Interested in recruiting a Postdoc

Project title
The curse or the cure: Notch signalling in liver cancer

Supervisor
Emma R Andersson, Dept of Biosciences and Nutrition, Karolinska Institutet
Email: emma.andersson@ki.se Phone: +46852487360
Home page: www.anderssonlab.com

Type of recruitment and qualifications of applicant
Postdoc (24 months)
The applicant should have a background in liver cancer and mouse handling.

Background
Hepatocellular carcinoma (HCC) is the most common form of liver cancer in adults, usually caused by infection or cirrhosis (often as a consequence of alcoholism), and is increasing world-wide. In children, HCC is relatively rare, but pediatric risk factors, including viral hepatitis, tyrosinemia, cirrhosis, and biliary atresia, dramatically up-regulate the childhood risk of acquiring HCC. Liver resection offers the best prognosis, but is not a viable alternative in most cases, since liver resection in patients with compromised liver function is associated with significant morbidity and the recurrence rate after resection is disappointingly high at 50-60%. Unfortunately, the 5-year survival for patients with HCC is as low as 28%, and drops rapidly to 2% with metastases, making this an area urgently in need of research to discover effective treatment options.
It has been suggested that Alagille syndrome (a *JAGGED1* genetic disorder affecting children, with severe liver disease) itself is a risk factor for developing HCC. Chronic liver disease is of course a significant risk factor for HCC, but the role of JAGGED1 in this is unclear, where both up-regulation, and down-regulation of JAG1 have been described. It is therefore currently controversial what the role of Notch in liver malignancy is. Understanding this is essential for the myriad of Notch-based therapies which are already in clinical trials.

Project description
We have developed a mouse model for Alagille syndrome that recapitulates the hallmarks of this genetic disorder. In this project, we ask whether “Alagille mice” are indeed at increased risk of HCC (in line with case reports) or are protected from developing HCC (in line with what is understood about Notch in liver). The results from these studies will be important for both patients with Alagille syndrome, and patients with HCC, as this will help identify the best therapeutic options.

Research group
Dr Andersson’s research group focuses on genetic control of embryonic development, in particular the hepatic, vascular, and central nervous systems. Since 2008, Dr Andersson has published 20 articles and reviews, and has an H-index of 15. She is the Chair of Karolinska Institutet’s Junior Faculty, and has been awarded several prizes, including the Sven and Ebba Christina Hagberg Award, and the 2017 Daniel Alagille Award from the European Association for the Study of the Liver (EASL).

Interested in recruiting a Postdoc

Project title

Development of a cutting-edge new technology to trace and manipulate the hematopoietic stem cell system in vivo

Supervisor

Emma R Andersson (main supervisor)
Dept of Biosciences and Nutrition
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Home page: www.anderssonlab.com

Niklas K Björkström (co-supervisor)
Dept of Medicine Huddinge
Karolinska Institutet
niklas.bjorkstrom@ki.se
+46706977195
ki.se/en/medh/niklas-bjorkstrom-group

Type of recruitment and qualifications of applicant

Postdoc (24 months)
The applicant should have a background in immunology and mouse handling.

Background

Development of the hematopoetic system is a multi-site process in which, at around E11.5, the liver becomes colonized by hematopoietic stem cells (HSCs), which expand, and then colonize the spleen, thymus and bone marrow. After birth, in adulthood, the bone marrow contributes HSCs to thymus and spleen. Tracing HSC proliferation and colonization, and performing high through put gain or loss of function in these systems has so far been challenging. Developing a technique to perform high throughput gain or loss of function, for genetic screens, would be a leap forwards in our scientific toolkit.

Project description

The aim of this project is to develop a cutting edge new tool to perform genetic manipulation of HSCs, or cells in the hematopoietic lineage. Using ultrasound-guided in utero nanoinjection, the candidate will map which HSC populations are targeted by lentiviral injection into embryonic liver at different stages, followed by mapping which sites of hematopoiesis are colonized by cells targeted at defined stages. After having established the optimal conditions, proof of principle experiments knocking down genes of interest in the hematoietic system will be used to demonstrate the technique's usefulness. Finally, a screen will be carried out to identify novel regulators of HSC fate determination and/or defined downstream immunological functions.

Research group

This project is a collaboration between Dr Emma R Andersson and Dr Niklas K Björkström's labs. The Andersson lab focuses on embryonic development and genetic control of morphogenesis, cell fate determination and differentiation. The Andersson lab has established ultrasound-guided in utero nano-injection as a method to manipulate gene expression in utero, in several different organs. A major interest in the lab is the Notch signalling pathway, and how this regulates embryonic development. The Björkström lab works with immune cell differentiation and function with a specific focus on innate and non-conventional lymphocytes.

Interested in recruiting a PhD student

Project title

For regeneration of insulin-producing β-cells

Supervisor

Olov Andersson, PhD, Principal Investigator
Department of Cell and Molecular Biology, Karolinska Institutet
Email: olov.andersson@ki.se home page http://ki.se/en/cmb/olov-anderssons-group

Type of recruitment and qualifications of applicant

PhD student. Master's degree in Biomedicine, Molecular Biology, or a similar subject

Project description

Diabetes can be controlled with insulin injections, but a cure is still lacking. One potentially curative approach is to increase the number of insulin-producing β-cells. Using a novel chemical screening approach in transgenic zebrafish for discovery, and transitioning to mouse and human studies for validation, we aim to identify and characterize enhancers of β-cell regeneration. In addition to expanding our whole-organism screening of small molecules in zebrafish, the PhD-student is to follow up on the tentative hits from our pilot screening to date. As a second independent approach, we are performing single-cell RNAsequencing to identify genetic signatures for formation of β-cells. The identified genes can be used as both markers and potential divers of β-cell regeneration. We can quickly test the functionality of identified genes by overexpressing them in the transgenic zebrafish monitoring β-cell regeneration. If treatment with the identified small molecules and genes (enhancers of β-cell regeneration) also lead to an improved regulation of glucose homeostasis in zebrafish, we will start translating the findings using mouse and human islets. Depending on the nature of the hit we might inject the small molecule or a secreted protein into diabetic mice for subsequent assessment of glucose-control and generation of β-cells. In sum, by performing whole-organism screens, characterizing mutant zebrafish, translating findings to mice and human islets, we will identify factors that could be used to treat diabetes.

Interested in recruiting a visiting researcher

Project title:
Induction of neural differentiation as a therapeutic approach in childhood medulloblastoma

Supervisor: Marie Arsenian Henriksson, Professor
Department of Microbiology, Tumor and Cell Biology (MTC),
KI Email Marie.Arsenian.Henriksson@ki.se
Homepage http://ki.se/en/mtc/marie-arsenian-henriksson-group

Research Focus: The MYC oncogenes in neuroblastoma and medulloblastoma pathogenesis and as targets for cancer therapies

Type of recruitment and Qualifications of applicant: Postdoctoral fellow
Applicants must have a PhD and preferentially three years postdoctoral experience in molecular and cell biology. The successful applicant should have expertise in cell culture, imaging, FACS and basic molecular biology techniques. Previous experience in metabolism and bioinformatics is an advantage. This is an excellent opportunity for an individual with experience in cellular and molecular biology and dedication to cancer research.
Very good knowledge of English language is prerequisite. Social skills and ability to cooperate are also important qualifications.

Short project description:
Medulloblastoma is the most common malignant brain tumor in children. Patients whose tumors exhibit overexpression or amplification of the MYC oncogene usually have a very poor prognosis. My group has previously identified the role of the miR-17~92 cluster and nuclear hormone receptors in MYCN driven neuroblastoma (Lovén et al., PNAS 2010; Ribeiro et al., Cell Reports 2016). Both these childhood tumors maintain an undifferentiated phenotype in part through their effect on nuclear hormone receptors levels and their role in differentiation processes. We have also shown that targeting MYC induces changes in neuroblastoma cell metabolism (Zirath et al., PNAS 2013). Here we aim to analyze the effect of targeting MYC and the miR-17~92 cluster on neural differentiation and metabolism in medulloblastoma cells. To this end, we will:

- evaluate the effect of targeting MYC with small molecules to induce differentiation and changes in cell metabolism.
- analyze the connection between the miR-17~92 cluster, nuclear hormone receptor expression and differentiation.

We already have preliminary data showing that targeting MYC in medulloblastoma cells results in neural differentiation as evaluated by morphological changes and expression of neural differentiation markers. We have also found that MYC inhibition results accumulation of lipid droplets and changes in metabolic flux as analyzed by Seahorse methodology. We will now further analyze these results as well as starting to analyze the role of the miR-miR-17~92 cluster and the nuclear hormone receptors in medulloblastoma differentiation.
A deeper knowledge of MYC-related control of differentiation and metabolism in medulloblastoma would provide information that could be the basis for novel potential therapeutic avenues to target MYC-driven medulloblastoma, which are associated with a particularly poor prognosis.

Interested in recruiting a PhD student/Postdoc/Visiting Researcher

Project title

Boosting Mucosal Immunity via induction of Antimicrobial Effector Molecules to Combat Multidrug Resistant Bacteria

Supervisor

Peter Bergman, MD, PhD, Assoc Prof, Groupleader
Department of Laboratory Medicine, Clinical Microbiology, Karolinska Institutet
Email: peter.bergman@ki.se Phone: +46708141684 Home page:
http://ki.se/en/labmed/research-group-bergmanagerberth-the-amp-group

Type of recruitment and qualifications of applicant

PhD-student/Postdoc/Visiting researcher. MD, MSc or PhD depending on the position, with relevant expertise in areas mentioned below.

Background

The applicant should have a suitable background for the intended work, including solid experimental experience from biochemistry, cell-biology and microbiology. Expert skills in cell-culture work, handling of BSL2-classified bacteria and experience from work with zebra-fish is a merit. This project can be either a 2-year Postdoctoral project or a 4 year PhD-project, depending on the academic level of the applicant.

Project description

Infections with multidrug resistant (MDR) bacteria constitute a significant problem for healthcare systems and patients worldwide. Especially, the spread of gram negative bacteria with resistance mechanisms against cefalosporins, carbapenems and colistin are a great concern. Thus, there is a great need to develop alternative strategies to treat infections with these bacteria. Here we develop a concept that is based on the induction of the host's own antimicrobial effector mechanisms, including antimicrobial peptides and proteins. The cytokine IL-22 is a key molecule for mucosal host defence since it regulates the expression of potent AMPs in epithelial cells, with the capacity to inhibit the growth of MDR bacteria, alone or together with antibiotics. Interestingly, the IL-22 system is conserved between fish and humans, and therefore a part of this project will use a recently developed infection model in zebra-fish to answer some fundamental questions about the regulation and control of the IL-22 antimicrobial axis in the host. Our goal is to obtain mechanistic insight into the IL-22 system and to translate this knowledge into clinical practise in the fight against MDR bacterial infections with a focus on carbapenemase producing *Klebsiella pneumomoniae.*

Research group

The AMP-group consists of 8 people, including the PI (Peter Bergman), 3 PhD-students, 2 PostDocs, 1 Senior scientist, 1 Senior Professor (Birgitta Agerberth). We study the regulation of antimicrobial mechanisms in innate immunity in order to utilize this knowledge for therapeutic strategies. We perform translational research and use patient-samples, primary cells and cell-lines and have recently developed an infection model in zebra-fish.

Interested in recruiting a PhD student

Project title: Mapping immune interactome circuits within human liver tumor

Supervisors
Niklas Björkström (MD, PhD, Associate Professor)
Martin Cornillet (PhD, postdoc)
Center for Infectious Medicine (CIM), Department of Medicine Huddinge, KI
Email: niklas.bjorkstrom@ki.se Phone: +46706977195
Home page: http://ki.se/en/medh/niklas-bjorkstrom-group

Type of recruitment and qualifications of applicant
PhD student (4 years/48 months)
The applicant should have a Master degree (or equivalent) and experienced experimental research in immunology (tumor immunology preferably). The applicant should also have an experience in flow cytometry which is the main technic used in the project. Experience in RNAseq would also be an advantage.

Background: Cancer of the human liver is the third most common cause of cancer-related death worldwide. Although not commonly thought of as an immunological organ, the liver contains large numbers of immune cells and is selectively enriched for natural killer (NK) cells, known for their capacity to recognize and eliminate tumor cells without prior sensitization. Yet, we have a limited understanding of how intrahepatic NK-cells are regulated and if they can target primary liver malignancies. The overall aim of the current research program is to acquire better insights into the role of NK cells and other intrahepatic lymphocytes in development of hepatocellular carcinoma (HCC).

Project description: Using advanced single cell technologies the aim is to provide a comprehensive mapping of the tumor immune-microenvironment using human liver samples from the tumor, the tumor-margin, and peripheral unaffected liver tissues. We will phenotypically and functionally characterise the human intrahepatic immune system and its interaction with liver tumors. For this, 26-color flow cytometry will be used. Original *in vitro* models will be developed to further investigate basic mechanisms including signaling pathway analysis using in-house developed phosphor flow. Cell sorting will be use to study cell subset of interest and combined with RNA sequencing to unravel differential transcriptional and non-coding profiles.

Research group: Our group is composed of scientists, clinicians, engineers, nurses, postdocs, PhD students, and master students all working with translational human immunology research, particularly tissue resident NK cells in the human liver and uterus. We combine unique human sampling settings, original experimental design, and strategic collaborations to answer basic and clinical questions in human immunology and medical research.

References: (1) J. M. Llovet, A. et al., Nat Rev Clin Oncol. 12, 408–424 (2015). (2) N. K. Björkström, et al., Nat Rev Immunol. 16, 310–320 (2016). (3) H.-G. Ljunggren, K.-J. Malmberg, Nat Rev Immunol. 7, 329–339 (2007). (4) C. Guillerey, et al., Nat Immunol. 17, 1025–1036 (2016). (5) J. H. Levine et al., Cell 162, 184-197 (2015). (6) S. C. Bendall et al., Science. 332, 687–696 (2011). (7) S. Krishnaswamy et al., Science. 346, 1250689 (2014). (8) E. L. Sylwestrak, et al., Cell. 164, 792–804 (2016).

Supervisors: Mattias Carlstrom (PharmD, PhD, Associate Professor), Jon Lundberg (MD, PhD, Professor) & Prof. Eddie Weitzberg (MD, PhD, Professor)

Affiliation: Department of Physiology and Pharmacology, Karolinska Institutet

Project title: Targetting microvascular oxidative stress in the triad of cardiovascular, metabolic and renal disease

Type of recruitment: Doctoral studies (PhD) 4 years

Qualifications of applicant: Previous experience using small animal models is mandatory. Assessment of renal and cardiovascular functions *in vivo* and *ex vivo* studies of vascular function will be an asset for this project. Previous experience in mitochondrial respirometry, redox signaling, oxidative stress, inflammation, histology, immunohistochemistry is also desirable. Proficiency in the English language, documented by an internationally recognized test (e.g. TOEFL or IELTS)

Short project description: Cardiovascular disease and type 2 diabetes are major health problems, affecting more than 1.5 billion people worldwide, and are often associated with chronic kidney disease. Oxidative stress implies increased production or decreased scavenging of reactive oxygen species (ROS), which is often associated with nitric oxide (NO) deficiency. NADPH oxidase (NOX)-derived O_2^- is a major source of ROS in the microcirculation and in the kidney, and increased NOX activity together with impaired mitochondrial function has been reported in the development or progression of cardiovascular, metabolic and renal disorders. We propose that novel strategies that reduce microvascular oxidative stress and increase NO signaling are proposed to have therapeutic value in these disorders.

