THE 2014-2015 COLLABORATION SUMMARIES

MAYO CLINIC

EDUCATION, RESEARCH & INNOVATION PLATFORM
Mayo Clinic and Karolinska Institutet have enjoyed a remarkable 21-year collaboration that began with a small annual scientific meeting focused on diabetes and metabolism. A formal agreement was celebrated in 2011, and the collaboration has expanded to include many areas of joint scientific, academic, and clinical interest.

In 2012, a joint competitive annual travel award program was initiated to promote short-term travel between institutions by faculty, staff, postdoctoral fellows and students to plan or conduct collaborative interactions during 2013. The following year, competitive project grants were added as a mechanism to build collaborative strength toward national or international project funding. In 2015, the awards program expanded to include funds for administrative projects.
2013

060 Mayo Clinic attendees at annual meeting in Stockholm
300 Total attendees
013 Mayo Clinic travelers at Karolinska Institutet funded by travel awards
015 Karolinska Institutet travelers at Mayo Clinic funded by travel awards

2014

059 Karolinska attendees at annual meeting in Rochester
330 Total attendees
011 Mayo Clinic travelers at Karolinska Institutet funded by project + travel awards
009 Karolinska travelers at Mayo Clinic funded by project + travel awards

2015

110 Mayo Clinic attendees at annual meeting in Stockholm
350 Total anticipated attendees
025 Mayo Clinic travelers at Karolinska Institutet funded by project + travel awards
021 Karolinska Institutet travelers at Mayo Clinic funded by project + travel awards
016 Stockholm County Council leaders at Mayo Clinic on Stockholm Health Care Senior Executive Study Tour
This project combines the MC Wireless Instantaneous Neurotransmitter Concentration System (WINCS), Mayo Investigational Neuro-modulation Control System (MINCS), and KI’s Organic Electronic Ion Pump (OEIP) to generate a novel device capable of wirelessly controlling an artificial synaptic system.

The recipients write: This grant provided an excellent opportunity to understand international collaboration and to build the foundation and storyline to publish our research with our collaborators at KI.

**Approaching the artificial synapse – electronically controlled neurotransmitter release and electrochemical sensing in an integrated closed-loop system**

*Erika Ross (MC)*  
*Dr. Kendall Lee (MC)*  
*Dr. Susanne Löffler (KI)*  
*Dr. Agneta Richter-Dahlfors (KI)*

This project seeks to determine whether a reagent called Brichos, which consists of a domain common to BRI protein and surfactant C precursor protein, can be therapeutic in a mouse model of Alzheimer’s disease. Dr. Kim’s lab obtained several unique antibodies generated by Dr. Johansson’s lab and successfully tested them. Several gene therapy vectors encoding BRICHOS domains were tested after brain injection.

The recipients write: This collaborative project would have not been initiated without the MC-KI collaborative grant program.
High-throughput discovery of RNA sequence specificities for RNA binding proteins

Estefania Mondragon (MC)
Dr. Jim Maher (MC)
Dr. Jussi Taipale (KI)

This project utilized robots and computers to determine which parts of RNA molecules bind to different proteins. It was an exciting collaboration involving the two groups that led to sustained PhD thesis research by Ms. Mondragon over two years of her Mayo Graduate School career including a travel grant visit in 2013 and project grant visit in 2014. Data for two potential publications and her PhD thesis project were obtained. These data are also raw material for future research studies.

The recipients write: The MC-KI travel and small grant program has been transformative for Estefania Mondragon and the participating laboratories. PhD training provides an ideal time for a graduate student to serve as a link between collaborating laboratories; in this case, living in Stockholm and working at KI for many months to conduct high-tech research in a setting with certain tools unavailable at her home institution. The cultural similarities between MC and KI, the excellence of the partner research programs, and the efficiency and determination of the facilitating administrative partners have been wonderful.
The significance of the immune-proteasome for the regulation of T cell differentiation and function in experimental atherosclerosis

Dr. Joerg Herrmann (MC)
Dr. Feilong Wang (MC)
Lisa Nesbitt (MC)
Dr. Göran Hansson (KI)
Dr. Anton Gisterå (KI)

The project initiated studies of the role of a special protein degradation system in immune cells involved in the hardening and narrowing of blood vessels. The award provided funding for Anton Gisterå from Dr. Göran Hansson’s laboratory to visit MC for three weeks to conduct the initial studies. Based on consistent, promising results in these early experiments, investigators are proceeding with subsequent steps using MC funding.

The recipients report: MC was fortunate to work with an extremely well-known group in this area, and this award brought valuable practical application to MC. In return, this program offered a PhD student the opportunity to come to the United States and MC. It also provided the nidus for future collaboration between the two institutions in the area of cardiovascular diseases.

High resolution definition of the memory B cell repertoire stimulated by measles virus vaccination

Dr. Chanakha Navaratnarajah (MC)
Dr. Roberto Cattaneo (MC)
Dr. Gunilla Karlsson Hedestam (KI)
Dr. Marjon Navis (KI)

This project attempts to characterize the diversity of the measles vaccine-induced antibody repertoire archived in memory B cells of experimentally vaccinated monkeys.

