

The Swedish Ear, Nose and Throat (ENT) specialty developed out of the surgical specialty for more than one hundred years ago. Stockholm with Karolinska Institutet became the first ENT center of Sweden, originally governed by the ENT-giant professor Gunnar Holmgren. In 1940s the Karolinska University Hospital was founded at the Solna site and later the Huddinge site was incorporated.

Today the Division of ENT diseases at Karolinska Institutet is a successful and leading national and international academic center for ENT. In this book we have gathered information concerning the Karolinska ENT history, some ongoing scientific projects and also presenting the current research groups among other things.

We, who have gathered and edited this information, are Britt Nordlander, Agneta Wittlock and Sten Hellström (see picture below)



ENT research at Karolinska Institutet meets the future



research at

**Karolinska Institutet**

**meets the future**

**ENT**

**research at**

**Karolinska Institutet**

**meets the future**

Who cares for and facilitates your day?  
Who specializes in the interplay,  
lets music, talk and noise into your head,  
helps understand a word that someone said.

What if those great opinions of your choice  
are stuck because of problems with your  
voice? Or, when you sit there in your stunning  
gown you find the party dinner won't go  
down?

Sometimes the aching nose is hard to blow  
yet there's a constant and annoying flow.  
It does not take a master mind to see  
that what you need is us from ENT!

*Per-Åke Lindestad*

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\*earlier presented in "Courage with ethics and responsibility. Scientific Report 2017" from the Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet







*Lars Olaf Cardell,  
Head of the Division, Professor*

When I spent the summer of 1982 at the Istituto Di Fisiologia Umana in Milan I came across an Italian expression, “futuro oggi”. It means the future today. I hope this book will give you just that. In it you will glimpse the tomorrow of the ENT field. Nine research groups present highlights of their ongoing scientific endeavors, providing an overview of the work of our division, and offering a peek into future trends in diagnostics and treatments. However, without an awareness of our history we will not be able to take necessary action to defend and develop our specialty. A brief history of Swedish ENT, from a KI perspective, has therefore been engrafted in this work.

Please enjoy,

**Post scriptum:** But why a book when everything can be found on the internet? A book, once printed, cannot be revoked. It is there and will always be there. It will not drown in the bombardment of information that flows from the continuous expansion of the electronic media. So, right or wrong it will be a time capsule that “seizes the day” of our institution.

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Professor Gunnar Holmgren Stockholm Suede =		
erfahre durch schwedischen Gesandten von der mich hoch beglueckenden Verleihung des nobelpreises und sage ihnen und durch sie der medicinischer facultat + stockholms meinen herzlichsten dank = dr barany kriegsgefangener		

## The history of ENT at the Karolinska

At the end of the 18<sup>th</sup> century otolaryngology began to separate from general surgery. The first clinic for ear, nose and throat (ENT) diseases in Sweden was established at the Royal Serafimer Hospital in the 1890s as an outpatient clinic. A few years later, governmental funds were raised for a teaching position at the Karolinska Institute for the teaching of otology, rhinology and laryngology at the Serafimer ENT clinic. ENT diseases became a mandatory course in medical school from 1907. That same year a department of otolaryngology was started at Sabbatsberg hospital under the leadership of Gunnar Holmgren, “the father of Swedish ENT”. In 1910, the first in-patient ENT ward was established at Sabbatsberg. The disease panorama was mainly complications to infectious diseases, i.e. diphtheria, tuberculosis, scarlatina, otitis media and pseudocroup. In this preantibiotic era fatal outcomes were common. Besides pioneer clinical work, such as introducing the binocular microscope in ear surgery allowing surgeons to perform fenestration surgery for otosclerosis, Gunnar Holmgren conducted major clinical and experimental scientific work. Gunnar Holmgren had a wide international network, was the president of the Swedish Association of Otorhinolaryngology for 17 years, a member of the Nobel committee and founder of the scientific journal *Acta Oto-Laryngologica* in 1918. He also recruited Robert Barany from Vienna who had been awarded the Nobel prize in 1914 for his work on the vestibular system, while he was a prisoner of war in Russia. Thanks to Gunnar Holmgren’s negotiations for an exchange of war prisoners Robert Barany was able to come to Stockholm two years later to receive his prize.



Many of the ENT surgeons trained at Sabbatsberg were later appointed heads of ENT departments that opened up throughout the country. Sabbatsberg became the ENT flagship clinic in Sweden until the Karolinska hospital was opened.

Karolinska hospital in Solna was inaugurated in 1940 and Torsten Skoog was appointed professor and the head of the department of otorhinolaryngology. Professor Paul Frenckner had laid the foundation for modern endoscopy during the 1930s during his stay at Sabbatsberg’s hospital. During his and professor Gunnar Holmgren’s leadership in the 1940s and 1950s ear surgery at the Karolinska hospital was developed in terms of both reconstructive ear surgery and otosclerosis.



In 1960, Carl-Axel Hamberger was appointed professor at the Karolinska and successor as the head of the department and remained so until he resigned in 1975. After his studies at Memorial Hospital in New York under John Conley he introduced advanced tumour surgery of the head and neck at the Karolinska, including transnasal surgery of the pituitary gland, which became the dominating approach for the following decades. A close cooperation was established with Radiumhemmet, the oncological institution at Karolinska and multidisciplinary conferences with representatives from head and neck surgeons and oncologists were introduced for all cancer patients. An Audiological section with Lennart Holmgren and later Bengt Barr was also established during this time.

At the research laboratory Gustav Vth at Karolinska an expanding “Ear-lab” was formed under Jan Wersäll. Important morphological animal studies were performed of the inner ear using electron microscopy, a novel technique at that time. With Åke Flock the field was expanded to physiological studies of the inner ear including studies of ototoxicity and physiology of single hair cells.

In the 1960s the ENT clinic comprised of four wards with altogether 86 beds. Thanks to improvement in methods of general anesthesia, improved treatment modalities and transition to outpatient surgery the number of beds have successively been reduced over decades. The question today is whether or not this reduction has gone too far, as the number of beds per inhabitant in Stockholm today is among the lowest in Sweden and in Europe.

In 1972 the Huddinge Hospital was opened and was at that time the largest hospital in Sweden. Two years later an ENT department was opened with professor Jan Wersäll as the head of this novel university clinic, fully staffed with a professor, teachers and teaching-assistants, and linked to the Karolinska Institute. Jan Wersäll returned to Karolinska Hospital in Solna as the head of the department after Carl-Axel Hamberger’s retirement in 1975.

During the 1990s and 2000s a series of reorganizations were promoted by the political regime of the county council including a new financial system. In 1997, all head and neck surgery in Stockholm was concentrated to Karolinska Hospital in Solna. The profile of Huddinge Hospital was advanced ear surgery, cochlear implants and phoniatriy.

In 2004 the Karolinska Hospital, Solna and University Hospital, Huddinge, joined together as Karolinska University Hospital.

In 2011, the previously separate Karolinska Institute ENT entities at Solna and Huddinge were joined together as one academic unit. Today there are 20 professors and associate professors, a large number of senior researchers who run their own independent projects and 31 doctoral students within this ENT division. The ENT division drives, as we shall see in this book, successful research at the scientific forefront of ENT diseases, of which some examples are:

- Cochlear implant research on children with hearing loss, focusing on aetiology, diagnosis and spoken language development.
- Obstructive Sleep Apnea in adults and children; diagnosis and treatment
- The development of a unique method for measurement of hearing.
- The connection between HPV and tumours of the head and neck region.
- The treatment of chronic rhinosinusitis with various anti-inflammatory antibodies against IgE

A major change and step forward for the ENT clinic will be moving into the New Karolinska University Hospital in the fall of 2018. Karolinska University Hospital is transitioning to a whole new operational model with a new thematic organization consisting of themes and functions, and is based on the patient's journey through the healthcare system. The ENT department will be split up and reorganized into 2 themes; Cancer and Trauma and Reparative Medicine (T12).

During the transition period, Karolinska will have two organizational models – one with divisions and departments, and the other with the new thematic organization.

The academic work at the ENT department in short:

Since the start of the ENT department at Karolinska, in 1942, 140 theses have been produced. Between 2000 and 2009 the number was 27 and between 2010 and 2017 the number of theses produced was 30. Within the last four years 286 articles have been published in international scientific journals. In December 2017, the number of registered doctoral students was 31, which provides a promising ground for a continuity of the scientific work at the department.

## Ongoing projects

Earlier presented in "Courage with ethics and responsibility. Scientific report 2017" from the Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet

## TO MAKE DEAF CHILDREN HEAR The cochlear implant – an amazing invention

It is a small miracle that electrical stimulation of the auditory nerve by a few electrodes, instead of thousands of sensory cells, may result in a hearing that gives a good understanding of speech and often even the possibility to talk on the telephone. The electrode array is inserted into the cochlea with a surgical procedure and to date hundreds of thousands of patients around the world have received implants.

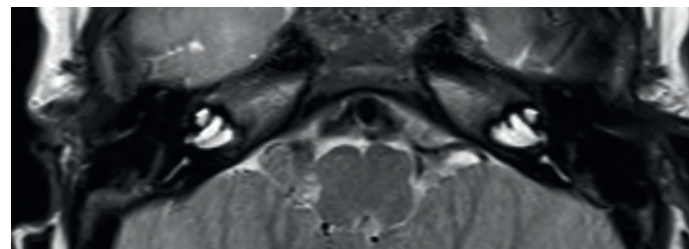
### Cochlear implantation of malformed inner ears – a prestigious *Rikssjukvårdsuppdrag*

Deafness is in most cases related to dysfunctioning or absent hair cells and most deaf patients have a normal anatomy of the inner ear. Some children born deaf have a cochlear malformation. In these cases special attention is required during surgery and speech and language training can be challenging. Since 2012 the Karolinska University Hospital is responsible for assessment, surgery and initial follow-up of all children in Sweden with a cochlear malformation (*Rikssjukvårdsuppdrag*).

(Right) The pictures show 3D-reconstruction(s) of Magnetic Resonance Images of the inner ear of a child with x-linked malformation. The white twisted structures on both sides are the cystic malformed cochleae with its unusually wide opening to the internal auditory canal.



*Cochlear perilymphatic space in white*



*Magnetic resonance image*



*Bilateral cystic malformation*



## WORDS MAKE A DIFFERENCE – a research program that examines the spoken language environment in young children

The prerequisites of listening and spoken language milestones change when a child is born with a hearing impairment (HI). The research program “Words make a difference” aims to explore the listening and spoken language environment in children aged 0–48 months, with and without HI and its possible effects on language, listening, cognitive and socioemotional development. The national research team is based at the Cochlear Implant Section (KI) in collaboration with international profile partners in Norway, Croatia, Italy and England.

A child performing play audiometry





## LENA – a new and Innovative research instrument

([www.lenafoundation.org](http://www.lenafoundation.org))

Language Environmental Analysis (LENA) – “a pedometer of words”, is an objective measurement instrument, with software that can distinguish between different audio-verbal communication parameters, e.g. automatically count the number of audio-verbal turns between a child and caregivers, number of child utterances and the number of adult words, during a whole recording day (12–16 hours), from the child's everyday environment. LENA also measures which kind of auditory environment the child was exposed to like silence, electronic sounds (iPad/TV), noise, speech close to the child (meaningful) and speech at a distance.

LENA is used in research and clinical work with norms in American English, and is so far also validated in Mandarin, Spanish and French, and soon also in Swedish. LENA will evaluate the spoken language environment of 0–48 month old children with HI and in comparison to age-matched children with normal hearing.





## Measurement of balance in small children

The balance organ, the posterior part of the inner ear, adjusts the muscle activity in response of balance stimulations. It can react even to loud sounds or skull vibrations. A clinical application, VEMP (Vestibular Evoked Myogenic Potential), evaluates the balance organ function by recording the neck muscles responses induced by sounds and vibrations. We have adapted the VEMP in a child friendly procedure to be applied in small children. We are studying the VEMP as a screening test for motor development delays due to balance organ failure, to address early habilitation.



Eye tracking lab/  
CI-section.

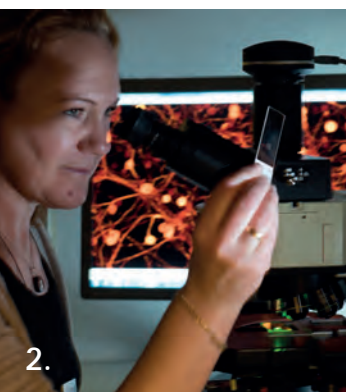
## What you see is where you hear – Eye-tracking for sound localization

Most daily sounds reach the left and right ear with subtle differences in time, and with different intensity. These interaural differences are subcortically processed, allowing humans to identify sound locations with accuracy. At Karolinska University Hospital, we study the effects of hearing loss on this remarkable ability and its development. The picture illustrates our recently developed setup—allowing analyses of sound localization from 6 months of age—based on an eye-tracking technique.

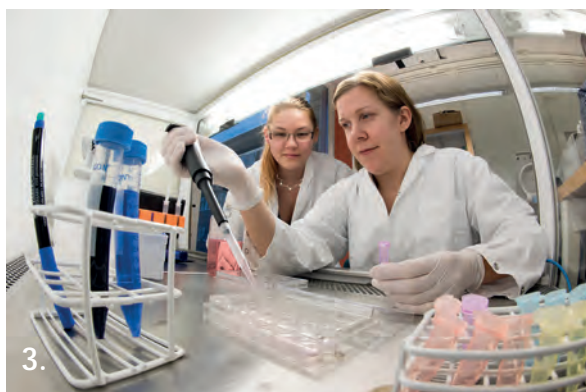




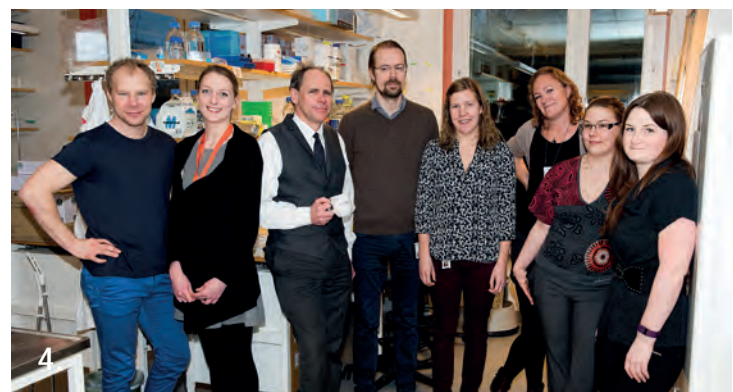
1.



2.



3.



4.

### The ENT Airway Inflammation Group

The group lead by professor Cardell, studies inflammation in: 1) Rhinitis and Asthma and 2) Head and Neck cancer. Inflammation is a key feature of both allergic and non-allergic rhinitis, nasal polyposis, asthma and epithelial derived cancer in the head and neck region. The mediators involved appear to be the same even though their profiles vary depending on the diseases involved.

1. Functional studies of freshly isolated airways from patients can be used to test and develop new medicines for allergy and asthma.

2. Microscopic visualization of nerve cell interaction unlocks the mysteries of neuro-immunology (how nerve signaling affects our immune system).

3. Biopsies and cell samples from patients obtained in the clinic are immediately processed in the lab in order to characterize diseases and the mechanisms involved in their origin.

4. The laboratory crew at Solna Campus (Eric Hjalmarsson Lab. Ing. Olivia Larsson PostDoc, Prof. Lars Olaf Cardell, Valtteri Häyry PostDoc, Lotta Tengroth PhD student, Susanna Kumlien Georén PhD Senior Lab Manager, Cecilia Draskog Msc, Sandra Ekstedt PhD Student).