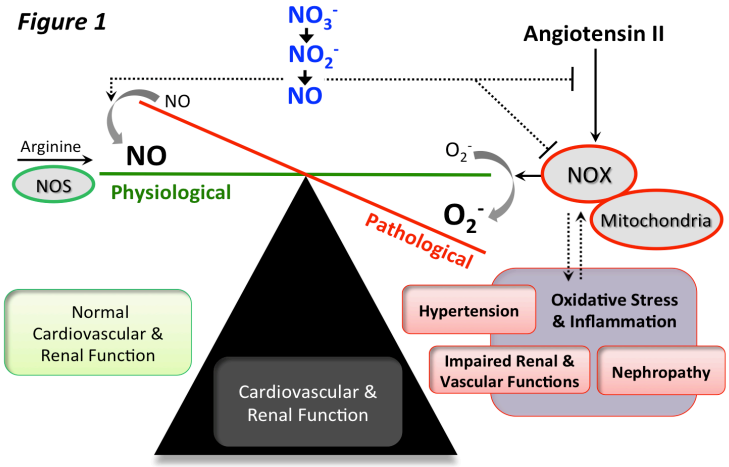
Inorganic nitrate (NO_3) and nitrite (NO_2) have long been considered inert end products of NO metabolism. However, we and other groups have shown that these anions, which are found in high concentrations in green leafy vegetables, via serial reduction steps can undergo bioconversion to NO independently of endothelial NO synthase (NOS) (*Figure 1*).

In the triad of cardiovascular, renal and metabolic disease, this translational project aims to further investigate the:

- Imbalance between NOX-derived O_2^- and NO signaling in the microvasculature, and associated immune cells activation.
- Therapeutic value of boosting the NO_3-NO_2-NO pathway in the triad of cardiovascular, renal and metabolic disease.

We hypothesize that novel strategies, such as stimulation of the NO_3-NO_2-NO pathway, can correct redox signaling by modulating ROS and NO generation, and hence halt progressive inflammation.

Figure 1



Approach	*in vivo*	*in vitro*	*Other analysis*
Experimental	**Cardiovascular function**	**Microvascular studies**	**Mesoscale**
-aging	*-telemetry*	*-vascular reactivity*	*-renal & vascular injuries*
-high fat diet	*-ambulatory blood pressure*	*-islet insulin release*	*-oxidative stress markers*
-ANG II infusion	**Renal function**	*-NO & ROS signaling*	*-metabolic markers*
-UNX+HS	*-autoregulation*	**NADPH oxidase function**	*-pro & anti-infl. cytokines*
-IRI	*-GFR & renal blood flow*	*-expression*	**Flow Cytometry (FACs)**
-transgenic mice	*-tubular reabsorption*	*-activity*	*-immune response*
Clinical	**Metabolic function**	**Primary cell culture**	**Biotin Switch**
-healthy subjects	*-glucose & insulin tests*	*-VSMC*	*-nitrosylation studies*
-patients	*-metabolism cages*	*-Inflammatory cells*	**Histology/Morphology**
	-DEXA scan		**Immunohistochemistry**

Methods: The research team has developed and accesses a broad, novel and advanced methodological platform to investigate novel signaling pathways in cardiovascular and renal disease. Unique combination of experimental (*in vivo* & *in vitro*) and clinical studies will be utilized in this project, which will result in novel mechanistic insights and ability to rapidly translate knowledge into practice.

Links to Home Page at the Karolinska Institutet:
http://ki.se/en/people/matcar
http://ki.se/en/people/jonlun
http://ki.se/en/people/eddwei

CSC Scholarship

Supervisors: Mattias Carlstrom (PharmD, PhD, Associate Professor), Jon Lundberg (MD, PhD, Professor) & Prof. Eddie Weitzberg (MD, PhD, Professor)

Affiliation: Department of Physiology and Pharmacology, Karolinska Institutet

Project title: Targetting microvascular oxidative stress in the triad of cardiovascular, metabolic and renal disease

Type of recruitment: Postdoctoral fellow (12-24 months)

Qualifications of applicant: Previous experience using small animal models is mandatory. Assessment of renal and cardiovascular functions *in vivo* and *ex vivo* studies of vascular function will be an asset for this project. Previous experience in mitochondrial respirometry, redox signaling, oxidative stress, inflammation, histology, immunohistochemistry is also desirable. Proficiency in the English language, documented by an internationally recognized test (e.g. TOEFL or IELTS)

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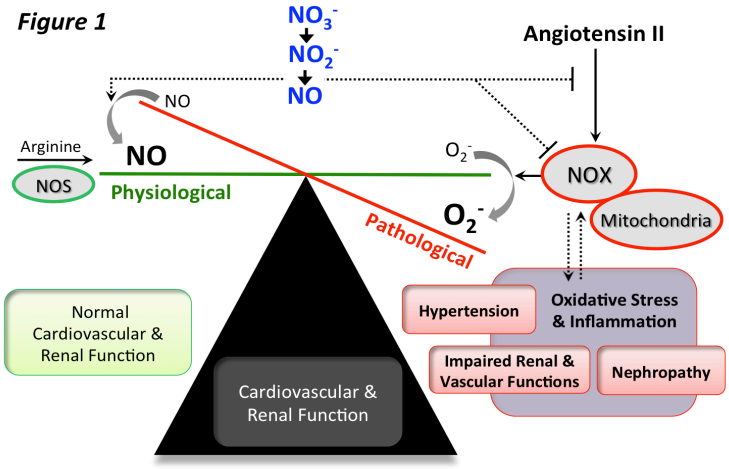
Figure 1



Approach	*in vivo*	*in vitro*	*Other analysis*
Experimental	**Cardiovascular function**	**Microvascular studies**	**Mesoscale**
-aging	*-telemetry*	*-vascular reactivity*	*-renal & vascular injuries*
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-transgenic mice	*-tubular reabsorption*	*-activity*	*-immune response*
Clinical	**Metabolic function**	**Primary cell culture**	**Biotin Switch**
-healthy subjects	*-glucose & insulin tests*	*-VSMC*	*-nitrosylation studies*
-patients	*-metabolism cages*	*-Inflammatory cells*	**Histology/Morphology**
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Methods: The research team has developed and accesses a broad, novel and advanced methodological platform to investigate novel signaling pathways in cardiovascular and renal disease. Unique combination of experimental (*in vivo* & *in vitro*) and clinical studies will be utilized in this project, which will result in novel mechanistic insights and ability to rapidly translate knowledge into practice.

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http://ki.se/en/people/matcar
http://ki.se/en/people/jonlun
http://ki.se/en/people/eddwei

Interested in recruiting a Postdoc

Project title

Drug safety and the epidemics of kidney disease

Supervisor

Juan-Jesus Carrero, Associate Professor, Senior Researcher
Department of Medical Epidemiology and Biostatistics, Karolinska Institutet
Email: juan.jesus.carrero@ki.se Phone: +46 (0)739636948
Home pages: https://www.researchgate.net/profile/Juan_Carrero2

Type of recruitment and qualifications of applicant

We are looking for a motivated postdoctoral researcher to join our team for a 24-months period. To be eligible for this position you must have A PhD in epidemiology, biostatistics, medicine or other relevant disciplines, and knowledge and experience in clinical epidemiologic data analysis; Qualifications of working independently and efficiently using excellent communication and collaborative skills are required; Fluency in English language (writing and speaking) and proficiency in analysis of data using SAS, R or other statistical programs are also required; Research in pharmacoepidemiology or in the renal-cardiovascular area is of merit.

Background

One in ten adults have chronic kidney disease (CKD), but a very small proportion is aware, visit a nephrologist or receive adequate treatment. The safety and efficacy of many drugs are affected by poor kidney function, and conversely, prolonged drug use may have long-term negative consequences on kidney function decline. Our goal is to improve the identification, prevention and management of CKD by studying real-world healthcare data.

Project description

The project focuses on evaluating the burden of CKD in society and documenting its impact on healthcare utilization, comorbidity incidence and life expectancy. In addition, it aims to quantify the extent of inappropriate prescription of "kidney-sensitive" medications and to explore the clinical risks and benefits of common drugs. To that end, the project will be primarily using data from the Stockholm CREAtinine Measurements (SCREAM) project, a complete healthcare utilization cohort of >1.5 Million individuals from the region of Stockholm. Priority areas of epidemiology research involve healthcare determinants of acute kidney injury and kidney function decline, pharmacosafety/ pharmacovigilance analyses, risk prediction algorithms and development of electronic decision-support applications to improve CKD management and prevent medication errors. The post-doctoral fellow will train under senior investigators to lead analyses, conduct, publish and present peer-review original research, mastering and carrying out epidemiological analyses of diverse complexity and wide range of exposures, with focus on longitudinal designs and causal inference.

Research group

Our research group consists of epidemiologists, pharmacists, clinicians, statisticians, and database administrators, and provides a vibrant and stimulating working atmosphere. We are committed to understanding the healthcare implications of CKD through a variety of national and international registers. We have strong collaborations with many leading centers worldwide and publish in the top ranking nephrology journals. For examples of our research, please see PubMed "carrero jj[author]".

We work at the Department of Medical Epidemiology and Biostatistics (MEB), which is among the largest departments of epidemiology in Europe with special focus on increasing our knowledge of the aetiology of different diseases. The department is situated at campus Solna. Further information can be found at http://ki.se/meb/start.

Interested in recruiting a PhD student

Project title

Internet-based cognitive behavioural therapy in dental care for children and adolescents with autism spectrum disorders

Supervisor

Professor Göran Dahllöf, Department of, Dental Medicine, division of Orthodontics and Pediatric Dentistry, Karolinska Institutet
Email: goran.dahllof@ki.se; Phone: 08 524 88 335; Home page: ki.se/dentmed

Type of recruitment and qualifications of applicant

PhD student, 4 years
The applicant should be a qualified dentist with special interest in pediatric dentistry. The successful applicant should be fluent in English language and have at least 2 years of clinical experience and experience of treating children with cognitive impairments.

Background

Autism spectrum disorder (ASD) is 1 of the most common developmental disorders diagnosed worldwide. ASD occurs in 1 of 68 children but is not related to ethnicity, nationality, or socioeconomic status. It is approximately 5 times more common in boys than girls. Although a high percentage of children with ASD have visited a dentist, many do not receive the level of care necessary to maintain good oral health. Children with ASD have impairment in communication and sensory modulation. Therefore, basic behavior guidance techniques that are effective with typically developing children may not be as effective with this population. We have recently developed internet based cognitive behavior treatment (CBT) for children with dental phobia.

Project description

Based on principles of visual preparation and individualized reinforcement, and 1000-learning, the aim of this study is to develop and test an internet-based CBT behavior management tool for children with autism. In Stockholm about 300 children are attached to autismcentrum for small children in Stockholm.

Supervisor group

Professor Göran Dahllöf
Assistant professor Shervin Shahnavaz, DENTMED, KI
Associate professor Erik Hedman, Klinisk Neurovetenskap, KI

References

SHAHNAVAZ S, HEDMAN E, KALDO V, REUTERSKIÖLD L, **DAHLLÖF G.** Internet-based cogntive behavioral therapy for dental fear and anxiety- an open trial. J Internet Medical Research. 2017;in press
SHAHNAVAZ S, HEDMAN E, GRINDEFJORD G, REUTERSKIÖLD L, **DAHLLÖF G.** Cognitive behavioral therapy for children and adolescents with dental anxiety – randomized controlled trial. JDR Clinical & Translational Research 2016;1(3):234–243.

Interested in recruiting a PhD student

Project title

Oral microbiome and metabolome in children with severe childhood caries – effects of three different preventive approaches

Supervisor

Professor Göran Dahllöf, Department of, Dental Medicine, division of Orthodontics and Pediatric Dentistry, Karolinska Institutet; Email: goran.dahllof@ki.se; Phone: 08 524 88 335; Home page: ki.se/dentmed

Type of recruitment and qualifications of applicant

PhD student, 4 years; The applicant should be a qualified dentist with special interest in pediatric dentistry. The successful applicant should be fluent in English language and have at least 2 years of clinical experience.

Background

Dental caries, one of the most prevalent diseases worldwide, is associated with dysbiosis of the tooth-colonizing microbiota, characterized by the accumulation of aciduric and acidophilic bacteria. A number of studies have also evaluated the complexity of the oral microbiota in dental caries, but results differ between studies, suggesting that the composition of the caries-associated microbiota has not been definitively identified.

Project description

The aim of this study is to characterize the oral microbiome and metabolomics in children with severe childhood caries and to study the effects of three different preventive approaches, one fluoride based prevention, one based on probiotics and one based on support for behavior change using health coachers. The goal is to identify the regime that is most effective in reversing the dysbiotic microbiota toward a healthy microbiota.
In Stockholm about 400 preschool children with extremely high caries prevalence and low age are treated under general anesthesia.
The metabolic profiles will be examined in collaboration with FIMM Metabolome Laboratory at Univ of Helsinki. Metabolite analyses will be performed using a high throughput triple quadrupole mass spectrometer (TQMS), allowing the detection of all metabolites present in a sample (semi) quantitative metabolomics. Fasted oral samples (fasted saliva, dental plaque) collected from treatment groups above will be used to determine the microbiome profile and inflammatory status of the oral cavity before and after respective treatment regiment. The oral microbiome will be examined by 16S gene deep sequencing using the Illumina amplicon library protocol and MiSeq instrument. Mapped and annotated OUT 16S centroid sequences will be aligned against the Human Oral Microbiome Database (HOMDB) to confirm the annotations.

Supervisor group

Professor Göran Dahllöf, Associate professor Margaret Chen, DDS, PhD in oral microbiology and virology, docent in infection biology, DENTMED, Kin Assistant professor Georgios Tsilingaridis, Dr. Rogier Gaiser (PhD in microbiology, DENTMED, KI

Interested in recruiting a PhD student

Project title

Shared and unique etiological risk factors across neuropsychiatric disorders: Population based studies in Sweden

Supervisor

Lorena Fernández de la Cruz, PhD – Assistant Professor (lorena.fernandez.de.la.cruz@ki.se)
Department of Clinical Neuroscience, Karolinska Institutet (KI)

Type of recruitment and qualifications of applicant

PhD student. We are looking for outstanding individuals with a degree in medical sciences or epidemiology/ biostatistics and a strong interest in psychiatric disorders. The successful applicant(s) will work with unique data sources (the Swedish National Registers, Swedish Twin Registers) and will get advanced training in epidemiological methods and biostatistics.