The recipients write: Based on the existence of this collaboration, Dr. Karlsson Hedestam has submitted an application for partial funding of a PhD student. The project stimulated an interesting collaboration that would not have been formulated otherwise.
Identification of a “molecular clutch” that inactivates E-cadherin in human cancer

Dr. Panos Anastasiadis (MC)
Dr. Lars Holmgren (KI)

This project attempts to determine how cancer cells migrate to and colonize distant organs. The investigators are studying the correlation between cell-adhesion changes and increased cell migration. We have shared unpublished data, reagents and ideas to elucidate further the mechanism of cell dissemination. We expect to continue this collaboration in the future, publish together, and eventually secure long-term funding.

The recipients report: The program is valuable, brings diverse expertise together and provides the potential to build long-term collaborations. Our studies are ongoing.

Mathematical modeling of the neuroendocrine signaling network dynamics in the model of mania induced by Lateral Hypothalamic Kindling (LHK)

Dr. Osama A. Abulseoud (MC)
Dr. Vlada Vukojević (KI)
Dr. Doo-Sup Choi (MC)
Dr. Man Choi (Ada) Ho (MC)

The goal of this study is to understand dynamic changes in the hypothalamic–pituitary–adrenal (HPA) axis activity in the lateral hypothalamic kindled rat mania model. The results show that the oscillatory changes in HPA axis response to mania-induction can be reliably quantified and modeled mathematically. The mathematical model can be used to study changes in HPA axis function in other disease models where HPA axis function is impaired.

The recipients write: This collaboration began when we met during the 2013 meeting. This partnership is an important initiative and well worth pursuing in the future.
**Exercise myokines in development – A novel role for irisin**

Dr. Yi Guo (MC)  
Dr. Pontus Boström (KI)

This study focuses on irisin, a novel myokine mediating the beneficial effects of exercise. Using precision genome engineering in a model organism, the project aims to address the fundamental function of irisin in the development and exercise training-promoted health span.

The recipients report: This program gave us the opportunity and funding support to collaborate not only on the exciting research program but also to educate graduate students. This fruitful collaboration will result in shared publications and long-term interaction between students, fellows, basic scientists, and clinicians from MC and KI.

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**Glutamate-NMDA receptor signaling in schizophrenia disorders**

Dr. Doo-Sup Choi (MC)  
Alfredo Oliveros (MC)  
Dr. Sophie Erhardt (KI)  
Xicong Liu (KI)

Schizophrenia is a severe brain disorder leading to abnormal thoughts and behaviors affecting approximately 1% of people in the general population. This disruption in normal thinking often results in severe interaction problems, placing a heavy burden on families and society. Out-of-control glutamate signaling may contribute to the severity of schizophrenia. The investigators have established a collaboration to elucidate how kynurenic acid and neurogranin regulate glutamate signaling in the brain.

The recipients write: We are truly appreciative of the leadership and staff organizing this legacy collaboration. The opportunity to receive this research award has not only furthered our understanding of this debilitating disease but also has strengthened the scientific training of our students and enhanced the research acumen of both institutions. Finally, we feel that the collaborative research award promotes our collaborative responsibility toward our common mission, which is to help our patients.
Stromal platelet-derived growth factor receptor (PDGFR) as a driver of breast cancer malignancy and potential therapeutic target

Dr. Derek Radisky (MC)
Dr. Arne Östman (KI)
Dr. Carina Strell (KI)
Dr. Janna Paulsson (KI)

We have found that stromal expression of two different forms of platelet-derived growth factor receptor can be detected even in benign breast biopsies, long before cancer develops. Our current plan is to determine the prognostic capability of the expression of these biomarkers, if they can be used to determine which women are more likely to develop breast cancer in the future, and if preventative steps can be taken to reduce their risk.

The recipients write:
It was an excellent experience; very well run and highly productive.

Skeletal muscle and adipose tissue cross-talk: Implications for aging

Dr. James Kirkland (MC)
Dr. Nathan LaBrasseur (MC)
Dr. Thomas Gustafsson (KI)
Anna Strömberg (KI)

We explored how fat cells and the factors they release may influence the health of skeletal muscles. Through strategic interdisciplinary collaboration, Dr. LeBrasseur and Dr. Gustafsson have the long-term goal of understanding the causes of skeletal muscle loss in the context of aging and disease. This collaboration was a result of discussions from the 2010 meeting.

The recipients write: The MC-KI Collaborative Award program is an outstanding opportunity for principal investigators and their laboratories. The funding is adequate to address focused questions through a select set of experiments.
Determining immunoglobulin isotypes and glycotypes using mass spectrometry

Dr. David Barnidge (MC)
Dr. David Murray (MC)
Dr. Susanna Lundstöm (KI)
Dr. Roman Zubarev (KI)

These investigators are developing better ways to diagnose patients with cancer and autoimmune diseases by using mass spectrometry to measure antibodies.