### Treatment of Bell's palsy sequelae is a challenge – a multiprofessional team means success

Bell's palsy is a relatively common acute unilateral weakness or paralysis of the face of unknown cause. It occurs more often in the age group 15 to 45 years. Seventy percent of patients will recover completely within 6 months without treatment. A big Nordic study (ENT/KI participated) showed that treatment with corticosteroid, within 75 hours of debut, shortens time to recovery and improves recovery rates. Viruses seem to be involved in the etiology, but antiviral treatment has no effect.

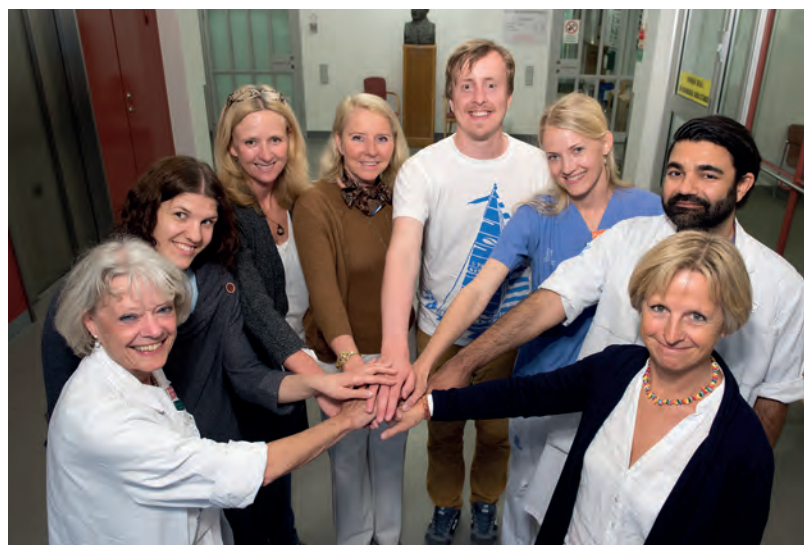
### Surgery followed by physiotherapy

*The more severe problems have to be solved by cross-facial nerve graft surgery and various kinds of static surgery to reduce synkinesis. Fysiotherapy is added to the surgical treatment.*

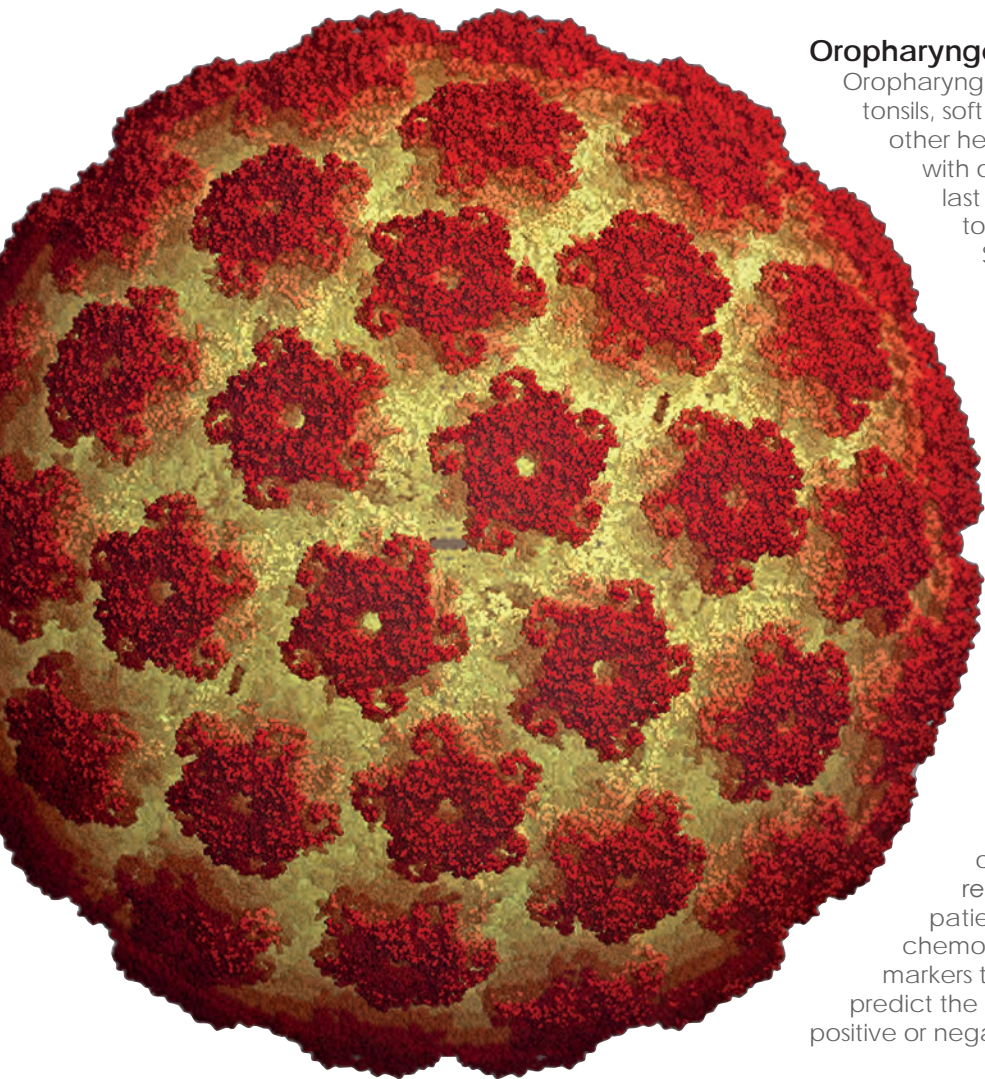
### Incapacitating symptoms

*If not recovered the affected persons will suffer from mild to severe sequelae like; absent capacity to move the mimetic muscles of one side of the face, difficulties closing the eye, running tears, problems eating and speech difficulties, muscle atrophy with contractures and synkinises (involuntary movements), cosmetic problems and psychological trouble.*

*(Below) The seriously affected patients need multiprofessional care-taking. A network of specialists is created around these patients; ENT and plastic surgeons, physiotherapists and speech therapists. Combined with an extensive research program, which will answer many questions and provide international guidelines for handling patients with Bell's palsy.*







Oropharyngeal cancer is increasing

Oropharyngeal cancer includes cancer of the base of the tongue, tonsils, soft palate and pharyngeal walls. In contrast to most other head and neck malignances the number of new patients with oropharyngeal cancer have markedly increased the last decades in Sweden. Together with malignant melanoma, tonsillar cancer has escalated most of all tumor types in Sweden. We have reported almost a doubling in the incidence of HPV-positive tumors per decade 1970-2007, and at a nationwide setting the incidence is continuing to rise.

Human papillomavirus caused tonsillar cancer:  
An epidemic of viral induced carcinoma?

Cancer in the head and neck region comprises 3-4% of all cancer cases in Sweden. Well known risk factors for head and neck cancer are tobacco usage and alcohol consumption. Although, during the past two decades human papilloma virus (HPV) has been recognized as a risk factor for the development of oropharyngeal cancer, which together with malignant melanoma is the tumor type that has increased the most the last decades in Sweden.

Future challenges

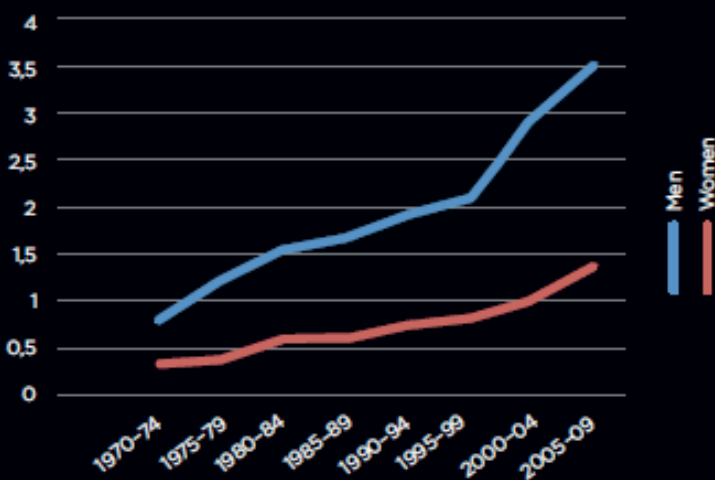
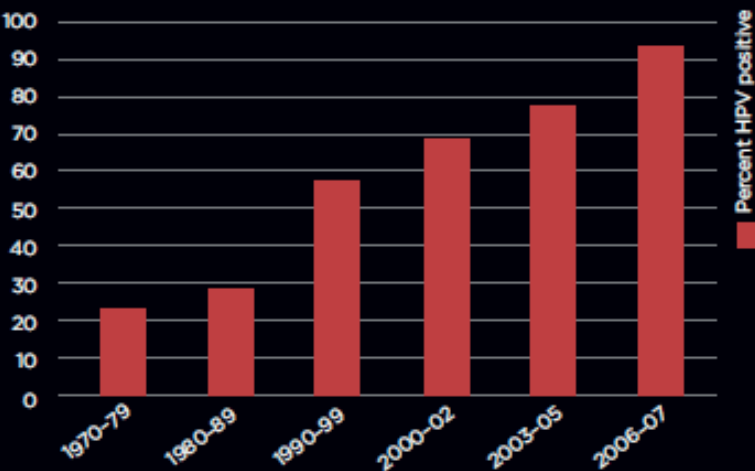
Patients with HPV positive oropharyngeal cancer have a significantly better survival than HPV negative oropharyngeal cancer. However a few patients respond poorly to treatment. A challenge is to find those patients with poor prognosis who will need intense chemotherapy. We have found a number of tumor markers that can distinguish them and created a model to predict the outcome. Another question is the predictive value of HPV positive or negative metastases.

Increased presence/prevalence of HPV  
in oropharyngeal cancer in Sweden

The prevalence of HPV in tonsillar cancer has increased dramatically in Stockholm over the latest decades, from 23% in the 1970s to today where over 80% of all tonsillar cancers are caused by HPV. This represent a sevenfold increase since the 1970s.

Incidence of oropharyngeal  
cancer in Sweden

Source Socialstyrelsen



## Head and neck cancer immunology

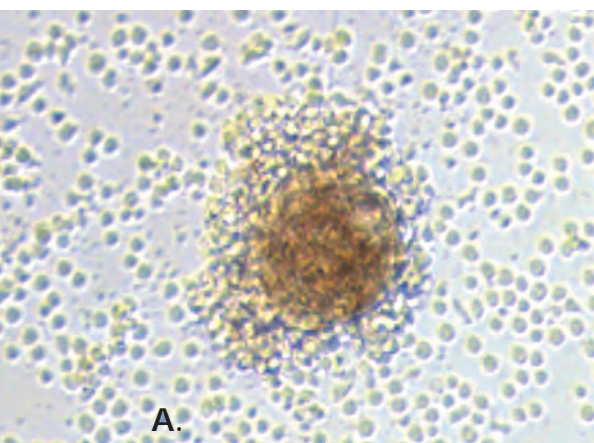
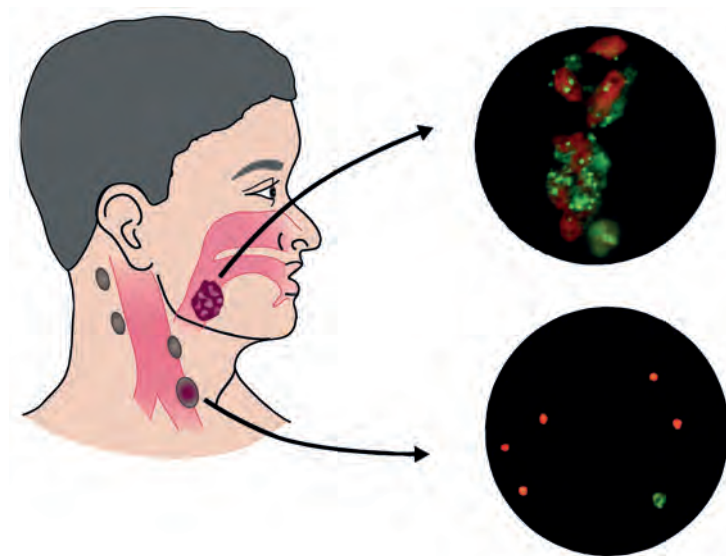
Loco-regional relapse and metastases are the most important reasons why head & neck cancer patients are not cured. The body's own immune system can destroy cancerous cells and prevent relapse, it could be directed and supported by immunotherapy.

### Metastatic cancer cells in the tongue

Metastatic cancer cells seeding from a primary tumor located in the tongue can be found in those lymph nodes

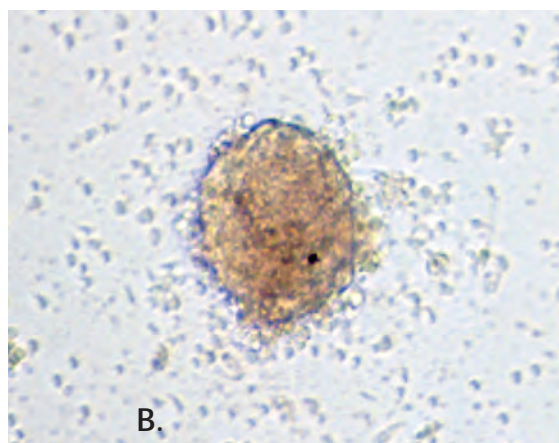
that drain the tongue in small numbers before a clinical metastasis is evident.

■ = lymphocyte  
■ = tumor cell



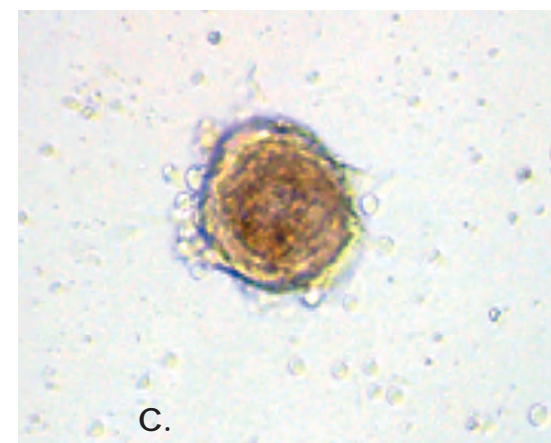
A.

Cancer cells cultured as 3-dimensional spheroids ("globes, balls") are exposed to lymphocytes:



B.

A. Lymphocytes from a healthy person rapidly attack and destroy the malignant cells.



C.

B. Lymphocytes from a tumor draining lymph node already previously exposed to tumor

proteins can mount a relatively strong reaction against the tumor spheroid.

