assisted diagnostics and surgery in oral and oropharyngeal cancer. With Rigshospitalet, Copenhagen.

* Outcome and treatment of advanced cutaneus squamous cell carcinoma in the head and neck area.

* A prospective study of the realtionship between relapse and circulating HPV-virus after treatment of orofaryngeal HPV-positive cancer. With Anna Oldaeus

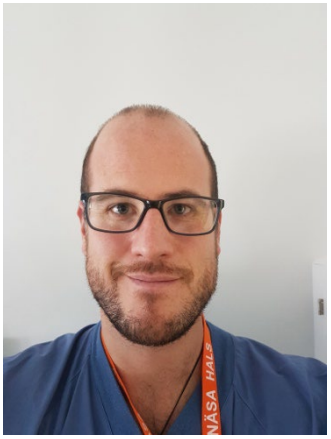
* Outcome after tracheostomies during the Covid-19 pandemic. With Clara Svenberg Lind.

Ethic permit No:

2015-548	2016-193	2016-275	2018-104	2019-03203

Publications 2022, 2023, 2024:

1. Hammarstedt Nordenvall L, Jortso E, von Beckerath M, Tani E, Nordemar S, Bark R. Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts. Acta Otolaryngol. 2022;142(1):100-5.
2. Nilsson O, Knutsson J, Landstrom FJ, Magnuson A, von Beckerath M. Ultrasound accurately assesses depth of invasion in T1-T2 oral tongue cancer. Laryngoscope Investig Otolaryngol. 2022;7(5):1448-55.
3. Nilsson O, Knutsson J, Landstrom FJ, Magnuson A, von Beckerath M. Ultrasound-assisted resection of oral tongue cancer. Acta Otolaryngol. 2022;142(9-12):743-8.
4. Ntouniadakis E, Sundh J, von Beckerath M. Monitoring Adult Subglottic Stenosis With Spirometry and Dyspnea Index: A Novel Approach. Otolaryngol Head Neck Surg. 2022;167(3):517-23.
5. Danielsson D, Hagel E, Dybeck-Udd S, Sjostrom M, Kjeller G, Bengtsson M, et al. Brachytherapy and osteoradionecrosis in patients with base of tongue cancer. Acta Otolaryngol. 2023;143(1):77-84.
6. Hammarstedt-Nordenvall L, Bark R, Elliot A, Von Beckerath M, Gahm C. Distribution of sentinel nodes from parotid tumors-A feasibility study. Cancer Med. 2023;12(19):19667-72.
7. Ntouniadakis E, Sundh J, Magnuson A, von Beckerath M. Balloon dilatation is superior to CO(2) laser excision in the treatment of subglottic stenosis. Eur Arch Otorhinolaryngol. 2023;280(7):3303-11.
8. Ntouniadakis E, Sundh J, Soderqvist J, von Beckerath M. How can we identify subglottic stenosis in patients with suspected obstructive disease? Eur Arch Otorhinolaryngol. 2023;280(11):4995-5001.
9. Almerén AO, Waenerlund M, Landström F, Beckerath M, Qvick A, Carlsson J, et al. 2024.
10. Nilsson O, von Beckerath M, Knutsson J, Landstrom FJ. Narrow band imaging in oral cancer did not improve visualisation of the tumour borders: a prospective cohort study. Acta Otolaryngol. 2024;144(11-12):652-6.
11. Nilsson O, von Beckerath M, Knutsson J, Magnuson A, Landstrom FJ, Bark R. Risk factors for local recurrence following marginal mandibulectomy in gingival cancer. Sci Rep. 2024;14(1):26347.



Name: Jeremy Wales
Title: Docent MD, PhD
Email: jeremy.wales@ki.se

Project title:

1. Temporal bone malformation.

2. Intraoperative assessment of the ossicular chain.

3. Bilateral bone conductive devices.

4. Late upper airway complications after trachesotomy during the COVID-19 pandemic

5. Cochlear implantation in otosclerosis

Supervision of PhD-student:

Clara Svenberg Lind	Main supervisor: ☒ Co-supervisor: ☐
Fatima Moumen Denanto	Main supervisor: ☐ Co-supervisor: ☒

Summary of project:

1. Temporal bone malformation.

Children with temporal bone malformations often present with a significant progressive hearing loss. Cochlea implantation is often needed to improve speech understanding and for the patient to develop the ability to communicate. We are assessing new methods in radiological diagnosis, implantation technique, hearing, implant programming and related neurological factors.

2. Intraoperative assessment of the ossicular chain.

Ossicular fixation in the middle ear is one cause of conductive hearing loss where there is no reliable objective system to assess this. We are developing a system (MIVIB)

utilising laser vibrometry to assess the movement of the ossicular chain to determine which operation and which prosthesis will give the best hearing result.

3. Bilateral bone conductive devices (BCD).

Bone-anchored hearing solutions are often implanted unilaterally. We are assessing whether patients have an imporved ability to localise sound and understand speech when background noise is present if they are provided with bilateral BCD.

4. Late upper airway complications after trachesotomy during the COVID-19 pandemic.

We have seen an increased incidence of late tracheal stenosis in patients that received a trachesotomy during the COVID-19 pandemic. We are assessing incidence, causative factors, screening and diagnostic methods for tracheal stenosis.

5. Cochlear implantation in otosclerosis

Cochlear implantation in far advanced otosclerosis is a rare indication for severe hearing loss. We will assess the hearing, speech and QOL results after implantation and those programming difficulties that occur. We will also utlise high definition Photon counting CT to assess the radiological indicators of facial nerve stimulation, a common side effect of this procedure.

Ethic permit No:

2020-02779	2022-05241-01	2022-04720-02		

Publications 2022, 2023, 2024:

Eklöf, M., Smeds, H., Karltorp, E., Wales, J. Progressive loss of sensitivity to electrical stimulation after cochlear implantation in X- linked incomplete partition type III deafness. Ear and Hearing 2024

Karpeta , N., Asp, F., Edholm, K., Bonnard, Å., Wales, J., Karltorp, E., Duam, M., Verrecchia, L. Vestibular function in children with vestibulocochlear nerve aplasia/hypoplasia. ACTA Otolaryngolgica 2024

Denanto, F.M., Wales, J., Tideholm, B., Asp, F. Differing bilateral benefits for spatial release from masking and sound localization accuracy using bone conduction devices. Ear and Hearing 2022

Wales, J., Smeds, H., Karltorp, E., Anderlid, B.M., Henricson, C., Asp, F., Anmyr, L., Lagerstedt-Robinson, K., Löfkvist, U. X-linked Malformation Deafness: Neurodevelopmental Symptoms Are Common in Children With IP3 Malformation and Mutation in POU3F4. Ear and hearing 2022;43(1):53-69

Name: Hui Wang
Title: PhD
Email: hui.wang@ki.se

Project title:
Lymphocytes differentiation and autoimmune diseases

Supervision of PhD-student:

Weixing Yan	Main supervisor: ☒ Co-supervisor: ☐
Li Du	Main supervisor: ☒ Co-supervisor: ☐

Summery of project:
My research aims to understand the molecular mechanisms of lymphocytes development and differentiation and their contribution to the pathogenesis of autoimmune diseases. We have mainly focused on T lymphocytes (J Clin Invest 2022 and Immunity 2024) and B lymphocytes (Front Immunol 2022; Cell Rep Med 2023). We have for the first time developed a Cre transgenic mouse model for tracing and targeting B1 lymphocyte (Front Immunol 2022). We are currently studying two mitotic kinases in regulating T and B cell differentiation and autoimmunity. We aims to repurpose the usage of the drugs inhibiting the mitotic kinases for treating autoimmune diseases.

Ethic permit No:

202211S011	201909A019			

Publications 2022, 2023, 2024:

1. Kou Y, Zhang S, Chen J, Shen Y, Zhang Z, Huang H, Ma Y, Xiang Y, Liao L, Zhou J, Cheng W, Zhou Y, Yang H, Liu Z, Wei Y, Wang H,Wang Y. *A mouse protozoan boosts antigen-specific mucosal IgA responses in a specific lipid metabolism- and signaling-dependent manner.* **Nat Commun**, 2024. 15(1):7914.
2. Ren J, Liu K, Hu L, Yang R, Liu Y, Wang S, Chen X, Zhao S, Jing L, Liu T, Hu B, Zhang X, Wang H,Li H. *An Efficient Probe-Based Quantitative PCR Assay Targeting Human-Specific DNA in*

ST6GALNAC3 for the Quantification of Human Cells in Preclinical Animal Models. **Mol Biotechnol**, 2024.

3. Schäfer S, Smelik M, Sysoev O, Zhao Y, Eklund D, Lilja S, Gustafsson M, Heyn H, Julia A, Kovács IA, Loscalzo J, Marsal S, Zhang H, Li X, Gawel D, Wang H,Benson M. *scDrugPrio: a framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases.* **Genome Medicine**, 2024. 16(1):42.
4. Zou X, Wang K, Deng Y, Guan P, Pu Q, Wang Y, Mou J, Du Y, Lou X, Wang S, Jiang N, Zhou S, Wang H, Du D, Liu X, Hu H,Zhang H. *Hypoxia-inducible factor 2alpha promotes pathogenic polarization of stem-like Th2 cells via modulation of phospholipid metabolism.* **Immunity**, 2024. 57(12):2808-2826 e8.
5. Gao S, Shi Y, Bai R, Li H, Ren J, Chen X, Hu L, Shi Z, Zhao S,Wang H. *Sputum basophils from allergic asthmatic patients do not express IL-7Rα that is essential for TSLP signalling.* **Scandinavian Journal of Immunology**, 2023. 97(1):e13236.
6. Lilja S, Li X, Smelik M, Lee EJ, Loscalzo J, Marthanda PB, Hu L, Magnusson M, Sysoev O, Zhang H, Zhao Y, Sjowall C, Gawel D, Wang H,Benson M. *Multi-organ single-cell analysis reveals an on/off switch system with potential for personalized treatment of immunological diseases.* **Cell Rep Med**, 2023. 4(3):100956.
7. Liu K, Hu L, Wang S, Chen X, Liu Y, Zhao S, Wang H, Li L,Li H. *An efficient qPCR assay for the quantification of human cells in preclinical animal models by targeting human specific DNA in the intron of BRCA1.* **Mol Biol Rep**, 2023. 50(11):9229-9237.
8. Xu M, Ren J, Jia W, Wang S, Liu Y, Chen X, Shi J,Wang H. *Regulation of B-1 cell numbers and B cell-mediated antibody production by Inpp4b.* **Scand J Immunol**, 2023:e13309.
9. Bai RX, Chen XZ, Ren JF, Hu L, Li H, Wang H,He C. *Toxoplasma gondii rhoptry protein (TgROP18) enhances the expression of pro-inflammatory factor in LPS/IFN-gamma-induced murine BV2 microglia cells via NF-kappaB signal pathway.* **Acta Trop**, 2022. 235:106650.
10. Chen X, Hu J, Wang Y, Lee Y, Zhao X, Lu H, Zhu G, Wang H, Jiang Y, Liu F, Chen Y, Kim BS, Zhou Q, Liu X, Wang X, Chang SH,Dong C. *The FoxO4/DKK3 axis represses IFN-gamma expression by Th1 cells and limits antimicrobial immunity.* **J Clin Invest**, 2022. 132(18).
11. He C, Gao S, Zhao X, Shi Y, Tang Y, Cao Y, Bai R, Ren J, Zhao S, Shi Z,Wang H. *An efficient and cost-effective method for the purification of human basophils.* **Cytometry Part A**, 2022. 101(2):150-158.
12. Li H, Tang Y, Ren J, Bai R, Hu L, Jia W, Cao Y, Hong L, Xu M, Gao S, Shi Y, Pan S, Wang L, Zheng K, Zhao S,Wang H. *Identification of novel B-1 transitional progenitors by B-1 lymphocyte fate-mapping transgenic mouse model Bhlhe41dTomato-Cre.* **Frontiers in Immunology**, 2022. 13.
13. Li X, Lee EJ, Lilja S, Loscalzo J, Schafer S, Smelik M, Strobl MR, Sysoev O, Wang H, Zhang H, Zhao Y, Gawel DR, Bohle B,Benson M. *A dynamic single cell-based framework for digital twins to prioritize disease genes and drug targets.* **Genome Med**, 2022. 14(1):48.

Name: Malin Wendt
Title: MD, PhD
Email: malin.a.wendt@regionstockholm.se

Project title:

Studies on laryngotracheal airway diseases

Summary of project:

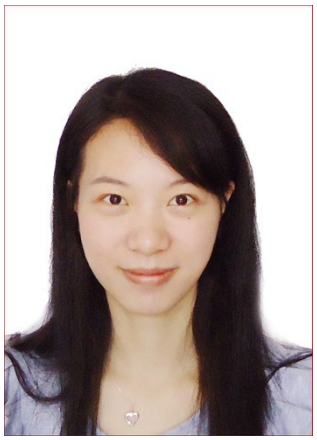
Long-term outcome of reconstructive airway surgery in pediatric and adult patients

- Pediatric tracheostomy - mortality, morbidity and long-term outcome
- Psychosomatic development and quality of life in pediatric patients with tracheostomy
- Supraglottoplasty for laryngomalacia in pediatric patients with comorbidities

Ethic permit No:

Publications 2022, 2023, 2024:

Medin G, Wendt M, Ekborn A, Andersson A, Gahm C. Supraglottoplasty for severe laryngomalacia can be effective and safe also in children with high-risk comorbidities - Experience from a tertiary center. Int J Ped Otorhinolaryngol. 2023 Aug:117:111632



Name: Yelin Zhao
Title: Postdoc Researcher
Email: yelin.zhao@ki.se

Project title:
Multi-Scale Modeling of Disease Trajectories to Identify Biomarkers for Cancer Prediction and Prevention

Summery of project:
Cancer remains one of the leading causes of death worldwide. Importantly, it does not arise suddenly, but rather evolves through a series of pathological events. By uncovering how these events form disease trajectories that culminate in cancer, we may enable earlier intervention and even prevention.

This project aims to develop and implement integrative strategies to identify disease trajectories by leveraging multiple layers of biological and clinical data. We begin at the population level by constructing a disease trajectory network based on clinical diagnoses from over 210 million individuals in the United States. While this large-scale view offers valuable insights, it is not sufficient on its own due to the complex and heterogeneous nature of cancer.

To address this limitation, we narrow our focus to specific disease trajectories using bulk RNA sequencing data, enabling investigation of how these diseases are linked at the molecular level. Since molecular alterations often arise through interactions among diverse cell types, we further refine our analysis by examining single-cell transcriptomic data from one representative disease trajectory. At this resolution, we explore how cell-type-specific gene expression changes and cellular communication networks contribute to cancer development.