Background

Obsessive-compulsive disorder (OCD), Tourette's syndrome (TS), attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorders (ASD) are neurodevelopmental conditions that generally appear early in life. These diagnoses have a complex etiology, with both genetic and environmental factors contributing to the expression of each one of them. This constellation of disorders (OCD-TS -ADHD-ASD) appears together in many occasions, which suggests that these conditions may share etiological pathways. While the overlap between TS and OCD has been more studied, supporting a genetic relation between them, the overlaps between OCD/TS and ADHD and ASD have been less explored. Additionally, the current literature on the shared etiology of these disorders has a number of methodological limitations, including limited sample sizes and lack of control of covariates.

Project description

The aim of this project is to investigate whether the co-occurrence of OCD, TS, ADHD, and ASD is due, in part, to shared genetic and/or environmental risk factors. Additionally, the project also aims to study to what extent these disorders share specific genetic/environmental risk factors (e.g., perinatal complications, polygenic risk scores) and how the comorbidity impacts certain outcomes (e.g., risk of suicide, educational outcomes, work marginalization). To explore this, we will use the rich data contained in the Swedish national registers and the Swedish Twin Register (the largest in the World). We will employ different epidemiological designs, including multigenerational family studies and multivariate twin studies in order to examine if the covariation between these disorders is due to shared vs unique genetic/environmental risk factors and the extent to which the familial associations are influenced by these genetic and shared environmental factors. In addition, we will have access to molecular genetic data from various large-scale genotyping efforts, such as NORDIC (http://www.crowleylab.org/nordic/).

Research group

The supervisor, Dr Fernández de la Cruz, is an Assistant Professor within the "Anxiety, obsessive-compulsive and related disorders across the lifespan" research group at Department of Clinical Neuroscience, KI. Her work focuses on epidemiology of OCD and related disorders. Currently, she leads a research program aimed to study the health outcomes, life expectancy, and causes of mortality in anxiety, obsessive-compulsive, and related disorders. Her research group is led by Prof David Mataix-Cols. He is an internationally leading expert in the field of OCD and related disorders. Prof Mataix-Cols' group has a strong link with Prof Henrik Larsson's group at the Department of Medical Epidemiology and Biostatistics, KI. Prof Larsson explores how genes and environments influence ADHD across the life span using epidemiological methods. The team has strong track record of working together and, as a group, they have published numerous epidemiological papers in high impact factor journals [for example, Fernández de la Cruz L, Rydell M, Runeson B, D'Onofrio BM, Brander G, Rück C, Lichtenstein P, Larsson H, Mataix-Cols D. (2016). Suicide in obsessive-compulsive disorder. Mol Psychiatry, in press; Brander G, Rydell M, Kuja-Halkola R, Fernández de la Cruz L, Lichtenstein P, Serlachius E, Rück C, Almqvist C, D'Onofrio BM, Larsson H, Mataix-Cols D. (2016). Association of perinatal risk factors with obsessive-compulsive disorder. JAMA Psychiatry, 73:1135-44]. The research group has strong ties with other groups at KI (e.g., Dr Christian Rück's group) and a large network of international collaborators.

Interested in recruiting a PhD student

Project title

Migration towards the next generation-a better understanding of mammalian germ cells

Supervisor

Qiaolin Deng, Assistant Professor
Department of Physiology and Pharmacology, Karolinska Institutet
Email: Qiaolin.Deng@ki.se Phone: 0046-8-52493933 Home page:
http://ki.se/en/fyfa/developmental-biology-and-reproductive-medicine

Type of recruitment and qualifications of applicant

Doctoral student (48 months)
The applicant has been awarded advanced/second-cycle/master qualification (i.e. master degree) or has satisfied the requirements for courses comprising at least 240 credits of which at least 60 credits were awarded in the second-cycle/master level, or has acquired substantially equivalent knowledge in some other way in Sweden or abroad.
The applicant is proficient in the English language, which can be documented by an internationally recognized test such as TOEFL or IELTS. More important, relevant educational background in developmental biology, molecular biology or cell biology is required.

Background

In the human population, about 10% of couples at reproductive age have trouble getting pregnant or carrying a baby to term. Such prevalence continues to increase due to the impacts from changing environment and life styles. Although infertility can result from many causes, abnormal specification of germ cells that in turn give rise to the functional gametes has the greatest potential to affect reproduction and even impair health outcomes transgenerationally. Moreover, migratory germ cells are pluripotent per se and display many properties of embryonic stem cells including expression of pluripotency marker genes and erasure of genomic imprinting. Notably, a significant fraction of germ cells never reach their final destination and many cells even go astray as they migrate from the hindgut to the gonads. In certain context, these vagrant germ cells are able to form germ cell tumors (GCTs) if they are not eliminated by apoptosis. GCTs represent a group of biologically complex malignancies due to varying subtypes reflected by their cell of origin and primary sites. GCTs affect people in various ages from children to adults and represent therapeutic challenge. Therefore, a better understanding of the biology of germ cells has a great implication in health care and disease treatment.

Project description

We are looking for one outstanding doctoral student to work on the large-scale single-cell transcriptome project during germ cell migration. In this project we will generate transcriptional landscape of mouse germ cells during migratory period in order to understand the molecular principles concerning their molecular competence, migration microenvironment as well as the elimination mechanism due to aberrant migration at a previously unprecedented level, using state-of-the-art single-cell RNA-seq and bioinformatics technologies. Therefore, we seek one doctoral student with passion and expertise for this comprehensive project.

Interested in recruiting a PhD student

Project title: **The potential influence of microbiome on human papillomavirus (HPV) related infection and cancers**

Supervisor: Main supervisor: Juan Du, Assistant Professor; juan.du@ki.se
Co-supervisor: Lars Engstrand, Professor
Department of Microbiology, Tumor and Cell biology, Karolinska Institutet,

Type of recruitment: PhD student (48 months)

Background: We all co-exist with bacteria and share our body with trillions of microbes, especially in our intestines, the number of bacteria outnumbering the cells by a factor of ten or more. Ever since the evolution, the microbial populations have evolved to form a complex ecosystem that allows many bacteria and their phages to intermingle with a large number of viruses as well as some fungi and archaea. Over the past decade, human microbiome has been established to be evolved in a growing list of disorders and diseases such as tumor development, enteric infectious diseases, aging processes, obesity, diabetes and neurological disorders. These evidences have propelled a vast expansion of our knowledge regarding our body and microbiome. In addition, with most studies conducted on intestinal microbiome, a growing body of evidences revealed microbiome in vaginal/genital and oral tract to also play roles in protecting our health.

Aim: In our group, we want to examine the diversity of genital microbiota in HPV infected young girls and evaluate its influence for persistent HPV infection and cervical cancer. We are also investigating the role of oral microbiota in infection and progression of head and neck cancer patients as well as studying the potential influence of the microbiota on patient response to treatments in order to increase patient survival and improve quality of life.

Work plan: Samples are collected from collaboration of hospital. DNA is extracted and HPV types are analyzed with Luminex. Microbiome is analyzed with 16S rRNA sequencing using the IlluminaMiSeq machine. The bacteria distribution data is divided according to HPV-, HPV+, HPV persistent and cancer group. Bacteria pattern that related to HPV infection and cancer progress are addressed. Microbiota variations after different treatments are also compared which provides information regarding how microbiota affects patients' survival and quality of life after therapy.

Significance: The proposed projects compare microbiome distribution with HPV infection and clinical and biomarker data from patients, giving a comprehensive analysis of microbiome contribution on cervical as well as head and neck cancer progression.

Interested in recruiting a Postdoc

Project title

Chromatin architecture and remodelling in quiescence

Supervisor

Mickael Durand-Dubief, PhD
Group of Pr. Karl Ekwall, Department of, Karolinska Institutet
Email: mickael.durand-dubief@ki.se Phone: 0033777046060
Home page: http://ki.se/en/bionut/epigenetics-chromatin-remodelling-and-cancer-karl-ekwall

Type of recruitment and qualifications of applicant

Postdoc (24months)

We are looking for enthusiastic and highly motivated candidate who have knowledge in genomics, molecular biology, genetics and/or biochemistry. Proven experiences in basic molecular biology techniques gene regulation studies are important. Experience with yeast technics and bioinformatics would be appreciated. The candidate should have strong interest in interdisciplinary technology development, and novel and creative thinking abilities are essential. The ideal candidate should be collaborative, scientifically adventurous, curiosity-driven, and should bring independent and original ideas into the project.

Background

The G0 phase is a resting phase of the cell cycle where cells are inactive, in a non-proliferative state. Cells exit of the cell cycle through G1 phase and enter in three different G0 states that can be reversible (quiescent) or irreversible (senescent and differentiated). Quiescence is a reversible resting phase characterized by the absence of proliferation, a decrease of RNA contents and a lack of proliferation markers. In nature, cells spend most of their time in the quiescent stage, dissecting chromatin regulation and expression could help in understanding senescence and cancer mechanisms.

Project description

In the fission yeast, entry into quiescence can be induced by nitrogen starvation in the absence of mating partner. Under these conditions quiescent G0 cells can stay viable and able to re-enter the cell cycle for several weeks. The fission yeast is a model of choice to study this specific state of the cell cycle. The project aims to explore the chromatin regulation at different stages of quiescence in *S. pombe* by studying different mutants identified previously from screenings using combined approaches with Chromosome Conformation Capture (HiC) and transcriptomic technics.

Research group

Epigenetics is the study of heritable changes for example chromosomal states, which are not associated with changes in the DNA sequence. The Ekwall group is taking a holistic approach towards understanding epigenetic regulation, unravelling mechanisms at work both in centromeres and gene regulation.

CSC Funded Postdoc Positions (2 year) in the Laboratory of Chemical and Synthetic Systems Biology

For our growing interdisciplinary and multi-national team, we are looking for highly skilled and motivated coworkers.

Histone proteins provide a dynamic packaging system for the eukaryotic genome. Chromatin integrates a multitude of signals to control gene expression, only some of which have the propensity to be maintained through replication and cell division. To unravel the molecular circuits that underlie epigenetic gene regulation and inheritance, my laboratory aims to develops methods methods for studying and manipulating chromatin in living cells with high spatiotemporal resolution and biochemical precision. In an interdisciplinary team, we will combine chemical and synthetic biology manipulation of living cells with systems-level (genomic and proteomic) readouts. For more information and latest news visit http://elsaesserlab.org.

We are located at the modern Science for Life Laboratory (SciLifeLab) in Stockholm, Sweden. SciLifeLab also houses numerous state-of-the art national core facilities. We are part of the Division of Translational Medicine and Chemical Biology, Department of Medical Biochemistry and Biophysics. Karolinska Institutet ranks as one of the world's leading medical universities.

1 Postdoc positions (scholarship)

Applicants should hold a doctoral degree or expect to defend in 2017. Excellent education and previous experience in bioinformatics a prerequisite. The ideal candidates have will have the following skills:

1) A PhD thesis in the field of bioinformatics, ideally in a laboratory that develops bioinformatics software.
2) extensive experience in ChIP-Seq, ATAC-Seq, DHS, or related next-generation sequencing data analysis.
3) extensive experience in R, Python, MatLab or related programming languages
4) robust mathematical and statistical background knowledge

The postdoctoral fellow will work closely with the main supervisor, Dr. Simon Elsässer, wet lab students and postdocs that generate the data, experienced bioinformaticians from the Wallenberg Bioinformatics Support Program (WABI), the Ming Wai Lau Center Bioinformatics Core.

Applications should include full CV including grades of degrees, motivation letter stating the reasons for being interested in my lab and *need to be accompanied by at least one reference letter* (can be sent separately to me by the mentor).

Interested in recruiting a PhD student

Project title

Effects of novel antipsychotic drugs on schizophrenia-like behaviour in animal models of schizophrenia.

Supervisor

Sophie Erhardt, PhD, Professor in Experimental Psychiatry
Dept of Phys & Pharm, Karolinska Institutet
Email sophie.erhardt@ki.se Home page http://ki.se/en/fyfa/neuropsychoimmunology

Type of recruitment and qualifications of applicant

PhD student. We are looking for a highly motivated candidate with a master in neuroscience or other relevant area. Experience or interest in working with animal models and behaviour, as well as advanced statistics is a significant merit, as is molecular biology training with experimental experience from pre-clinical research. Excellent communication skills and an ability to interact socially and scientifically with other students and post docs in the laboratory and with collaborators in various networks are essential.

Project description

Schizophrenia is a highly heritable disorder, in most cases leading to chronic, severe loss of function. The unfavorable outcome of therapy in schizophrenia is related to our lack of insight into pathophysiological mechanisms, preventing treatment directed at causative targets. Furthermore, the absence of disease biomarkers hampers patient stratification as well as detection of patients early in the disease phase. We hypothesize that brain immune activation, leading to increased production of the NMDA receptor antagonist kynurenic acid (KYNA), is an underlying cause of schizophrenia. Based on this hypothesis, we have developed several animal models of schizophrenia. In parallel, we have, together with SciLifeLab, initiated a drug discovery program aiming at attenuating brain immune activation and production of KYNA.

Preclinical models will be used to evaluate a drug candidate's potential for clinical research, including pharmacokinetics, efficacy, pharmacodynamics, validation of normalization of immune activity and KYNA production, initial assessment of therapeutic windows, combinability, and tolerability.

The effects of identified drug candidates on KYNA levels will be investigated with microdialysis in the brain of naïve rodents and in our validated animal models of schizophrenia (see Erhardt et al., Biol Psychiatry. 2016 Dec 16. pii: S0006-3223(16)33112-2. doi: 10.1016/j.biopsych.2016.12.011. [Epub ahead of print]; Larsson et al., Neurochem Res. 2016 Sep;41(9):2243-55)..

Drug candidates that are able to reduce the synthesis of KYNA will be investigated with regard to their effects on behavior in our validated animal models of schizophrenia. The effects will be compared to the effects of other immune-blocking agents (such as minocycline and COX-2 inhibitors) as well as existing antipsychotic drugs (such as haloperidol and clozapine).

Interested in recruiting a Postdoc or Visiting Researcher

Project title

Somatic mutation load and its implication to tissue aging

Supervisor

Name, title: Maria Eriksson, PhD, Docent, Research group leader
Department of Biosciences and Nutrition, Karolinska Institutet
Email: maria.eriksson.2@ki.se Phone: 08-52481066 Home page:
http://ki.se/en/bionut/searching-for-genetic-mechanisms-that-affect-aging-maria-eriksson

Type of recruitment and qualifications of applicant

Postdoc or senior visiting scholar (24 months).

The applicant is expected to play a leading role in experimental design, experimentation, analysis, and presentation/publication of research results. The research work includes standard molecular biological techniques, next generation applications for genome-wide analysis, and previous experience from this type of research is important. He/She should have a PhD degree in Biomedicine, Bioinformatics, Molecular biology or similar. The applicant should be able to take a leading roll, provide suggestions and contribute significantly to fulfill the aim to study the contribution of somatic mutations to functional tissue decline and prepare results for publication.