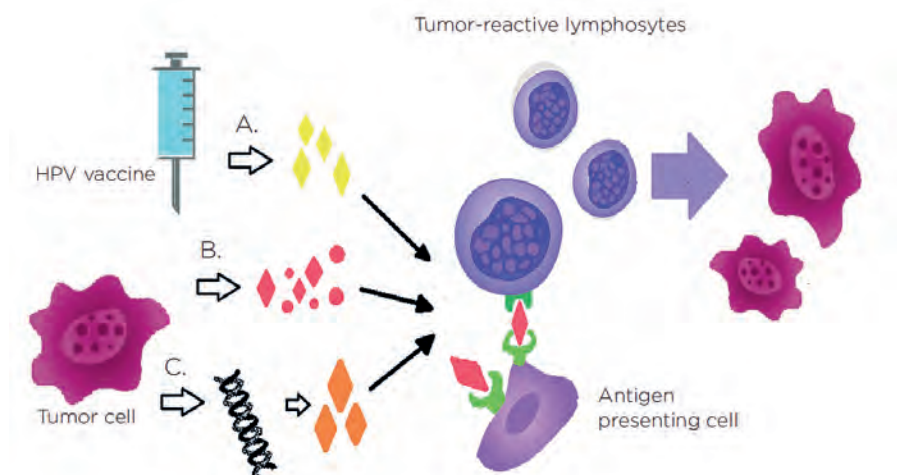
C. Unprepared lymphocytes from the cancer patient do not recognize the tumor and leave it undisturbed.

### Three possible means to enhance the anti-tumor immune response:

A. In human papilloma induced tumors (HPV+) vaccination with viral peptide.

B. Stimulating the immune system directly with tumor derived protein extract.

C. Feeding antigen presenting cells with cancer-specific immunogenic mutated peptides.





## Breathing obstruction during sleep – dangerous to health

Obstructive sleep apnea syndrome (OSAS) is common (~10% of the population), and could be dangerous with increased morbidity (cardio-vascular diseases, impaired cognition), and even mortality.

The obstruction site is often the soft palate in adults, and tonsil hyperplasia in children. A research group of specialists in sleep medicine and in ENT has several ongoing randomized controlled trials on surgery for sleep apnea in children and in adults as well as collaboration studies with maxillofacial surgeons, Rehabilitation Medicine for chronic fatigue syndrome, the Stress Research Institute at Stockholm University among others.

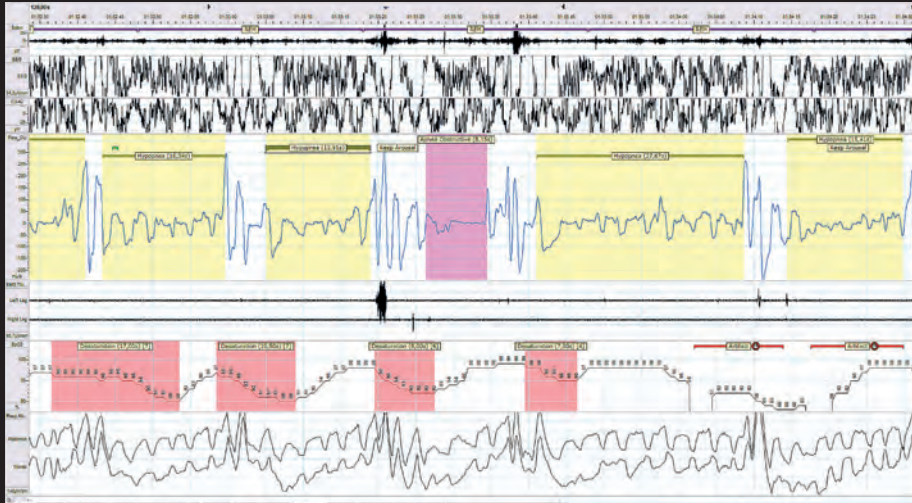
## The sleep laboratory

We investigate both children and adults with a capacity of more than 800 full-night, in-lab polysomnographies each year. This provides a unique possibility to perform high quality research in the field of sleep medicine, with focus on OSAS.



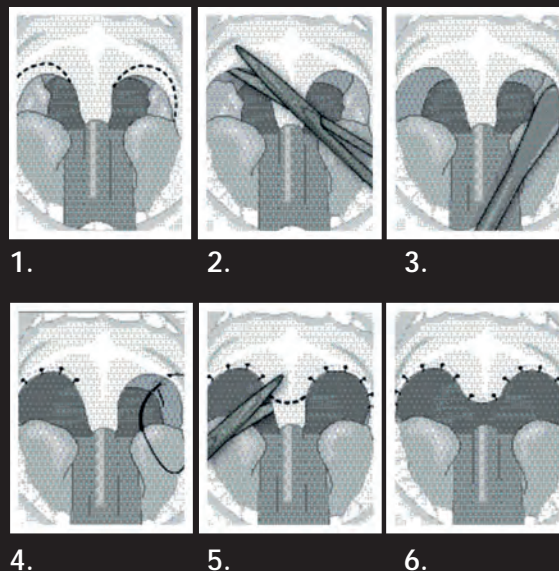
## Polysomnography

is the gold standard to diagnose OSAS (Left) This is an example of monitoring of a child with obstructed airways during Rapid-Eye-Movement, (dream) sleep, showing repetitive obstructive hypopneas, apneas and desaturations.



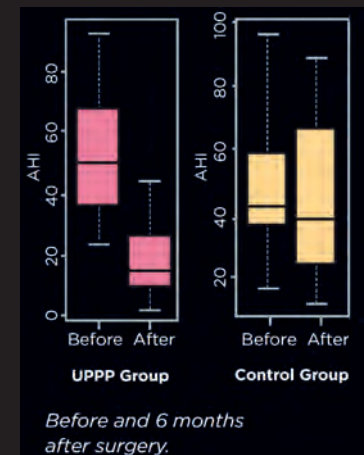
## Karolinska Uvulo-PalatoPharyngoPlasty (UPPP)

UPPP at Karolinska is a modification of earlier more aggressive techniques and vital tissues are preserved resulting in less side effects. It is performed during general anesthesia to treat OSAS in adults who do not tolerate non-surgical treatment (CPAP, dental device).



## Evidence based surgery

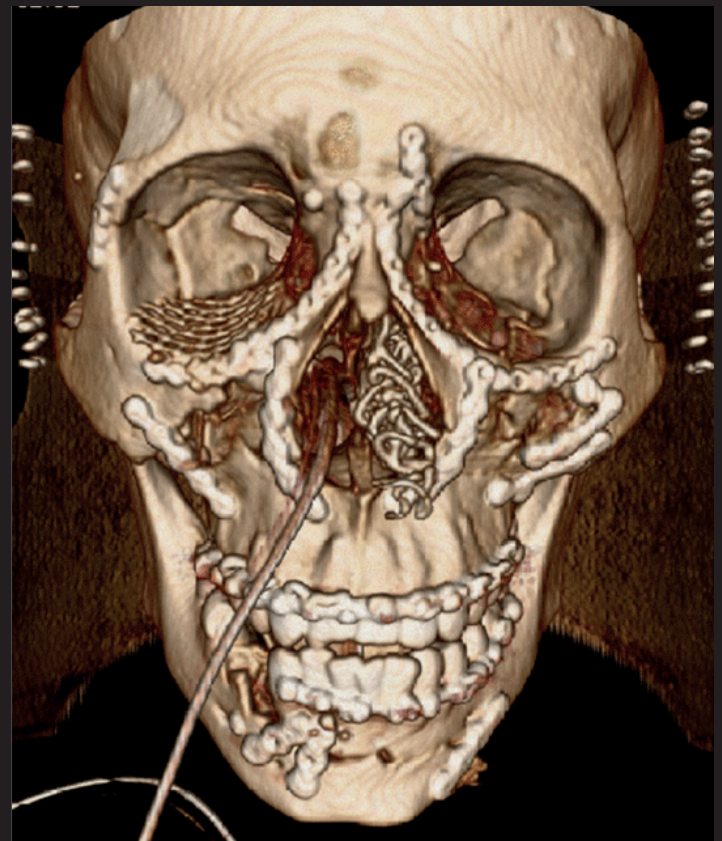
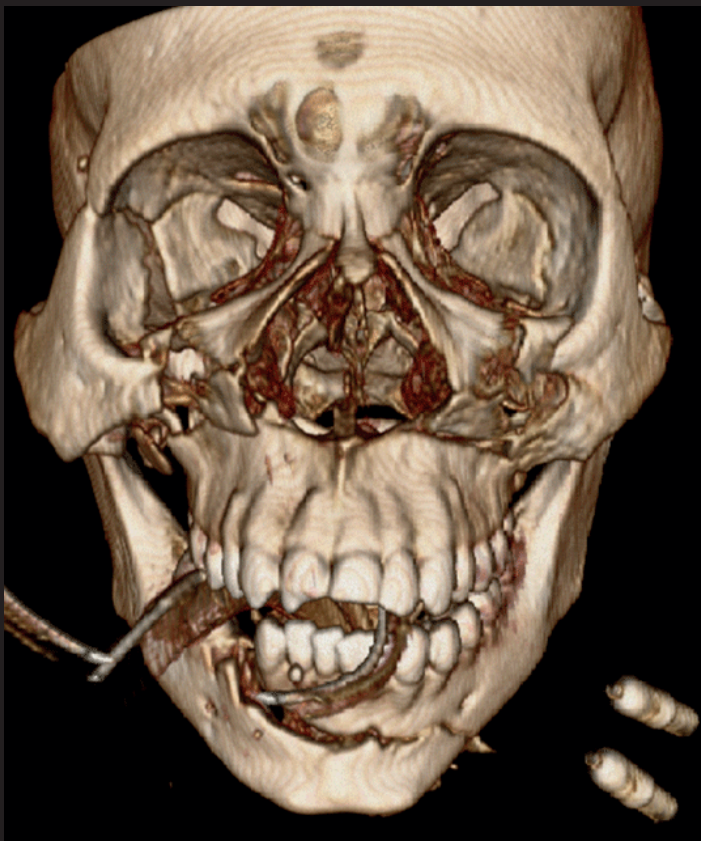
This is the first published randomised controlled trial comparing surgery (UPPP) with an untreated control group, in 65 adults with moderate to severe OSAS. The results show a highly significant and clinically relevant group difference in nocturnal respiration (AHI reduction), in favor of UPPP. With courtesy to Thorax, Browaldh et al 2013.



### Evidence-based treatment of facial fractures

About 500 patients with facial trauma are treated at Karolinska University hospital every year. Early assessment of the significance of the fracture and a decision on the type of treatment are crucial for an optimal result. Despite recommendations, there are considerable

differences in opinion regarding the management of facial trauma patients due to a lack of a reliable evidence. We are performing prospective studies in the management of facial trauma to offer an evidence based and reliable treatment for our patients.



Figures visualizing computed tomography scan of a patient with multiple fractures of the facial skeleton (A), and the result after open reduction and internal fixation of the fractures (B).





### **Botox for health**

Botox is most known for its use in the cosmetics industry, but has long before been used for different medical disorders with muscular overactivity, i.e. spasticity. The purified bacterial toxin decreases or inhibits the release and the uptake of acetylcholine with resulting distal denervation and subsequent reinnervation which explains the normal effect duration of 3 months. At that point the botox has left the body long since.

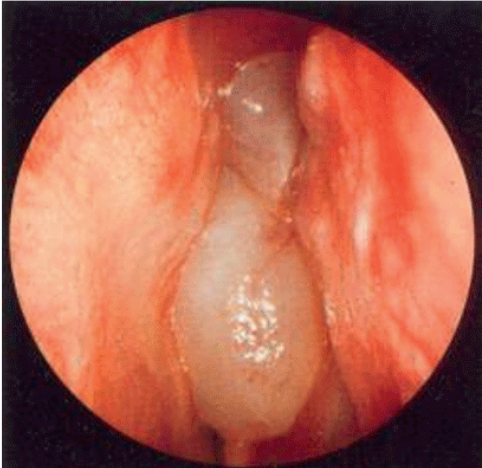
*The use of Botox in ENT includes injection treatment of spasmodic dysphonia, i.e. vocal cramps (picture), laryngeal dystonia, biting and mouth opening dystonia, bruxism, drooling, treatment of abnormal sweating after parotid surgery and treatment of heavy tension headaches.*

# Treating nasal polyps with an antibody

Chronic inflammation in the nose and sinuses with presence of nasal polyps (CRSwNP) is a rather prevalent disease affecting approximately 4 % of the population. Some patients present with a severe type of CRSwNP and their polyps recur despite frequent surgery.



Normal nostril



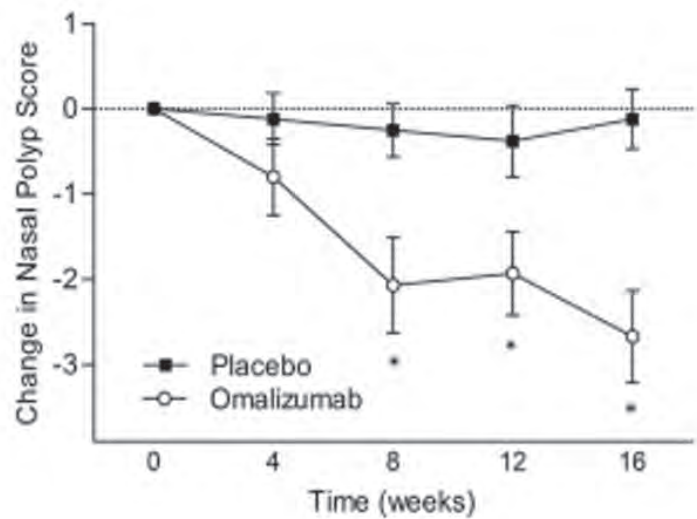
Nasal polyp obstructing the nostril

## A remarkable improvement

Currently a series of patients with severe CRSwNP\* are treated with a monoclonal antibody (Omalizumab), which reduces inflammatory mediators and is approved for treatment of severe asthma.

A remarkable improvement has been shown. The polyps disappear and the patients experience markedly improved symptoms. One patient, with 30 previous surgeries, has even had his smell returned for the

first time since the 70' and a 13 year old boy, who had recurrent polyps a few weeks after surgery, is now free of polyps and symptoms. The new medication is expensive, but we will continue to expand this treatment at the clinic.



Change in total nasal polyp score from baseline  
In placebo group and Omalizumab group

\* CRSwNP = Chronic Rhinosinusitis with Nasal Polyps





From left: Susanna Kumlien Georén, Nele de Klerk, Åsa Kågedal, Julia Arebro, Eric Hjalmarsson, Lars Olaf Cardell, Olivia Larsson, Sandra Ekstedt, Cecilia Drakskog, Laila Hellkvist, Lotta Tengroth, Karin Jonstam

#### Five most valuable publications from the research group 2014-2017

1. Arebro J, Tengroth L, Razavi R, Kumlien Georén S, Winqvist O, Cardell LO. Antigen-presenting epithelial cells can play a pivotal role in airway allergy. *J Allergy Clin Immunol* (IF: 12.5), 2016;137:957-60.e7.
2. Larsson O, Tengroth L, Xu, Y, Uddman R, Kumlien-Georén S, Cardell LO. Substance P represents a novel first-line defense mechanism in the nose. *J Allergy Clin Immunol*. (IF: 12.5), 2017;S0091-6749(17)30241-5.
3. Arebro J, Ekstedt S, Hjalmarsson E, Winqvist O, Kumlien Georén S, Cardell LO. A possible role for neutrophils in allergic rhinitis revealed after cellular subclassification. *Sci Rep*. (IF: 5.2), 2017;7:43568.
4. Häyry V, Kågedal Å, Hjalmarsson E, Farrajota Neves da Silva P, Drakskog C, Margolin G, Georen S, Munck-Wikland E, Winqvist O, Cardell LO. Nodal staging of neck dissection specimens with flow-cytometry. *Br J Cancer*. (IF: 6.2) 2017 Nov 21. doi: 10.1038/bjc.2017.408.
5. Westman M, Stjärne P, Bergström A, Kull I, Toskala E, Cardell LO, Wickman M, Holmström M. Chronic rhinosinusitis is rare but bothersome in adolescents from a Swedish population-based cohort. *J Allergy Clin Immunol* (IF: 12.5), 2015;S0091-6749(15)00268-7.