This high-resolution view of molecular perturbations along disease trajectories holds promise for identifying biomarkers that can predict cancer onset and inform preventive strategies. To evaluate their predictive value, candidate biomarkers will be validated using plasma proteomics data from over 50,000 individuals.

Ethic permit No:

6798/18	202012A162	M75-08/2008		

Publications 2022, 2023, 2024:

1. **Zhao, Y**., Li, X., Loscalzo, J. et al. Transcript and protein signatures derived from shared molecular interactions across cancers are associated with mortality. J Transl Med 22, 444 (2024).

2. Smelik, M.*, **Zhao, Y.***, Li, X. et al. An interactive atlas of genomic, proteomic, and metabolomic biomarkers promotes the potential of proteins to predict complex diseases. Sci Rep 14, 12710 (2024).

3. Smelik, M., **Zhao, Y.**, Mansour Aly, D. et al. Multiomics biomarkers were not superior to clinical variables for pan-cancer screening. Commun Med 4, 234 (2024).

4. Schäfer, S., Smelik, M., Sysoev, O., **Zhao, Y.**, et al. scDrugPrio: a framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases. Genome Med 16, 42 (2024).

5. Lilja S, Li X, Smelik M, Lee EJ, Loscalzo J, Marthanda PB, Hu L, Magnusson M, Sysoev O, Zhang H, **Zhao Y**, Sjöwall C, Gawel D, Wang H, Benson M. Multi-organ single-cell analysis reveals an on/off switch system with potential for personalized treatment of immunological diseases. Cell Rep Med. 2023 Mar 21;4(3):100956

6. Li, X., E. J. Lee, S. Lilja, J. Loscalzo, S. Schäfer, M. Smelik, M. R. Strobl, O. Sysoev, H. Wang, H. Zhang, **Y. Zhao**, D. R. Gawel, B. Bohle and M. Benson. A dynamic single cell-based framework for digital twins to prioritize disease genes and drug targets. Genome Medicine. 2022 14(1): 48.

Research fellows

At the Division of Ear, Nose and Throat Diseases

Name: Sigurdur Arnason
Main supervisor: Barbro Hedin Skogman
Supervisor: Åsa Laestadius, Elin Marsk, Malou Hultcrantz
Registered (date): 2019-09-27
Half time control (date): 2022-12-02
Date for Dissertation: 2025-11-28

Project title:
Facial nerve palsy in children; treatment and clinical outcome.

Conclusion of the project:
Facial palsy in children is a common and worldwide occurrence and the role of cortisone for children has been a matter of discussion for decades. Our randomized placebo-controlled trial aims to answer the long-standing question of the role of cortisone for children with acute peripheral facial palsy. We report the incidence and etiology of facial palsy in children in the Stockholm area and look into different methods of evaluation the children affected with facial palsy.

Summery of project:
I. Peripheral facial nerve palsy in children in a Borrelia high endemic area: epidemiology and evaluation of clinical recovery. A retrospective follow-up. To identify the incidence, etiology and prognosis of acute peripheral facial nerve palsy (FNP) in children in the Stockholm area. A retrospective study identifying children from 0-17 years of age visiting a pediatric emergency department for acute FNP during a one-year period from 2014-2015 (77 patients).

II. Efficacy of cortisone vs. placebo in children with idiopathic facial nerve palsy and Lyme neuroborreliosis facial nerve palsy. Participation in the FACE study (Facial nerve palsy And Cortisone Evaluation in children), a multicenter randomized placebo-controlled study on the efficacy of cortisone treatment in children with acute facial nerve palsy. For inclusion the cause of FNP will be either Lyme neuroborreliosis (LNB) or idiopathic facial palsy. Children with LNB will be treated with antibiotics according to present guidelines in combination with the treatment provided in the study (cortisone vs. placebo). Follow-up will take place via telephone and with follow-up visits at 1 and

12 months. Subjects will be graded according to the House-Brackmann and the Sunnybrook facial grading scales and specific standardized facial palsy questionnaires.

III. Long term outcome and neurophysiologic findings in idiopathic facial nerve palsy in a pediatric population. This study will aim to highlight the long-term prognosis of 50 children affected by idiopathic facial nerve palsy. The aim is to follow-up the children with idiopathic facial palsy and record subjective, objective and neurophysiological findings.

IV. Detection of brain damage markers S-100B and NSE in serum in children with Lyme neuroborreliosis for evaluation as prognostic marker for clinical outcome. The brain damage markers S-100 B and NSE (Neuron-specific enolase) will be analyzed in serum in children with LNB and in a non-neuroinflammatory group

Ethic permit No:

2016/1937-31/4	2017/554	2010/106	2021-01926	2022-03295-02

Publications/manuscript 2022, 2023, 2024:

1. Arnason S, Skogman BH. Effectiveness of antibiotic treatment in children with Lyme neuroborreliosis - a retrospective study. BMC Pediatr. 2022 Jun 9;22(1):332.

2. Arnason S, Molewijk K, Henningsson AJ, Tjernbeg I, Skogman BH. Brain damage markers neuron-specific enolase (NSE) and S100B in serum in children with Lyme neuroborreliosis – detection and evaluation as prognostic biomarkers for clinical outcome. Eur J Clin Microbiol Infect Dis. 2022 Jul;41(7):1051-1057

Name: Rasmus Blomkvist
Title: PhD
Email: rasmus.blomkvist@ki.se

Project title:
Predictive markers for laryngeal cancer

Supervision of PhD-student:

Linda Marklund	Main supervisor: ☒ Co-supervisor: ☐
Björn Palmgren	Main supervisor: ☐ Co-supervisor: ☒
Lalle Hammarstedt Nordenvall	Main supervisor: ☐ Co-supervisor: ☒
Antti Mäkitie	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:
Cancer of the vocal cords, laryngeal cancer, is one of the most common tumor types in the head and neck region with approximately 180 new cases each year in Sweden. Whereas the survival rate for small tumors (T1) is relatively good, more advanced disease (T2-T4) is associated with poor outcome and has not improved significantly in recent decades. In Sweden and in Stockholm according to national guidelines, patients with T2 and T3 laryngeal cancer are treated with radiotherapy (RT) or chemoradiotherapy (CRT) to preserve the patient's larynx, while patients with T4-tumors are treated surgically with laryngectomy, i.e. resection of the entire larynx and upper trachea often in combination with adjuvant RT/CRT. Our own data and other studies show that there is poorer survival for patients with T3 compared with T4 laryngeal cancer. It is clear that many patients with tumors classified as T3 are undertreated. The question is how to identify which laryngeal tumors that are in need of extended treatment to avoid recurrence and death from laryngeal cancer.

All our sub-studies in this research project aim to identify clinically useful markers and methods that can help us to optimize the choice of treatment strategy for patients with advanced laryngeal cancer.

Ethic permit No:

2019-04829	2021-06907-02	2024-07341-02

Publications 2022, 2023, 2024:

Blomkvist, R, Marklund, L, Hammarstedt-Nordenvall, L, Gottlieb-Vedi, E, Mäkitie, A, Palmgren, B. Treatment and outcome among patients with laryngeal squamous cell carcinoma in Stockholm—A population-based study. Laryngoscope Investigative Otolaryngology. 2023; 1- 9.

Name: Torsten Buddee Roos
Main supervisor: Julia Arebro
Supervisor: Åsa Bonnard, Luca Verecchia, Anna Granath

Registered (date): 25-03-25

Project title:
Acute labyrinthitis – risk factors and outcome predictors

Summery of project:
AOM is defined as an infection of the middle ear, and it can be viral, bacterial or both. In rare cases, the infection can spread to the inner ear causing an acute labyrinthitis. The incidence of labyrinthitis due to AOM is highly unknown as well as potential risk factors. Bacteriological as well as radiological findings are scarcely described in previous literature. The impact of the COVID-19 pandemic along with the social distancing it implied gives us a unique chance to study the effects of a pandemic on other infectious diseases.

The overall aim of this project is to improve the knowledge, understanding and management of complications due to acute otitis media in adults and children. Moreover, we wish to

- Describe the incidence of AOM with labyrinthitis in the Stockholm County during 2020-2024. Determine what impact the COVID-19 pandemic had on this incidence. Describe cases with modiolus erosion.
- Epidemiologically map the incidence of AOM with labyrinthitis in Sweden during 2016-2024. Determine what impact the COVID-19 pandemic had on this incidence.
- Prospectively study patients with AOM with labyrinthitis in the Stockholm County during 2024-2028 including the radiological findings.
- Evaluate the effect of acute mastoidectomy on clinical outcomes (e.g., hearing) for patients with AOM and labyrinthitis. Moreover, map whether these patients have a deranged immunological pattern in their mucosa, making them susceptible to this complication.

Ethic permit No:

2024-04249-01	2022-06851-01	2025-00795-02

Publications/manuscript 2022, 2023, 2024:

Name: Malin Dahlby Skoog
Main supervisor: Ulrika Löfkvist
Supervisor: Eva Karltorp, Björn Lyxell, Tamara Kalandadze

Registered (date): 21-09-06
Half time control (date): 23-12-08

Project title:
Long-term effects of early cochlear implantation on metaphor comprehension and executive functions in Swedish adolescents and young adults

Conclusion of the project:
Our results indicate that early implanted adolscents and young adults have a metaphor comprehension similar to peers with typical hearing, and that earlier age at 1st CI is associated with better metaphor comprehension.

Summery of project (max 2 000)**:**
This study is part of the TAYACI (Teenagers and young adults with cochlear implants) project. Early age at cochlear implantation (CI) in congenitally deaf children has positive effects on early spoken language by reducing the period of auditory deprivation. However, the research regarding long term effects of cochlear implantation on higher linguistic and cognitive skills is scarce.

The aim of this project is to investigate long term effects of early cochlear implantation on the development of executive functions and metaphor comprehension. The cohort consists of 44 individuals between 12 and 22 years old, fitted with CI before 30 months of age at the Hearing Implantation Center at Karolinska university hospital. There is also a control group with 27 typically hearing indviduals.

Since there is no standardized test targeting metaphor comprehension in Swedish, a multiple-choice task was created för this study (that can be found here https://doi.org/10.6084/m9.figshare.26029144.v1). Linguistic skills (vocabulary and reading) were assessed with standardized tests. Executive functions were assessed by task performance (reading span, non word repetition and trail making test) as well as by the BRIEF questionnaire.

The next step is to analyze the executive function skills of the cohort, then further investigating the role of executive function and vocabulary organization in metaphor comprehension as well as a qualitiative analysis of responses on the metaphor task.

Ethic permit No:

2021-04345

Publications/manuscript 2022, 2023, 2024:

Dahlby-Skoog, M., Kalandadze, T., Karltorp, E., Lyxell, B., & Löfkvist, U. (2025). Hearing Early Opens More Doors: Long-Term Effects of Age at Implantation on Metaphor Comprehension in Adolescents and Young Adults with Cochlear Implants. *Journal of speech, language, and hearing research: JSLHR*, *68*(3), 1105–1125. https://doi-org.proxy.kib.ki.se/10.1044/2024_JSLHR-24-00480

Löfkvist, U., Dahlby-Skoog, M., Persson, A., Asp, F., Verrecchia, L., Gripenberg, S., Karpeta, N., Eklöf, M., & Karltorp, E. (2025). Teenagers and Young Adults with Cochlear Implants: A Multidisciplinary Follow-Up Study Approach and Baseline Characteristics. *Audiology research*, *15*(1), 16. https://doi-org.proxy.kib.ki.se/10.3390/audiolres15010016

Name: Björn Eriksson
Main supervisor: Caroline Gahm
Supervisor: Martin Halle, Lalle Hammarstedt, Liv Eidsmo

Registered (date): 180129
Half time control (date): 221209
Date for Dissertation: VT26

Project title:
Inflammatory changes of soft tissue after radiotherapy

Conclusion of the project:
Epidemiologic data from our cohort indicate an elevated risk of infection and fistula formation in previously irradiated patients undergoing free tissue transfer.

Plasminogen Activator Inhibitor-1 is elevated in the arteries and veins of previously irradiated patients undergoing free tissue transfer.

Summary of project:
Reconstruction with free tissue transfer is a well established treatment modality for patients with advanced head and neck cancer. A majority of these patients also receive pre- or postoperative radiotherapy. Radiation-induced injury to surrounding healthy tissue is an important limitation of radiotherapy. Epidemiologic studies have shown an increased risk for cardiovascular events, e.g. stroke and myocardial infarction, in patients that have been irradiated. Biopsies from arteries and veins in this patient group have demonstrated acute and chronic inflammatory changes, believed to contribute to post-treatment complications and a decreased quality of life. Preoperative radiotherapy affects tissue healing properties and increased the risk of postoperative infections and fistulas in our material. Through investigations with immunohistochemistry and gene expression analysis of irradiated and non-irradiated skin biopsies from patients as well as from a murine model, we aim to contribute to the understanding of post-therapeutic inflammation and tissue fibrosis in skin after radiotherapy.

Ethic permit No:

2006/834-31	2012/1663-32	2016/1578-32	2008-484-31/2	2008/114-31

Publications/manuscript 2022, 2023, 2024:

Eriksson, B.O, Gahm C., Halle, M; Long-term presence of macrophages in irradiated skin in head and neck cancer patients, with comparisons to a murine model (partial manuscript, 2024-2025)

Name: Ola Fridman Bengtsson
Main supervisor: Pär Stjärne
Supervisor: Ola Sunnergren, Anna-Lena Hulting, Charlotte Höybye

Registered (date): 111222
Half time control (date): 210122
Date for Dissertation:

Project title:

Pituitary tumors; clinical aspects of treatment and expression of Galanin,- and pattern recognition receptors

Conclusion of the project:

The aims of this thesis were initially to evaluate treatment strategies regarding pituitary adenomas in Karolinska University Hospital regarding treatment outcomes, complications and overall survival. The results of this study has been published, as well as evaluation of different approaches in perioperative cortisone treatment in patients undergoing pituitary surgery in Karolinska University Hospital.

The other half of the thesis aimed to evaluate receptor expression in pituitary adenomas and compare these to normal pituitary tissue, where the latter was collected from organ donors adjacent to harvest of organs for transplantation. The latter has proven to be difficult to perform and only 12 samples have been collected, why we decided to include samples from healthy pituitary tissue that were available from other projects. Our aim has also been to compare these samples from the aspect of inflammatory markers, to see if we could detect any differences between adenomas and healthy pituitary tissue.

Summery of project:
The laboratory part of this thesis has proven to be difficult to accomplish, due to different circumstances. We therefore have decided to investigate if we can change the project plan for the thesis and include two studies concerning measurements and evaluation of nasal airflow instead. This process will proceed during 2025.