Background

The postdoc/researcher is expected to be part of the group and to develop in accordance with the common group goals and research interests. He /She should be highly motivated, responsible, able to function well in the group, able to perform his /her own experiments and to provide suggestions and support in experimental design.

Project description

Age-related increased somatic mutation burden may play a role in the functional decline of the tissue seen with increased age. Efforts to characterize somatic mutation load in normal tissues have been hindered by technical limitations of available DNA sequencing technologies to detect low-frequency genetic variation within a tissue sample. During recent years we have developed a protocol to analyze somatic mutation load in single stem cells from human tissues. Our unpublished data from these studies show that stem cells accumulate 100-1000s of mutations with increased age (similar range as seen in cancer), and suggest that this is dependent on mechanisms involved in the function of DNA repair. However, it remains unknown how somatic mutations are propagated in the tissue and contribute to tissue homeostasis decline associated with increased age. Further analysis of somatic mutagenesis and age-related mutational processes will be important for aging and cancer. In the next years we plan to further define the role of age-related somatic mutations in human tissue and identify the under laying mechanism(s), to be used for the intervention of age-associated disease.

Research group

The research group of Maria Eriksson aims to identify novel genetic mechanisms of aging with a special focus on somatic mutations and their contribution to the functional declined tissue homeostasis with increased age. The research involves the use of both in vitro and in vivo model systems, in addition to human patient samples.

Interested in recruiting a Postdoc

Project title

Molecular and cellular studies of the Alarmin HMGB1 and its role in inflammatory conditions

Supervisor

Helena Erlandsson Harris, Professor
Department of Medicine, Solna, Center for Molecular Medicine, Karolinska Institutet
Email: Helena.Harris@ki.se Phone: +46-8-5177 6746
Home page: http://www.cmm.ki.se/field/reumatologi/

The research group of Erlandsson Harris is part of the Rheumatology unit, Dept Medicine. The laboratory is situated at the Center for Molecular Medicine, a center within Karolinska Institutet for translational inflammation research.

Type of recruitment and qualifications of applicant

Postdoc (24 months)
The applicant is expected to conduct high quality research in a collaborative manner. The postdoctoral fellow will be responsible for the planning of the project as well as data acquisition, preparation and analysis, manuscript writing and other activities for disseminating the results. Work is also to seek external research funding from external funding agencies.
The work will involve both cell and molecular work as stated in the project description below. Thus, documented knowledge of these techniques is required. Experience from disease-oriented work is considered favourable. The applicant must be organized, thorough, proactive and a talented problem solver.

Background

HMGB1 (high mobility group box chromosomal protein 1) is a structural nuclear protein present in all eukaryotic cells. Stressed and dying cells release HMGB1 which then acts as an Alarmin, a signal of danger and an initiator of inflammatory reactions. As an alarmin, HMGB1 has the potential to induce cytokines and prostaglandins, to induce cell migration and cell differentiation by interaction with multiple receptors (TLR2, -4, -9, RAGE, TIM-3 and others have been suggested). The interaction of HMGB1 with its receptors and the functional outcome is regulated by the redox status of HMGB1 and of complex formation with different ligands. HMGB1 has been suggested to be a mediator of pathology in multiple conditions, including arthritis, stroke and cancer. The interaction of HMGB1 with TLR4 is well defined whereas its interaction with the other receptors needs to be better defined.

Project description

The applicant is expected to conduct a research project focused on the molecular interactions of HMGB1 with its suggested receptors, the importance of post-translational modifications for the interactions and the consequences for the functional outcome. Additionally, the project involves revealing the molecular mechanisms active for two therapeutic agents neutralising HMGB1 activity. Methodologies used in the project are molecular cloning, protein expression and purification. Cell culture and in vitro assays such as Western blotting, ELISAs, Luminex, FACS, Nanostring and RNAseq.

Interested in recruiting a Ph.D. student/

Project title
Investigation of the functional role of antibodies to citrullinated proteins in rheumatoid arthritis and experimental animal models

Supervisor
Changrong Ge, Assistant Professor
Department of Medical Biochemistry and Biophysics, Karolinska Institutet
Email: changrong.ge@ki.se
Phone: 46 (0) 76-287 80 29
Homepage: http://www.inflam.mbb.ki.se

Type of recruitment and qualifications of applicant
Ph.D. (48 months)
The applicant must have successfully passed an education in medicine or biological science including a master education, which also shows scientific ability. Laboratory experience and excellence is a requirement, in particular in immunology and biochemistry. Experience in experimental animal research is needed. Computer skills and bioinformatic knowledge are needed. Fluent English is a requirement.

Background
The first antibodies that appear and predicts the development of Rheumatoid arthritis (RA) are rheumatoid factors and antibodies to citrullinated proteins (ACPA). The function of these antibodies, i.e. if and how they cause disease or if they, in fact, could regulate the disease, is unknown and the current project aimed to investigate the function of isolated monoclonal antibodies from RA.

Project description
The project includes analysis and validation of posttranslationally modified epitopes recognized by autoreactive B cells, of relevance for rheumatoid arthritis as well as studies of the function of cloned antibodies. A new preliminary diagnostic test has been developed which contain major epitopes recognized by antibodies in sera from RA patients and individuals at risk of developing RA. This first test will be validated in both animal models and in human RA cohorts. The project will focus on epitope-specific antibodies that are associated with protection against the disease. These antibodies have been shown to also protect against experimental models of arthritis. The structural interactions between the antibodies and its epitope will be analyzed by crystallization. The therapeutic mechanisms will also be analyzed in both experimental models and in patients with RA and individuals at risk of developing RA.

Research group
Medical Inflammation Research, MBB, Holmdahl

Interested in recruiting a PhD student

Project title

Regulation of mast cell differentiation, maturation, and function in health and disease

Supervisor

Gunnar Nilsson, professor
Immunology & Allergy unit, Department of Medicine, Karolinska Institutet
Email: gunnar.p.nilsson@ki.se ; Phone: +46 8 517 70205
Home page: http://ki.se/en/meds/gunnar-nilsson-group

Type of recruitment and qualifications of applicant

PhD student
The applicant should have a Master degree from a medical or biomedical program. The ideal candidate has previous experience in translational research with focus on molecular biology and bioinformatics. Fluency in English is a requirement.

Background

Mast cells are hematopoietic cells known for their role in allergic diseases, but they contribute to the pathology of many different diseases. The cells have been difficult to study as they are tissue-bound, and knowledge about their development and regulation of function is still very limited. We analyse mast cells in mastocytosis, a disease characterized by increased numbers of mast cells, which have increased reactivity. We use this as a model to gain knowledge about mast cell development and regulation of its function.

Project description

The major aims for this project are: i) To investigate the transcriptional networks in aberrant mast cells from mastocytosis patients using single cell RNAseq; ii) To reveal the transcription factor networks that regulates cell fate decisions in myeloid progenitors, with focus on mast cells. Methods that will be used in the project include single cell fluorescence-activated cell sorting (with indexing), single cell RNA sequencing, bioinformatic analysis, cell culture, and PCR. Primary cells are used in all projects. Sources include mouse bone marrow, blood, and peritoneal cavity. Human cells are from bone marrow and blood from both healthy subjects as well as patients with systemic mastocytosis or other haematological disease. The ultimate and long-term goal for the project is to decipher the transcription factor networks during haematopoiesis, and to identify deregulated genes during mast cell differentiation that can be used as therapeutic targets.

Research group

The research group on Mast Cell Biology consists of prof. Gunnar Nilsson, 1 senior lab manager, 2 post docs and 2 PhD students. The research is performed in an interdisciplinary setting with strong collaborations with clinical departments and other national and international research groups.

Interested in recruiting a PhD student

Project title

Identification of novel fusion proteins in neoplasms and neurodegenerative disease

Supervisor

Johan Holmberg, PI, PhD.
Department of Cell and Molecular Biology, Karolinska Institutet
Email: johan.holmberg@ki.se Phone: +46-722212702
Home page: http://ki.se/en/cmb/johan-holmbergs-group

Type of recruitment and qualifications of applicant

PhD student; The applicant must have experience in standard cell culture and molecular biology. It is considered a merit if the applicant have experience from animal experiments. The applicant must be prepared to work with mouse models. Bioinformatic skills will also count as a merit. The applicant should be able to communicate well in English.

Background

The relative paucity of mutations has hampered efforts to understand the pathogenesis in several pediatric cancers. Neuroblastoma (NB) arises from precursor cells of the sympathetic nervous system and is the most frequent extracranial solid childhood cancer. It exhibits a high degree of clinical heterogeneity ranging from spontaneous regression to swift progression accompanied by fatal outcome despite intense treatment intervention. Despite several sequencing efforts, the frequency of detected recurring mutations remains low in NB. This relative absence of identified mutations can be translated into a lack of candidates for drug targeting.

Project description

We intend to identify novel fusion genes through bionformatic analysis of sequenced NB patient material. Once identified, selected candidates will be validated in an independent NB cohort. To reveal functional properties, transcripts will be cloned and expressed both in vitro and in vivo. We will also explore the mechanisms through which they that affect key aspects of NB biology. To understand if selected candidates affects NB growth in vivo NB cells overexpressing the fusion transcripts will be transplanted to immunodeficient mice. Analysis will focus on cellular processes important for NB biology (e.g. proliferation, apoptosis, differentiation etc.) as well as the global transcriptional response through RNAseq analysis. **Preliminary results:** We have identified and validated fusion transcripts that occur at high frequency in high-risk NB. Several candidates have been cloned into expression vectors. For one candidate, *ZNF451-BAG2*, we have functional data revealing that it blocks maturation of NB cells in vitro and neuronal progenitors in vivo.
Significance: The high frequency through which these read-through fusion events occur imply that they represent an overlooked mechanism that could provide high risk neuroblastoma with a critical growth advantage. Besides shedding light on the fundamental biology of NB, we hope that our effort also will provide novel druggable targets.

Research group

PI: Johan Holmberg
Post-docs: Yao Shi, Erik Södersten, Vilma Rraklli
PhD-student: Isabelle Westerlund, Konstantinos Toskas

Interested in recruiting a Post-doc student

Project title
Identification of novel fusion proteins in neoplasms and neurodegenerative disease

Supervisor
Johan Holmberg, PI, PhD.
Department of Cell and Molecular Biology, Karolinska Institutet
Email: johan.holmberg@ki.se Phone: +46-722212702 Home page: http://ki.se/en/cmb/johan-holmbergs-group

Type of recruitment and qualifications of applicant
Post-doc; The applicant must have experience in and master standard cell culture and molecular biology techniques. The applicant should have experience from working with mouse models. It is considered a merit if the applicant have experience from xenograft models of tumorigenesis and of in utero electroporation. Bioinformatic skills will also count as a merit. The applicant should be able to communicate well in English.

Background
The relative paucity of mutations has hampered efforts to understand the pathogenesis in several pediatric cancers. Neuroblastoma (NB) arises from precursor cells of the sympathetic nervous system and is the most frequent extracranial solid childhood cancer. It exhibits a high degree of clinical heterogeneity ranging from spontaneous regression to swift progression accompanied by fatal outcome despite intense treatment intervention. Despite several sequencing efforts, the frequency of detected recurring mutations remains low in NB. This relative absence of identified mutations can be translated into a lack of candidates for drug targeting.

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Significance: The high frequency through which these read-through fusion events occur imply that they represent an overlooked mechanism that could provide high risk neuroblastoma with a critical growth advantage. Besides shedding light on the fundamental biology of NB, we hope that our effort also will provide novel druggable targets.

Research group
PI: Johan Holmberg
Post-docs: Yao Shi, Erik Södersten, Vilma Rraklli
PhD-student: Isabelle Westerlund, Konstantinos Toskas

Interested in recruiting a PhD student, Postdoc or a visiting researcher

Project title

Mechanical forces control morphogenesis and cancer

Supervisor

Lars Holmgren, Professor, Department of Oncology and Pathology, Karolinska Institutet
Email: Lars.Holmgren@ki.se Home pages: http://ki.se/en/people/larhol http://ki.se/en/onkpat/lars-holmgrens-group; https://se.linkedin.com/in/lars-holmgren-74648bb

Type of recruitment and qualifications of applicant

Post-doc, PhD student or visiting scientist. Experience in molecular and cell biology techniques are required.

Background

Transmission of mechanical force via cell junctions is an important component that molds cells into shapes consistent with proper organ function. Of particular interest are the cadherin transmembrane proteins that play an essential role in connecting cell junctions to the intra-cellular cytoskeleton. Understanding how these biomechanical complexes orchestrate intrinsic and extrinsic forces is import for our understanding of the underlying mechanisms driving morphogenesis and invasion. We have previously identified the Amot protein family, which are scaffold proteins that integrate polarity, junctional, and cytoskeletal cues to modulate cellular shape. Methods: Analysis of protein expressin in human and mouse tumors. Using genetic inactivation approaches in endothelial cells, zebrafish and mice we have characterized the function of the protein family in normal development as well as in tumor progression. Results: Expression analysis shows that p60 AmotL2 is regulated by hypoxia and is induced in colon, breast, prostate and glioma cancer patients. We provide a novel mechanism how tumor cells escape the mechanical constraint exerted by neighboring cells and become plastic and highly invasive.

References:

AmotL2 disrupts apical-basal cell polarity and promotes tumor invasion. Mahdi Mojallal, Yujuan Zheng, Sara Hultin, Stéphane Audebert, Tanja van Harn, Per Johnson, Claes Lenander, Nicolas Fritz, Christin Mieth, Martin Corcoran, Marja Hallström, Johan Hartman, Nathalie Mazure, Thomas Weide, Dan Grandér, Jean-Paul Borg, Per Uhlén, and Lars Holmgren. Nature Communications, 2014 Aug 1;5:4557.

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Interested in recruiting a PhD student or a Postdoc

Project title

Mechanisms of blood vessel formation and function in CNS development and cancer

Supervisor

Lars Jakobsson, PhD, group leader
Department of Medical Biochemistry and Biophysics, Karolinska Institutet
Email: Lars.jakobsson@ki.se Phone: +46(0)8-52487124
Home page: http://ki.se/en/mbb/lars-jakobsson-group

Type of recruitment and qualifications of applicant

PhD student (48 months) or a postdoc (24 months)
The applicant should have a master's degree in molecular biology/bioinformatics or similar with a true interest in developmental biology. The candidate must be able to work with mice and experience thereof would be a merit. The candidate should be open-minded, curious, creative and collaborative. A good knowledge of spoken and written English is required.

Background

Blood vessel malformation and malfunction have major impact on the development and treatment of multiple diseases such as cancer, psoriasis, stroke, diabetes complications and vascular anomalies. In order for the blood vasculature to adapt to changing demands from tissue, the endothelial cells (ECs) of the vessel wall need to collectively re-organise to form new functional branches, involving precise co-ordination of migration, differentiation and proliferation. Failure of ECs to interpret the instructive tissue- or serum -derived signals may cause life-threatening malformations and malfunction.