The Role of Inflammation in; 1) Airways 2) Head and Neck cancer

*Lars Olaf Cardell, Professor and Head of the Division*

Inflammation is a key feature of allergic rhinitis, nasal polyposis, asthma and epithelial derived cancer in the head and neck region. The mediators involved appear to be the same even though their profile varies depending on the diseases involved. Hence, a similar methodological approach could be used regardless of the specific nature of the disorder. Our group has an ambitious agenda focusing on the dissection of the immunologic mechanisms behind the origin and development of these diseases with a primary goal of finding prognostic markers for disease development as well as future therapeutic targets.

<p><b>Julia Arebro</b>, MD. PhD , Specialist in ENT</p> <p>This project investigates whether the sentinel node can be identified in patients with head and neck malignant melanoma, if melanocytes in lymph nodes can be identified with flow cytometry and what immunological pattern the sentinel nodes show. In the long run, we aim to determine what impact these metastases and eventual immunological responses have on the prognosis of the individual patient.</p>	<p><b>Mats Holmström</b>, MD, PhD, Specialist in ENT</p> <p>Dr Holmström supervises PhD-student S Moren, Uppsala Univ. in a project entitled Nasal aspects on unilateral Cleft-, Lip- and Palate. He is the co-supervisor of other PhD students, in the area of sleep apnea syndrome and children with chronic rhinosinusitis. Together with another PhD student from Uppsala, C Bengtsson, the correlation between compliance and nasal function during CPAP is evaluated.</p>	<p><b>Valtteri Häyry</b>, MD. PhD , Specialist in ENT</p> <p>This project is centered around lymph node metastases of head and neck carcinoma (HNSCC). We have developed a new method for the detection of metastatic deposits in cervical lymph nodes, and are constructing a multiparametric method to evaluate the immunological tumor response in patients and <i>in vitro</i> that could be applied in the treatment of HNSCC with immune checkpoint inhibitors.</p>	<p><b>Susanna Kumlien Georén</b>, PhD, Senior Lab Manager</p> <p>The nature of the interaction between the innate and the adaptive parts of the immune system in disease development is still partly unknown. We are in this translational project, involving primary cell cultures, <i>in vivo</i> and <i>in vitro</i> models and patients, focused on the role of innate cells, Toll and NOD-like receptors in allergy, rhinitis, asthma and head and neck cancer.</p>
<p><b>Olivia Larsson</b>, PhD, Assistant Professor</p> <p>The concept of neuro-genic inflammation was described in the 1980s, but has since been hard to demonstrate in humans. The overall goal of the project is to identify a role for neuropeptides in allergic exacerbations, with focus on viral disease. In addition, the possible interaction between sensory nerve signalling and neutrophil subset activity will be studied.</p>	<p><b>Petter Olsson</b>, MD. PhD, Specialist in ENT, Associated Researcher</p> <p>Dr Olsson specializes in nasal and sinus disorders, with special interests in the epidemiology of non-allergic rhinitis, the medical and surgical management of chronic rhinosinusitis with or without nasal polyps, the relation between upper and lower airway disease and more recently, health economy in sino-nasal disease. He is currently an associated researcher at the Division.</p>	<p><b>Marit Westman</b>, PhD, M.D. Specialist in ENT-diseases</p> <p>Allergic rhinitis and chronic rhinosinusitis are two of the most common chronic diseases in the population and are often associated with asthma. Prediction of disease severity and prognosis is essential for decision on treatment, such as allergen immunotherapy or monoclonal antibodies. We study possible predictive biomarkers for these diseases in both population based and patient material.</p>	



**Sandra Ekstedt***PhD-student*

Previous studies have focused on eosinophils as the main contributors to allergic asthma with less attention given to neutrophils. This project introduces a new concept for neutrophils, one that includes a primary role for a specific, active subset of neutrophils. It conjures a translational approach including bronchial provocation, *in vitro* analysis and *in vivo* animal experiments.

**Eric Hjalmarsson***PhD-student*

This project investigates how intra lymphatic immunotherapy (ILIT) induces tolerance in grass and birch allergic patients. Fine needle aspirates from the allergen injected lymph node are analysed along with samples from peripheral blood and brush samples from nasal mucosa. The immunological analyses are mainly focused on B and T-cell differentiation.

**Åsa Kågedal***MD, PhD-student*

Cancer Immunology is a fast-developing field of research. Our use of flow cytometry to investigate the metastatic status of the lymph nodes shortens the time to diagnosis. It will also provide new information about the immunological status of the cancer, with a special focus on sentinel nodes, something that, might provide a better guide for future treatment decisions.

**Laila Hellkvist***MD, Specialist in ENT, PhD-student*

Intralymphatic immunotherapy for allergic rhinitis is proposed as a safer and faster alternative to conventional subcutaneous administration. The safety and clinical effects of this therapy is evaluated in a series of clinical trials. Markers predicting a successful outcome are assessed by collecting samples from nasal mucosa, blood and lymph node tissue for immunological investigations.

**Karin Jonstam***MD, PhD-student*

This project is designed to further determine the inflammatory pathophysiology of chronic rhinosinusitis with and without nasal polyps. This includes the identification of potential biomarkers for endotyping, investigation of the role ALK-receptors and neutrophins and development of novel treatments as well as different surgical approaches.

**Magnus Starkhammar***MD, PhD-student*

Respiratory tract infections are a common cause for acute asthma exacerbations. The overall aim of this project is to analyze the role of Toll-like receptors (TLRs) in the development of local airway hyperresponsiveness (AHR). TLRs with an ability to identify viruses are investigated in an *in vivo* mouse model, where the AHR and the inflammatory response are used as read outs.

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**Claus Bachert**

*Professor in ENT in Ghent, MD., Associated Researcher*

Dr Bachert is heading a project centered around inflammatory pathophysiology of chronic rhinosinusitis (CRS). This includes the identification of potential biomarkers for endotyping and evolution of novel treatments as well as different surgical approaches. He is also involved in several other ongoing CRS related project at the ENT div. at KI.

**Antti Mäkitie**

*M.D., Ph.D. Affiliated Researcher*

We have established research collaboration between KI and Univ. of Helsinki in Head and Neck Cancer focusing on epidemiological, clinical outcome and translational studies. The aim is to provide clinical and molecular prognostic and predictive markers for the management as well as to unify their treatment protocols. Hospital and national registry-based data as well tumour specimens are applied.



**Valtteri Häyry, MD. PhD , Specialist in ENT**  
and

**Antti Mäkitie, M.D., Ph.D. Affiliated Researcher**

*Research nurses*

**Anna Drevland** and **Agneta Karlsson**  
examine a patient together with  
Bo Tideholm.





*From left in the back: Gregory Margolin; Eva Munck-Wikland, Alexandra Elliot, Björn Palmgren, David Landin, Daniel Danielsson  
From left in front: Rusana Bark, Linda Marklund, Lalle Hammarstedt Nordenvall, Andrea Vlastos*

### Five most valuable publications from the research group 2014-2017

1. Wendt M, Romanitan M, Näsman A, Dalianis T, Hammarstedt L, Marklund L, Ramqvist T, Munck-Wikland E. Presence of human papillomaviruses and p16 expression in hypopharyngeal cancer. *Head and Neck* Jan;36(1):107-12, 2014.
2. Danielsson D, Brehwens K, Halle M, Marczyk M, Sollazzo A, Polanska J, Munck-Wikland E, Wojcik A, Haghdoost S. Influence of genetic background and stress response on risk of mandibular osteoradionecrosis after radiotherapy of head and neck cancer. *Head&Neck* Oct 28. Doi:10.1002/hed.23903, 2014.
3. Sivars L, Landin D, Haegglblom L, Tetipis N, Grün N, Bersani C, Marklund L, Ghaderi M, Näsman A, Ramqvist T, Nordfors C, Munck-Wikland E, Tani E, Dalianis T. Human papillomavirus DNA detection in fine-needle aspirates as indicator of human papillomavirus-positive oropharyngeal squamous cell carcinoma: A prospective study. *Head Neck* 2016 Nov 29. Doi:10.1002/hed.24641
4. Wangsa D, Chowdhry SA, Ryott M, Gertz EM, Elmberger G, Auer G, Åvall Lundqvist E, Kuffer S, Ströbel P, Schäffer AA, Schwartz R, Munck-Wikland E, Ried T, Hesselmeier-Haddad K. Phylogenetic analysis of multiple FISH markers in oral tongue squamous cell carcinoma suggests that a diverse distribution of copy number changes is associated with poor prognosis. *Int J Cancer* Jan 1;138(1):98-109, 2016.
5. Bersani C, Sivars L, Haegglblom L, DiLorenzo S, Mints M, Ährlund-Richter A, Tertipis N., Munck-Wikland E, Näsman A, Ramqvist T, Dalianis T. Targeted sequencing of tonsillar and base of tongue cancer and human papillomavirus positive unknown primary of the head and neck reveals prognostic effects of mutated FGFR3. *Oncotarget* May 23;8(21): 35339-35350, 2017

## Head and Neck Cancer

**Eva Munck-Wikland**, *Affiliated Professor, Senior Consultant*

Already in 1994 we found HPV-DNA in tonsillar cancer and then demonstrated a striking increase in tonsillar and base of tongue cancer incidence due to HPV as well as the important favorable impact HPV has on prognosis.

Head and neck cancer incidence and certainly the proportion of survivors are increasing why quality of life after treatment has become very important. The ambition to provide more effective and intensified treatment is now balanced by a need for personalized treatment in order to not overtreat with life long severe side effects. We continue to identify clinically useful predictive and prognostic markers for head and neck cancer.

Osteoradionecrosis is a late complication after radiotherapy in 3-15% of all head and neck cancer treated patients. Symptoms include disabelling pain, trismus, infections, impaired nutrition, oro-cutaneous fistulas and fractures of the mandible. We have identified 8-oxo-dG and single-nucleotide polymorphism rs1695 in glutathion s-transferase p1 as risk markers for ORN. We prospectively study QOL in patients who have been treated with mandibular microvascular reconstruction after osteoradionecrosis.

**Rusana Bark**  
*PhD, Senior Consultant*

- The risk for regional metastasis in patients with gingival cancer (2000-2016) in relation to tumor size, localization (maxilla/mandible), T-class, histopathology.
- Retrospective study on the prevalence of cystic metastases in patients who had undergone surgery for lateral branchial cleft cyst at Karolinska between 2003-2017.
- Longitudinal prospective study of the hearing in women with breast cancer.

**Caroline Gahm**  
*MD, PhD, Senior Consultant*

- The impact of irradiation on acute and long-term changes in human blood vessels and skin in paired biopsies from all previously irradiated patients who underwent head and neck cancer surgery reconstruction with free autolog tissue transplantation at the Karolinska University Hospital since 2004
- Study underlying mechanisms of irradiation-induced changes in blood vessels and skin using an interventional experimental mouse model
- To validate the sentinel node technique in parotid cancer
- To validate a histopathological risk model for patients with parotid cancer.

**Lalle Hammarstedt Nordenvall**, *MD, PhD, Senior Consultant*

- Tumor budding and thickness in oral cancer to predict the risk of local recurrence and regional disease.
- To validate the sentinel node technique in oral cancer.
- Nasopharyngeal cancer, epidemiological aspects and association to EBV and HPV.
- HPV prevalence and its effect on outcome in patients with non tonsillar, non base of tongue cancer of the oropharynx.
- To validate a histopathological risk model for patients with oropharyngeal cancer.

**Linda Marklund**  
*MD, PhD, Senior Consultant*

Linda Marklund has for many years focused her research on prognostic markers in Head and Neck cancer in order to optimize and individualize treatment for the patients. Special focus has been on the HPV-positive oropharyngeal tumors the later years. Linda is also co-supervisor to 3 ongoing PhD projects.



**Daniel Danielsson**  
*PhD-student, Head of Patient flow, Craniofacial Diseases*

Main research interest is adverse effects after irradiation due to head and neck cancer. Current focus areas include detection of biomarkers for individual radiosensitivity and prospective quality of life analysis for patients treated with mandibular microvascular reconstruction after grade III osteoradionecrosis.

**David Landin**  
*MD, PhD-student*

Does Human papillomavirus (HPV) analysis safely distinguish branchial cleft cysts from cystic metastases? To distinguish branchial cleft cysts from cystic metastases can be challenging. Today, many centers oncologically treat cystic lesions on the basis of cytology results only, with the support of HPV positivity and thus many patients are spared neck dissection. In order to do so safely we need to investigate whether HPV DNA and p16 protein expression can be found exclusively in cystic metastasis and not in branchial cleft cysts.

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**Malin Wendt**  
*MD, PhD-student, Senior Consultant*

Benign cysts in the head and neck area such as ranulas and branchial cleft cysts are traditionally treated with surgery. A less harmful method that is used treating other cystic lesions is sclerotherapy with OK 432. To evaluate this treatment as an alternative to surgery also for benign cysts in the head and neck area we are running a prospective, randomized, double-blinded placebo-controlled study.





Babak Alinasab, Ola Fridman Bengtsson, Pär Stjärne

#### Five most valuable publications from the research group 2014-2017

1. Schollin Ask L, Hultman Dennison S, Stjärne P, Granath A, Srivastava S, Eriksson M, Lindstrand A, Ryd Rinder M. Most preschool children hospitalised for acute rhinosinusitis had orbital complications, more common in the youngest and among boys. *Acta Paediatr.* 2017 Feb;106(2):268-273.
2. Alinasab B, Qureshi AR, Stjärne P. Prospective study on ocular motility limitation due to orbital muscle entrapment or impingement associated with orbital wall fracture. *Injury.* 2017 Jul;48(7):1408-1416.
3. Elliot A, Marklund L, Håkansson N, Song H, Ye W, Stjärne P, Hammarstedt-Nordenvall L. Incidence of IP and risk of malignant transformation in the Swedish population 1960-2010. *Eur Arch Otorhinolaryngol.* 2017 Mar;274(3):1445-1448.
4. Elliot A, Jangard M, Marklund L, Håkansson N, Dickman P, Hammarstedt-Nordenvall L, Stjärne P. Sinonasal malignancies in Sweden 1960-2010; a nationwide study of the Swedish population. *Rhinology.* 2015 Mar;53(1):75-80.
5. Westman M, Stjärne P, Bergström A, Kull I, Toskala E, Cardell LO, Wickman M, Holmström M. Chronic rhinosinusitis is rare but bothersome in adolescents from a Swedish population-based cohort. *J Allergy Clin Immunol.* 2015 Aug;136(2):512-4.



## Upper Airway Inflammation, Skull Base, Sino-Nasal Tumours, Facial Fractures

**Pär Stjärne**, MD/PhD, Professor, Senior Consultant

The research group has three main areas of interest:

1. Inflammation in the upper respiratory tract; mechanistic mapping and evaluation of medical and surgical intervention. The project contains two parts:
  - Studies of mechanisms in pregnancy rhinitis and its effect on the pregnant woman's quality of life.
  - Epidemiological studies on acute rhinosinusitis in children.
 The overall objective is to understand the basic epidemiology and mechanisms and to improve the treatment of these patient groups.
2. Zygomatic and orbital blow out fractures; diagnosis and evaluation of treatment. The project includes both retrospective studies and prospective randomized trials and aims to improve the management of patients with facial fractures.
3. Studies of sinonasal tumors and pituitary adenomas: We have created an interdisciplinary network that aims to study sinonasal tumors and pituitary adenomas. The network, which covers most aspects from "bench to bedside", has all prerequisites to get powerful synergies both in terms of basic knowledge about the tumors as well as clinical treatment.