Ethic permit No:

2012/1689-31/4 (2019-01941	2012/891-31/2			

Publications/manuscript 2022, 2023, 2024:

None

Name: Evelina Gille
Main supervisor: Lalle Hammarstedt Nordenvall
Supervisor: Antti Mäkitie, Elin Marsk

Registered (date): 2020-05-25
Half time control (date): 23-05-17
Date for Dissertation: Maj 2026

Project title:
Studies on Nasopharyngeal Cancer – a characterization of a rare disease

Summery of project:
I: To describe the pattern of recurrence in patients treated for nasopharyngeal cancer in Stockholm. Hypothesis: Local recurrences occur outside target volume. Retrospective single institution study. Data from medical records and target volume, will be correlated to recurrence and place of recurrence, ie outside or inside target volume. Pattern of failure will teach us more on how to design treatment models in this disease. If recurrences occur outside treatment volume that might be an indication to improve treatment planning. Also to describe the distribution of different histopathological subgroups to assess the viral correlation.

II: A register-based cohort study of Nasopharyngeal Carcinoma in Sweden, using SweHNCR: outcome, failure rate and site of failure Hyphothesis: Local regional failure is more common than distant failure Data from Swedish Head and Neck Cancer Registry (SweHNCR). All patients in Sweden diagnosed with Nasopharyngeal carcinoma, histology codes for Squamous cell carcinoma, Lymfoepithelioma or undiffe rentiated carcinoma will be included. This study will describe the pattern of failure in Sweden and thus indirectly characterize the disease as resembling either the endemic type or the non-endemic type.

III: To explore the risk of NPC among migrants and their children in Sweden. The possible improvement in outcome over time is to be compared with outcome of non-migrants. Hypothesis: Several studies indicates that there is a strong familial risk of NPC.

IV: To dentify occupations and work-related exposure agents linked to NPC in the Nordic countries. The study is based on a large cohort of almost 15 million persons from the Nordic countries diagnosed with NPC in 1961-2005. The study suggests that NPC may be associated with exposure agents that are work-related such as smoking, kitchen air pollution and solvents.

Ethic permit No:

2019-01933

Publications/manuscript 2022, 2023, 2024:

Carpén T, Gille E, Hammarstedt-Nordenvall L, Hansen J, Heikkinen S, Lynge E, et al. Occupational risk variation of nasopharyngeal cancer in the Nordic countries. BMC cancer. 2022;22(1):1130.

Manuscript 2025:

The Burden and Outcome of Nasopharyngeal Carcinoma in Sweden

Name: Susanne Gripenberg
Main supervisor: Luca Verrecchia
Supervisor: Cecilia Lidbeck, Sten Hellström
Registered (date): 2022-08-24

Project title:
Vestibular function and motor functioning in children with hearing loss, balance disorders and motor delays, included in research projects: TAYACI and MOVEST.

Conclusion of the project:
My project aims to explore how vestibular loss affects motor functioning in children and teenagers with hearing loss and also to evaluate the feasibility of an early intervention designed for infants and children with motor delay related to vestibular loss.

Summery of project:
TAYACI is an interprofessional project aiming to ascertain the functional level of TeenAgers and Young Adults, CI recipients since infancy. In the first TAYACI study, we explore how motor functioning relates to vestibular function in a group of teenagers and young adults who received CI in early childhood. The participants are assessed for vestibular function by a MD and a parallel blinded assessment of motor function using motor tests, is conducted by a physiotherapist. Self-reported physical activity and experience of balance are measured with questionnaires. In the second study, we collect data from children in the first study, with inertial sensors applied on different body parts. We analyze with the help of machine learning. The principal question is whether a computerized system based on inertial sensors may implement the clinical evaluation of motor patterns in children with or without vestibular impairment in comparison with age-matched peers. Data analysis is ongoing.

MOVEST is a project aiming to investigate the role of pediatric physiotherapy in children with vestibular loss. In the first MOVEST study, we assess if clinical motor assessments can detect vestibular impairment in infants with hearing loss or motor delay. The infants are tested with age-appropriate test batteries and scores of motor function will be analyzed concerning vestibular function. Data collection is ongoing. The second study will be a feasibility study, where we will design and evaluate a vestibular rehab

intervention aimed to enhance motor functioning in children with vestibular impairment and motor delay. This study is under planning.

Ethic permit No:

2021-04345	2021-00165	2021-04345	2022-00863-02	2025-00695-01

Publications/manuscript 2022, 2023, 2024:

“A manageable and challenging fall prevention intervention with impact on society” - Older women's perspectives on participation in the Stay Balanced training programme.
C Halén*, S Gripenberg*, K Skavberg-Roaldsen, A Ståhle, A Halvarsson.
doi.org/10.1080/09593985.2021.1972498

Teenagers and Young Adults with Cochlear Implants: A Multidisciplinary Follow-Up Study Approach and Baseline Characteristics.
Ulrika Löfkvist, Malin Dahlby-Skoog, Anna Persson, Filip Asp, Luca Verrecchia, Susanne Gripenberg, Niki Karpeta , Martin Eklöf and Eva Karltorp.
doi.org/10.3390/audiolres15010016

Name: Sofie Henecke
Main supervisor: Johan Lundström
Supervisor: Ylva Tiblom Ehrsson
Evelina Thunell
Registered (date): 2022-11-14

Project title:
Quality of life in patients with sensory dysfunctions

Experiencing a good quality of life is the end goal of most clinical treatments. Yet relatively little is known how individuals with sensory dysfunctions experience their life quality. This project aim to explore this issue from multiple angles. The project will assess; 1) how the quality of life is for individuals with olfactory dysfunction compared with patients with similar dysfunction but for the sense of hearing and whether similarities or differences exist between quantitative or qualitative dysfunctions; 2) determine clinical or demographical parameters differentiating sub-groups with increased quality of life; 3) longitudinally, how quality of life change over time for patients with a qualitative smell dysfunction (parosmia and/or hyposmia); and 4) how different treatment regimes, online or in person, affect patient's quality of life and treatment satisfaction.

Ethic permit No:

2023-02619-01	2024-05264-02

Publications/manuscript 2022, 2023, 2024:

Winter, A. L., Henecke, S., Lundström, J. N., & Thunell, E. (2023). Impairment of quality of life due to COVID-19-induced long-term olfactory dysfunction. Frontiers in psychology, 14, 1165911. https://doi.org/10.3389/fpsyg.2023.1165911 Lundkvist

Winter, A.L., Henecke, S., Thunell, E., Swartz, M., Martinsen, J., Johansson, P., & Lundstrom, Johan. (2024). Olfactory training using nasal inserts more effective due to increased adherence. 10.1101/2024.06.26.24309521

Name: Sofia Hultman Dennison
Title: MD, PhD
Email: sofia.hultman-dennison@regionstockholm.se

Project title:
Complications to acute rhinosinusitis in children.
Pneumococcal vaccine.

Summery of project:
PhD june 2021: Complications to acute rhinosinusitis in children. 2024: Co-author of article regarding pneumococcal vaccine.

Publications 2022, 2023, 2024:
”The pneumococcal conjugate vaccine had a sustained effect on Swedish children 8 years after its introduction”. Acta Paediatr. 2024 Jan 12. doi: 10.1111/apa.17108. Online ahead of print.PMID: 38217260

“Complications to acute bacterial rhinosinusitis in children - a prospective study; bacterial cultures, virus detection, allergy sensitization and immunoglobulins”. Rhinology. 2023 Oct 1;61(5):412-420. doi: 10.4193/Rhin22.168. PMID: 37338824

Name: Maryam Jafari
Main supervisor: Lars Olaf Cardell
Supervisor: Susanna Kumlien Georén, Eric Hjalmarsson, Laila Hellkvist

Registered (date): 2022-09-29
Half time control (date): 2024-10-18
Date for Dissertation: 2025-11-21

Project title:

Exploring Subcutaneous Vaccination, Immunoglobulin Modulation, and Glycosylation in Allergic Rhinitis, and the Immunological Mechanisms Underlying Chronic Rhinosinusitis with Nasal Polyps

Conclusion of the project:
Overall, this thesis advances our understanding of the complex immune mechanisms underlying AR and CRSwNP by revealing key alterations in both innate and adaptive immune responses. The findings emphasize the importance of neutrophil function, B cell-mediated antibody regulation, and post-translational modifications in shaping allergic inflammation and immune tolerance. These insights provide a foundation for developing improved, targeted therapeutic strategies for chronic upper airway diseases.

Summery of project (max 2 000)**:**
This doctoral thesis explores immune dysregulation in allergic rhinitis (AR) and chronic rhinosinusitis with nasal polyps (CRSwNP), focusing on type 2 inflammation and its clinical consequences. It investigates neutrophil dysfunction in CRSwNP and highlights the roles of B cell responses, immunoglobulin class switching, and mucosal tolerance following subcutaneous immunotherapy (SCIT) in AR. Additionally, the thesis examines the impact of protein glycosylation, particularly O-GlcNAcylation, on T cell function, offering new insights into immune regulation and potential therapeutic targets in respiratory allergies.

Ethic permit No:

021-03633	2021-00325	2021-06514-02

Publications/manuscript 2022, 2023, 2024:
CLINICAL AND TRANSLATIONAL ALLERGY. 2024;14(3):e12347
Delayed neutrophil shedding of CD62L in patients with chronic rhinosinusitis with nasal polyps and asthma: Implications for Staphylococcus aureus colonization and corticosteroid treatment
Jafari M; Cardenas EI; Ekstedt S; Arebro J; Petro M; Karlsson A; Hjalmarsson E; Arnarson D; Ezerskyte M; Kumlien Georen S; Cardell LO

Name: Marcus Jansson
Main supervisor: Caroline Gahm
Supervisor: R. Bark, A. Elliot

Registered (date): 241204
Half time control (date): 2027
Date for Dissertation: 2029

Project title:
Studies on precision medicine in salivary gland cancer – regional lymph node management with sentinel node analyses

Summery of project:

Salivary gland cancer affects approximately 100 patients per year in Sweden. The disease can arise in the major salivary glands or in minor salivary glands located in the oral cavity and pharynx. Aggressive tumor types are associated with low survival rates if treated incorrectly. There is currently no consensus regarding the recommended surgical treatment for aggressive tissue types without suspected lymph node metastases. Some centers advocate prophylactic radical neck dissection, while others favor active surveillance. The former carries the risk of overtreatment and increased morbidity, while the latter may result in undertreatment and increased mortality.

The literature on whether sentinel node (SN) technique can be used as a precision diagnostic method in salivary gland cancer is sparse. Our group published a prospective study in 2023 on patients with tumors in the parotid gland, demonstrating the usefulness of the SN technique. We have now initiated further validation studies on SN diagnostics for tumors in all salivary glands. The aim is to evaluate the impact of the SN technique on staging and treatment decisions compared to current preoperative lymph node diagnostics (radiological examination with computed tomography and/or magnetic resonance imaging). The technique could potentially provide higher precision in staging, thereby improving conditions for individualized surgical treatment while reducing the risk of under- and overtreatment.

Research questions:

1. Metastatic pattern of malignant tumors in the parotid gland – in what proportion of patients were metastases detected in region 1 versus region 5?
2. In what proportion of patients with malignant salivary gland tumors but radiologically normal cervical lymph nodes were occult metastases detected in SN? How many had bilateral metastases?
3. In what proportion of salivary gland cancer patients did SN diagnostics affect pre-therapeutic TNM classification and treatment decisions in recommended cancer treatment (according to the national cancer care guidelines for head and neck cancer) compared to if SN technique had not been used?
4. In what proportion were occult metastases detected in SNs outside those lymph node stations planned for removal during neck dissection in N+ disease, if SN-assisted dissection had not been performed (specificity – so-called false-negative sentinel node)?
5. Did recurrence rates and/or disease-free survival differ in patients where SN technique was used as guidance in neck dissection?

Ethic permit No:

2019-0521	2022-05287-02	2024-06940-02

Publications/manuscript 2022, 2023, 2024:

-

Name: Gabriel Johansson
Title: ST-läkare
Email: gabriel.johansson@regionstockholm.se

Project title:
The impact of isolated tumour cells and micrometastasis on prognosis in oral squamous cell carcinoma patients.

Supervision of PhD-student:

Rusana Bark	Main supervisor: ☒ Co-supervisor: ☐
Krzysztof Piersiala	Main supervisor: ☐ Co-supervisor: ☒
Linda Marklund	Main supervisor: ☐ Co-supervisor: ☒

Summary of project:

Oral squamous cell carcinoma (OSCC) is an aggressive malignancy with significant morbidity and mortality rates. The presence of lymph node metastasis is a critical factor influencing prognosis, guiding treatment decisions, and determining follow-up protocols. However, the role of isolated tumor cells (ITC) and micrometastasis (Mi) in lymph nodes remains inadequately understood in OSCC, despite evidence suggesting that Mi may negatively impact survival in other cancers, including breast and colorectal cancers.

Despite substantial research, there is no consensus on the prognostic impact of ITCs and Mi in OSCC. While some studies suggest that the presence of ITCs or Mi may be associated with worse survival outcomes, others find no statistically significant impact, leading to inconclusive results across the literature. This lack of uniformity in findings can be attributed to differences in histological assessment techniques, sample sizes, and inclusion criteria, as well as variation in how ITCs and Mi are classified and reported across studies.

In light of these contradictory findings, it is crucial to reassess the clinical implications of ITCs and Mi in OSCC. Understanding their prognostic relevance may refine staging

systems and treatment protocols, potentially leading to more tailored approaches to patient management. This study aims to address these gaps by analyzing a comprehensive dataset of OSCC cases at Karolinska University Hospital, providing insight into the impact of ITCs and Mi on patient outcomes and contributing to the development of standardized guidelines for their assessment in OSCC.

Ethic permit No:

2019-03518	2021-01265			

Publications 2022, 2023, 2024:

-

Name: Hanna Josefsson Dahlgren
Main supervisor: Cecilia Engmér Berglin
Supervisor: Filip Asp

Registered (date): 20170407
Half time control (date): 20220902

Project title:
Bone Conduction Devices and Active Middle Ear Implants in Children with Unilateral Aural Atresia- Functional and Qualitative Assessments

Conclusion of the project:
The project aims to investigate the effects of habilitation with bone conduction implants and active middle ear implants in children with congenital unilateral conductive hearing loss.

Summery of project:
Individuals with unilateral hearing loss are known to have difficulties in situations requiring binaural processing of sounds, such as listening in noisy environments and localizing sound. This project focuses on children born with unilateral aural atresia causing a conductive hearing loss on the affected side. We aim to study the effect of habilitation with bone conduction devices (BCD) on audiological outcomes such as sound localisation ability (SLA) and speech recognition (SCS), surgical outcomes and the degree of patient satisfaction.

Study 1: Horizontal Sound Localization Ability and Speech Perception in Competing Speech in Children with Unilateral Aural Atresia Using Percutaneous BCD.

Children age 5-10 years with BCD is recruited for testing of PTA, SCS and SLA using corneal eye tracking.