Project description

The purpose of our studies is to understand the molecular mechanisms in control of the organisation of individual ECs into the hierarchical blood vasculature of arteries, capillaries and veins and why this fails in cancer and in the genetic vascular disease HHT/Osler. To this end, we utilize unique transgenic mouse lines with EC-specific ubiquitous or conditional endogenous fluorescent reporters, tumour models as well as inducible mosaic gene deletion, mimicking HHT with severe arteriovenous malformations (see our paper, *Jin et al, Nature Cell Biology, 2017* for details). We apply single-cell RNA sequencing followed by bioinformatic analysis to gain information at individual cell level, potentially revealing novel vascular targets. To study cell dynamics at single cell level during vascular morphogenesis, and to evaluate the effects of presumptive targeting, we utilize ex vivo and in vivo multi-photon confocal time-lapse imaging. All methods have either been established in the Jakobsson lab or are available in collaboration. We believe that these projects will provide novel data that may reveal fundamental mechanistic insight on processes of angiogenesis and vascular malformation with significance in cancer, stroke, diabetes and vascular anomalies.

Research group

Lars Jakobsson, PI; Yixin Wang, PhD student; Yi Jin, postdoc (part time affiliated);
Postdoc in recruitment

Interested in recruiting a Postdoc or PhD student

Project title
B cell memory in autoimmune diseases

Supervisor
Mikael Karlsson, Professor
Department of Microbiology, Tumor and Cellbiology, Karolinska Institutet
Email: Mikael.Karlsson@ki.se Home page: http://ki.se/en/mtc/mikael-karlsson-group

Type of recruitment and qualifications of applicant
Postdoc or PhD student
The applicant should preferably have experience in immunological methods and both in vivo and in vitro work

Background
The focus of this proposal is to define the mechanisms behind activation and regulation of innate inflammatory processes in disease with emphasis is on B cells. I propose to study their recruitment and interaction with other immune cells and the role they play in cardiovascular disease including the formation of memory to self-antigens and effector functions beyond antibody production. Since cardiovascular disease is closely linked to autoimmunity and in particular Systemic Lupus Erythematosus (SLE), I propose to compare these two diseases using both mouse models and patient samples and bridge knowledge available in the fields of cardiovascular and rheumatology research.

Project description
The final goal of this proposal is to gain understanding on how to interfere with mechanisms leading to faulty B cell activation and disease development and to define new disease markers that can be used in the clinic.
Aim I – Define key cellular mechanisms that recruit B cells in atherosclerosis with focus on cellular interactions and subsets.
Aim II – Investigate how to modulate B cell activation and evaluate potentially novel disease markers related to B cell activation.
Aim III – Assess how targeting of different B cell mediated disease mechanisms can be used for treatment in models for atherosclerosis.
Aim IV – Translate knowledge gained from animal models to investigate human disease and develop novel diagnosis tools as well as verify the potential use of B cell directed treatments.

Research group
At the moment the group consists of four PhD student and two postdocs. We have access to all the necessary facilities to complete this project. Also, this project is done in collaboration with groups at Harvard Med School in the US and the Rheumatology clinic at Karolinska hospital, Sweden.

Interested in recruiting a Postdoc

Project title
Immunometabolic control of atherosclerosis

Supervisor
Daniel Ketelhuth, PhD, Associate Professor
Department of Medicine Solna, Karolinska Institutet
Email: daniel.ketelhuth@ki.se Phone:+468 51776419 Home page:http://ki.se/en/people/danket

Type of recruitment and qualifications of applicant
Postdoc (24 months) The applicant is to perform research in cardiovascular immunology and metabolism to identify novel therapeutic targets against inflammation, lipid metabolism, and atherosclerosis. We expect that the holder of the job will have proven experience in field of immunology, and/or be very knowledgeable in the fields of biochemistry, pharmacology, metabolism and atherosclerosis research

Background
The immune system has been implicated as a key regulator linking multiple metabolic risk fact ors, e.g. dyslipidemia, diabetes, obesity, and fatty liver disease, with the pathological process in vessel wall leading to atherosclerosis and cardiovascular diseases. Hence, metabolism and activation are fully integrated in immune cells, and systemic and microenvironmental changes in metabolism have been shown to modulate their responses. In pioneer work, we demonstrated that tryptophan metabolism, through the production of metabolites in the Kynurenine pathway, plays a protective role in atherosclerosis by reducing pro-inflammatory responses of macrophages, T cells, and smooth muscle cells in the vessel wall, and influencing plasma lipids.

Project description
Our research indicates that metabolites are not just ‘fuels’ in their pathways, but that they can also act as signalling molecules in different immune cells and influence atherosclerosis. It is our aim to identify and understand the immunometabolic reactions controlling immune responses during the process of atherosclerosis in order to develop new therapies to prevent and treat cardiovascular disease (CVD).

Research group
The “Ketelhuth team” is part of the Cardiovascular Medicine Unit, led by Prof. Per Eriksson. Our unit is an example of multi-professional environment omprising expertise in basic, experimental, and clinical molecular research, and thus a great supporting factor to the development of our projects. At present, in addition to myself, our team counts with two MD-PhD students, and three postdoctoral fellows. Our research is supported by grants from the Swedish Heart and Lung foundation, Novo Nordisk foundation, and pharmaceutical industry.

Interested in recruiting a PhD student

Project title: Cerebral small vessel disease, genetic susceptibility, and cognitive phenotypes in aging: a population-based study

Supervision

Main supervisor: Miia Kivipelto, MD, PhD, Professor, Division of Clinical Geriatrics and Aging Research Center (ARC), Department of Neurobiology, Care Sciences and Society (NVS), Karolinska Institutet (KI). Contact person: Dr Chengxuan Qiu, email: chengxuan.qiu@ki.se.
Co-supervisors: Chengxuan Qiu, PhD, Associate Professor; Rui Wang, PhD; Erika J Laukka, PhD, ARC, Department of NVS, KI, Stockholm Sweden; Tiia Ngandu, MD, PhD, Associate Professor, National Institute for Health and Welfare, Helsinki, Finland.

Type of Recruitment: A 4-year full-time doctoral (PhD) position in the major of medicine (geriatric epidemiology), supported by a scholarship from CSC (50%) and a project grant (50%).
Qualifications of the Applicant: General requirements for the applicant: (a) a bachelor degree or equivalent of education in medicine, biology or public health plus a master degree in biostatistics or epidemiology or neurology; (b) experiences or skills of using common statistical software such as SPSS, Stata or SAS; (c) documents/certificates to demonstrate the proficiency in English language; and (4) communication skills and ability to interact effectively and work productively with others in a multidisciplinary research group.

Brief information of the project

Background and aims: In the past decade, evidence has been accumulating that cerebral small vessel diseases (SVDs) are associated with increased risk of cognitive decline and dementia in old age. In this project, we seek to clarify the following research questions: (a) how do various SVDs distribute in older people? (b) Do imaging markers of various brain lesions have differential effects on specific cognitive domains? (c) Do SVDs have an interactive effect with individual or clustering susceptible genes that are related to cardiovascular diseases (e.g., APOE, ACE, IDE, and FTO) on risk of dementia and cognitive decline in aging? (d) To what extent, do certain compensatory factors (e.g., education and leisure activities) modify the detrimental effects of SVDs on cognitive decline, and delay the onset of dementia? ***Methods***: This doctoral project will be based on 2 population-based imaging studies of old people from Sweden and Finland: the Swedish National study on Aging and Care (SNAC-K)/SNAC-K MRI Study (web: http://ki-su-arc.se/longitudinal-studies) and the Finnish Cardiovascular Risk Factors, Aging and Dementia (CAIDE; web: www.uef.fi/en/web/caide), and an intervention study of the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER; web: www.thl.fi/en). In all the three studies, data on demographics, lifestyles, health-related behaviors, health conditions, use of medications, global cognitive function and dementia were collected and assessed following standardized procedures and criteria at baseline and each follow-up. Markers of brain vascular and neurodegenerative lesions were assessed on brain MRI scans among the sub-sample of each study. Different statistical approaches will be utilized to address those specific research questions. ***Relevance***: From a clinical perspective, this project may provide sound evidence supporting the view that vascular pathways can be potentially targeted for therapeutic intervention. From a public health perspective, research findings may pave the way for preventive interventions to delay the onset of brain aging-related cognitive disability (e.g., dementia) by targeting vascular and cognitive compensatory pathways.

Aging Research Center (ARC) at Karolinska Institutet (KI) (http://ki-su-arc.se/; http://ki.se/en/)
ARC at NVS/KI is a multidisciplinary center devoted to studying health in aging. Researchers at ARC conduct scientific research, educate the next generation of aging researchers, and disseminate information about our research findings within and outside the scientific world. Our research group includes senior researchers, postdocs, doctoral students, and visiting scientists. We study the transitional process of health in aging from medical and psychosocial perspectives.

supervisor: Claudia Kutter, PhD

academic title: Assistant professor — SciLifeLab fellow

affiliation: Karolinska Institutet, MTC
Nobels väg 16
171 77 Stockholm, Sweden

SciLifeLab Stockholm
Tomtebodavägen 23B
171 65 Stockholm, Sweden

project title: "Gene regulation and transcriptional control in liver metabolism"

type of recruitment: postdoctoral researcher (24 months) in genomics and RNA biology

qualifications of applicant: The applicant will apply genome- and transcriptome-wide approaches (epigenome profiling and RNA-sequencing) to study functionality of regulatory sequences in the DNA and processed transcripts in liver tissues and cultured cells. The work implies original research in computational biology, designing computational methods and implementing analytical pipelines to infer underlying molecular mechanisms. A strong background in genomics, computational biology, statistics and/or genetics is required. Experience in eukaryotic RNA biology, gene regulation, transcriptome-wide studies and mammalian tissue culture techniques are important. Prior knowledge in bioinformatics (implementing analytical pipelines) and R programming for statistical computing and graphics is an asset. Since the work will be conducted in a vibrant and interdisciplinary group, the ideal candidate should be collaborative, scientifically adventurous, curiosity-driven, and brings independent and original ideas into the project. The applicant should have good communication skills and be proficient in spoken and written English.

project description: Liver cells ensure metabolic homeostasis by regulating synthesis and breakdown of nutrients. Activating specific gene regulation programs facilitates homeostasis. Deregulation of genes has been observed upon increased and unbalanced food consumption and is linked to developing liver diseases[1-4]. The aim of this project is to:

(i) identify how transcriptional programs are regulated to maintain cellular plasticity by using state-of-the-art ChIP- and RNA- sequencing in human and mouse primary hepatocytes and multiple liver cancer cell lines

(ii) investigate how gene regulatory programs get unhinged during high- and low-fat diet and measure the effect upon applying hormonal treatments in human and mouse by using comparative genomics

(iii) determine predictive measurements in gene deregulation by using machine learning approaches

This research project contributes to our understanding of the molecular mechanisms employed in liver metabolism. Since deregulation of liver metabolism can lead to severe diseases, the aim is to benefit patients by providing novel prognostic and therapeutic markers.

The work will be conducted in collaboration with Cecilia Williams (KI, KTH) and Adil Mardinoglu (KTH, Chalmers) who will complement the project's success with experimental and computational expertise, respectively to ensure maximum success.

group home page: ki.se/en/mtc/claudia-kutter-group
scilifelab.se/researchers/claudia-kutter/
orcid.org/0000-0002-8047-0058

1. Kutter C. *et al.*, **PLoS Genetics** (2012) 8(7), e1002841
2. Du J *et al.*, **Epigenetics & Chromatin** (2016) 9: 28
3. Lee S. *et al.*, **Molecular Systems Biology** (2017) 13: 938
4. Rodriguez H. *et al.*, **Molecular Aspects of Medicine** (2017) 54

Recruitment of a PhD student

Project title

Investigation of the regulatory role of antibodies to cartilage specific proteins

Supervisor

Pernilla Lagergren, Professor of Surgical Care Science, Surgical Care Science group, Department of Molecular medicine and Surgery, Karolinska Institutet.
Email: pernilla.lagergren@ki.se Home page: http://ki.se/en/mmk/surgical-care-science

Type of recruitment and qualification of the applicant

Doctoral student for 48 months of full-time work. This corresponds to a PhD in medicine at Karolinska Institutet. Completed undergraduate medical exam, e.g. surgeon, physician, nurse. Knowledge in epidemiological and biostatistical methods is a merit. Important personal characteristics include curiosity, engagement, and good collaboration skills. Excellence in oral and written English is required (with required test results).

Project description

Oesophageal cancer is common worldwide, particularly in China, and is afflicted by poor prognosis. Curative treatment includes extensive surgery (oesophagectomy) usually preceded by neoadjuvant chemoradiotherapy. The surgery is often followed by severe complications and the recovery is extraordinarily long and complex. Minimally invasive surgery may potentially reduce the risk of complications and facilitate recovery after surgery, and this is currently a very important topic in oesophageal cancer therapy. However, there is a need for much more research on this topic. This PhD project will use data from a Swedish nationwide and population-based cohort study, named OSCAR (Oesophageal Surgery on Cancer patients – Adaptation and Recovery). OSCAR is uniquely comprehensive and includes almost all patients who have undergone surgery for oesophageal cancer in Sweden from 2013 onwards. The patients are interviewed 1 year after surgery and respond to several well-validated patient-reported outcome measures during a visit by a research nurse. Patients are then followed up repeatedly (at 1½, 2, 2½, 3, 4 and 5 years) after surgery with established questionnaires. Patient and treatment details are collected from medical records.

Specifically, the project will examine:

1) If minimally invasive surgery reduces the risk of post-operative complications compared to open surgery;

2) If postoperative complications are risk factors for post-traumatic stress after surgery;

3) If minimally invasive surgery is associated with better postoperative body image compared to open surgery;

4) If minimally invasive surgery is associated with better physical performance and nutritional status one year after surgery compared to open surgery.

Interested in recruiting a Postdoc

Project title

Validation of protein markers to stratify and guide breast cancer therapy

Supervisor

Janne Lehtiö, Professor
Department of Oncology-Pathology, Karolinska Institutet
Email: janne.lehtio@ki.se Phone: 08-524 814 16 Home page:
http://ki.se/en/onkpat/janne-lehtios-group & http://www.lehtiolab.se

Type of recruitment and qualifications of applicant

Postdoc (24 months)
The applicant is highly motivated to join our research team to work validate protein biomarkers in large independent clinical cohorts. The candidate is creative and should have a degree in molecular life sciences, molecular biology, biomedicine, medicin, bioinformatics or equivalent. The applicant should have basic laboratory skills and knowledge of cell biology. The applicant should have good communication skills and ability to work productively in a team of researchers. The majority of work will be around validation of biomarkers in clinical cohorts and therefore emphasis is placed on personal ability and previous experience of working with and evaluating tumor stainings. Pathology background in preferred but not required. Excellent ability to express themselves in speech and writing, including scientific writing, in English is a requirement. Previous experience in programming (for instance R and Python), statistical analyses, and in the fields of proteomics, molecular biology, tumor biology and protein chemistry is considered as an advantage for this project.