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**Babak Alinasab**  
MD/PhD

Orbital Blow Out Fracture (BOF). To operate or not to operate – that is the question. When deciding whether to operate or not on a BOF, it is important to recognize that a surgical indication upon functional impairment is limited to muscle motility restriction. Regarding the decision making around surgical treatment due to aesthetic deformities, patient's involvement is crucial since the patient's experience of the importance of facial asymmetry is individual.

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**Ann Abrahamsson**  
MD, PhD-student

Local inflammatory parameters in women with pregnancy rhinitis. The cause of pregnancy rhinitis is not known. It is also not known to what degree the pregnancy rhinitis affects the pregnant woman. Furthermore, the incidence of OSAS among pregnant women with and without pregnancy rhinitis is unknown. In order to find answers to these questions we have studied 40 healthy pregnant women with and without pregnancy rhinitis.

**Alexandra Elliot**  
MD, PhD-student

Inverted papilloma (IP); Incidence, etiology and prognosis. The aim of this project is to increase the knowledge about IP, a benign tumour of the sino-nasal mucosa; What is the incidence and risk of malignant transformation? Is HPV involved in the pathogenesis? Does the host immunity have an impact on the pathogenesis? The studies are epidemiological and experimental (using immuno-histo-chemistry and PCR). We collaborate with Tumor and Virological lab at KI (CCK).

**Ola Fridman Bengtsson**  
MD, PhD-student

Pituitary Adenomas – Clinical aspects of treatment and expression of galanin and pattern recognition receptors. The project consists of clinical evaluation of patients undergoing surgery for pituitary adenomas as well as preclinical studies aimed at analysing different mechanisms that influence tumor pathophysiology, which affects clinically important aspects such as tumor biology and recurrence by studying various receptors in adenomas as compared to healthy pituitary tissue.

**Sofia Hultman Dennison**  
MD, PhD-student

Complications of rhinosinusitis in children. The aim of the project is to study all children up to 18 years old with complications due to acute rhinosinusitis in Stockholm County to get a better understanding of which children are at risk of developing such complications and how we can predict and avoid these complications. Another goal is to study the impact on complications after the introduction of pneumococcal vaccine in Stockholm County.





From left in front: Pia Froissart Nerfeldt, Anna Borgström, Nanna Browaldh, Danielle Friberg  
From left in the back: Joar Sundman, Gert Henriksson, Johan Fehrm

### Five most valuable publications from the research group 2014-2017

1. Browaldh N, Nerfeldt P, Lysdahl M, Bring J, Friberg D. SKUP3 randomised controlled trial: polysomnographic results after uvulopalatopharyngoplasty in selected patients with obstructive sleep apnoea. *Thorax* 2013 Sep;68(9):846-53. doi: 10.1136/thoraxjnl-2012-202610
2. Sundman J, Friberg D, Lowden A, Bring J, Nagai R, Browaldh N. Sleep quality after modified uvulopalatopharyngoplasty: Results from the SKUP3 randomized controlled trial. *Sleep*. Accepted for publication, Sleep October 2017.
3. Fehrm J, Friberg D, Bring J, Browaldh N. Blood pressure after modified uvulopalatopharyngoplasty: results from the SKUP3 randomized controlled trial. *Sleep Med*. 2017 Jun;34:156-161
4. Borgström A, Nerfeldt P, Friberg D. Adenotonsillotomy vs Adenotonsillectomy in pediatric obstructive sleep apnea – a randomized clinical trial reporting polysomnographic data. *Pediatrics* 2017;139(4):e20163314
5. Borgström A, Nerfeldt P, Friberg D, Sunnergren O, Stalfors J. Trends and changes in paediatric tonsil surgery in Sweden 1987- 2013: a population-based cohort study. *BMJ Open*. 2017 doi: 10.1136/bmjopen-2016-013346

## Surgical treatment of obstructive sleep apnea (OSA) and lower respiratory tract stenosis

**Pia Froissart Nerfeldt**, MD, PhD, Senior Consultant, ENT-specialist and Sleep-specialist

We evaluate the treatment effect of stents in the lower airway with spirometry and quality of life questionnaires.

Further, the group has research in surgical treatment of obstructive sleep apnea (OSA) in adults and children. We perform epidemiological studies concerning tonsil surgery in Sweden. The group run five randomized controlled trials (RCT), by evaluating the patients at the ENT-clinic's sleep lab with full night polysomnography (PSG).

The main focus for adult OSA is to evaluate uvulopalatopharyngoplasty including tonsillectomy (UPPP), compared to expectancy, and to tonsillectomy.

In children, the main focus is to compare different techniques; adenotonsillotomy with adenotonsillectomy (ATE), ATE with additional suturing of the pillars (APP), and ATE compared to expectancy. Patients are evaluated with both objective and subjective parameters such as PSG findings, vigilance, daytime sleepiness, quality of life, blood pressure, inflammatory markers etc. Also, to evaluate surgical treatment of children with Down Syndrome and OSA.

### **Anna Borgström**

MD, PhD, Senior Consultant, ENT-specialist

The research project focuses on surgical treatment of pediatric obstructive sleep apnea (OSA), comparing total and subtotal tonsillectomy; i. e. tonsillectomy (TE) and tonsillotomy (TT). A group of 79 children with OSA have been randomized to TE or TT and several outcomes are compared between the groups, e.g. changes in polysomnographic variables. The aim is to improve treatment for childhood OSA.

### **Nanna Browaldh**

MD, PhD, Senior Consultant, ENT-specialist and Sleep-specialist

We studied uvulopalatopharyngoplasty for obstructive sleep apnea syndrome in adults in an RCT. Uvulopalatopharyngoplasty was effective in improving nocturnal respiration, daytime sleepiness, blood pressure and quality of life. Our results aim to improve the selection of patients for surgical treatment. We will also study the long-term results as well as side-effects of surgical treatment.

Co-worker within the research group:

### **Danielle Friberg**

MD, PhD, Senior Consultant, ENT-specialist and Sleep-specialist, Uppsala University.

Started the Sleep lab at the Karolinska ENT-clinic 2007.

Main Supervisor to 6 PhD students in the OSA group. Principal Investigator of the 5 randomized controlled studies in adults and children.

### **Gert Henriksson**

MD, PhD, Senior Consultant, ENT-specialist

In the first study we compare subjective and objective measurements before and after airway stenting because of malignant diseases obstructing the lung. In the second study we compare the same measurement before and after endoscopic surgery of significant subglottal stenosis. We want to point out the positive effects achieved by airway stents and our endoscopic operation on subglottal stenosis.

### **Johan Fehrm**

MD, PhD-student, ENT-resident

This project includes two RCTs in children. One evaluates if children with mild-moderate OSA benefit from ATE, the standard surgical treatment. The other evaluates if children with severe OSA are better treated with a modified ATE.

OSA is a risk factor for hypertension and change in blood pressure after UPPP in adult patients with OSA are evaluated.

### **Joar Sundman**

MD, PhD-student, ENT-resident

My thesis concerns obstructive sleep apnea and the evaluation of patient selection for surgical intervention, evaluation of subjective sleep quality after surgery, the long-term effect of surgery and also a randomized controlled trial assessing the efficacy of two different surgical methods for treating OSA, namely tonsillectomy and uvulopalatopharyngoplasty.



Malin Siegbahn, Hanna Josefsson, Malou Hultcrantz, Cecilia Engmér Berglin

### Five most valuable publications from the research group 2014-2017

1. Hultcrantz M, Lanis A. A five year follow-up on the osseointegration of bone-anchored hearing aid implantation without tissue reduction. *Otol Neurotol* 2014 Sep;35(8):1480-5. PMID: 24770406.
2. Johansson, M.L., Stokroos, R.J., Banga, R., Hol, M.K., Mylanus, E.A., Jones, H.S., Tysome, J.R., Vannucchi, P., Hof, J.R., Brunings, J.W., van Tongeren, J., Lutgert, R.W., Banerjee, A., Windfuhr, J.P., Caruso, A., Giannuzzi, A.L., Bordin, S., Hanif, J., Scharf-Morén, N., Singam, S., Cantus, C. Jonhede, S., Holmberg, M. Cremers, C.W., Hultcrantz, M. Short-term results from seventy-six patients receiving a bone anchored hearing implant installed with a novel minimally invasive surgery technique. *Clin Otolaryngol.* 2017 Oct;42(5):1043-1048. PMID: 27930877.
3. Moverare T, Hultcrantz M, Lohmander A, Sjögreen L. Peripheral facial palsy: Speech, communication and oral motor function. *European Annals of Otorhinolaryngology, Head and Neck diseases* 2017;134(1):27-31. PMID: 27836742.
4. Bylund N, Jansson D, Enghag S, Berg T, Marsk E, Hultcrantz M, Hadziosmanovic N, Rodriguez-Lorenz A, Jonsson L. Synkinesis in Bell's palsy in a randomised controlled trial. *Clin Otolaryngol.* 2017;42 (3): 673-680. PMID: 27882653.
5. Berglund M, Florentzon R, Fransson M, Hultcrantz M, Eriksson PO, Englund E, Westman E. Myringoplasty outcomes from the Swedish National Quality Register. *Laryngoscope* 2017 Apr 20. doi: 10.1002/lary.26523.

1. Single Sided Conductive Hearing Loss Associated with Ear Canal Atresia in Humans and in Experimental Animals. Use of bone anchored hearing aids.
2. Facial Palsy in Adults and Children.
3. A Swedish National Quality Register for Myringo- and Ossiculoplasty

**Malou Hultcrantz MD, PhD, Professor Emerita**

1. In patients born with single sided canal atresia, the central hearing pathways are described in humans using functional magnetic resonance imaging (fMRI, in co-operation with the Royal Technical High School). A comparable rat model is investigated in the same way. A new model for testing binaural hearing in humans has been implemented. Implantable hearing aids are the treatment of choice and a new device is under construction (Sahlgrenska Akademien/Chalmers, Gothenburg). (3 PhDs).
2. Patients with Bells palsy are investigated using a network of experts, including ENTs, plastic surgeons, pediatricians, ophthalmologists, physiotherapists and neurophysiologists. Patients with bad outcome are randomized to surgery/no surgery (cross facial surgery). A national project concerning Quality of Life in children is ongoing. (3 PhDs).
3. A National Quality Registry in Sweden includes patients having had an ear operation. The control group in Sweden is working to describe inclusion, outcome and complications. (1 PhD).

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**Åsa Bonnard**  
MD, PhD

In Turner Syndrome (an endocrine syndrome with loss of one X-chromosome) estrogen is missing and severe hearing problems follow. Ongoing projects look at hearing after estrogen loss in women after breast cancer treatment. Pendred's syndrome, also an endocrine syndrome, is connected to a severe inner ear malformation and children with these problems are followed and mapped.

**Cecilia Engmér Berglin**  
MD, PhD

Central auditory pathways in adults who have not been habilitated with BAHA and children who have, as well as in rats with experimental unilateral atresia, will be analysed using different modes of MRI. Conventional hearing tests, a new method for directional hearing, the eye reflex test and questionnaires for self or parent assessed hearing handicap will also be analysed in the human subjects.

**Elin Marsk**  
MD, PhD

Bell's palsy can cause disfigurement of the face, impair eating, drinking and speech, and seriously affect the patient's quality of life in both adults and children. Different aspects of Bell's palsy are studied in both retrospective and prospective manners, to find prognostic clinical signs for non-recovery. Alterations in the patients' quality of life are measured using QoL- questionnaires.

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**Hanna Josefsson**  
MD, PhD-student

The project aims to investigate the development of the central hearing pathways in children with unilateral aural atresia and associated conductive hearing loss. Human study participants will undergo testing of hearing, sound localization abilities, speech perception in competing speech and MRI. We also have an ongoing histological study of rat brain and cochleae.

**Lovisa Lansing**  
MD, PhD-student

Since 2015 I have joined the group studying Peripheral Facial Palsy at Karolinska Institutet since June 2017 was appointed as a PhD-student. In my studies, I investigate Bell's palsy during pregnancy and puerperium (first six weeks after childbirth). Previous studies have shown an increased risk of Bell's palsy in pregnancy, but little is known and further studies are needed.



**Andreas Kaiser**  
MD, PhD-student

I work in a group that is presently based in a laboratory in Uppsala. Our overall aim is to facilitate nerve restoration in the auditory system. We mainly do *in vitro* work, with running projects using human stem and progenitor cells. We have established an auditory nerve system model that we utilize to serve as cell transplantation target and to evaluate cell transplant strategies.

**Malin Siegbahn**  
MD, PhD-student

Congenital unilateral hearing loss affects educational results when untreated. Knowledge about the effects on the central auditory pathways, caused by untreated congenital aural atresia and associated conductive hearing loss is limited. This project aims to examine these effects, through MRI, of both adult human patients and animal models.

**Rebecka Ohm**  
MD, PhD-student

I aim to describe the cohort of patients that develop long term sequelae after inflammatory peripheral facial palsy and to study whether early cross facial nerve transplantation will give patients good facial function without the need of additional microvascular muscle transplantation. I will also study the occurrence of synkinesis and surgical treatment options for patients with severe synkinesis.

**Stefan Toth**  
MD, PhD-student

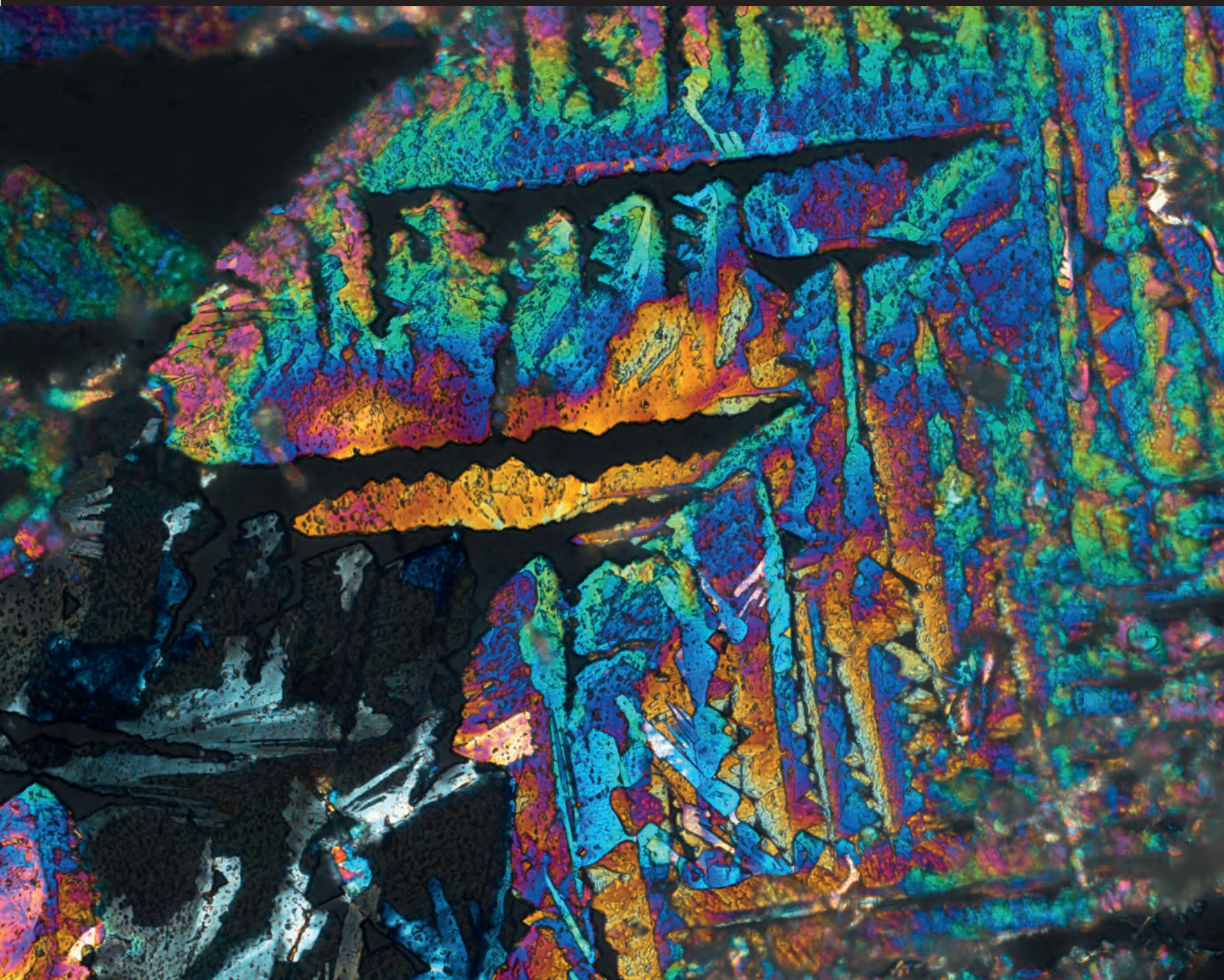
My PhD-project focuses on peripheral facial palsy of unknown origin (Bell's palsy) and neuroborreliosis. Bell's palsy can cause severe sequelae and subjective suffering but is poorly investigated. This study about incidence, outcome and subjective suffering will therefore be of great importance for increasing the knowledge of this disease. It will also add value for new guide lines.