Study 2: Evaluation of Bone Anchored Hearing Systems, Audiology and Fixture Mechanics.

Children with congenital conductive hearing loss suited for implantation with percutaneous BCD using a titanium fixture are included in this study that evaluates a new type of titanium screw, BHX. In collaboration with Oticon Medical.

Study 3: A Retrospective Chart Study of BCD Usage in Children with Aural Atresia at Karolinska University Hospital.

A retrospective chart review of children with aural atresia treated with percutaneous BCD at Karolinska University Hospital.

Study 4: Patient Satisfaction and Long-Term Usage of Percutaneous BCD

Subjects aged 0-18 operated with percutaneous BCD at Karolinska University Hospital 2010-2020 are asked to fill out a questionnaire regarding usage of their implant, and reasons for possible non-usage.

Study 5: BHAMBI, Binaural Hearing in Children with Unilateral Atresia Using Active Middle Ear or Bone Conduction Implants

Subjects aged 4-18 eligible for implantation with an active middle ear implant or an active transcutaneous BCD. Per- and postoperative surgical complications are registered. Subjects will participate in standard clinical audiometry, SLA and SCS.

Ethic permit No:

2012/1661-313	2018/864-31	2021-02984

Publications/manuscript 2022, 2023, 2024:

Josefsson Dahlgren H, Engmér Berglin C, Hultcrantz M and Asp F (2023) A pilot study on spatial hearing in children with congenital unilateral aural atresia. Front. Pediatr. 11:1194966. doi: 10.3389/fped.2023.1194966

Name: Evelina Jörtsö
Main supervisor: Linda Marklund
Co-supervisors: Rusana Bark, Anders Näsman

Registered (date): 2022-08-24
Half time control (date): 2025-05-09

Project title:
Predictive Markers for Head and Neck Tumors

Conclusion of the project:
In this doctoral project I focus on neck lesions, my main focuses are how we best can use the HPV markers for predicting histopathological outcome in a neck lesion; what information we can get from HPV status on a malignant neck lesion; and also, if there is a neck lesion we need to surgically remove, and it is hard or non-palpable – can an ultra-sound guided wire be helpful?

Summery of project:
Study I: Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts

436 patients were included. Re-evaluation of the cytology including HPV-analysis was performed. Cystic metastases were demonstrated histologically after surgical excision in 13 patients (3%). In patients over 18 years of age, the prevalence of cystic metastasis regardless of the primary tumour type was 3.3%.

Study II: Fine needle aspiration cytology including the analysis of human papilloma virus (HPV) DNA enhances the diagnostic workup of solitary cystic neck lesions in a population with a high incidence of HPV positive oropharyngeal cancer

Morphology and HPV-DNA in FNAC were reevaluated preoperatively and correlated to final diagnosis of 304 BrCC and CUP patients at Karolinska University Hospital during 2016-2023. All 176 cases finally diagnosed as BrCC were HPV-DNA negative in the preoperative FNAC. HPV-DNA was present in 100/128 (78.1%) of the FNAC with a solitary cystic neck metastasis and in 3/3 CUPs separately investigated on surgical

specimens. A FNAC with a benign morphology and the absence of HPV-DNA indicated a BrCC, while an HPV-DNA positive aspirate irrespective of morphology suggested an HPV-DNA positive cancer or CUP.

Study III: HPV and p16 prevalence, discordance and impact on survival in head and neck CUP: A retrospective cohort 2000-2024

This is a study that aims to investigate the prevalence of HPV and p16 in head and neck CUP – if there is discordance between HPV DNA and p16, and if the discordance affects the prognosis.

Study IV: OPSCC incidence, and HPV and p16 prevalence in OPSCC: A retrospective cohort 2000-2022

Sweden is one of the countries in the world with the highest incidence of HPV+ OPSCC. Incidence data for Sweden and Stockholm have been collected from the National Board of Health and Welfare and Statistics Sweden, SCB. HPV and p16 data have been collected from 2000-2022. We will also look at the three subsites of OPSCC: tonsillar, base of tongue and "other".

Study V: Is ultrasound-guided anchor technique useful in extirpation of a non-palpable lesion in the neck? A prospective randomized controlled study

Evaluation of a surgical method for enabling an extirpation of a non-palpable neck lesion. An ultra-sound guided anchor which is compared to only use of ultra-sound.

Ethic permit No:

2005/431-31/4	2005/1330-32	2009/1278-31/4	2010/1117-32	2015/0157-32
2023-05249-01	2024-06394-02	2017/1035-31/2	2023-03476-01	2020-00448
2021-00697	2024-06451-02			

Publications/manuscript 2022, 2023, 2024:

Hammarstedt Nordenvall L, Jörtsö E, von Beckerath M, Tani E, Nordemar S, Bark R. Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts. Acta Otolaryngol. 2022 Jan;142(1):100-105. doi: 10.1080/00016489.2021.2016951. Epub 2021 Dec 28. PMID: 34962438.

Jörtsö E, Marklund L, Harper Hysek M, Näsman A, Hammarstedt-Nordenvall L, Von Beckerath M, Dalianis T, Bark R. Fine needle aspiration cytology including the analysis of human papilloma virus (HPV) DNA enhances the diagnostic workup of solitary cystic neck lesions in a population with a high incidence of HPV positive oropharyngeal cancer. Acta Oncol. 2025 Feb 17;64:276-283. doi: 10.2340/1651-226X.2025.42078. PMID: 39962709; PMCID: PMC11848946.

Name: Sofia Karlsson
Main supervisor: Barbro Hedin Skogman
Supervisor: Elin Marsk, Malou Hultcrantz

Registered (date): 20181008
Half time control (date): 20240115

Project title:
Corticosteroid treatment in children with acute facial nerve palsy

Summery of project:
Children with acute peripheral facial nerve palsy cannot yet be recommended corticosteroid treatment based on evidence. Adults with idiopathic facial nerve palsy are treated with corticosteroids, according to guidelines resulting from a meta-analysis comprising two major randomized placebo-controlled trials. Corresponding trials in children are lacking. Furthermore, acute facial nerve palsy in childhood is frequently associated with Lyme neuroborreliosis, caused by the spirochete Borrelia burgdorferi. The efficacy and safety of corticosteroid treatment of acute facial nerve palsy associated with Lyme neuroborreliosis, has not yet been determined in prospective trials in children. The FACE study is a placebo-controlled double blinded randomized trial that aims to determine the efficacy of prednisolone treatment in children with acute facial nerve palsy of either idiopathic etiology or associated to neuroborreliosis and forms the basis of the doctoral project. Within the framework of the project a patient reported outcome meusure (PROM) will be evaluated using Rasch analysis, a method derived from modern test theory.

Ethic permit No:

2017/554	2019-01546	2021-01926	2009/156-31/2	2022-00501-02

Publications/manuscript 2022, 2023, 2024:
Nilsonne G, Wieschowski S, DeVito NJ, Salholz-Hillel M, Ahnström L, Bruckner T, m.fl. Results reporting for clinical trials led by medical universities and university hospitals in the nordic countries was often missing or delayed. J Clin Epidemiol. 01 februari 2025;181:111710.

Karlsson S, , Janeslätt G, Hultcrantz M, Marsk E, Skogman BH. A modern test theory approach to evaluating the FaCE scale – a patient reported outcome measure (PROM) for patients with facial nerve palsy. In manuscript

Name: Niki Karpeta
Main supervisor: Maoli Duan
Supervisor: L. Verrecchia, S. Hellström

Registered (date): 19-09-10
Half time control (date): 23-09-28

Project title:
Development of objective balance testing in newborns and young children

Conclusion of the project:
Pending

Summery of project:
Vestibular function plays a key role in the child's motor development especially during the first two years of life. It is the only active sensory system at birth and is fully integrated at teenage. Normally a baby can achieve head control at 4 months and go a few steps at 12 months old.Kimura and Kaga with coworkers showed delayed motor skills in children with reduced vestibular reflexes in studies in 2018 and 2019, respectively. Moreover, vestibular problems are associated with falls without deflect movements navigation problems and reading difficulties.It has been reported that preoperatively 40% of CI candidates, have an accompanied vestibular dysfunction. The surgical operation itself is an independent risk factor for vestibular injury.We propose a systematic methodology for testing newborns and young chilfren with two child friendly and scientifically approved methods (VEMP, vHIT). The identification of the optimal testing approach for vestibular screening in clinical praxis is also of great importance as the identification of a possible vestibular dysfunction will lead to a correct assessment of balance and thus an early intervention with physiotherapy. This will improve the child's motor development in the long term and will also affect unnecessary health care contacts.

Ethic permit No:

2015/1296-31/2	2022-02135-02

Publications/manuscript 2022, 2023, 2024:

Teenagers and Young Adults with Cochlear Implants: A Multidisciplinary Follow-Up Study Approach and Baseline Characteristics.

Audiol Res. 2025 Feb 12;15(1):16. doi: 10.3390/audiolres15010016. PMID: 39997160; PMCID: PMC11851589.

Löfkvist U, Dahlby-Skoog M, Persson A, Asp F, Verrecchia L, Gripenberg S, Karpeta N, Eklöf M, Karltorp E.

Vestibular function in children with vestibulocochlear nerve aplasia/hypoplasia
https://doi.org/10.1080/00016489.2023.2285453

Acta Oto-Laryngologica, Volume 143, 2023 - Issue 1

Niki Karpeta, Filip Asp, Kaijsa Edholm, Åsa Bonnard, Jeremy Wales, Eva Karltorp, Maoli Duan & Luca Verrecchia

other research publications outside the project

1.

Comorbidities and laboratory changes of sudden sensorineural hearing loss: a review.

Xie W, Karpeta N, Tong B, Liu Y, Zhang Z, Duan M.Front Neurol. 2023 Apr 18;14:1142459. doi: 10.3389/fneur.2023.1142459. eCollection 2023.PMID: 37144001

2.

Etiological analysis of patients with sudden sensorineural hearing loss: a prospective case-control study.

Xie W, Karpeta N, Tong B, Liu J, Peng H, Li C, Hellstrom S, Liu Y, Duan M.Sci Rep. 2023 Mar 30;13(1):5221. doi: 10.1038/s41598-023-32085-7.PMID: 36997587

3.

Diagnosis, differential diagnosis, and treatment for sudden sensorineural hearing loss: Current otolaryngology practices in China.

Chen N, Karpeta N, Ma X, Ning X, Liu X, Song J, Jiang Z, Ma X, Liu X, Zhong S, Sun Q, Liu J, Chen G, Duan M, Yu L.Front Neurol. 2023 Feb 23;14:1121324. doi: 10.3389/fneur.2023.1121324. eCollection 2023.PMID: 36908605

4.

Efficacy of intratympanic or postauricular subperiosteal corticosteroid injection combined with systemic corticosteroid in the treatment of sudden sensorineural hearing loss: A prospective randomized study.

Xie W, Karpeta N, Liu J, Peng H, Li C, Zhang Z, Liu Y, Duan M.Front Neurol. 2023 Apr 6;14:1138354. doi: 10.3389/fneur.2023.1138354. eCollection 2023.PMID: 37090982

Name: Aeneas Kolev
Main supervisor: Lars-Olaf Cardell
Supervisor: Linda Marklund, Gregori Margolin

Registered (date): 2020-05-14
Half time control (date):
Date for Dissertation:

Project title:
Sentinel node in head and neck cancer

Conclusion of the project:

Summery of project:
Sentinel node biopsy is a technique used to investigate if a cancer with lymphatic dissemination has metastasized. By injecting a radioactive and fluorescent tracer near the tumor, the sentinel nodes, which are the first lymph nodes to receive drainage from the tumor site, can be identified, removed, and examined. The sentinel nodes are the first locations where metastases typically occur. This research project focuses on the application of the sentinel node technique in oral and oropharyngeal cancer and its potential for further development.

One area of interest is the distribution of the sentinel node, which can sometimes deviate from established lymphatic drainage pathways. In the first sub-study, the sensitivity of the technique as used at the clinic is investigated, along with the the topographic placement of sentinel nodes and occult metastases in patients with N0 tongue cancer.

In the second study, the application of the sentinel node technique in radiation planning for oral cancer treatment is being investigated. Although traditionally used as a diagnostic technique by surgeons, the sentinel node could also be used to individualize radiation plans by reflecting the true lymphatic pathways.

In the third sub-study, the use of the sentinel node technique in oral cancer with regional metastasis (N+) is being evaluated. The technique can be used as a guide to a more radical neck dissection.

The fourth study will explore the applicability of the sentinel node technique in tonsil cancer. We will investigate the distribution of sentinel nodes. As tonsil cancer is

primarily treated with radiation therapy to the primary tumor and neck lymph nodes, the sentinel node technique could eventually be of interest to oncologists in radiation planning.

Ethic permit No:

2013/1943-31/4	2019-03518	2021-01265	2024-02635-01	

Publications/manuscript 2022, 2023, 2024:

Name: Lovisa Lansing
Title: MD PhD
Email: lovisa.lansing@gmail.com

Project title:
Bell's palsy in pregnancy and puerperium

Summary of project:

Background of my doctoral thesis:
Bell's palsy is a disorder with unknown etiology, suspected to be more common among pregnant and puerperal women, although the underlying cause for this remains unclear. The prognosis for recovery seems to be worse among the pregnant and puerperal patients with Bell's palsy. Still, since all prospective randomized treatment studies have excluded pregnant women, it is impossible to draw conclusions regarding corticosteroid treatment. Women affected by Bell's palsy during pregnancy and puerperium have been an unprioritized group in studies, likely due to the perceived risks for the unborn fetus or the newborn child. Being pregnant or a new mother can be physically and psychologically stressful for a woman, as well as being affected by an acute facial palsy. Hopefully, with better knowledge about Bell's palsy, concerning clinical course, prognosis, and associated risk factors in pregnant and puerperal women, caregivers can provide better and more customized care for these patients.

My doctoral thesis concludes that:

- The incidence of pregnancy-associated Bell's palsy in Sweden from 2005 to 2015 was determined to be 171.6 per 100,000 births.
- Pregnant women with Bell's palsy had a poorer outcome than puerperal and non-pregnant women with Bell's palsy.
- Similar depression scores were seen in women with pregnancy-associated Bell's palsy compared to pregnant and puerperal women without Bell's palsy.

- Patient-reported facial disability (FDI) and facial palsy-specific quality of life assessment scales (FaCE) correlated well with depression scores (EPDS) in women with pregnancy-associated Bell's palsy.
- Physician-graded facial functioning scales (Sunnybrook) had a poor correlation to depression scores (EPDS) in women with pregnancy-associated Bell's palsy.
- High BMI, geographical origin from Asia, Africa, and South America, multiple pregnancy, preeclampsia, and gestational diabetes were more common in pregnant and puerperal women with Bell's palsy than without.
- Bell's palsy during pregnancy was not associated with adverse neonatal outcomes.
- Adverse neonatal outcomes were associated with a higher risk for Bell's palsy in the puerperium.