Background

Breast cancer (BC) is the most common form of cancer among females with about 1.7 million new patients annually in the world. Breast cancer ranks as the fifth cause of death from cancer overall (522,000 deaths). Despite advances in treatment, in age group of 45 year old women, breast cancer is responsible for 20% of all death.
Treatment decisions are based upon tumor histology and on the status of three biomarkers: estrogen receptor (ER), progesterone receptor (PR), and HER2. In addition, BC molecular subtypes can be defined by mRNA expression levels based on a set of 50 genes (PAM50) or by surrogate immunohistochemistry (IHC) markers (ER, PR, HER2, Ki67). Multigene expression assays (e.g. MammaPrint, Oncotype DX, Prosigna ROR) are not readily available for all patients, and despite progress in patient stratification by current pathology-based surrogate markers, they are suboptimal with 1 out of 3 patients potentially misclassified (Coates et al., 2015; Prat et al., 2015; Senkus et al., 2015).
How the tumor proteome forms subtypes and markers for tumor stratification is less well studied, even though proteins provide the major molecular phenotype and proteins constitute the majority of drug targets. In addition, mRNA is suboptimal surrogate measurement of protein levels as mRNA and proteins display varying correlation (Mertins et al., 2016; Zhang et al., 2014).
To study BC on the phenotypic protein level we have used the by us developed MS technique, high-resolution isoelectric focusing (HiRIEF) nanoLC-MS/MS based proteomics

(Branca et al., 2014) and generated 2 comprehensive quantitative proteome datasets. The first BC proteome cohort constitutes of 45 tumors representing all mRNA defined subtypes with a protein depth of 10.000 across all tumors. Correlation analysis of this dataset have identified functional protein modules with enrichment of protein complexes that are related to known and novel tumor groups. The functional modules also include FDA approved drug targets and provide a basis to suggest combination therapy and stratify tumors based on the phenotypic proteome. We have also identified 2 novel clusters of extracellular matrix proteins that are related to outcome. The second proteome cohort (Promix) constitutes of tumor samples from a neoadjuvant study of patients that received chemotherapy. Comparing responders versus none responders we have identified proteins predictive of chemotherapy response. In addition, the cohort includes samples before and after chemotherapy treatment making it possible to follow drug response in the tumor and suggest markers to monitor therapy.

Project description

Breast cancer has come a long way towards personalized therapy, however, additional biomarkers are needed to truly tailor therapy based on each tumor. In this work, we aim to validate protein biomarkers from discovery proteomics in clinical cohorts using the routinely used immunohistochemistry (IHC) technique, and proximity ligation (PLA), to add a new dimension of functionality via measurement of protein interactions. Three different aims are planned, all with validation of biomarkers in clinical cohorts.

1. Validate protein marker expression from 2 of us newly discovered extracellular matrix (ECM) clusters and their relation to tumor biology and outcome in clinical cohorts.
2. Validate the interaction of potential novel drug target combinations we have discovered using protein correlation networks.
3. Validate protein marker expression to evaluate response to chemotherapy.

The project is done in collaboration with Prof. Anne-Lise Børresen-Dale, Pathologist MD PhD Hege Russnes and PhD Kristine Kleivi Sahlberg in Oslo. In Stockholm we have collaboration related to the Promix cohort with Clinical PI Thomas Hatscheck, Karolinska Hospital & Institutet and pathologist Johan Hartman.
In house, the project is led by PhD Henrik Johansson and pathologist Fabio Socciarelli.

Research group

The Lehtiö group carries out research projects within proteomics, a field aiming to study global changes in a proteome, for example, to determine the function of a specific protein in the context of a biological network. The Lehtiö research group develops mass spectrometry based methods and applies them to cancer research with the overall aim to improve cancer therapy. As such, one of our main projects involves proteome scale analysis in order to obtain a proteome view of a system. Our proteomics research project is performed in a translational frame-work within a large collaborative network with preclinical and clinical researchers in Sweden and around the world.

Interested in recruiting a Postdoc/Visiting Researcher

Project title

Platelet-regulated inflammatory mechanisms in atherosclerosis

Supervisor

Nailin Li, associate professor
Karolinska Institutet, Department of Medicine-Solna, Clinical Pharmacology Group
Email: Nailin.Li@ki.se Phone: +46-8-517 739 96

Type of recruitment and qualifications of applicant

Postdoc (24 months) or visiting researcher (12 months)

Applicants to this position must have a doctoral degree in medicine, biomedicine, or life sciences conferred during last five years. The applicant should be self-motivated, and wish to conduct research independently. The successful applicant should have expertise in cell culture, flow cytometry, and basic cellular and molecular biology techniques. Previous research experience in T cell and macrophage immune/inflammatory responses and/or animal studies of atherosclerosis is an advantage. Good communication skill in English is a prerequisite. Teamwork spirit is also an important qualification.

Project description

Atherosclerosis is an inflammatory and thrombotic disease. Platelets, as the principle cellular component in thrombosis, have also emerged as a versatile regulator of inflammatory mechanisms in atherogenesis. We and others have recently shown that platelets distinctly regulate immune responses of different $CD4^+$ T cell subsets, and that platelets closely regulate macrophage functions. Aim of the project is thus to elucidate the impact of platelet-regulated vascular inflammation on the development of atherosclerotic lesions. We are investigating the mechanisms underlying platelet regulation of $CD4^+$ T effector responses of T helper (Th1 and Th17) cells and regulatory T (Treg) cells. We will study platelet influence on M1 and M2 polarization and plasticity. Using various murine models, we are studying how platelet deficiency of specific inflammatory mediators affects $CD4^+$ T effector responses and M1-M2 balance in vivo and how the deficiency influences atherosclerotic lesion formation in a pro-atherosclerotic mouse model. The work may lead to novel therapeutic developments for atherosclerotic disease management.

Interested in recruiting a Postdoc/Visiting Researcher

Project title

Platelet-cancer cell cross-talk in cancer progression: Clarifying mechanisms for efficient interventions

Supervisor

Nailin Li, associate professor
Karolinska Institutet, Department of Medicine-Solna, Clinical Pharmacology Group
Email: Nailin.Li@ki.se Phone: +46-8-517 739 96

Type of recruitment and qualifications of applicant

Postdoc (24 months) or visiting researcher (12 months)

Applicants to this position must have a doctoral degree in medicine, biomedicine, or life sciences conferred during last five years. The applicant should be self-motivated, and wish to conduct research independently. The successful applicant should be skilled in cellular and molecular biology laboratory work. Previous research experience in cancer biology, thrombosis, and/or animal studies of atherosclerosis is an advantage. Good communication skill in English is a prerequisite. Teamwork spirit is also an important qualification.

Project description

Platelets facilitate cancer metastasis and growth. Better understandings of platelet-cancer cell interactions can help to optimize cancer therapeutics. Thus, the project aims to: a) elucidate novel mechanisms of cancer cell-platelet cross-talk that promote cancer metastasis and growth; b) study how selective release of platelet pro- and anti-angiogenic factors influences on cancer progression; c) investigate the impact of miRNA-regulated de novo synthesis of platelet angiogenic factors on tumor angiogenesis; d) evaluate the true effects of antiplatelet treatments on cancer metastasis using novel models of cancer metastasis.

We will study how cancer cells “educate” platelets, and if cancer cell-educated platelets and platelet-primed cancer cells collaborate to facilitate cancer progression, and how platelet releasate promotes distal interactions of metastatic tumours using multiple models of cancer metastasis. We are studying the mechanisms underlying platelet selective release of pro- or anti-angiogenic factors upon different stimuli, and evaluating the impact of pro-angiogenic platelet releasate and anti-angiogenic platelet releasate on cancer growth and metastasis. Possible regulation of de novo synthesis of platelet angiogenic factors by microRNAs, especially the ones derived from cancer cells, will also be explored. The true effects of antiplatelet treatments on cancer metastasis will be evaluated using novel and pathophysiologically relevant murine models of cancer metastasis.

Interested in recruiting a PhD student/Postdoc/Visiting Researcher

Project title

International comparison and collaboration: a basis for establishing and implementing a culture appropriate maternal mental health care model

Supervisor: Helena Lindgren, Associate Professor, Head of Department of Reproductive Health, Institute of Women's and Children's Health, Karolinska Institutet Email: Helena.lindgren@ki.se Phone: +46 733-44 25 99 Home page: http://ki.se/en/kbh/reproduction-childbirth-and-parenting

Coordinator: Simone Schwank, MS MA Msc lic Psychotherapist, PhD candidate Department of Reproductive Health, Institute of Women's and Children's Health, Karolinska Institutet

Type of recruitment and qualifications of applicant

Qualification: PhD student, Postdoc, Guest Researcher, Guest Professor
Requirements: economic or public health, reproductive health, psychiatry

Background

In 2015 China shifted from a one-child policy introduced in 1979 to a two-child policy. The policy shift is intended to countermeasure the demographic development of an aging population, skewed sex ratios, and a shrinking labour supply. The child policy shift has an immense impact on Chinese society, families, and the economy of the PRC. We aim to analyze the judgment and decision-making in reproductive health and family planning, and how the former one-child policy contributes to the families' reflections. This research in collaboration with Fudan University, Redhouse Hospital, School of Nursing and School of Public Health will provide insight into the factors contributing to parents' deciding whether to have a second child, and investigate the policy shift's effect on perinatal family health.

Project description

Maternal mental health problems have adverse impact on maternal and child health. However an appropriate care model has not yet been developed in China. The NSFC research project "construction of maternal mental health care model (MAMM) and intervention study based on social learning theory" aimed to develop a maternal mental health care model and a specific intervention program. This intervention program will be base of the current China-Sweden joint research and education project. Multi-center RCT will be performed in order to study the effect of mental health intervention during pregnancy provided by midwives (intervention) vs. standard care (obstetrician led care) focused on factors that can reduce mental health problems and adverse outcomes in pregnant women and postpartum. The research project is in a key stage, initiating the development of the intervention program and training of perinatal health care professionals. Based on the governmental request of developing a midwifery education program, the maternal mental health care model shall be integrated in the working scope of the midwives. The collaboration project further includes the up-scaling of midwifery education programs on bachelor, master and PhD level, supported by both Karolinska Institutet, Fudan University, and the Chinese government.

Interested in recruiting a PhD student

Project title

Gene-environment interplay in traits related to quality of life throughout adulthood and into old age.

Supervisor

Miriam A. Mosing, Assistant Professor
Dep of Medical Epidemiology and Biostatistics & Dep of Neuroscience, Karolinska Institutet
Email: Miriam.Mosing@ki.se Phone: +467 2532 2230

Type of recruitment and qualifications of applicant

The applicant should have a Master's or honours degree in Psychology, Public Health, Biomedicine, Statistics or Gerontology (or similar) and should be enthusiastic about aging research and the application of (standard) statistical methods. The student should possess excellent written and spoken English skills.

Background

The idea of predicting Quality of Life (QoL) has received great attention with the hope of developing early intervention strategies to increase positive affect leading to better health outcomes especially in the aged. Simple measures of QoL such as subjective well-being/health (SWB) are often superior to objective clinical assessment for predicting an individuals' morbidity and mortality, suggesting that QoL in itself is a powerful predictor of future health. But what drives the predictive value of SWB over and above objective health? Environmental factors, e.g. stressful life events and loneliness, are important influences on mental, somatic and cognitive health, although QoL related traits have been shown to be at least partly genetic. However, still little is known about the interplay between genetic and environmental influences affecting QoL and healthy aging. For example, are such 'environmental' variables (e.g. loneliness and stress) causal risk factors for bad health outcomes? Or are there underlying shared genetic vulnerabilities? These are important questions to answer in order to understand whether such variables truly qualify as starting points for intervention.

Project description

The present project explores factors contributing QoL in terms of mental and somatic health throughout adulthood and into old age and aims to determine underlying genetic and environmental influences and their interplay to produce QoL. This will be achieved using a combination of longstanding and novel methods such as cross-sectional, longitudinal and survival analyses, the classical twin and co-twin control design, and genetic risk-prediction. The proposed project has the advantage of using rich samples including phenotypic and genetic data based on several registries in Sweden, but also from other countries through existing collaborations, thereby providing a unique resource toward answering questions that are key to QoL and healthy ageing in the 21st century.

Research group

The student will join Prof. Nancy Pedersen's aging research group, a group of about 15 researchers and PhD students with a large variety of backgrounds, research projects, and interests as well as different methods applied. The research environment is very pleasant and collaborative and the student will have access to staff statisticians.

Interested in recruiting a Postdoc

Project title

Reciprocal crosstalk between innate and adaptive immunity in disease progression in HIV-1 positive Elite Controllers

Supervisor

Ujjwal Neogi, PhD, Assistant Professor
Department of Laboratory Medicine, Karolinska Institutet
Email: ujjwal.neogi@ki.se
Home page: http://ki.se/en/labmed/multi-omics-research-team

Type of recruitment and qualifications of applicant

Postdoc (24 months)

The applicant should have strong knowledge in cell culture related work and PhD in Medical Science/microbiology/other Life Science field. Prior experience with FACS, confocal, siRNA knockdown experiments is desired. Student should also had proven scientific credentials with first author publications in reputed peer reviewed English journals. Knowledge in miRNA, and modern molecular biological techniques like RCA, PLA etc are plus. Candidate should check the group profile.

Background

The purpose of this research program is through basic and translational research integrating the multi-omics techniques and the clinical data to understand the disease progression mechanism in a group of HIV-1 positive individuals, who control viral replication and restrained progression to AIDS, without any antiretroviral therapy for a longer duration of time (controller). In a systemic approach, I shall apply the molecular data-first approach to classify persistent genetic variants or expression patterns in order to reduce host influenced heterogeneity among the controllers followed by the phenotypic profiling, virological and immunological characterizations of the disease progression mechanism in ECs, with the long-term goal of functional HIV-cure and vaccine development.

Project description

Most of the studies to identify the viral control in controllers conducted to date have either focused on genomic co-relation of immune protection or have focused on individual immunological aspects. Despite the scientific evidence suggested that controllers are heterogeneous, most of the studies were conducted to specific predefined molecules or pathways ignoring the systemic, interconnected immunological programmes that individual immune defence mechanisms are associated with. Currently available data indicate that the natural control of HIV-1 replication have multiple underlying mechanisms of immune defence.

Research group

The Research term is nested in Sonnerborg Group and work mainly with big data multi-omics technologies. The team members are working in multidisciplinary fields from immunology, nano-biotechnology, high throughput sequencing, bioinformatics, proteomics, metabolomics etc.,

Interested in recruiting a Postdoc

Project title

The role of interactions between gut microbiota and immunity in development of active Mycobacterium tuberculosis infection.