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### **Other co-workers within the reseach group**

**Malin Berglund**, MD, PhD student, SUS/NÄL, Gothenburg  
**Måns Eeg-Olofsson**, MD, Docent, University of Gothenburg  
**PO Eriksson**, MD, PhD, Uppsala  
**Bo Håkansson**, Professor, Chalmers University of Technology  
**Mervi Kanerva**, MD, Docent, Helsingfors Univ. Finland  
**Rodrigo Moreno**, Docent, Royal Technical Highschool, Stockholm  
**Eva Westman**, MD, PhD, lecturer, Umeå









Stellan Hertegård



Per-Åke Lindestad



Riitta Möller



Emma Malmström

#### Five most valuable publications from the research group 2014-2017

1. Hertegård S, Larsson H. A portable high speed camera system for vocal fold examinations. *Journal of Voice*. 2014. Jul 5. pii: S0892-1997(14)00070-8. doi: 10.1016/j.jvoice.2014.04.002. [Epub ahead of print]
2. Svensson B, Nord C, Nagubothu RS, Hultman I, M.S, Cedervall J, Ährlund-Richter L, Tolf A, Hertegård S. Stem cell therapy in injured vocal folds – a three months analysis of human embryonic stem cells. *Biomed Research International*. 2015;2015:754876. doi: 10.1155/2015/754876. Epub 2015 Oct 18. Hindawi Publishing Corporation. Article ID 754876. 2015
3. Möller R, Safa S, Östberg P. Validation of the Swedish Translation of Eating Assessment Tool (S-EAT-10). *Acta Otolaryngologica* 2016; DOI: 10.3109/00016489.2016.1146411
4. Geneid A, Lindestad PÅ, Granqvist S, Möller R, Södersten M. Long-Term Follow-Up of Patients with Spasmodic Dysphonia and Improved Voice despite Discontinuation of Treatment. *Folia Phoniatica et logopaedica* 2016;68(3):144-151. doi: 10.1159/000449100. Epub 2016 Dec 3
5. Malmström E. , Hertegård S. Epidemiological study of vocal fold scarring and sulcus vocalis- background factors and Swedish Voice Handicap Index data. *Folia Phoniatica et logopaedica*. 2017. In press

## Reconstruction of Vocal Fold Scarring with Mesenchymal Cells

**Stellan Hertegård**, MD PhD. Adjunct Professor in Phoniatics (until 2017-12-31)

The research of the phoniatic research group at Karolinska is focused on severe voice disorders such as vocal fold (VF) scarring and neurologic voice disorders, and dysphagia. Other projects concern the development of improved diagnostics for voice disorders.

Dr Hertegård's research concerns development of diagnostic methods of voice disorders, in particular analysis of laryngeal examinations with high-speed imaging. A prototype low cost high speed imaging camera with software for recording and analysis had been developed (1). Another research area is development of treatment of vocal fold scarring (2). Previous experiments on damaged rabbit VFs has shown great potential for mesenchymal stromal cells (MSC) to heal vocal fold damage and prevent scarring. A clinical study with autologous MSC treatment in patients with severe voice problems and VF scarring has shown positive results with improved VF vibration function, without side effects.

**Per-Åke Lindestad**

MD, PhD, Associate Professor in Phoniatics

Research in neurologic voice disorders, e.g., treatment of spasmodic dysphonia (SD) and oromandibular dystonias. McLeods syndrom (feeding dystonia) was successfully treated with botulinum toxin. In a recent study on 28 SD patients, who refrained from treatment > 10 years ago due to normalized voice, 10 showed few or no symptoms. Botulinom toxin has lasting results in selected SD patients, in particular males who started treatment early after symptom occurrence (4).

**Riitta Möller**

MD, PhD, Associate Professor in ENT and Phoniatics

Dysphagia is a common problem that can cause nutritional deficiencies and lead to pneumonia. There is a great need for a simple instrument that measures the severity of the dysphagia based on the patient's perspective. We have therefore recently translated and culturally validated EAT-10 questionnaire into Swedish and want now to further analyze and ensure the clinical validity of S-EAT-10 (3).

**Emma Malmström**

MD, PhD-student

The aim of the project is to analyse treatment results in transfeminine patients treated with laryngeal surgery (kondroplasty, Adams apple reduction) and/or vocal fold surgery (glottoplasty, vocal fold shortening) in order to treat voice- and gender dysphoria. Dr Malmström has also analysed background factors in vocal fold scarring and sulcus vocalis (5), and validated the new Swedish VHI-10 voice evaluation scale widely used in voice clinics.

### Other co-workers within the reseach group

**Srinivasa Rao Nagubothu** Msc. PhD student . Main supervisor Professor Katarina LeBlanc, Hertegård co-supervisor (PhD-student at Lab Med Inst).

**Ahmed Geneid** MD. PhD, Associate professor in Phoniatics, post doc researcher since 2015 from University of Helsinki Finland





From left in the back: Henrik Smeds, Filip Asp, Eva Karltorp, Erik Berninger, Elisabet Engström, Martin Eklöf, Jeremy Wales

From left in front: Inger Uhlén, Åsa Bonnard, Marlin Johansson

#### Five most valuable publications from the research group 2014-2017

1. Asp, F., A. Olofsson and E. Berninger (2016). "Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy from 6 Months of Age." *Ear Hear.* 37(2): e104-118.
2. Berninger, E., A. Olofsson and A. Leijon (2014). "Analysis of click-evoked auditory brainstem responses using time domain cross-correlations between interleaved responses." *Ear Hear* 35(3): 318-329.
3. Chilosi, A. M., A. Comparini, P. Cristofani, M. Turi, S. Berrettini, F. Forli, G. Orlandi, A. Chiti, N. Giannini, P. Cipriani and G. Cioni (2014). "Cerebral lateralization for language in deaf children with cochlear implantation." *Brain Lang.* 129:1-6.
4. Rance, G., K. Saunders, P. Carew, M. Johansson and J. Tan (2014). "The use of listening devices to ameliorate auditory deficit in children with autism." *J Pediatr.* 164(2): 352-357.
5. Smeds, H., J. Wales, F. Asp, U. Lofkvist, B. Falahat, B. M. Anderlid, L. Anmyr and E. Karltorp (2017). "X-linked Malformation and Cochlear Implantation." *Otol Neurotol.* 38(1): 38-46.

## Scientific Center for Advanced Pediatric Audiology

**Erik Berninger**, MScEE, PhD, Associate Professor

The center is aimed to promote sustained research on hearing impairment in newborns, infants, and children. Our research forms a foundation for the very best treatment for each infant suffering from a life-long burden that hampers communication and education. Binaural stimulation during a sensitive period of development will be the key to accelerate the stimulus-driven maturation of the central auditory pathways, thereby avoiding permanent and detrimental reorganization of the brain.

A clear-cut etiology is paramount for optimizing the care of each child.

We have a unique opportunity due to our highly efficient newborn hearing screen, two continuously updated regional databases, large clinic (25% of the uptake in Sweden), National Medical Care Center for children with inner ear malformations requiring cochlear implantation, long tradition of very early intervention and bilateral cochlear implantation in young children, and advanced clinical laboratory facilities.

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**Filip Asp**  
MScCS, PhD

Spatial hearing is fundamental to human communication. We study the effects of hearing loss and various interventions on spatial hearing from 6 months of age, using rapid and objective techniques. The goal is to alleviate the negative impact of hearing impairment on spatial hearing, and increase our understanding of how impaired hearing affects humans during critical periods in development.

**Åsa Bonnard**  
MD, PhD

About 20% of children with cochlear implants have a malformed inner ear and large vestibular aqueduct with incomplete partition type 2 malformation as the most common one. Descriptive, retrospective and prospective studies regarding natural history, long-term hearing and language outcome and vestibular and motor function in cochlear implanted children with this malformation are ongoing.

**Anna Granath**  
MD, PhD

PhD 2010. Co-tutor for Sofia Dennison-Hultman (KI) and Johanna Westerberg (Linköping)  
Ongoing project: Effects of aging on treatment with cochlear implants  
Co-workers Luca Verrecchia and Jeremy Wales.  
The project is at present in a startup phase. The aim is to investigate the impact of cochlear implants on vestibular function, cognition, hearing results and social abilities.

**Sten Hellström**  
Senior Professor, Senior Consultant

The research focuses on two avenues; supervising the development of a "Scientific Center for Advanced Pediatric Audiology" and on studying plasminogen (plg) and healing of tympanic membrane perforations and other chronic wounds. The latter in collaboration with Canadian PROMETIC Life Sci Inc. Clinical trials on pig in diabetic foot ulcers and chronic TM perforations will start in springtime 2018.

**Eva Karltorp**  
MD, PhD

We study different etiologies to hearing impairment such as congenital cytomegalovirus infection and malformations of the inner ear as large vestibular aqueduct syndrome and X-linked deafness.

**Ulrika Löfkvist**  
Cert. Spoken Language Pathologist,  
PhD, Associate Professor

The overall purpose is to find factors that explain the variation of outcome in individuals with hearing impairment across the life-span. The research is especially focused on gaining new knowledge about lexical-semantic abilities and cognitive functioning, in relation to e.g. auditory deprivation, cause of deafness, comorbidity, multi-lingualism, quantity and quality of language stimulation.

**Mircea Romanitan**  
MD, PhD

The long-term aim is to find the causes and mechanisms behind various nonsyndromic congenital bilateral cochlear hearing losses, and to identify or develop future treatment options. Specifically, infectious exposures, genetic contribution, cochlear morphology, and cochlear function is studied in relation to for example unaided and aided recognition of speech in competing speech along with questionnaires.

**Inger Uhlén**  
MD, PhD

The present research project aims at investigating the prevalence and etiology of congenital and late onset childhood hearing impairment. Through studies of the regional (Stockholm County Council) databases *Audioscreen* and *Audiohab*, the efficacy, sensitivity and specificity of the universal newborn hearing-screening program will be evaluated. The EU-project EUSCREEN will provide similar information.

**Henrik Smeds**  
MD, PhD

Incomplete Partition type 3, classified on radiology, is linked to a gene on the x-chromosome, *POU3F4*. Our subgroup of 10 x-linked recipients has been examined related to genetics, radiology, hearing and language showing that cochlear implantation is a feasible and safe procedure for rehabilitation. Results from several international centers are compared; e.g., neurodevelopmental symptoms.

**Jeremy Wales**  
MD, PhD, ENT resident

Hearing loss can be related to immobility of the middle ear bones where surgery will provide the best chance to improve hearing. The subjective assessment of this immobility is often performed manually during the surgical procedure. We are developing an objective measuring system using laser vibrometry to measure middle ear bone vibration with simulated noise from a magnetic coil.

**Bo Tideholm**  
MD, PhD

The research scope is to elucidate language development in children with bilateral and unilateral cochlear implantation. Furthermore, to study how binaural hearing with cochlear implants effect the ability to detect and localize sound sources and its relation to language acquisition and communication outcomes.

**Martin Eklöf**  
MScEE, PhD-student

The PhD project involves development of a method to assess latencies in a horizontal sound localization task. The measure is extracted from optimization of an arctangent function to the eye tracking data from each sound shift. This technique is used to study the coding of fine structure in the stimulation strategies of cochlear implants (CIs). Lateralization seems to depend on CI processing parameters.

**Marlin Johansson**  
MSc, PhD-student

The overall aim is to describe the causes and mechanisms behind pediatric congenital unilateral sensorineural hearing loss (uSNHL), as well as the effect of early intervention on auditory abilities and maturation of the central auditory pathways. Congenital uSNHL is studied with objective and subjective methods from birth in order to identify and develop the most appropriate treatment protocols.

**Elisabet Engström**  
MD, PhD-student

Cognitive development and central auditory processes are studied in children with hearing aids and/or cochlear implants. A specific purpose is to examine how a phonological intervention programme can affect neurophysiological and cognitive development and reading skills. The children were between 5-7 years old with a follow-up after 3 years. Language development is dependent on training.

**Satu Turunen-Taheri**  
MSc, PhD-student

The study will present the quality and the usefulness of audiological rehabilitation and examine sex equality in the Swedish hearing health care for patients with severe-to-profound hearing loss. We will study reasons for not being rehabilitated with cochlear implants, prevalence of mental fatigue in this patient group, experiences and factors affecting daily life for patients with deaf-blindness.

**Stefano Berrittini***Professor, Affiliated Researcher*

We have established a research collaboration between Karolinska Institutet and University of Pisa in the area of audiology and otology, focusing on deafness in adults and children and on cochlear implant procedure. Regarding cochlear implant procedure the joint research regards various aspects, such as cochlear implantation in malformed cochleas and cochlear implantation outcome in bilingual children. We are also conducting a research project about Language Environmental Analysis (LENA), an advanced technique to record a child's listening and language environment, with the aim to correlate it to language development both in normal-hearing and deaf children.