Ethic permit No:

2016-03-09 (2015/2349-31)	2020-09-23 (2020-01295)	2022-01-19 (2021-06768-02)	2022-09-06 (2022-04464-02)

Publications 2022, 2023, 2024:

Lansing, L., Wendel, S.B., Hultcrantz, M. and Marsk, E. (2023), Bell's Palsy in Pregnancy and Postpartum: A Retrospective Case-Control Study of 182 Patients. Otolaryngol Head Neck Surg, 168: 1025-1033. doi: 10.1002/ohn.188.

Lansing L, Brismar Wendel S, Wejde Westlund E, Marsk E. A longitudinal study of facial function, quality of life, and depression in Bell's palsy during pregnancy and puerperium. Sci Rep. 2024 Oct 22;14(1):24890. doi: 10.1038/s41598-024-75552-5. PMID: 39438586; PMCID: PMC11496803.

Name: Andra Lazar
Main supervisor: Maoli Duan
Supervisor: Luca Verrechia, Inger Uhlén, Anna Persson

Registered (date): 2022.06.15

Project title:
Follow up of Children with moderate-severe bilateral sensorineural hearing loss

Conclusion of the project:

Summery of project:
This study focuses on the analysis of the regional registry Audiohab for pediatric hearing habilitation in Stockholm together with audiological data from the software platform Auditbase and regional public health electronic database. The pediatric hearing loss is investigated in its clinical, etiopathological and psychosocial aspects in older children enrolled in the Hearing habilitation Centre for Children and youth in Stockholm. We also investigate the family's knowledge about the cause of the hearing loss to better understand the importance for these children and parents of further investigations of their hearing loss.

Ethic permit No:

2020-07203	2023-01762-02	2024-03470-01

Publications/manuscript 2022, 2023, 2024:

Name: Vilma Liljeström
Main supervisor: Lars Olaf Cardell
Supervisor:
Susanna Kumlien Georén
Eva Munck-Wikland
Krzysztof Piersiala

Registered (date): 2021-01-25
Half time control (date):
2023-12-06

Project title:
Immunologic characterization of tumor draining lymph nodes in head and neck squamous cell carcinoma

Conclusion of the project: N/A

Summary of project:
Many patients with head and neck squamous cell cancer (HNSCC) present regional spread to the cervical lymph nodes (LN), while distant metastases are rare. Nodal involvement is the most important factor adversely affecting both the treatment and outcome. The treatment involves surgical removal of primary tumour, and removal of LN from one or more anatomical regions of the neck. However, extensive neck dissection is not without risks for severe complications. We want to provide an improved perioperative staging, so that only patients diagnosed with metastasis or unfavorable immunological features in sentinel node will receive a full neck dissection. Our preliminary results, clearly indicate that patients with low T-cells activation in LN have significantly higher risk of recurrence and death. Moreover, the development of new cancer treatments, especially immune checkpoint inhibitors (CPI), have changed the field of oncology. However, less than 20% of patients with HNSCC treated with CPI responds to this treatment. This is why, in order to fully benefit from this paradigm shift we have to improve the way we select patients for various treatment alternatives.

The overall goal is to provide a better outcome prognostic marker as well as introduce an improved selection of patients who need more rigorous follow-up and those who would benefit from CPI. The overall aims are firstly to provide a detailed characterization of different B cellular components of a lymph node. Secondly, to comprehensively investigate the humoral immune response against various tumour-associated antigens

(TAAs) and lastly, to explore the mechanism of B cell cellular interactions and B cell mediated immune suppression in

patients with oral cancer.

Ethic permit No:

2019-03518	2021-01265

Publications/manuscript 2022, 2023, 2024:

1. Eric H, Piersiala K, Lagebro V, Farrajota Neves Da Silva P, Petro M, Starkhammar M, Elliot A, Bark R, Margolin G, Kumlien Georén S, Cardell LO. High expression of PD-L1 on conventional dendritic cells in tumour-draining lymph nodes is associated with poor prognosis in oral cancer. Cancer immunology, immunotherapy : CII 2024 73;9 165-

2. Piersiala K, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, Bark R, Elliot A, Marklund L, Margolin G, Georén SK, Cardell LO. Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma. Frontiers in immunology 2024 15; 1455426-

3. Lagebro V, Piersiala K, Petro M, Lapins J, Gryback P, Margolin G, Georen SK, Cardell LO. A Novel Method Using Fine Needle Aspiration from Tumor-Draining Lymph Nodes Could Enable the Discovery of New Prognostic Markers in Patients with Cutaneous Squamous Cell Carcinoma. CANCERS 2023 15;13

4. Ekstedt S, Lagebro V, Kumlien Georén S, Cardell LO. Prolonged inflammatory resolution in allergic asthma relates to dysfunctional interactions between neutrophils and airway epithelium. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology 2023 131;3 349-355.e3

5. Piersiala K, Hjalmarsson E, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georén SK, Cardell LO. Regulatory B cells producing IL-10 are increased in human tumor draining lymph nodes. International journal of cancer 2023 153;4 854-866

6. Piersiala K, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georen SK, Cardell LO. Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells. TRANSLATIONAL ONCOLOGY 2022 23; 101469-

Name: Ellinor Lundberg
Main supervisor: Jesper Lagergren
Supervisor: Fredrik Mattsson, Eivind Gottlieb

Registered (date): 22-01
Half time control (date): 24-12-04

Project title:
Survival after surgery for esophageal cancer

Conclusion of the project:
To increase survival after esophageal cancer surgery

Summery of project:
Same as above

Ethic permit No:

2017/141-31/2

Publications/manuscript 2022, 2023, 2024:
https://pubmed.ncbi.nlm.nih.gov/35190948/

https://pubmed.ncbi.nlm.nih.gov/39962004/

Name: Anahita Mobargha
Main supervisor: Mathias von Beckerath
Supervisor: Zhenya Pencheva & Lalle Hammarstedt Nordelvall
Registered (date): 18/10/2024
Half time control (date): not decided
Date for Dissertation: not decided

Project title:

Oral tongue squamous cell carcinoma; a study of factors affecting spread and survival

Conclusion of the project: not decided

Summery of project:

My research as a PhD student at Karolinska Institutet focuses on improving prognostic tools and personalized treatment for early-stage oral tongue squamous cell carcinoma (OTSCC), a common and aggressive type of oral cancer. Despite advancements in treatment, challenges remain in accurately predicting survival and recurrence, particularly for patients who appear to have no regional spread at diagnosis. OTSCC traditionally affects individuals with a history of smoking and alcohol use, but a rising number of younger patients without these risk factors now face this disease. Accurate staging is essential, yet current methods such as elective neck dissection (END) may miss micro-metastases in up to 16% of cases. Sentinel lymph node biopsy (SNB) offers a promising, less invasive alternative, but its broader clinical impact requires further study. This retrospective study analyzes patients treated between 2008 and 2022 at Karolinska University Hospital and consists of four sub-studies: 1.Recurrence Patterns: Examines recurrence and survival trends in T1-T2 OTSCC and evaluates the prognostic utility of the 8th TNM classification. 2.Prognostic Factors: Investigates the influence of histopathological features and surgical margins on survival to define high-risk vs. low-risk patients. 3.Neck Management Strategies: Compares recurrence and survival outcomes between patients treated with SNB versus END. 4.Immune Response: Explores the prognostic significance of immune cell infiltration in tumor samples, aiming to enhance risk models with immune markers. The goal is to refine risk stratification, personalize treatment, and optimize neck management—potentially reducing overtreatment. This research may also pave the way for integrating immune markers into future prognostic models and inspire clinical guidelines or trials using less invasive approaches

Publications/manuscript 2022, 2023, 2024:

In process

Name: Agnes Modée Borgström
Main supervisor: Åsa Bonnard
Supervisor: Cecilia Engmér Berglin , Johan Knutsson

Registered (date): 2021-11-02

Project title:
Adverse events in cholesteatoma surgery - risk, contributing factors and quality of life

Conclusion of the project:
Thus far, an association between mucosa-affecting diseases of the upper airways and cholesteatoma has been found.

Summery of project (max 2 000)**:**
Surgery for cholesteatoma is performed in an area defined by the facial nerve, the sigmoid dura, the middle fossa dura plate, the labyrinth, the temporomandibular joint and the posterior wall of the ear canal. Sensitive structures that may be affected during surgery.

The aim of the thesis is analyzing different aspects of adverse events and effects on quality of life after cholesteatoma surgery as well as risk factors for the disease. This has been studied in a national registry based study. And will further on be studied in a regional retrospective study and two prospective survey based studies.

Ethic permit No:

2020-05935	2019-05190	2020-00245

Publications/manuscript 2022, 2023, 2024:
Modée Borgström, A., Mogensen, H., Engmér Berglin, C. *et al*. Occurrence of mucosa-affecting diseases of the upper airways in middle ear cholesteatoma patients: a nationwide case–control study. *Eur Arch Otorhinolaryngol* **281**, 4081–4087 (2024)

Name: Fatima Moumèn Denanto
Main supervisor: Filip Asp
Supervisor: Jeremy Wales, Bo Tideholm, Sten Hellström

Registered (date): 20-04-20
Half time control (date): 02-06-22
Date for Dissertation: -

Project title:
Bilateral Bone Anchored Hearing Devices, Bilateral Cochlear Implants and Binaural Hearing

Summary of project:
Binaural hearing is important for everyday listening tasks. The ability to localize sound and understanding speech in a noisy environment is dependent on the difference in time and level at which the sound reaches the two ears. In bone conducted sound this ability is affected due to the properties of the skull and surrounding tissue. With bilateral cochlear implants a difference in the electrode angular insertion depth between the ears causing place-of-stimulation mismatch might affect the binaural hearing abilities.

In my doctoral project we study whether a bilateral fitting of bone conduction hearing devices (BCD) gives a better hearing compared to one device in terms of horizontal sound localization accuracy and speech understanding in spatially co-located or separated competing speech. In addition, self-perceived benefit and quality of life will be assessed. Normal hearing subjects as well as patients with bilateral conductive/mixed hearing loss that are using one BCD will be assessed and tested with bilateral fitting compared to unilateral BCD.

We are also assessing the electrode angular insertion depth mismatch in adolescent bilateral cochlear implant users (a subgroup of a larger cohort in The Teenager and Young Adults Cochlear Implant, TAYACI, study) using photon-counting CT and correlating that to the ability to localize sounds on the horizontal plane.

Ethic permit No:

2019-04696	2021-04345	2022-00863-02	2023-01945-02	

Publications/manuscript 2022, 2023, 2024:

Differing Bilateral Benefits for Spatial Release From Masking and Sound Localization Accuracy Using Bone Conduction Devices, Ear and Hearing 43(6):p 1708-1720, November/December 2022. |DOI:10.1097/AUD.0000000000001234

Name: Lina Nygren
Main supervisor:
Supervisor:

Registered (date):
Half time control (date)
Date for Dissertation: 200206

Project title:
Post doctoral studies as part of the project SweChole regarding cholesteatoma in Sweden.

Summery of project:
I) Prospective study regarding hearing in patients undergoing cholesteatoma surgery. Hearing is tested before surgery as well as six months, one year and five years post surgery. The hearing test methods are pure tone audiometry (PTA), horizontal sound localization and speech in competing speech. PTA is used in clinical practice to measure the hearing of the cholestetoma patients. We want to evaluate if the other two methods are better to represent the useful hearing in the patients, compare the data to normal hearing subjects and describe eventual auditory plasticity in spatial hearing over time. II) Retrospective study of cholesteatoma patients in Sweden using the Swedish Patient Registry and the Swedish Quality Registry for Ear Surgery. We will combine these registries to evaluate the risk of developing cholesteatoma after myringoplasty. We will analyze parameters such as time from myringoplasty to cholesteatoma surgery and also parameters regarding surgical procedure of the myringoplasty and complications during the healing period.

Ethic permit No:

2022-04517-02	2020-05935			

Name: Rebecka Ohm
Main supervisor: Birgit Stark
Supervisor: Elin Marsk, Fredrik Brännström, Filip Farnebo

Registered (date): Dec 2017
Half time control (date): May 24 2024
Date for Dissertation: Planned 2027

Project title:
Observations on chronic facial dysfunction after peripheral facial palsy

Summery of project:
Persistent sequelae of peripheral facial palsy imposes a great reduction in quality of life. This thesis aims to evaluate sequelae from different perspectives; - Investigate incidence of long term sequelae and treatment needs after peripheral facial palsy

- Identify patients at risk for eye complications in a prospective study in collaboration with S:t Eriks Eye Hospital

- Evaluate highly selective neurectomy as a surgical method to treat synkinesis, i.e. mass muscle movements, following peripheral facial falsy.

-Validate different methods to assess symptoms of chronic facial palsy; a self reported questionnaire for dry eye symptoms (DEQ5) for use in Swedish, and EMG as a method to evaluate severity of synkinesis.

Ethic permit No:

2019-00421 2021-00246 2024-06985	2023-00761-01 2024-06413-02	2021-01380 2024-08033-02		

Publications/manuscript 2022, 2023, 2024:
Ohm R, Stark B, Brännström F, Marsk E. Sequelae Treatment Needs Following Peripheral Facial Palsy: Retrospective Analysis of 525 Patients. Otol Neurotol. Mar 21 2024;doi:10.1097/mao.0000000000004162

Name: Eirini Paziou
Main supervisor: Lars Olaf Cardell
Supervisor: Laila Hellkvist,
Monika Ezerskyte
Registered (date): 20231017

Project title:
Allergic rhinitis, evaluation of novel methods for nasal provocation and allergen specific allergen vaccination with or without vitamin D supplementation, as well a quest for new biomarkers and exploration allergen specific B-cells in lymphatic node

Summery of project:
Allergic rhinitis (AR) is a chronic condition with a 30% prevalence in Sweden. Despite widespread availability and frequent use of standard of care medication most patients are unsatisfied and report a marked impairment in their quality of life. The high prevalence of AR and lack of satisfactory treatment led to loss in productivity (presenteeism) resulting in high costs for the society.

AIT is currently the only treatment that incudes long-lasting relief of symptoms. It can be administered either traditionary as subcutaneous injections (SCIT) every 6–8 weeks or as a sublingual alternative (SLIT) where a tablet is placed under the tongue every day. Both routes involve treatment during at least three years. Problems with side effects and adherence respectively limit the use.

Ten years ago, intralymphatic injections were proposed as a new route for AIT. Since then, several small studies have investigated the effect on cat allergy, grass and/or birch pollen allergy or combinations of house dust mite, dog and cat allergy. Most trials have indicated improvement on allergen triggered symptoms and had few and mild side effects with allergen in low doses.