Supervisor

Piotr Nowak, M.D., PhD

Department of Medicine Huddinge, Karolinska Institutet

Email: Piotr.Nowak@ki.se

Home page: http://ki.se/en/medh/team-microbiota-inflammation

Type of recruitment and qualifications of applicant

Postdoc (24 months)

The applicant should have strong knowledge in molecular biology/immunology and a PhD in Medical Science/Microbiology/other Life Science fields. Prior experience of sequencing, FACS, immune assays and cell culture experiments is desired. Student should also have proven scientific credentials with first author publications in reputed peer reviewed English journals. Knowledge in bioinformatics, microbiome analysis and metabolomics are of extra interest.

Background

The purpose of this research program is through basic and translational research to understand aspects of reactivation of Mycobacterium tuberculosis from latency to active infection. We will integrate the data obtained by multi-omics techniques, and immune assays with clinical phenotype to understand the role of the microbiome and the metabolome in M. tuberculosis reactivation. The pathways of M. tuberculosis control, suggested by the multiomics / phenotype integration will be later studied in *in vitro* systems.

Project description

There are several line of evidence that the reactivation of M. tuberculosis infection is dependent on several factors not only associated with classical ''immune suppression'' status but also dependent for example on nutrition and metabolic status of individuals. In our prospective study of patients with latent and active Mycobacterium infection we aim to investigate several features of the immune response as well as microbiome/metabolome in order to obtain a holistic picture of M. tuberculosis infection. Thus, data obtained from analysis of the microbiome and the metabolome will be linked to immune and meta-data. Additionally the pathway mechanisms that will be revealed by the analysis will be applied in *in vitro* systems to further study the mechanism of latency control during M. tuberculosis infection.

Research group

Our Research team is a part of Professor A. Sonnerborg Group at Department of Medicine Huddinge/Laboratory medicine and focus on translational/patient-orientated research. The experiments are performed at the new-build top-modern laboratory at Campus Flemingsberg. Presently, two Chinese students from the CSC-programme and also an ongoing collaboration with Prof Yiming Shao, director of the Division of Research on Virology and Immunology of NCAIDS, China CDC. We adapt the data multi-omics technologies addressing clinical questions. The team members are working in multidisciplinary fields from immunology, nano-biotechnology, high throughput sequencing, bioinformatics, proteomics, metabolomics etc., We have broad collaboration with key leaders in immunology, microbiome sciences at both KI and National Institute of Health, USA.

Interested in recruiting a Postdoc or PhD student

Project title: Worms as vectors for bacteria and parasites

Supervisor :Susanne Nylén, PhD Associate Professor MTC, KI
Department of Microbiology Tumor and Cellbiology, Karolinska Institutet
Email: Susanne.nylen@ki.se Phone: +46852486736
Home page: http://ki.se/en/mtc/susanne-nylen-group

Type of recruitment and qualifications of applicant

Postdoc (24 months) or possibly PhD student
The applicant should be proficient in the English language. Background in microbiology and immunology is a merit as is previous work with research animals, in particular rodents. For post doc, a PhD in a field related to the project (i.e. microbiology or immunology)

Background

Helminth infections are common in all animals. Most infections are relatively benign while other may with time cause severe disease. Intestinal nematodes are the most common worms in humans as well as animals.
We live in symbiosis with the microbiota that we carry and the composition of microbiota have implication on several aspects of our development, in particular development of immune response. The microflora itself may also contribute control of pathogens by preventing their establishment though occupation of a niche or by secretion of substances harmful to the pathogen. The presence of worms modulates the intestinal flora for better and worse.
One rarely considers that parasitic worms are also animals in their own right with their own intestinal tract that is colonized by bacteria and protozoa (and possibly other worms). Just as for other animals the worms need their bacteria and in their absence many worms fail to develop or do not develop normally.

Project description

We and other have shown that intestinal worm can modulate host immunity and mute immune responses to secondary infection and vaccines. The most potent down regulatory effect of worms on host immunity are seen in the close proximity to the worm. This could make worms attractive carriers/vectors for other microbes as dampening of immune responses and modulation of host microbiota may facilitate establishment and survival of other microbes in a target niche.
We are interested in the role intestinal helminths and their microflora have on our microflora and in particular if they can act as vectors, mediating transfers of bacterial and / or protozoa from one host to another. There are reports indicating that pinworms may take up the protozoa Dientamoeba fragilis, but if these eggs can transmit the protozoa is less clear.

In this project the following research questions will be addressed:

- Microbiota of the worms and their eggs
- How do the worms own microbiota evolve? Unique, environmental or host origin?
- Can bacteria/protozoa transfer worms to/from their host and the environment? If so what type of microbes can utilize the worm.

Studies will be conducted in experimental models as well as on human samples.

Interested in recruiting a Postdoc

Project title
Human Computer Interactions (HCI) for Stress Reduction

Supervisor
Walter Osika, MD, PhD, Associate Professor
Department of Clinical Neuroscience, Karolinska Institutet
Email: walter.osika@ki.se Phone: +46704530546 Home page: http://ki.se/en/people/walosi

Type of recruitment and qualifications of applicant
Postdoc (6 months). The applicant should have a background in health & human computer interaction design, and have experience in working with different stakeholders (both researchers, designers and end product users) relevant for the development of novel stress reducing interventions. Experiences from international research collaborations is favourable.

Background
High levels of stress and an increasing information overload contributes to the global burden of disease at great societal costs. There is therefore an urgent need for both preventive interventions aimed at reducing the adverse effects of stress, as well as new effective treatment strategies. Lately there has been a rapid increase of interactive applications for health and wellbeing integrating medicine and Human–computer interaction (HCI) research, and people increasingly turn to digital technology to handle stress, anxiety, social isolation and negative emotions, and e.g. stress management methods such as mindfulness practices are moving to digital devices. In our initial market search we found only few devices delivering e.g. mindfulness practices that satisfied customers with HCI technology and wearable technology, and that were evidence based from a medical point of view.
New research collaborations including HCI researchers, psychologists, neuroscientists, designers and engineers are hence needed to explore the behavioral impact of these new technologies and applications, as well as to develop them in user-friendly and evidence based ways.

Project description
This post doc project focuses on the use of HCI technology to reduce stress. Our research group has already performed studies where we designed digital technologies and bio-sensing technology for stress reduction [Zhu et al 2017]. Our prototypes are based on multi-sensory experience (e.g. visual, auditory, olfactory and tactile sensation) for flexible & effective usage in daily life. The post doc is supposed to collaborate on the further development of HCI based stress reducing interventions and test them in randomized controlled studies with healthy subjects & with patients with stress related problems.

Research group
Ass prof Osika/Prof Gumpert, Centre for psychiatry research, Dep of Clinical Neuroscience

Reference
Zhu, B., Hedman, A., Feng, S., Li, H., & Osika, W. (2017). Designing, Prototyping and Evaluating Digital Mindfulness Applications: A Case Study of Mindful Breathing for Stress Reduction. *Journal of Medical Internet Research*, *19*(6), e197. DOI: 10.2196/jmir.6955

Interested in recruiting a Postdoc/Visiting Researcher

Project title:
Uncovering the role of atypical ubiquitination in health and disease

Supervisor:
Magdalena Paolino
Assistant Professor
Department of Medicine
Karolinska Institutet
Center for Molecular Medicine L8:03
Karolinska University Hospital Solna
171 76 Stockholm, Sweden
Email: magdalena.paolino@ki.se

Type of recruitment: the project is suitable for a postdoc or a visiting researcher

Project description: Ubiquitination is a post-translational modification by which ubiquitin, a small 76-amino acid protein, is covalently attached to a substrate protein in order to regulate and diversify protein functions. Protein ubiquitination is essential to maintain cellular homeostasis and several human pathologies have been linked to alterations in ubiquitin-dependent networks. Thus, it is of paramount importance to better understand the molecular and cellular processes regulated by ubiquitin. In particular, we still do not fully understand the relevant functions of the different types of ubiquitin chains that exist in cells. This project aims to elucidate physiological roles for atypical ubiquitin chains, a relatively neglected area of research. The project integrates genetic, cellular, and molecular studies at the interface of basic and translational research with the ultimate goal of revealing the molecular basis of relevant ubiquitin-dependent human diseases, and in doing so, to uncover novel strategies for therapeutic intervention.

Qualifications of applicant: The applicant will apply comprehensive studies and state-of-the-art approaches encompassing 3D cultures, gene expression, biochemical, proteomics, and cell-based functional assays to uncover the physiological role(s) of atypical ubiquitin chains. The project requires the usage of gene editing, cell culture, reporter assays, transcriptome profiling as well as mass spectrometry and ubiquitination assays. A strong background in biochemistry, molecular biology and mammalian tissue culture techniques is required. Previous knowledge on working with retro- and lentiviruses as well as usage of gene editing techniques, such as CRISPR/Cas9 and inducible shRNA knockdown systems is an asset. Also experience from working with ubiquitin-related enzymes and performing ubiquitination assays will be important. The ideal candidate should be able to work independently and take a strong lead in managing the project. Moreover, the applicant should be highly motivated and collaborative, and is expected to work in a diligent way to generate properly controlled data. Finally, the applicant should have good communication skills and be proficient in spoken and written English.

Group: The research group of Dr. Magdalena Paolino is part of the Cardiovascular Medicine Unit at the Department of Medicine in Solna. We are recruiting an integrated team of talented experimental researchers, who will work together to help elucidate what are the cellular and physiological functions of atypical ubiquitin chains.

Relevant publications:

1.Paolino M., et al (2014) *Nature*, 507 (7493), 508-512.
2.Suriben R.**,**Kaihara K., **Paolino M**., et al. (2015). *Cell*, 163 (6), 1457-1467.
3.Paolino M., et al. (2011).. *J Immunol,* 186 (4), 2138-2147.

Interested in recruiting a Postdoc

Project title: Genome-wide study of transcriptional and epigenetic heterogeneity in cancer drug resistance.

Supervisor's name: Vicente Jose Pelechano Garcia, PhD. Assistant Professor.
Karolinska Institutet. Department of Microbiology, Tumor and Cell Biology. Science for Life Laboratory Fellow. Email vicent.pelechano@scilifelab.se
Home page http://pelechanolab.com/

Type of recruitment and qualifications of applicant

Postdoctoral Fellow. The postdoctoral fellows will have the opportunity to learn and develop a variety of experimental and computational genome-wide tools. Applicants to this position should have a PhD in molecular biology, genomics, epigenetics or computational biology. Preferred experience also includes familiarity with eukaryotic transcription, ChIP-Seq, cancer biology, single-cell analysis and molecular biology techniques. A strong interest in interdisciplinary technology development, and novel and creative thinking abilities are essential. The successful candidate is expected to be highly motivated and take a strong lead on his/her project and start to develop independent ideas. The candidate should be able to communicate scientific results by writing up scientific papers and attending scientific meetings in English. The ideal candidate is also expected to participate in the general duties of the team and to effectively communicate with scientists of very diverse backgrounds in a highly interdisciplinary and international environment. Applicants wishing to integrate computational and experimental biology approaches are especial encouraged to apply.

Project description

One of the biggest challenges in biology is to understand how identical information encoded in a genome generates diversity between cells and tissues. Different cells in a population can present varying responses to the same stimulus. In some cases these differences are attributable to genetic mutations. However, in other cases, identical (clonal) cells can also display phenotypically heterogeneous responses. This phenotypic heterogeneity has a poorly understood origin but a significant impact on biology and human health. To understand how these divergent phenotypes arise, it is necessary to study the factors that control gene expression variability across cells.

We will use novel genome-wide approaches to investigate the transcriptional basis of the non-genetic heterogeneity driving divergent gene expression responses to drugs in cancer cells. We will study both the transcriptome complexity and epigenetic heterogeneity of those populations. We will expand our current approaches to interrogate also single-cell variations. To study the functional relevance of those variations, we will sort cells according to their phenotypic response to drugs and analyze the effect of drug re-exposure. Once we identify potential mechanisms implicated in the appearance of phenotypically divergent cells, we will characterize selected targets using biochemical and molecular biology tools.

The proposed work will use experimental and computational tools to improve our knowledge of epigenetics and transcription regulation and to what degree it underpins cell-to-cell differences and bet-hedging strategies.

This project will be performed in the context of a long-term collaboration with Prof. Wei Wu laboratory (PICB Shanghai & Stanford University).

Interested in recruiting a PhD student, Postdoc or a visiting researcher

Project I: *Regulation of immunoglobulin class switch recombination in human B cells*

The project is aimed at understanding the complex molecular mechanisms involved in DNA editing, repair and recombination during immunoglobulin class switch recombination (CSR) and somatic hypermutation (SHM) and their involvement in the pathophysiological processes leading to immunodeficiency, genome instability and cancer development in humans.

Project II: *Discovery of therapeutic targets in B cell lymphoma*

The project is aimed at identifying potentially treatable molecular targets in mature B cell lymphomas (with focus on diffuse large B cell lymphoma, follicular lymphoma and mantle cell lymphoma) by next generation-sequencing (whole genome and exome sequencing, RNA-seq) and other high-throughput technologies such as proteomic analysis and genome-wide CRISPR/cas9 loss- or gain-of-function screening.

Supervisor

Qiang Pan-Hammarström, MD, PhD, Professor
Department of, Karolinska Institutet
Email: qiang.pan-hammarstrom@ki.se Phone: +46 8 52483592

Type of recruitment and qualifications of applicant

PhD students (4 years)
The applicant is eligible to apply if he or she has obtained a master degree in the fields of Medicine, Biology, Genetics, Oncology and Immunology, or related fields, and fulfils all academic entry requirements set by the Karolinska Insitutet.

Postdoc or Visiting Scientist (12-24 months)
The applicant is eligible to apply if he or she has obtained a PhD in the fields of Medicine, Biology, Genetics, Oncology, and Immunology, or related fields.

The applicants for all positions should be talented and highly motivated students or researchers who are able to work within a team environment.

The candidates are expected to possess a strong background in immunogenetics or cancer genetics and master several molecular biology techniques, equivalent to their carrier ages. Good knowledge of molecular biology, cell culture, FACS, the CRISPR/Cas 9 technology or skills in analysing large-scale data, is an advantage. Furthermore, the candidate should possess excellent communicating and writing skills in English.

Research group

Our group currently consists of one lab manager, 4 postdocs, 2 PhD students and several visiting students and scientists. For details please visit our website:
http://ki.se/en/labmed/research-group-qiang-pan-hammarstrom

Interested in recruiting a Postdoc/Visiting Researcher

Project title

TIME COURSE OF ALLOIMMUNISATION DURING PREGNANCY: CONSEQUENCES FOR OPTIMISATION OF SCREENING AND PROPHYLAXIS

Supervisor

Marie Reilly, Professor
Department of Medical Epidemiology and Biostatistics, Karolinska Institutet
Email: marie.reilly@ki.se Phone: +46 8 5248 3982 Home page: http://ki.se/en/people/mareil

Type of recruitment and qualifications of applicant

Postdoc or Visiting Researcher (6 months).