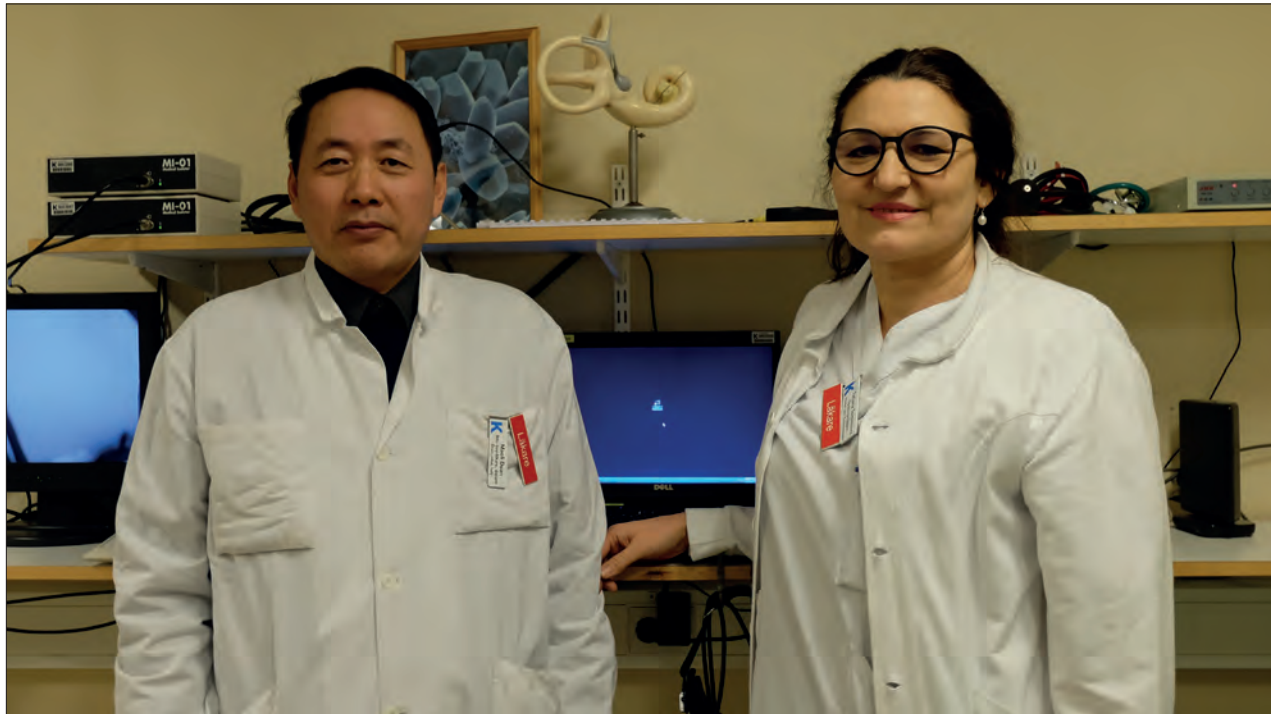
A paper about cochlear implant and bilingualism has been accepted for publication on the International Journal of Pediatric Otolaryngology and papers about LENA and cochlear implant in malformed cochleas are under preparation.

**Wolf-Dieter Baumgartner***Professor in ENT in Ghent, MD., Associated Researcher*

Dr Baumgartner is a collaborative researcher to the ENT.div at KI in the area of cochlear implant surgery. He has a particular interest in children and adults suffering from partial deafness, where so called Electric Acoustic Stimulation Cochlear Implantation is needed. This is a combination of natural acoustic hearing together with electric stimulation via cochlear implant on the same ear.







Maoli Duan and Tatjana Tomanovic

#### Five most valuable publications from the research group 2014-2017

1. Tomanovic T, Bergenius J. Vestibular findings in patients with persistent geotropic positional nystagmus: the "light cupula" phenomenon. ? Acta Otolaryngol 2014 Sep;134(9):904-14.
2. Zhang X1, Xu X, Ma W, Zhang Q, Tong B, Yu H, Xu M, Ren T, Rosenhall U, Anniko M, Duan M. A clinical study of sudden deafness. Acta Otolaryngol. 2015;135(10):1030-5. doi: 10.3109/00016489.2015.1060629. Epub 2015 Jun 24.
3. Strömberg AK, Olofsson Å, Westin M, Duan M, Stenfelt S. Changes in cochlear function related to acoustic stimulation of cervical vestibular evoked myogenic potential stimulation. . Hear Res. 2016 Oct;340:43-49. doi: 10.1016/j.heares.2015.12.022. Epub 2015 Dec 25.
4. Verrecchia L, Westin M, Duan M, Brantberg K. Ocular vestibular evoked myogenic potentials to vertex low frequency vibration as a diagnostic test for superior canal dehiscence. Clin Neurophysiol. 2016 Apr;127(4):2134-9. doi: 10.1016/j.clinph.2016.01.001. Epub 2016 Jan 12.
5. Zhou L, Feng M, Huang X, Duan M. Fatigue analysis of tympanic membrane after ossiculoplasty. Acta Otolaryngol, 2017 Jul;137(7):679-685. doi: 10.1080/00016489.2016.1277264. Epub 2017 Jan 26.



Hearing Loss and Vestibular Disorders

**Maoli Duan**, MD/PhD, Associate Professor, Senior Consultant

Hearing and vestibular disorders are two of the common diseases affecting both children and adults.

1. Vestibular disorders projects include PhD students, Luca Verrecchia and Pedro Marques: To develop VEMP methods to diagnose vestibular and middle ear disorders, and to test if permeability of the round window membrane to aminoglycosides and cortocosteroids differ between normal and hydropic ears.
2. Hearing impairment (HI) in newborns - the importance of early diagnosis and early intervention. This project will focus on developing new objective diagnostic methods for determination of hearing loss in young infants and newborn children.
3. Evaluation of noise-induced hearing loss by electrical drilling for otological surgery and by acoustic stimulation with VEMP tests will be carried out by PhD student Anna-Karin Strömberg at Linköping University. The project is a collaboration between KI and Linköping University with dr Duan as a co-supervisor.
4. Geotropic variant of the persistent positional direction-changing nystagmus (PPDCN) will be studied by Dr Tomanovic

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**Tatjana Tomanovic**  
MD/PhD, Senior Consultant

Persistent positional nystagmus

Geotropic variant of the persistent positional direction-changing nystagmus (PPDCN) can be recorded in patients with peripheral vestibular disorders. This nystagmus patterns could be explained by disturbances in the density relation between the cupula and the endolymph, where the cupula has become lighter. Ongoing work on the different variants of peripheral positional dizziness and vertigo.

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**Luca Verrecchia**  
PhD-student

The diagnosis of cochlear and vestibular hypersensitivity in superior canal dehiscence syndrome

The research project for this PhD program focuses on the cochlear and vestibular hypersensitivity in superior canal dehiscence syndrome (SCDS). The diagnostic role of vestibular evoked myogenic potentials has been stated in 2 published articles and further explored in 2 ongoing works. A third article explores the SCDS cochlear hypersensitivity by a special application of bone conducted hearing test.

**Other co-workers within the research group**

**Anna-Karin Strömberg**, PhD student in Linköping University.

**Pedro Marques**, PhD student Faculdade de Medicina da Universidade do Porto, Portugal.



Per Östberg, Jenny Häggström, Christina Hederstierna, Ulf Rosenhall  
Esma Idrizbegovic

#### Five most valuable publications from the research group 2014-2017

1. Idrizbegovic E, Hederstierna C, Rosenhall U. Mismatch negativity and ear laterality in Alzheimer's disease and in mild cognitive impairment. *J Alzheimers Dis.* 2016 Jul 1;53(4):1405-10. doi: 10.3233/JAD-160323.
2. Rosenhall U, Idrizbegovic E, Hederstierna C, Rothenberg E. Dietary habits and hearing. *Int J Audiol.* 2015;54 Suppl 1:53-6. doi: 10.3109/14992027.2014.972524. Epub 2014 Dec 30.
3. Hardy J, Bogdanovic N, Winblad B, Portelius E, Andreassen N, Cedazo-Minguez A, Zetterberg H. Pathways to Alzheimer's disease. *Journal of Internal Medicine.* 2014, 275; 296–303.
4. Cederlöf M, Östberg P, Pettersson E, Anckarsäter H, Gumpert C, Lundström S, Lichtenstein P. Language and mathematical problems as precursors of psychotic-like experiences and juvenile mania symptoms. *Psychol Med.* 2014;44(6):1293-302.
5. Wardi T, Alkass K, Bogdanovic N, Druid H. Alcohol addiction and its effect on stem cells, migrating immature and proliferating cell populations in the adult human hippocampus, *Neuropsychopharmacology.* 2017. [Epub ahead of print].

Aging, cognition and central auditory function

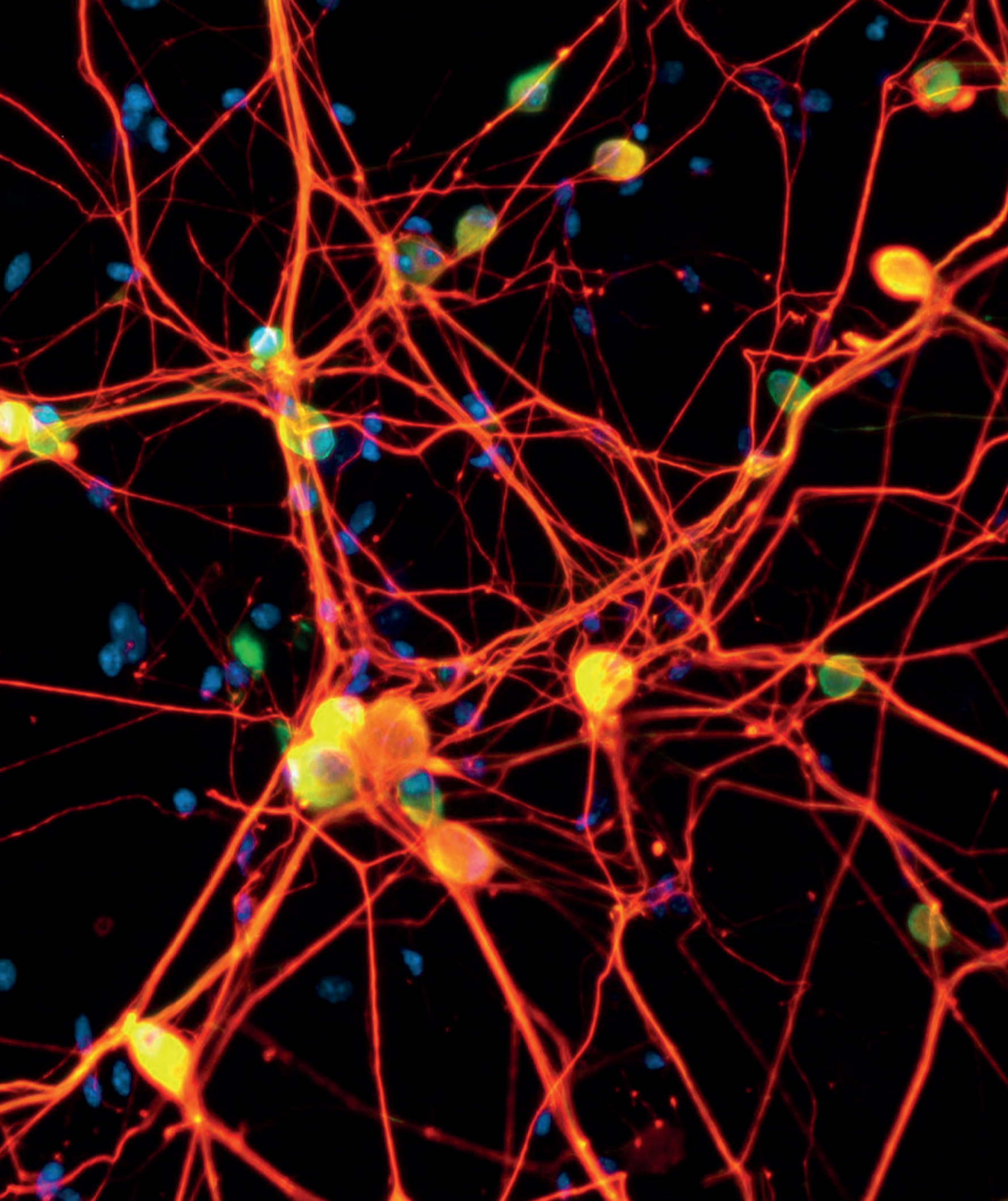
*Esma Idrizbegovic, Associate Professor, MD, PhD*

Our research group study relationships between aging, cognitive decline, and central auditory function. Hearing deteriorates with age and age-related hearing loss is a complex phenomenon. Many elderly retain adequate sensitivity to sound but are poor at recognizing relevant sounds such as speech in back-ground noise. This indicates central auditory dysfunction (CAD). Persons with CAD have limited benefit from standard hearing aids. We aim to validate diagnostic methods for assessing central auditory dysfunction (CAD) in individuals with different degrees of cognitive impairment. The hypothesis is that combined assessment of CAD and cognitive function will help to identify individuals with both hearing impairment and cognitive decline, cognitive level of the patient and thus possibly contribute to better communication abilities and quality of life in this group. Jenny Häggström is a PhD student, EI is the main supervisor, and CH, PÖ and NB are co-supervisors

<i>Christina Hederstierna</i> MD, PhD	<i>Esma Idrizbegovic</i> Associate Professor, MD, PhD	<i>Ulf Rosenhall</i> Professor Emeritus
Collaboration in projects about: Hearing and cognition; Hearing in the elderly - epidemiology; Noise-induced hearing loss; Prevention of cisplatin ototoxicity and Hearing preservation in vestibular schwannoma.	Per Östbergs research covers cognitive communication disorders in geriatric populations, especially neurodegenerative disease and stroke.	Part of UR's research is carried out at KI together with three research groups. One project is a study of the central auditory function in cognitive disorders (head: E Idrizbegovic). Another is a study of prevalences of pediatric hearing loss (head: I Uhlén). A third is the influence of noise on the fetus during pregnancy (head: J Selander). UR has a special competence in audiological epidemiology.