ILIT delivers allergen directly to the lymph nodes (in the groin) and as tolerance induction primarily is centred to the lymph nodes this method provides the maximal chance for tolerance induction. ILIT uses the same allergen-based vaccine as in SCIT but with a 100 times lower concentration. Three injections with an interval of four weeks results in a

comparable clinical effect as three years of traditional AIT with fewer side effects and better compliance.

Vitamin D (vitD) has immunomodulatory effects on allergen-induced inflammatory by acting via Vitamin D receptor (VDR). Supplementation of vitD in animal allergic models and in some human studies has been shown to attenuate allergic symptoms in animals and to improve response to SCIT and SLIT in humans.

The time of initiation of AIT (off pollen season) overlaps the time of the year when the level of naturally produced vitamin D (vitD) might be at its lowest. VitD deficiency or insufficiency and its influence on AIT comes into question, especially in countries located in higher latitudes such as Nordic countries.

Although highly effective, some patients do not respond to AIT, regardless of it is SCIT, SLIT or ILIT. An ability to predict the outcome would greatly increase the incitement to use AIT. So far, no definite cellular or humoral biomarkers has been able to predict the clinical outcome of AIT.

Nasal provocation (NAC) can be used to confirmation AR and it is especially helpful when there appears to discrepancies between the medical history and the results of tests. Unfortunately, the pollen extracts ('Aquagen') that we in Sweden and most part of Europe have routinely used for NAC has been discontinued and is therefore no longer available. Hence, there is therefore a need to test alternative sources of pollen extracts. One such sores of grass pollen is Grazax, a freeze-dried tablet intended for allergen-specific immunotherapy (AIT), has recently been successfully evaluated by a head-to-head comparison of Grass Aquagen and Grazax tablets (dissolved). No alternative for birch has so far been tested.

Aims

• To establish a method for NAC using dissolved Itulazax tablets

•Study the role of lymph node allergen specific B-cells in AR

•Investigate if supplementation of vitD in parallel with ILIT increases the efficacy of AIT

•Compare the treatment efficacy of ILIT with SLIT

•Explore immunological changes in blood, lymph nodes and nasal lavage (NAL) before and during the pollen season to identify clinically usable biomarkers

Ethic permit No:

2023-06100-02	2021-05597-01

Publications/manuscript 2022, 2023, 2024:

Manuscript February 2025: Nasal allergen challenge with dissolved Birch Tree pollen tablets

Name: Malin af Petersens
Main supervisor: Elisabet Örtqvist
Supervisor: Tomas Wester, Anna Löf Granström, Anna Svenningsson
Registered (date): 2024-08-29

Project title:
Outcomes of anorectal malformations

Conclusion of the project:
This doctoral project aims to provide valuable insights into the centralization of advanced pediatric surgery and the long-term outcomes of anorectal malformations (ARM). By evaluating the impact of centralization on short-term complications, as well as gastrointestinal health-related quality of life (HRQoL) and delivery outcomes in patients with ARM, this research seeks to improve patient care and outcomes of ARM.

Summery of project:
Background:
ARM comprise a spectrum of congenital anomalies. Over the last decades, the advancement of surgical techniques and neonatal care have improved survival rate of children born with ARM. The focus of care has therein shifted from survival to optimizing functional outcomes as well as reducing the negative impact on their quality of life. Data indicate that concentration of complex care and procedures in specialized centers improves quality of care in adult surgery. However, there is insufficient data to determine if centralization has a similar impact in pediatric surgery.

Purpose:
This doctoral project aims to improve understanding and patient care for ARM. The impact of centralizing advanced pediatric surgery has not been evaluated. The project will also adress the lack of data on long-term outcomes as well as delivery in females with ARM to improve patient care.

Issue:
1&2: Does centralization of the surgical management of anorectal malformations (ARM) and bladder exstrophy epispadias complex (BEEC) have an impact on short-term complications?

3: Does ARM have a negative impact on gastrointestinal health-related quality of life (HRQoL) in children and adolescents?
4: Assess delivery mode and delivery complications in females with ARM

Method:
The first two studies are national retrospective observational studies, comparing short-term outcomes before and after centralization of ARM (n=349) and BEEC (n=40). The third study will assess HRQoL including all patients aged 2-18 treated for ARM in Sweden (n≈400). The fourth study will be a national register-based cohort study assessing delivery in females with ARM from 1964 to 2005 (n≈1000).

Executive plan:
I started my doctoral project on August 29, 2024 and plan to complete it by spring 2029. I am submitting the manuscript of the first study this spring

Ethic permit No:

2023-02650-01.	2022-00983-01.			

Name: Petronella Pettersson
Main supervisor: Rusana Bark
Co-supervisors:
Linda Marklund, Elin Marsk

Registered (date): 250306
Half time control (date): VT2028
Date for Dissertation: VT2030

Project title:
Predictive markers and diagnostic methods for improved outcome in laryngeal cancer patients.

Conclusion of the project:
Yet to be determined.

Summary of project:

BACKGROUND
Head and neck cancer (HNC) is primarily treated with surgery, radiotherapy (RT), chemotherapy (CT), and more recently immunotherapy, though the latter is mainly used palliatively (1). Small tumors typically receive single modality treatment, while advanced stages involve combination therapy. Due to the proximity to vital organs, surgery is often limited, and organ-preserving RT/CT is the treatment of choice (2-4). HNC is a heterogeneous group, with variation in tumor aggressiveness and treatment response. While HPV/p16 serves as a prognostic marker for tumors of the tonsils and base of tongue (5,6), in other HNC we lack clinical markers for predicting which tumors will respond well to RT/CRT or which should be treated surgically.

Laryngeal cancer, one of the most common HNCs, has around 180 new cases annually in Sweden, with a good survival rate in small tumors but much poorer outcomes in advanced stages (T2-T4) (1,7-9). In Sweden, T1 tumors are usually treated locally through surgery, while T2-T3 tumors often receive RT or chemoradiation (CRT) for larynx preservation. T4 tumors require surgical total laryngectomy. In T2-T3 tumors where RT/CRT fails to work (residual/recurrent tumor), patients are also treated with laryngectomy, referred to as secondary or salvage laryngectomy.

It remains unclear why some T2-T3 tumors are resistant to RT, leading to a higher risk of residual tumors or recurrence. Several studies have shown that T2-T3 laryngeal cancer treated with RT/CRT have worse survival rates compared to T4 laryngeal cancer (10-12).

Identifying predictive markers for more aggressive, and less radiosensitive, T2-T3 tumors therefore is critical in being able to choose an optimal course of treatment.

Prognostic Markers: There are no known markers for determining RT/CRT sensitivity in laryngeal tumors. Studies suggest OCT4 expression is linked to radiation resistance (13), while alpha B-crystallin and LIMA 1 correlate with poor prognosis (14-15). Mutations in TERT are associated with aggressive thyroid cancer (16). Our research group has shown that high levels of CD8(+) tumor-infiltrating lymphocytes predict better prognosis in HPV+ tonsil cancer (17). We aim to explore if these markers can predict RT/CRT efficacy and prognosis in T2-T4 laryngeal cancer.

Complications after Laryngectomy: A common complication of laryngectomy is the formation of a pharyngocutaneous fistula (PCF). These can be challenging to treat, leading to extended hospital stay and delayed swallowing and voice rehabilitation. Severe cases may require advanced surgical reconstruction, and in some instances, fistulas become chronic. Studies report a 10-60% incidence of fistulas, but exact risk factors remain unclear (18-19).

Sentinel Node Technique in Laryngeal Cancer: HNC primarily spreads to cervical lymph nodes. Sentinel node (SN) technique can map the lymphatic drainage and identify the first nodes affected by cancer, critical for staging and treatment planning. This technique is established for breast cancer and melanoma, but not routinely used for laryngeal cancer, despite promising results in smaller studies. Its application in laryngeal cancer is more complex and hasn't been evaluated for advanced stages (T3, T4, N+) (20-21).

PLANNED SUBSTUDIES

Study I: Complications after total laryngectomy; risk factors for PCF.

Research questions: What was the prevalence of PCF in patients who underwent laryngectomy at Karolinska University Hospital during year 2000-2001? What patient-, tumor-, and treatment-related factors influence the risk of PCF after laryngectomy?

Material and method: Retrospective study on consecutive patients diagnosed with laryngeal cancer in the Stockholm-Gotland region between 2000-2021 identified from the Head and Neck Cancer Registry. A total of 753 patients were identified, of which 160 patients underwent laryngectomy, either primary or secondary. Data on patient demographics, tumor characteristics, comorbidities, primary treatment, and surgical details will be analyzed. The impact of factors like smoking, diabetes, BMI, blood values, postoperative care, laryngectomy type, tumor stage, and postoperative complications on cutaneous fistula formation will be assessed. A comparison between primary and secondary laryngectomy groups will also be conducted.

Study II: Survival, recurrence rate, and prevalence of dysphagia and voice problems after laryngectomy.

Research questions: Do prognosis and recurrence patterns differ between patients who underwent primary versus secondary laryngectomy? Is there a difference in the

prevalence and severity of complications such as dysphagia and voice problems after primary versus secondary laryngectomy?
Material and method: Retrospective observational study on same cohort as study I. Data will be supplemented with survival (overall and disease free), time and location of recurrence, presence of dysphagia, and voice problems. Speech therapist notes regarding dysphagia, need for PEG, consistency-adjusted diet, aspiration risk, and muscle-strengthening exercises will be collected if available. Data on voice problems requiring ongoing contact with a speech therapist or the need for alternative communication methods (e.g., electrolarynx or writing board) will also be collected.

Study III: Complications related to voice prosthesis use; incidence and causes.
Research questions: How common are complications related to voice prosthesis use and replacement? What factors influence the risk of these complications? Is there a difference in the prevalence and type of voice problems, voice rehabilitation interventions and the risk of permanent non-functioning voice for patients with laryngeal cancer who underwent primary vs secondary laryngectomy?
Material and method: Retrospective observational study on same cohort as study I/II. Data will be supplemented with voice prosthesis-related data, such as type of voice prosthesis, location of the prosthesis, the interval between voice prosthesis replacements, etc. These data will be correlated with the occurrence of various complications related to the voice prosthesis, as well as the reasons for voice prosthesis replacement (e.g., granuloma, narrow laryngostomy, incorrect size of voice valve, non-optimal tracheoesophageal fistula, RT/given, or other comorbidities). Comparison of primary vs secondary laryngectomy will be made.

Study IV: Predictive markers for tumor aggressiveness and RT sensitivity in laryngeal cancer.
Research questions: Can TERT, OCT-4, LIMA 1, alpha-B crystallin, and CD8 be used as predictive and prognostic markers for patients with laryngeal cancer? Can these markers predict which T2/T3 patients will require laryngectomy?
Material and method: Retrospective study on 453 consecutive patients diagnosed with laryngeal cancer stage T2-T4 at Karolinska University Hospital between years 2000–2021. The presence of tumor markers TERT, OCT-4, LIMA 1, alpha-B crystallin, and CD8 will be analyzed on formalin-embedded tumor blocks and correlated with overall survival and disease-free survival.

Study V: Sentinel node technique and mapping of lymphatic drainage in laryngeal cancer.
Research questions: What does the lymphatic drainage pattern look like in T2-T4 laryngeal cancer on SPECT-CT? In which regions can sentinel nodes be found in glottic, supraglottic, and subglottic laryngeal cancer?
Material and method: All patients diagnosed with T2-T4 laryngeal cancer will be invited to participate in the study. A total of 15 patients are planned for inclusion. During the examination under anesthesia (endoscopy) the radioactive tracer, Technetium-99-m

Nanocolloid (Nanocoll, GE Healthcare), will be injected peritumorally by an experienced head and neck surgeon. After at least one hour, SPECT-CT, which combines Single Photon Emission Computed Tomography (SPECT) and Computed Tomography (CT). All is performed in accordance with Karolinska's sentinel node protocol. Patient data and results from SPECT-CT will be compiled for statistical analysis.

PhD Project Objective and Significance:
This PhD project aims to improve individualized treatment selection for laryngeal cancer patients by developing clinically applicable predictive markers for tumor aggressiveness, RT sensitivity, and complication risks. By identifying which T2-T3 tumors will respond poorly to RT/CRT and better understanding lymphatic drainage patterns and complication risk factors, we can optimize treatment strategies to enhance survival and reduce treatment-related morbidity. The findings will directly support clinical decision-making regarding primary treatment choice (surgery vs. RT/CRT).

References:

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10. Patel SA et al. Comparing surgical and nonsurgical larynx-preserving treatments with total laryngectomy for locally advanced laryngeal cancer. Cancer. 2019;125(19):3367-77.

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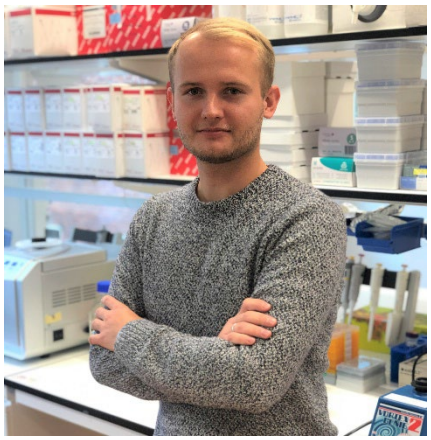
Ethic permit No:

Dnr 2019–04829	Dnr 2021–01265	Dnr 2024-07341-02	Dnr 2023-05249-01	Dnr 2024-07785-02



Name: Krzysztof Piersiala
Title: MD PhD
Email: Krzysztof.piersiala@ki.se

Project title(s):

1. Prognostic Biomarkers and Immune Mechanisms in Oral Cancer: Profiling Tumor-Draining Lymph Nodes

2. Lip Cancer – Improving Survival and Quality of Life

3. Emerging Trends in ENT Infectious Diseases: Epidemiology, Resistance, and Implications for Patient Care

Supervision of PhD-student:

Pétur Rafnsson	Main supervisor: ☒ Co-supervisor: ☐
Anna Bruckova	Main supervisor: ☒ Co-supervisor: ☐
Oscar Solmell	Main supervisor: ☐ Co-supervisor: ☒
Vilma Liljeström	Main supervisor: ☐ Co-supervisor: ☒

Summery of project:

Prognostic Biomarkers and Immune Mechanisms in Oral Cancer: Profiling Tumor-Draining Lymph Nodes

This project investigates the immunological role of tumor-draining lymph nodes (TDLNs) in oral squamous cell carcinoma (OSCC). By analyzing immune cell profiles and checkpoint molecules in TDLNs, the study aims to identify prognostic biomarkers that predict disease progression and response to treatment. The findings could improve patient stratification and guide personalized therapeutic approaches, particularly in the context of immune checkpoint inhibitor therapy.