The recipients write: Thank you for this wonderful opportunity to work at KI. The MC-KI Collaboration is a great initiative. The findings from our efforts suggest we may have identified a new form of an immunoglobulin kappa light chain.

Administrative support for joint grant applications

Dr. Björn Kull (KI)
Eva Björndal (KI)
Dr. Laura Plant (KI)
Dr. Ylva Linderson (KI)
Dave Moertel (MC)
Jon Zurn (MC)
Tracey Anderson (MC)
Janice Grace (MC)

The investigators are developing a collaborative platform to support joint grant applications and administration at the pre- and post-award stage.

The recipients write: The KI staff visit to MC as part of our collaborative project was useful and informative. We have identified areas of interest and are pursuing them. Support for the meetings has enabled us to develop collaboration and assemble a solid work plan and infrastructure for future project development. Two applications to the European Union involving MC-KI researchers are currently receiving support as a result of the collaboration.
Leading for change: Education leadership for residency program directors in Sweden

Dr. Thomas Viggiano (MC)
Dr. Jonas Nordquist (KI)

The investigators developed a competency-based curriculum in residency training, which was presented to residency program directors in Sweden.

The curriculum incorporates various strategies used in the United States and the United Kingdom for applying competency-based learning to Graduate Medical Education.

The recipients write: The MC-KI collaborations have unlimited potential. Both institutions will benefit from both identifying productive areas for innovative approaches to improving the effectiveness and efficiency of education programs.

Differential diagnosis of childhood apraxia of speech

Dr. Edythe Strand (MC)
Dr. Anita McAllister (KI)
Dr. Per Östberg (KI)
Dr. Ellika Schalling (KI)

The investigators established a Swedish Dynamic Motor Speech Test, designed a study for establishing reliability and validity, provided lectures on motor speech disorders, dynamic assessment and progressive aphasia, and apraxia of speech.

The recipients write: This was a superb way to expand current collaborative work to include additional researchers with complementary skills and knowledge. The cross-linguistic work discussed in particular would not be possible without this collaboration. This research is important both theoretically and in providing better patient care.
**ADAPT**  
(ADHD medication and predictors of treatment outcome)  

*Dr. Linda Halldner Henriksson (KI)  
Dr. Jyoti Bhagia (MC)*

This project studied patients ages 4-17 with ADHD in Rochester and Stockholm, and investigated the association of gene polymorphisms with treatment response and side effects for ADHD medications. We mapped symptoms, side-effects, and predictors of treatment outcome in patients in the ordinary clinical settings.

The recipients write: It was a very unique experience to learn about the research programs offered by MC and KI. Clinical expertise at MC and research expertise at KI are synergistic. The Travel Award program is a fantastic opportunity to exchange both clinical, scientific, and logistic experiences. Travelling to each site has been invaluable to exchange experiences from clinical work, identify differences in clinical practice, and to plan a two-site study with a good collaborative partner.

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**Epigenetic glutamate dysregulation in rapid cycling bipolar disorder: Development of biomarkers**

*Dr. Marin Veldic (MC)  
Dr. Catharina Lavebratt (KI)  
Dr. Martin Schalling (KI)  
Dr. Lena Backlund (KI)  
Dr. Mark Frye (MC)  
Dr. Doo-Sup Choi (MC)*

This project investigates the role of the neurotransmitter glutamate in severe forms of bipolar disorder with the goal of developing biomarkers for early accurate diagnosis and selection of individualized treatment options.

The recipients write: My hosts were Dr. Schalling and Dr. Lavebratt, and without exaggeration, I could say that I never had better hosts in my entire life. The MC-KI Collaborative Awards program is an excellent idea and every effort should be made to ensure that this program continues in the future.
Genomics of lymphoma prognosis

Dr. James Cerhan (MC)
Dr. Karin Ekström Smedby (KI)

An initial goal for this award was to identify how best to harmonize prospective data collection to facilitate later pooling of data for multiple projects. Our joint site visits allowed us to understand existing data sources and patient populations, identify publication and grant opportunities, and meet with related collaborators (clinicians, hematopathologists, translational immunologists). This work will develop a broad team approach to understanding and predicting lymphoma risk and patient outcomes in order to better understand lymphoma genesis. Topics include etiologic factors, improved risk stratification, enhanced prognostication and enhanced overall survivorship.

The recipients write: The program has been an unexpected boost to accelerating some existing low-level collaborations (mainly through InterLymph), which are now much deeper between MC and KI. The value of the face-to-face and “on-the-ground” interactions enabled by travel award funds cannot be underestimated.
“The MC-KI collaborations have unlimited potential. Both institutions will benefit from both identifying productive areas for innovative approaches to improving the effectiveness and efficiency of education programs.”

Dr. Thomas Viggiario (MC)
Dr. Jonas Nordquist (KI)
MARK YOUR CALENDAR
22nd Annual Research Meeting
September 8–9, 2016
Mayo Clinic, Rochester, Minn., USA

VISIT
ki.se/mayo
for grant information, travel details, collaboration history, news and much more