<i>Jenny Häggström</i> MD, PhD-student	<i>Other co-workers within the reseach group</i>
The first part of the project is a longitudinal study of central auditory function in adults with different levels of cognitive decline. Secondly, measures of central auditory function will be validated against biomarkers for Alzheimer's disease. Thirdly, central auditory function will be compared across different dementia diagnoses.	<i>Nenad Bodganovic</i> , Professor in Geriatrics, Department of Neurobiology, Care Sciences and Society (NVS), Division of Clinical geriatrics, Karolinska Institutet  <i>Per Östberg</i> , Associate Professor, PhD, Department of Clinical Science, Intervention and Technology, Division of Speech and Language Pathology, Karolinska Institutet





## Doctoral dissertations from the opening of the ENT clinic at Karolinska University Hospital in 1942 to present 2018

- Babak Alinasab 2017  
*Orbital blow out fracture. To operate or not to operate – that is the question.*
- Julia Arebro 2017  
*Innate Mechanisms in Upper Airway Inflammation with focus on Epithelium and Neutrophils.*
- Lotta Tengroth 2017  
*Nasal Epithelial Cells: Innate Immunity and Inflammation.*
- Anna Borgström 2017  
*Pediatric obstructive sleep apnea – evaluation of questionnaire and surgical treatment.*
- Henrik Smeds 2016  
*Cochlear Implantation: Experimental and Clinical Studies.*
- Louise Honeth 2016  
*Determinants of hearing impairment in Swedish hunters, an e-epidemiological approach.*
- Yuan Xu 2016  
*Nicotine and endotoxin in airway hyperreactivity and inflammation.*
- Filip Asp 2015  
*Bilateral Cochlear Implants in Children - Clinical and Methodological Studies.*
- Victoria Hellberg 2015  
*Pharmacokinetics and inner ear transport of cisplatin.*
- Marit Westman 2014  
*"Hay fever" in children - the real story.*
- Daniel Carlberg 2014  
*Genetic association studies in allergic rhinitis.*
- Lena Anmyr 2014  
*Life circumstances of children and adolescents after cochlear implantation.*
- Tatjana Tomanovic 2014  
*Persistent geotropic nystagmus : a different kind of cupula pathology.*
- Camilla Rydberg Millrud 2014  
*Pattern-recognition receptors and neutrophils in cancer inflammation.*
- Eva Karltorp 2013  
*Congenital CMV infection and connexin 26 mutations in childhood deafness: intervention with early cochlear implantation.*
- Nanna Browaldh 2013  
*Upper airway surgery in obstructive sleep apnoea : descriptive, observational and randomised controlled studies.*
- Terese Hylander 2013  
*Novel potential targets for treatment of airway inflammation.*
- Elin Marsk 2012  
*Bell's palsy : study design, prognosis and quality-of-life.*
- Karin Lundkvist 2012  
*Pharyngeal surgery and epidemiology in sleep apnea.*
- Per Attner 2012  
*Clinical Implications of Human Papilloma Virus (HPV) in oropharyngeal cancer.*
- Bengt Svensson 2012  
*Restoration of scarred vocal folds with stem cell implantation: analyses in a xenograft model.*
- Ylva Tiblom Ehrsson 2011  
*Nutritional follow-up of patients with head and neck cancer.*
- Björn Palmgren 2011  
*Regeneration of the auditory nerve - a cell transplantation study.*
- Cecilia Engmér Berglin 2011  
*Local pharmacological treatment of inner ear disorders.*
- Anna-Karin Ekman 2011  
*Pattern-Recognition Receptors in Airway Inflammation.*
- Alexander Ahlberg 2010  
*Patients with head and neck cancer - aspects on treatment, complications and rehabilitation.*
- Michael Ryott 2010  
*Predictive and prognostic biomarkers in oral tongue squamous cell carcinoma.*
- Anna Granath 2010  
*Clinical and pathogenic aspects of otitis media.*
- Petter Olsson 2009  
*Prevalance of upper airway symptoms and aspects on treatment of nasal polyposis.*
- Christina Forshell Hederstierna 2009  
*Hearing in menopausal women and in women with Turner syndrome, a model for hearing matured in an estrogen-deficient environment.*
- Rusana Simonoska 2009  
*Sex steroid hormone receptors: Inner ear & hearing.*
- Pia Nerfeldt 2008  
*Weight reduction and alcohol abuse in sleep apnea patients.*
- Anders Ehnhage 2008  
*Nasal and bronchial testing as well as treatment of patients with airway hyperresponsiveness and inflammation focusing on the united airway concept.*
- Susanna Kumlien Georén 2008  
*Endogenous and exogenous glucocorticoid effects in a model of allergic airway inflammation.*
- Lalle Hammarstedt 2008  
*Tonsillar cancer : Incidence, prevalence of HPV and survival.*
- Karin Toll 2007  
*Pregnancy rhinitis : Pathophysiological effects of oestrogen and treatment with oral decongestants.*
- Ion Tcacencu 2005  
*Regenerative medicine of the airway cartilage: A morphological and immunohistochemical study with focus on cricoid cartilage defects treated with BMP-2.*
- Caroline Gahm 2005  
*Nitric oxide in brain contusion.*
- Gert Henriksson 2004  
*Clinical, immunological and olfactory aspects of sinusitis and nasal polyposis: With special reference to patients with cystic fibrosis.*



## Doctoral dissertations

- Stig Rudblad 2004  
*Nasal mucosal reactivity after long-time exposure to building dampness.*
- Jörgen Palm 2004  
*Nasal airway nitric oxide : Methodological aspects and influence of inflammation.*
- Sushma Nordemar 2004  
*Methods for early diagnosis of head and neck cancer.*
- Ebba Hedén Blomqvist 2004  
*Evaluation of medical and/or surgical treatment of anosmia/hyposmia in association with inflammatory disease of the upper airway.*
- Andreas Ekborn 2003  
*Cisplatin induced ototoxicity : Pharmacokinetics, prediction and prevention.*
- Georgios Papatziarnos 2003  
*Immunological studies of adenoids in children. Relation and atopy.*
- Anne-Charlotte Hessén Söderman 2002  
*Morbidity in Meniere's disease; aspects on quality of life and triggering factors.*
- Christina Larsson 2002  
*Stiffness changes of the tympanic membrane in otitis media.*
- Michael Lysdahl 2002  
*Rhynchopathy: Long-term clinical results after palatal surgery.*
- Esma Idrizbegovic 2001  
*Calcium binding protein immunoreactivity in the central auditory system correlations with the auditory periphery. The effects of noise and aging in mice.*
- Annika Elmqvist Stenberg 2001  
*Ear and hearing problems in Turner syndrome.*
- Urban Knutsson 2000  
*Individual glucocorticoid sensitivity in the human.*
- Erik Berninger 2000  
*Quinine as a model for the study of cochlear hearing loss in humans.*
- Karin Lindberg 2000  
*Nasopharynx and mucosa associated lymphatic tissue. Studies on mucosal immunity, nasopharyngeal colonization with non-encapsulated non-typhable *Haemophilus influenzae* and local administration of immunoglobulin in the upper respiratory tract.*
- Hans Grudemo 2000  
*Rhinostereometry and laser doppler flowmetry. Simultaneous measurements of inflammation and steroid effects in normal and allergic human nasal mucosa.*
- Marie Forseni Flodin 2000  
*Inflammation mediators and immunocompetent cells in the middle ear with particular regards to otitis media and tympanosclerosis.*
- Karin Forsgren 1999  
*Mucosal regeneration following sinus surgery.*
- Anders Westermarck 1999  
*On inferior alveolar nerve function after sagittal split osteotomy of the mandible.*
- Anders Högmo 1999  
*Squamous cell carcinoma and preneoplastic lesions of the oral cavity. Biological factors and prognosis.*
- Wanje Jäger 1998  
*Physiological aspects of cochlear excitation and neurotransmitter release.*
- Mats Lidégran 1998  
*Effects of drugs and irradiation on the laryngeal mucosa of the rat, with special reference to mast cells and neuropeptides.*
- Karin Ågren 1997  
*Immune response in human tonsil tissue.*
- Danielle Friberg 1997  
*Nerve lesions in pharynx - an aetiology of obstructive sleep apnoea.*
- Tomas Norlander 1997  
*Effects of the inflammatory response and formation of polyps in the nasal and sinus mucosa.*
- Wiveka Westergren 1997  
*Ventilator-associated sinusitis.*
- Jonas Karling 1997  
*Speech and velopharyngeal function in patients with hypernasality.*
- Anders Samuelsson 1994  
*Non-encapsulated *Haemophilus influenzae*. Aspects of epidemiology and pathogenicity with special reference to recurrent respiratory tract infections.*
- Joachim Forsgren 1994  
*Nasopharyngeal host-parasite interactions with special reference to non-encapsulated *Haemophilus influenzae*.*
- Xi Zheng 1994  
*Studies on etiological factors in nasopharyngeal carcinoma.*
- Magnus von Unge 1994  
*Mechanical properties of the tympanic membrane. An experimental study.*
- Claes Hemlin 1994  
*Secretory otitis media. Bacteriology and immunology of the nasopharynx.*
- Hans Hallén 1994  
*Nasal mucosa reactivity in healthy subjects, in patients with non-allergic nasal hyperreactivity and in patients with nasal polyps.*
- Peter Graf 1994  
*Overuse of oxy- and xylometazoline nasal sprays. Changes in nasal mucosal swelling and histamine sensitivity in healthy subjects and in patients with rhinitis medicamentosa.*



## Doctoral dissertations

- Håkan Larsson 1993  
*Obstructive Sleep Apnea Syndrom. Aspects on evaluation, etiology and treatment.*
- Karl Magnus Westrin 1992  
*The course of experimental sinusitis. Histological, microbiological and biochemical aspects.*
- Göran Laurell 1991  
*Ototoxicity of the anticancer drug cisplatin. Clinical and experimental aspects.*
- Per-Olle Haraldsson 1991  
*Rhynchopathy a treatable traffic hazard.*
- Pär Stjärne 1991  
*Sensory and motor reflex control of nasal mucosal blood flow and secretion: Clinical implications in non-allergic nasal hyperreactivity.*
- Kjell K. Karlsson 1990  
*On quinine and hearing.*
- Magnus Holst 1989  
*Elective cricothyroidotomy. Clinical and experimental studies on respiratory mechanics, complications and postoperative voice function.*
- Mats Holmström 1989  
*Effects of formaldehyde and wood dust on the upper airways.*
- Eva Munck-Wikland 1989  
*Cancer in esophagus. A clinical and experimental investigation of prognostic and diagnostic methods.*
- Mats E. Nilsson 1988  
*The upper esophageal sphincter. A simultaneous cineradiographic and manometric study of healthy subjects and of patients with Zenker's diverticulum.*
- Pontus Stierna 1988  
*Experimental and clinical studies of maxillary sinusitis. Energy metabolism, bacteriology and histology with special reference to acute pneumococcal sinusitis in rabbits.*
- Olof Berg 1988  
*Etiological Diagnosis in sinusitis.*
- Lars Fredelius 1988  
*Degeneration pattern in the guinea pig organ of corti after pure tone acoustic overstimulation.*
- Sven Olof Wikström 1987  
*Microchemical and morphological characterization of inner ear development.*
- Kajsa Tunér 1986  
*Studies on beta-lactamase producing anaerobic bacteria in recurrent tonsillitis and peritonsillitis.*
- Gunnar Marklund 1986  
*Tonsillar Angina and Host Response During Infectious Mononucleosis.*
- Louise Widemar 1985  
*Membrane Shrapnelli and its mast cells. A structural and biochemical study in the rat with special references to experimentally induced otitis media with effusion.*
- Malou Hultcrantz 1985  
*Structure and function of the adult inner ear in the mouse following prenatal irradiation.*
- Jan Kumlien 1984  
*Blood flow measurements in sinus and nasal mucosa. Methodological studies with special references to induced sinusitis in rabbits.*
- Bo Wilhelmsson 1984  
*Effects of wood dust on the nasal mucosa. A clinical and experimental study.*
- Lars Lundblad 1984  
*Protective reflexes and vascular effects in the nasal mucosa elicited by activation of capsaicin-sensitive substance P-immunoreactive trigeminal neurons.*
- Anders Freijd 1983  
*The otitis-prone child. A clinical, immunological and bacteriological study.*
- Aron Sobin 1983  
*Vestibular sensory cell pathology in a strain of the waltzing guinea pig. A morphological study on hereditary labyrinthine pathology.*
- Stefan Engquist 1983  
*Granulocyte function in maxillary sinusitis.*
- Britt Carlsson (Nordlander) 1982  
*On granulocyte protease and protease inhibitors in otitis media.*
- Hans Nordemar 1982  
*Differentiation of the inner ear structures in vivo and in vitro. An experimental study.*
- Richard Kuylenstierna 1981  
*Cryosurgery of the mandible. An experimental study in rabbits.*
- Britta Rynnel-Dagöö 1978  
*Adenoid tissue. Effect of adenoidectomy and in vitro immunological studies on adenoid lymphocytes.*
- Matti Anniko 1978  
*Atoxyl induced pathological changes of the inner ear. A model system for the study of ototoxicity.*
- Jan-Erik Juto 1977  
*Rhinostereometry.*
- Christer Carenfelt 1977  
*Maxillary sinusitis.*
- Dan Bagger-Sjöbäck 1977  
*The basilar papilla of the lizard.*
- Arthur Nathansson 1977  
*Bony repair of defects in non-irradiated and irradiated mandibulars. An experimental study in rabbits.*
- Jan Siegborn 1975  
*Interaction between the otolith organs and the semicircular canals.*
- Magnus Lind 1974  
*A symmetry detector method for gammaencephalography.*

## Doctoral dissertations

- Anders Änggård 1974  
*Autonomic nervous control of blood circulation and secretion in the nasal mucosa.*
- Christer Lundberg 1974  
*Concentration of penicillin and tetracycline in maxillary sinus mucosa and secretion.*
- Jan Kinnman 1973  
*Acromegaly. An ultrastructural analysis of 51 adenomas and a clinical study in 80 patients treated by transanthro-sphenoidal operation.*
- Stig Haglund 1973  
*Electromyography in the diagnosis of laryngeal motor disorders.*
- Rolf Leandersson 1972  
*On the functional organization of facial muscles in speech.*
- Stefan Ernstson 1972  
*The waltzing guinea pig. A study on inherited inner-ear degeneration.*
- Lennart Mendel 1971  
*Vestibular recruitment.*
- Ulf Engzell 1971  
*Aspiration biopsy of metastatic carcinoma in lymphnodes. Clinical and experimental investigations.*
- Henry Andersson 1969  
*Acoustic intra-aural reflexes in clinical diagnosis.*
- Bertil Mårtensson 1967  
*Transconioscopy.*
- Lars Änggård 1965  
*An electrophysiological study of the development of cochlear functions in the rabbit.*
- Helge Schiratzki 1965  
*Studier över extra thorakala luftvägsmotståndet hos normala och patienter med en eller dubbelsidig recurrenspares.*
- Per-Gotthard Lundquist 1965  
*The endolymphatic duct and sac in the guinea pig. An electron microscopic and experimental investigation.*
- Åke Flock 1965  
*Electron microscopic and electrophysiological studies on the lateral line canal organ.*
- Gösta Ewert 1965  
*On the mucus flow rate in human nose.*
- Tomas Gejrot 1965  
*Diagnostik och behandling av glomus jugulare tumörer.*
- Carl Magnus Eneroth 1964  
*Histological and clinical aspects on parotid tumors.*
- Bo Enfors 1962  
*The parotid and submandibular secretion in man.*
- Ingemar Klockhoff 1961  
*Middle ear muscle reflexes in man. A clinical and experimental study with special reference to diagnostic problems in hearing impairment.*
- Jan Wersäll, 1956  
*Studies on the structure and innervation of the sensory epithelia of the cristae ampullares in the guinea pig*
- Bengt Barr 1955  
*Pure tone audiometry for pre-school children.*
- Gunnar Lidén 1954  
*Speech audiometry. An experimental and clinical study with Swedish language material.*
- Herman Diamant 1954  
*Cholinesterase inhibitors and vestibular function.*
- Lars-Erik Floberg 1953  
*Vestibular symptoms in carbon monoxide poisoning after unilateral ligation of the common carotid artery.*
- Gunnar Nilsson 1952  
*The immediate improvement of hearing following fenestration operation.*
- Tore Lundborg 1952  
*Diagnostic problems concerning acoustic tumor.*
- Erik Wedenberg 1951  
*Auditory training of deaf and hard of hearing children.*
- Gunnar Mårtensson 1950  
*Dental injuries following radical surgery on the maxillary sinus.*
- Rutger Heyden 1950  
*The respiratory function in laryngectomized patients.*
- Erik Carlens 1943  
*Otitic infections due to pneumococcus type 3.*
- Carl-Axel Hamberger 1942  
*Über die behandlung der otitis media acuta und gewisser otogener komplikationen mit sulfanilamidderivaten.*

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***Staffan Larsson***

The head photographer and editor of photography of this scientific report. He has an AS degree in photography and holds a national certificate in digital image workflow delivery systems. Staffan Larsson has forty-five years of experience in medical and scientific photography. He has worked at Karolinska Institutet, Stockholm County Council and the Royal Institute of Technology (KTH). As a photographer his work has illustrated science and medicine. He is co-author of The Focal Encyclopedia of Photography and the recently published Laboratory Imaging and Photography. Staffan Larsson was instrumental in the formation of the Lennart Nilsson Award and developed numerous initiatives supporting its mission.