Lip Cancer – Improving Survival and Quality of Life

This research focuses on optimizing treatment and follow-up strategies for patients with lip cancer. The project explores prognostic factors affecting survival and investigates strategies to enhance post-treatment quality of life. A key component is the introduction of sentinel lymph node biopsy (SLNB) into clinical practice for better staging and treatment planning, especially in patients with advanced stages. The study also evaluates long-term functional and aesthetic outcomes, aiming to balance oncological control with patient well-being.

Emerging Trends in ENT Infectious Diseases: Epidemiology, Resistance, and Implications for Patient Care

This project examines the evolving landscape of infectious diseases in otorhinolaryngology (ENT), with a focus on epidemiological trends, antimicrobial resistance, and emerging pathogens. Research includes the study of peritonsillitis, its recurrence patterns, possible association with head and neck malignancies, and bacterial resistance mechanisms. Another aspect explores the impact of HPV vaccination on oral HPV prevalence. Additionally, the project investigates epiglottitis and supraglottitis, analyzing incidence trends, microbial etiology, resistance patterns, and clinical outcomes. The overall goal is to provide data-driven insights that improve diagnostic strategies, treatment guidelines, and infection prevention measures in ENT practice in Sweden.

Ethic permit No:

2019-03518	2021-01265	2023-05724-02	2024-01475-02	2024-02635-01

Publications 2022, 2023, 2024:

1. Eric H, **Piersiala K**, Lagebro V, Farrajota Neves Da Silva P, Petro M, Starkhammar M, Elliot A, Bark R, Margolin G, Kumlien Georén S, Cardell LO. High expression of PD-L1 on conventional dendritic cells in tumour-draining lymph nodes is associated with poor prognosis in oral cancer. Cancer immunology, immunotherapy : CII 2024 73;9 165-

2. Locatello LG, Costantino A, Maniaci A, Fermi M, Barillari MR, Sampieri C, Bellini E, Serafini E, Jiang SRA, Nocera F, Asaro A, Midolo M, Rodio A, **Piersiala K**, Sooriyamoorthy T, Dimitriadis PA, Mannelli G. Does sex influence the prognosis of laryngeal cancer? A systematic review and a meta-analysis. AMERICAN JOURNAL OF OTOLARYNGOLOGY 2024 45;2 104195-

3. Ekstedt S, **Piersiala K**, Kolev A, Farrajota Neves da Silva P, Margolin G, Kumlien Georén S, Cardell LO. Phenotypical differences of neutrophils patrolling tumour-draining lymph nodes in head and neck cancer. British journal of cancer 2024 131;12 1893-1900

4. **Piersiala K**, Hjalmarsson E, Lagebro V, Farrajota Neves da Silva P, Bark R, Elliot A, Marklund L, Margolin G, Georén SK, Cardell LO. Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma. Frontiers in immunology 2024 15; 1455426-

5. Kakabas L, **Piersiala K**, Kolev A, Kumlien Georén S, Cardell LO. Allergic sensitization does not influence advancement or survival in oral cancer. Scientific reports 2023 13;1 21696-

6. Lagebro V, **Piersiala K**, Petro M, Lapins J, Grybäck P, Margolin G, Kumlien Georén S, Cardell LO. A Novel Method Using Fine Needle Aspiration from Tumor-Draining Lymph Nodes Could Enable the Discovery of New Prognostic Markers in Patients with Cutaneous Squamous Cell Carcinoma. Cancers 2023 15;13

7. **Piersiala K**, Hjalmarsson E, da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georén SK, Cardell LO. Regulatory B cells producing IL-10 are increased in human tumor draining lymph nodes. International journal of cancer 2023 153;4 854-866

8. Bark R, Kolev A, Elliot A, **Piersiala K,** Näsman A, Grybäck P, Georén SK, Wendt M, Cardell LO, Margolin G, Marklund L. Sentinel node-assisted neck dissection in advanced oral squamous cell carcinoma-A new protocol for staging and treatment. Cancer medicine 2023 12;11 12524-12534

9. **Piersiala K**, Kakabas L, Bruckova A, Starkhammar M, Cardell LO. Acute odynophagia: A new symptom of COVID-19 during the SARS-CoV-2 Omicron variant wave in Sweden. Journal of internal medicine 2022 292;1 154-161

10. Ekstedt S, **Piersiala K,** Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO. A prolonged innate systemic immune response in COVID-19. Scientific reports 2022 12;1 9915-

11. Weinreb SF, **Piersiala K**, Dhar SI, Hillel AT, Akst L, Best SRA. Impact of human immunodeficiency virus status on laryngeal cancer survival and locoregional control. LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY 2022 7;1 153-160

12. Cardenas EI, Ekstedt S**, Piersiala K,** Petro M, Karlsson A, Kågedal Å, Kumlien Georén S, Cardell LO, Lindén A. Increased IL-26 associates with markers of hyperinflammation and tissue damage in patients with acute COVID-19. Frontiers in immunology 2022 13; 1016991-

13. **Piersiala K**, Weinreb SF, Akst LM, Hillel AT, Best SR. Laryngeal disorders in people living with HIV. American journal of otolaryngology 2022 43;1 103234-

14. Kałużny J, Klimza H, Tokarski M, **Piersiala K**, Witkiewicz J, Katulska K, Wierzbicka M. The holmium:YAG laser lithotripsy-a non-invasive tool for removal of midsize stones of major salivary glands. Lasers in medical science 2022 37;1 163-169

15. Saibene AM, Allevi F, Ayad T, Lechien JR, Mayo-Yáñez M, **Piersiala K,** Chiesa-Estomba CM. Treatment for parotid abscess: a systematic review. Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale 2022 42;2 106-115

16. **Piersiala K,** da Silva PFN, Lagebro V, Kolev A, Starkhammar M, Elliot A, Marklund L, Munck-Wikland E, Margolin G, Georen SK, Cardell LO. Tumour-draining lymph nodes in head and neck cancer are characterized by accumulation of CTLA-4 and PD-1 expressing Treg cells. TRANSLATIONAL ONCOLOGY 2022 23; 101469-

Name: Samin Rahbin
Main supervisor: Babak Alinasab
Supervisor: Ola Sunnergren, Hatef Darabi, Pär Stjärne
Registered: 2020-08-18
Half time control: 2021-10-22
Date for Dissertation: 2025-12-05 (prel)

Project title:
Zygomaticomaxillary Complex Fractures: Aspects of Diagnostic Methods, Treatments and Complications

Conclusion of the project:
A first description of the loss of lower eyelid bags in patients surgically treated for orbital fractures
A first description of the volume difference along the external surface (VDAES) of the zygomatic bone (a novel computer-based method of measuring zygomatic bone asymmetry)
High patient satisfaction with facial appearance at long-term follow-up of ZMC fractures
Differences in patient and surgeon perspectives with regards to sequelae following ZMC fractures
An inadequacy in predicting malar asymmetry on CT scans in patients with ZMC fractures
Selected ZMC fractures can be treated with less invasive methods

Summary of project:
Zygomaticomaxillary Complex (ZMC) fractures are one of the most common types of facial fractures and frequently managed at Karolinska University Hospital (KUH). Treatment usually consist of either conservative management or surgery, either by closed reduction (CR) or open reduction with internal fixation (ORIF). Although long-term functional complications are rare, treatments are still guided by surgeon training, experience and preference rather than systematic evidence.

The project consists of a long-term follow-up of patients treated for ZMC fractures at KUH and a computer-based method of evaluating zygomatic bone asymmetry.

Ethic permit No:

2017/960-31/1	2018-302/31

Publications/manuscript 2022, 2023, 2024:

1. S Rahbin, O Sunnergren, E McBride, H Darabi, B Alinasab: Does More Invasive Surgery Result in Higher Patient Satisfaction? A Long-Term Follow-Up of 136 Zygomaticomaxillary Complex Fractures. Craniomaxillofacial Trauma & Reconstruction 2024, Vol. 17(4) NP271–NP280. DOI: 10.1177/19433875241286544.

2. S Rahbin, O Sunnergren, E McBride, H Darabi, B Alinasab: Differences Between Patient and Surgeon Perspectives: A Long-Term Follow-Up of 180 Patients With Zygomaticomaxillary Complex Fractures Following Either Conservative or Surgical Treatment. Craniomaxillofacial Trauma & Reconstruction 2024, Vol. 17(4) NP121–NP130. DOI:

10.1177/19433875231208463

3. Rahbin S, Toufani T, Al-Khabbaz AM, Lindblom J, Sunnergren O, Darabi H, Qureshi A R, Alinasab B: The Volume Difference Along the External Surface of the Zygomatic Bone: A Novel Method of Measuring Zygomatic Bone Asymmetry J Craniofac Surg. 2022 Mar/Apr 01;33(2):463-468. DOI: 10.1097/SCS.0000000000008186 (2022).

4. S Rahbin, M Kjellberg, M Söderlind & A Ekborn: Well-planned rather than rushed extraction of airway foreign body in 532 g preterm neonate Acta Oto-Laryngologica Case Reports. 6:1, 85-87. DOI: 10.1080/23772484.2021.2002153 (2021).

5. Rahbin, S; Liakos, A; Alinasab, B: Loss of Malar Bags in Lower Eyelid in Orbital Blow Out Fracture Reconstruction Following Pre- or Retro-Septal Transconjunctival Incision J Craniofac Surg. May/Jun 2020;31(3):769-771. DOI: 10.1097/SCS.0000000000006103 (2020)

Name: Pétur Rafnsson
Main supervisor: Krzysztof Piersiala
Supervisor: Linda Marklund and Alexandra Elliot

Registered (date): 2024-10-23
Half time control (date): 2026
Date for Dissertation: 2028

Project title:
Treatment of lip cancer in Stockholm, Uppsala and Örebro. A retrospective study of treatment and overall survival in 2000-2022.

Conclusion of the project:
The project has not finished yet, data still being gathered.

Summery of project (max 2 000)**:**
Lip cancer is one of the most prevalent oral tumors with about 23000 new cases yearly through out the world. In Sweden about 140 patients are diagnosed yearly and registered at SweHNCR, 60% men and 40% women. Known risk factors are tobac and UV-light exposure. Usually the patients are older (median 75 years) and the lower lip is more prone to cancer compared to the upper lip. The majority of the tumors are diagnosed in the early stages with a relatively good prognoses and a 92% 5-year overall survival in Sweden. Globally the treatment varies for lip cancer and even in Sweden. Surgery and radiotherapy (and or brachytherapy) are the main treatment options either as a combined therapy or stand-alone.

In Stockholm and Örebro there is a strong tradition of using brachytherapy for T2-T3 tumors aswell as relapses however in Uppsala most patients are treated with surgery and in rare cases with postoperative external radiotherapy. By including patients from these 3 different regions we believe we will get representative data regarding the different treatment modalities and thereby evaluate its effectiveness.

The questions we want to answer are:

What treatment do these patients in these regions get and what is their overall survival in regards to tumorstadium?

Is there a correlation between treatment of T2-T3 tumors and different complications, relapse rate and overall survival?

How do we treat relapses and what is the overall survival for such a treatment?

Ethic permit No:

2024-02635-01	2024-01475-02	2023-00134-01	2023-05724-001265	

Publications/manuscript 2022, 2023, 2024:

Name: Elnaz Sepehri
Main supervisor: Julia Arebro
Supervisor: Magnus von Unge,
Per Olof Eriksson
Registered (date): 2019-03-18
Half time control (date): 2023-09-29
Date for Dissertation: 2025-

Project title:
Regenerative closure of tympanic membrane perforations- clinical and experimental studies

Conclusion of the project:
Tympanic membrane perforation is a common condition and most often heal spontaneous due to its regenerative capacity. Why some perforations fail to heal and become chronic is an enigma. This PhD-project aims to map the inborn regenerative capacity in the human tympanic membrane and identify risk factors for unsuccessful outcome upon myringoplasty.

Summary of project:

In laboratory studies we try to identify stem cells and proliferative zones in normal human tympanic membranes as well as in tympanic membranes that has been mechanically and chemically injured in vivo. The aim is to better understand the normal inborn healing mechanism.

Plasminogen is an endogenous protein and has a role in cell migration and wound healing and has been identified as a possible drug for medical treatment of chronic tympanic membrane perforation. In a clinical trial different doses of plasminogen are injected close to the tympanic membrane in the ear canal in patients with chronic perforations and the feasibility and effect on healing of the ear drum is evaluated. With this project we aim to increase knowledge about the normal healing process and to improve the treatment of tympanic membrane perforations with the aim to design a simple, out-patient procedure without the need for advanced surgery.

In a fourth project we use SwedEar, one of the world's largest national registers in oto-surgery, to identify risk factors for unsuccessful surgical outcome upon myringoplasty.

Ethic permit No:

Dnr 2018/364	Dnr 2017/2011-31	2022-06108-01	2018/362-32

Publications/manuscript 2022, 2023, 2024:

Risk factors for unsuccessful healing upon myringoplasty - a register-based study (*Manuscript*)

Mapping the Regenerative Pattern in the Human Tympanic Membrane (*Manuscript/ submitted*)

Plasminogen - safe for treatment of chronic tympanic membrane perforation: a phase 1 randomized, placebo-controlled study. Acta Otolaryngol. 2024 Jul-Aug;144(7-8):439-45

Name: Carl Skröder
Main supervisor: Lars-Olaf Cardell
Supervisor: Ulla Westin, Laila Hellkvist

Registered (date): 200514
Half time control (date): 250404

Project title:

Examining therapeutic interventions for pollen-induced allergic rhinitis and dog allergy: Systemic steroids, allergen immunotherapy and economic implications

Conclusion of the project:

1. **Evaluation of systemic steroids for birch pollen-induced AR:** Systemic corticosteroids show efficacy in alleviating symptoms of allergic rhinitis during the birch pollen season, although with limited advantages compared to topical treatments. The efficacy could potentially be enhanced by increasing the dosage, but this would correspondingly increase the risk of adverse effects.
2. **Safety profile of systemic steroids in treating birch pollen-induced AR:** The short-term use of systemic corticosteroids is associated with well-documented acute side effects; however, with careful management, this treatment can be considered safe in the short term. The long-term safety profile, particularly over several years, is less well understood and poses significant concerns.
3. **Comparative impact of systemic versus topical steroids on quality of life:** There is no significant enhancement in quality of life when using systemic corticosteroids compared to topical steroids for the treatment of birch pollen-induced allergic rhinitis.
4. **Cost-effectiveness of SLIT versus topical treatments in Sweden:** SLIT proves to be a cost-effective alternative to topical treatments for managing allergic rhinitis, offering both financial benefits and effective symptom control.

Summary of project:

Allergic rhinitis (AR) is a chronic condition with a 30% prevalence in Sweden. Despite widespread availability and frequent use of standard of care medication the majority of patients are unsatisfied and report a marked impairment in their quality of life. When standard of care treatment fails, like in the middle of a severe pollen season, short-term systemic corticosteroids are often prescribed, especially in private practice. However, injected corticosteroids is not recommended in modern guidelines, due to risk for side effects and lack of documented efficacy. Despite this, the longstanding praxis of giving a pre-

seasonal intramuscular injection methylprednisolone remains at several places around the world.

Aims:

- Evaluate the efficacy of systemic steroids for treating birch pollen-induced allergic rhinitis (AR).
- Assess the safety profile of systemic steroids in the management of birch pollen-induced AR.
- Compare the impact of systemic versus topical steroids on quality of life in patients with birch pollen-induced AR.
- Analyze the cost-effectiveness of sublingual immunotherapy (SLIT) versus topical treatments for allergic rhinitis in Sweden.
- Investigate the effectiveness of Alutard SQ Dog in treating patients with canine allergies.

Ethic permit No:

2016/2158	2017/947	2018/11

Publications/manuscript 2021, 2023, 2024:
Publications:

1. HealthSWEDE: Costs with sublingual immunotherapy - a questionnaire study

Petter Olsson, Carl Skröder, Lars Ahlbeck, Frida Hjalte, Karl-Olof Welin, Ulla Westin, Morgan Andersson, Cecilia Ahlström-Emanuelsson & Lars-Olaf Cardell. Allergy, Asthma & Clinical Immunology volume 17, Article number: 55 (2021)

2. Comparison of prednisolone tablets versus antihistamine tablets for seasonal allergic rhinitis: A randomized controlled trial

Carl Skröder, Laila Hellkvist, Ulla Westin, Pernilla Sahlstrand-Johnsson, Åslög Dahl, Leif Bjermer, Lars Olaf Cardell, Clin Transl Allergy. 2024;e70017

3. Limited beneficial effects of systemic steroids when added to standard of care treatment of seasonal allergic rhinitis

Carl Skröder, Laila Hellkvist, Åslög Dahl, Ulla Westin, Leif Bjermer, Agneta Karlsson, Lars Olaf Cardell

Sci Rep. 2023. PMID: 37950032

Name: Martin Smelik
Main supervisor: Mikael Benson
Supervisor: Lars-Olaf Cardell, Xinxiu Li, Oleg Sysoev, Claudio Cantu

Registered (date): 26.5.2021
Half time control (date): 14.2.2024
Date for Dissertation: 26.5.2025

Project title:
System-Level Approaches for Biomarker Discovery in Complex and Malignant Diseases

Conclusion of the project:
This thesis demonstrates the potential of systems-level approaches in biomarker discovery, providing insights into disease mechanisms and paving the way for personalized medicine. The studies highlight the importance of considering disease heterogeneity and the need for tailored biomarker strategies, ultimately contributing to earlier diagnoses and improved patient outcomes.

Summery of project:
Early diagnosis and effective treatment of complex and malignant diseases are critical challenges in modern medicine. These diseases exhibit significant heterogeneity, manifesting differently across patients and involving diverse genes and pathways. This variability complicates the identification of universal biomarkers, necessitating innovative, system-level approaches to uncover robust and predictive biomarkers across various biological contexts.

This dissertation addresses these challenges by leveraging both knowledge-based and data-driven methods to analyze multi-omics data, including spatial and single-cell transcriptomics, as well as bulk data. The goal is to prioritize potential biomarkers that can provide system-level insights into disease mechanisms, ultimately facilitating personalized medicine. The findings of this thesis promise to transform biomarker discovery, leading to earlier diagnoses, improved treatment outcomes, and enhanced patient care.

The thesis encompasses four comprehensive studies:

1. **Multi-organ single-cell analysis reveals an on/off switch system with potential for personalized treatment of immunological diseases**: We analyzed scRNA-seq data from mice and humans with immune-mediated inflammatory diseases (IMIDs). We identified upstream regulators acting as on/off switches, which collectively serve as candidate biomarkers and potential drug targets. These findings were validated in a study involving sera from nearly 300 systemic lupus erythematosus patients.

2. **An interactive atlas of genomic, proteomic, and metabolomic biomarkers promotes the potential of proteins to predict complex diseases**: Using multiomics data from UK Biobank (UKBB), we identified reliable biomarkers for nine complex diseases and constructed an interactive atlas to explore their performance. Proteomics outperformed other omics types in most of the diseases.

3. **Multiomics biomarkers were not superior to clinical variables for pan-cancer screening**: We analyzed multiomics data to find early diagnostic biomarkers for cancers. While proteomics data from peripheral blood did not outperform routine clinical variables for most cancers, promising biomarkers were identified for cancers in highly vascularized organs.

4. **Combining spatial transcriptomics and pseudotime to find urine biomarkers for prostate cancer**: We analyzed spatial transcriptomics data of prostate cancer to identify transcripts correlated with malignant transformation. Using pseudotime and machine learning, we validated the diagnostic accuracy of these transcripts in various samples from over 2,000 patients and controls.

Ethic permit No:

Ethical Committee Board, Norra Stockholms Djurförsöksetiska nämnd	6798/18			
Animal Experimental Ethics Committee of Xuzhou Medical University	202012A162			

Regional Ethics Review Board in Linköping	M75-08/2008			

Publications/manuscript 2022, 2023, 2024:

Sandra Lilja*, Xinxiu Li*, **Martin Smelik***, Eun Jung Lee, Joseph Loscalzo, Pratheek Bellur Marthanda, Lang Hu, Mattias Magnusson, Oleg Sysoev, Huan Zhang, Yelin Zhao, Christopher Sjöwall, Danuta Gawel, Hui Wang, Mikael Benson. Multi-organ single-cell analysis reveals an on/off switch system with potential for personalized treatment of immunological diseases. Cell Rep Med. 2023 Mar 21;4(3):100956.

Martin Smelik*, Yelin Zhao*, Xinxiu Li, Joseph Loscalzo, Oleg Sysoev, Firoj Mahmud, Dina Mansour Aly, Mikael Benson. An interactive atlas of genomic, proteomic, and metabolomic biomarkers promotes the potential of proteins to predict complex diseases. Sci Rep 14, 12710 (2024).

Xinxiu Li, Eun Jung Lee, Sandra Lilja, Joseph Loscalzo, Samuel Schäfer, **Martin Smelik**, Maria Regina Strobl, Oleg Sysoev, Hui Wang, Huan Zhang, Yelin Zhao, Danuta R Gawel, Barbara Bohle, Mikael Benson. A dynamic single cell-based framework for digital twins to prioritize disease genes and drug targets. Genome Med 14, 48 (2022).

Yelin Zhao, Xinxiu Li, Joseph Loscalzo, **Martin Smelik**, Oleg Sysoev, Yunzhang Wang, A. K. M. Firoj Mahmud, Dina Mansour Aly, Mikael Benson. Transcript and protein signatures derived from shared molecular interactions across cancers are associated with mortality. J Transl Med 22, 444 (2024).

Samuel Schäfer, **Martin Smelik**, Oleg Sysoev, Yelin Zhao, Desiré Eklund, Sandra Lilja, Mika Gustafsson, Holger Heyn, Antonio Julia, István A Kovács, Joseph Loscalzo, Sara Marsal, Huan Zhang, Xinxiu Li, Danuta Gawel, Hui Wang, Mikael Benson. scDrugPrio: a framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases. Genome Med 16, 42 (2024).

AKM Firoj Mahmud, Dina Gamaleldin Mansour Aly, Yelin Zhao, Mikael Benson, **Martin Smelik**, Oleg Sysoev, Hui Wang, Xinxiu Li. Proteogenomic analysis reveals Arp 2/3 complex as a common molecular mechanism in high risk pancreatic cysts and pancreatic cancer. Sci Rep 15, 3902 (2025).

Name: Mikolaj Stachurski
Main supervisor: Åsa Bonnard
Supervisor: Eva Westman, Per Olof Eriksson, Hanna Mogensen

Registered (date): 2024-08-28

Project title:
Clinical and epidemiological aspects of middle ear cholesteatoma

Summary of project:

I: International studies show the incidence of middle ear cholesteatoma ranging from 6.8 to 12.6 cases per 100 000 adults and 3 to 15 cases per 100 000 children but the data from Sweden is lacking. The aim of this project is to determine the incidence of cholesteatoma in Sweden and its changes over the past 30 years.

II: Craniofacial malformations are one of the causes of chronic middle ear infections that can lead to the development of cholesteatoma. Studies show that children with cleft lip and palate have an increased risk of acquiring cholesteatoma. With this project we intend to answer the question whether other facial malformations pose an increased risk for cholesteatoma development.

III: The treatment for cholesteatoma is surgery. There is limited material describing the risk of postoperative complications. With this study we are going to establish whether the risk for pulmonary embolism and deep vein thrombosis following cholesteatoma surgery is increased.

IV: Current research has shown a lack of association between prolonged waiting time until cholesteatoma surgery and recidivism, however, data is lacking regarding postoperative hearing results. The aim of this study was to determine if waiting time until cholesteatoma surgery affects hearing outcome and patients' satisfaction.

Ethic permit No:

2019-05190	2020-000245	2021-05727-02	2021-06440-01	

Publications/manuscript 2022, 2023, 2024:

1. Stachurski M, Eriksson PO, Westman E, Mogensen H, Bonnard Å. The impact of waiting time on hearing outcome and patients' satisfaction after cholesteatoma surgery. Acta Otolaryngol. 2023 Aug;143(8):662-668.

Name: Clara Svenberg Lind
Main supervisor: Jeremy Wales
Supervisor: Jessica Kåhlin, Mathias von Beckerath, Lalle Hammarstedt Nordenwall

Registered (date): 20230101
Half time control (date): 20230601

Project title:
Tracheostomy in the era of Covid-19

Conclusion of the project:
The Covid-19 pandemic led to an unprecedented amount of patients requiring tracheostomy. We analyse the immediate, short- and long-term complications of this technique when performed by otolaryngologists or intensivists.

Ethic permit No:

2020-2779	2022-05241-01

Publications/manuscript 2022, 2023, 2024:
Globalsurg Collaborative, Covidsurg Collaborative. SARS-CoV-2 infection and venous thromboembolism after surgery: an international prospective cohort study. Anaesthesia 2022 Jan;77(1):28-39.

Submitted artikel (april 2025): Laryngotracheal pathologies associated with patient-care factors one year after critical care in a COVID-19 cohort.

Name: Zheer Tawfique
Main supervisor: Luca Verrecchia
Supervisor: Bo Håkansson, Sabine Reinfeldt, Karl-Johan Freden-Jansson

Registered (date): 2023-11-02

Project title:
Bone conducted stimulation in audiology and neurotology: new perspectives

Conclusion of the project:
Through our research project we aim to further expand upon the use of bone conduction stimulation (BC) in diagnostics and treatment within neurotology. By this, we hope to improve the current management of specific fields within clinical neurotology.

The research project comprises of four studies.

Two are diagnostic studies:

1) The diagnostic accuracy of ankle audiometry for superior canal dehiscence syndrome in patients affected by pulsatile tinnitus and/or autophony.

2) The role of a balance screening by VEMP in infants alongside the newborn hearing screening program.

Two are intervention studies:

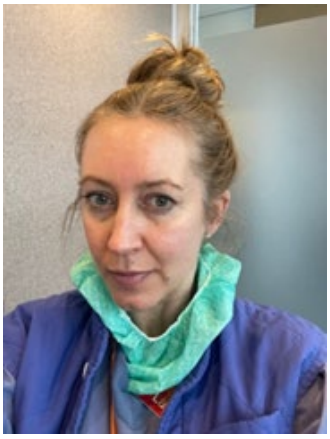
1) BC stimulation in the treatment of benign paroxysmal positional vertigo.

2) BC stimulation in the treatment of bilateral vestibulopathy.

All studies are still in their planning phases.

Ethic permit No:

2020-04214	2023-04525-02



Name: Karin Åberg
Main supervisor: Marit Westman

Supervisors: Marianne van Hage**,** Anna Asarnoj**,** Mats Holmström

Registered (date): 17.12.21
Half time control (date): 23.11.14
Date for Dissertation: Mars 2026

Project title:
"Predictors of upper airway symptoms in the BAMSE birth cohort"

Conclusion of the project:
In the first study, we concluded that:

- Molecular diagnostics for grass pollen allergy can be useful in a clinical setting in difficult cases.
- IgE antibodies against natural Phl P 4 is a hitherto unknown early biomarker for grass pollen allergy.

In study 2 we concluded that:

- The prevalence of CRS in young adults in Stockholm is around 2-4 %.
- There is significant association between CRS and atopic disease in young adults.
- The cytokine profile in cells from nasal lavage from young adults with CRS show signs of type 1 inflammation.

Summery of project:
Background: Rhinitis and rhinosinusitis are inflammatory diseases in the upper airways, often associated with asthma. *Allergic rhinitis* (AR) is an IgE-mediated disease. It is one of the most costly diseases to the society. Sensitization is a strong risk factor for later development of AR and, in some cases, asthma. During the last decade, there has been a rapid increase in knowledge about specific allergen proteins (allergen components). This has primarily been used within food allergy to be able to separate life threatening allergies from cross reactions (component resolved diagnostics). *Chronic rhinosinusitis (CRS)* is a multifactorial inflammatory disease in the upper airways, with several different endotypes. The prevalence is somewhat uncertain since the diagnosis is

difficult to ensure via questionnaires. To be able to estimate prognosis and decide on treatment for these diseases, there is a need for prognostic biomarkers.

Aim: The overall aim of this project is to identify early prognostic factors for upper airway disease and to increase the understanding of the relationship between symptoms from the upper and lower airways.

Methods: We use data from the population based birth cohort BAMSE (Barn Allergi Miljö Stockholm Epidemiologi) consisting of 4089 children. The children have been followed repeatedly by questionnaires. At 4, 8, 16 and 24 years of age clinical examinations were performed, including blood samples for specific IgE. We have also performed a subgroup study of the 24-year-olds with CRS symptoms. The data from this study has recently been submitted in Rhinology.

Ethic permit No:

93:189	98:175	2007/1634-31	2010/1474-31/3	2016/1380-31/2

Publications/manuscript 2022, 2023, 2024:

Westman M, Åberg K, Apostolovic D, Lupinek C, Gattinger P, Mitterman I, Andersson N, Melèn E, Bergström A, Antò J M, Bousquet J, Valenta R, Wickman M, van Hage M
"Longitudinal assessment of sensitization to grass pollen allergen molecules in a birth cohort – the importance of Phl p 4 for diagnosis and prediction of grass pollen allergy."
JACI April 2020

Åberg K, Asarnoj A, Georén SK, Cardell L.O, Kull I, Bergström A , Melén E, Holmström M, van Hage M, Westman M
"The prevalence of primary chronic rhinosinusitis in young adults from a Swedish birth cohort"
Rhinology Mars 2025