This project is suitable for a medical or health science PhD graduate with good quantitative skills, a keen interest in population health issues such as screening and maternal/neonatal health. The project would ideally suit a postdoc or researcher with experience of handling large population databases and statistical software tools (such as SAS). Good communication skills and a capacity to collaborate are essential as the project is multi-disciplinary spanning clinical medicine, health services and epidemiology.

Background

Screening for red blood cell antibodies, follow-up of alloimmunised pregnancies, and prophylaxis of Rhesus negative women immunised with anti-D antibody, are standard components of maternal care in many countries. Immunisation due to anti-D or other antibodies is rare, raising questions about the cost-effectiveness of screening and the potential for optimisation, of not just who but when to screen, monitor and treat. Despite the accumulation of extensive electronic records, protocols vary widely between (but also within) country.

Project description

Aim: To investigate how information on the time course of alloimmunisation can help optimise the identification, follow-up and prophylaxis of pregnancies at risk. The **specific aims** are to: (1) model alloimmunisation risk during pregnancy to identify a "risk window" (2) compare the timing and severity of immunisations due to prior transfusion or pregnancy , (3) use repeated titres to estimate the effect of accumulated antibody exposure on adverse pregnancy outcomes, (4) investigate if anti-D prophylaxis in late pregnancy provides protection through delivery.
Methods: Using a large population register, we will model the "risk-window" for optimal screening (Aim 1 and 2). Using a regional quality register, we will compare the severity of early alloimmunisations due to different prior exposures (Aim 2), and apply methods from toxicology to investigate how the accumulated antibody exposure impacts on fetal health (Aim 3). In a prospective cohort of 100 Rhesus-negative women carrying a Rhesus-positive fetus, a pharamokinetic study will investigate the protective levels of anti-D IgG at full-term following prophylaxis at week 28-30 (the current routine) and a booster at week 38.
Significance: Our findings can provide timely and relevant evidence for expert groups working on optimising and harmonising screening programs and contribute to the development of more equitable and cost-effective protocols.

Research group

The postdoc or visiting researcher will join a multidisciplinary collaborative team. The principal investigator, **Marie Reilly**, is a full-time professor of Biostatistics with a keen interest in blood-related research. Co-investigator **Agneta Wikman** is a qualified specialist in immunology and transfusion medicine at Karolinska University Hospital, where she is responsible for the blood group serology laboratories in the county of Stockholm. Co-investigator **Eleonor Tiblad** is an MD specialised in fetal medicine and combines her clinical work at Karolinska University Hospital with research in fetomaternal immunology.

Interested in recruiting a Postdoc/Visiting Researcher

Project title

DESIGN AND ANALYSIS OF EFFICIENT EPIDEMIOLOGICAL STUDIES

Supervisor

Marie Reilly, Professor
Department of Medical Epidemiology and Biostatistics, Karolinska Institutet
Email: marie.reilly@ki.se Phone: +46 8 5248 3982 Home page: http://ki.se/en/people/mareil

Type of recruitment and qualifications of applicant

Postdoc or Visiting Researcher (6 months).
This project is suitable for a PhD graduate in statistics or biostatistics with an interest in extending the design and analysis of epidemiological studies to make more efficient use of existing data resources and stored biological material. The postdoc or researcher should be familiar with standard epidemiological analyses, have good data analysis and programming skills in one or more statistical software packages, and an interest in applying their skills in the intersection of biostatistics, epidemiology and clinical research.

Background

Case-control designs are widely used in genetic and molecular studies due to their cost efficiency. The investment in the collection and measurement of biomarkers has generated new interest in developing statistical methodology to enable re-use of these data or to extend the efficiency advantages of case-control sampling to other designs. Our work focuses on methods of analysis that remove the bias in re-used data resources by using appropriate weights to correct for the sampling strategy that gave rise to the data. We also extend the well-known advantage of matched case-control designs to the study of continuous outcomes, such as biomarkers.

Project description

Aim: To develop statistical methods and software to enable valid analysis of non-standard epidemiological designs. The **specific aims** are to (i) Extend the methodology for re-use of controls from prior nested case-control studies, (ii) Develop modified case-control designs for informative sampling from biobank material, (iii) Introduce matched study designs and methods of analysis for continuous outcomes, (iv) Provide software for the analysis of extended designs

Methods:

For the re-use of case-control data or the analysis of modified case-control designs, we use a weighted likelihood approach where the weights essentially "reconstruct" the underlying cohort. For the analysis of continuous outcomes, we are developing rank-order logit models that use stratification for confounder adjustment.

Significance: Our work will provide methods and software that enable optimal use (and re-use) of scientific data being generated in various designs, allowing for flexibility in the sampling and optimal use of biological material contributed by volunteers.

Research group

The postdoc or visiting researcher will join an international collaborative team. The principal investigator, **Marie Reilly**, is a professor of Biostatistics with a keen interest in epidemiological design. Co-investigator **Chuen Seng Tan** is an assistant professor of biostatistics at the National University of Singapore, working with methods for using electronic medical records. Co-investigator **Nathalie Stoer** is a biostatistician at the Norwegian Cancer Register and the author of the R package. *multipleNCC* for extended analysis of nested case-control data. Other collaborators include prostate cancer researchers from Sweden and the Harvard School of Public Health.

Interested in recruiting a Postdoc Researcher

Project title

Charting the molecular landscape in chronic lymphocytic leukemia

Supervisor

Prof Richard Rosenquist Brandell, MD, PhD
Department of Molecular Medicine and Surgery, Karolinska Institutet
Email: richard.rosenquist@ki.se Phone: +4670-6253384 Home page:http://ki.se/people/richro

Type of recruitment and qualifications of applicant

Postdoc (24 months)
We aim to recruit a highly motivated postdoctoral researcher with experience of advanced molecular analysis in hematological malignancies. The research is focused on applying next-generation sequencing (NGS) technologies to explore key molecular events linked to the ontogeny and evolution of chronic lymphocytic leukemia (CLL) that ultimately can be used to predict therapy response and clinical outcome. The applicant is required to have completed a doctoral degree or higher in a field related to the position, such as cancer genetics, molecular hematology, biotechnology or similar.

Background

CLL is clinically and biologically heterogeneous with varying clinical outcome. Although new drugs have been approved in the last few years, there is still no curative treatment and there is an urgent need for new therapeutics and predictive biomarkers. To overcome this gap of knowledge, we believe that the optimal strategy is to identify patient subgroups with distinct features that respond differently to therapy. We recently described a novel subgrouping of CLL into clinically and biologically distinct categories. In our perspective, further molecular characterization of these subgroups using high-throughput technologies, including NGS, will increase the possibility to identify novel biomarkers, resistance mechanisms and subgroup-specific treatment targets.

Project description

Taking advantage of our large, well-annotated CLL cohort, we employ a spectrum of state-of-the-art NGS technologies and innovative molecular tools to investigate clinically relevant and homogeneous CLL patient groups. By applying such approach, we will obtain an unprecedented, compartmentalized picture of the complex molecular landscape in CLL. Ultimately, this comprehensive characterization will lead to an improved risk stratification with far-reaching implications for the biology and management of the disease, the identification of novel predictive biomarkers that can guide treatment decision, and the definition of novel treatment targets in this incurable disease. The project is translational in its nature with possibilities to link molecular data to clinical records.

Research group

The research group is led by prof Richard Rosenquist Brandell and located at Center for Molecular Medicine, Karolinska Institutet, Stockholm, and includes PhD students, postdoctoral researcheres, and bioinformaticians. The group will move to a new laboratory building in Jan 2018, BioClinicum, at Karolinska University Hospital. The group works closely with Clinical Genetics at Karolinska university Hospital and Science for Life Laboratory (www.scilifelab.se).

Interested in recruiting a Postdoc/Visiting Researcher

Project title

Role of SOCS and STATs in the regulation of immunity to Mycobacterium tuberculosis

Supervisor

Martin Rottenberg,
Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet
Email: Martin.Rottenberg@ki.se Phone: +468 5248 6711 Home page: **http://ki.se/en/people/marrot**

Type of recruitment and qualifications of applicant

Postdoc/ Visiting researcher (12-24 months)
We are looking for a highly motivated and self-going postdoctoral fellow or visiting researcher to perform cutting-edge infection immunology research in a leading research group at the Dept of Microbiology, Tumor and Cell Biology, Stockholm, Sweden.
The applicant should have a PhD in the field of cellular or molecular immunology, and preferably interested in T cell responses. Methods including FACS analysis and sorting, real time PCR, primary cell culture and differentiation, histopathology and immunohistochemistry are an advantage. Part of the studies planned are done in murine and to a lesser extent in guinea pig experimental models of infections.

Background

Tuberculosis (TB) is a global health problem. The challenges to control it are enormous: BCG, the only available vaccine against TB, is only partially protective in adults. SOCS3 protein inhibits STAT3. The activation of STAT3 transcription factor by different cytokines, growth factors and hormones and is critical in regulation of immunity and inflammation. We believe these molecules to control the infection with *Mycobacterium tuberculosis*, the causative agent of TB.

Project description

We have previously shown that SOCS3 in both myeloid and lymphoid cells independently and via distinct mechanisms the control of murine infection with *M. tuberculosis.*
We propose an in depth investigation of SOCS3-STAT3 mediated control of *M. tuberculosis* infection. Specifically, we will:

1. Investigate the role of myeloid SOCS3 and STAT3 expression in activation of dendritic cells and in the regulation of *Mtb* specific T cell-mediated protection.
2. Evaluate the role of STAT3 in T cells during *M. tuberculosis* infection, specifically in the development of T cell memory cells populations.
3. A novel imaging technique based on the bar code sequencing of pad lock amplified probes allowing the *in situ* simultaneous detection of > 200 transcripts on a tissue section will be employed to map the development and immunobiology of the granuloma and the role of SOCS3 and STAT3 in granuloma formation and maintenance.
4. Diabetes increases the risk of developing TB. SOCS3 regulates insulin resistance which underlies the onset of diabetes. Whether SOCS3 expression also influences the TB and diabetes comorbidity will be analysed in appropriate genetically modified animals.

The project will contribute, through an in depth assessment of the control of cytokine responses, to the improvement of the design of specific vaccines and to a better understanding of the relationships between the bacteria and the immune system.

Research group

The Department of Microbiology, Tumor and cell Biology (MTC) is dedicated to the fight against infections and cancer worldwide are two of the major goals of research at MTC. The merge of infection biology, immunology and cancer research provides a unique platform where fruitful interactions are developed. MTC is a leading institution, both at the national and international level, in science and education. The research group is composed of 3 post docs and 3 PhD students.
The research group, headed by Professor Martin Rottenberg, studies the regulation of bacterial load and pathology during infection with *M. tuberculosis* in experimental models of infection. The role of different cell populations, cytokines, chemokines and transcription factors are studied in part within a EU-funded TB-vaccine project.

Interested in recruiting a PhD student or Postdoc

Project title

Cyclic di-nucleotide signalling in *Salmonella typhimurium*

Supervisor

Ute Römling, professor in Medical Microbial Physiology
Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet
Email: Ute.Romling@ki.se Phone: +46-8-524 87319
Home page: http://ki.se/en/mtc/ute-romling-group

Type of recruitment and qualifications of applicant

Postdoc (24 months) or PhD student
The applicant can have a Master education in Biochemistry, Biology, Chemistry, Medicine or related subjects. High engagement, outstanding performance and interest in scientific questions is a must. The PhD education should aim to be the basis for a later career in science.

Background

The secondary messenger cyclic di-GMP (c-di-GMP) has been established as an almost ubiquitous signaling molecule in Bacteria. Originally discovered as an allosteric activator of a cellulose synthase, c-di-GMP signaling regulates biofilm formation, motility, the cell cycle, virulence properties, resistance phenotypes and other phenotypes such as photosynthesis and production of antibiotics.
C-di- GMP is a life style switch regulator, which adjusts the transition between the sessile and the motile and between the acute virulent and the persistence or commensal status of bacteria on the single cell level. Cyclic di-GMP concentrations in the cell are regulated by a complex signaling network whereby up to over 100 c-di-GMP metabolizing proteins can control the c-di-GMP level in the cell. Only some highly adapted host pathogens lack the c-di-GMP signaling system. These cumulative data point out c-di-GMP as the most important secondary messenger in Bacteria.

Project description

This project aims to unravel the cyclic di-GMP signalling network in *S. typhimurium*. C-di-GMP signalling is involved in biofilm formation, motility and virulence in this species. In this project, the role of individual gene products of the cyclic di-GMP turnover network involved in biofilm formation and virulence phenotypes will be assessed. Comparisons to homologous gene products in other species will be made. Methodology applied spans from genetic manipulation over biochemical approaches and microscopy techniques to bioinformatic analysis.

Research group

Ute Römling group

Interested in recruiting a Postdoc

Project title: **Postdoctoral Fellow - Computational Cancer Biology**

Supervisor: Susanne Schlisio, Associate Professor; Karolinska Institute - MTC
Box 240, Nobels vag 3; SE-171 77 Stockholm; SWEDEN
Email: susanne.schlisio@ki.se Phone: ++46-8-52487117
Home page: http://ki.se/en/mtc/susanne-schlisio-group and
http://www.ludwigcancerresearch.org/location/stockholm-branch/susanne-schlisio-lab

Type of recruitment and qualifications of applicant

Postdoc (12 months)
The applicant in computational analyses of single-cell RNA-seq data should have a strong background in genome-wide bioinformatics, programming and linux environment. Previous experience with RNA-seq data analyses is required and additional experience with single-cell data, post-transcriptional gene regulation (e.g. splicing) or machine learning is a strong merit.

Background

How and when during development does childhood neuroblastoma (NB) and pheochromocytoma (PCC) arise? We aiming to elucidate the origin and heterogeneity of human neuroblastoma (NB) and pheochromocytoma (PCC). NB is a cancer of early childhood that arises from the developing sympathetic nervous system births that despite its relative rareness accounts for 15% of childhood cancer mortality. While primary NB tumors occur in sympathetic neural tissue, most commonly arising in the adrenal medulla their precise origin is poorly understood. In pediatric tumors such as NB the underlying developmental processes are considered to be important, and NB can be considered as a failure of differentiation of neural crest cells underscoring the importance of understanding this process as it proceeds normally. The clinical hallmark of childhood neuroblastoma is heterogeneity, ranging from spontaneous regression to relentless progression. The cell of origin is thought to be a developing sympathoblast. However, its precise cell of origin remains unknown and the genetic basis of neuroblastoma remains obscure. Identifying the developmental cell of origin will reveal the causes of disease heterogeneity and clinical behavior. Understanding what triggers spontaneous neuroblastoma regression would provide critical clues for the development of therapeutic strategies that are currently missing in high risk neuroblastoma.

Project description

We are looking for one outstanding researcher to work on the computational analyses of a large-scale single-cell transcriptome project on neuroblastoma and pheochromocytoma. In this project we will generate “molecular encyclopedias” of this tumor in order to understand the molecular principles concerning the origin, progression and subtypes of this tumor at a previously unprecedented level, using state-of-the-art RNA-seq and bioinformatics technologies. Therefore, we seek one postdoctoral research fellow with expertise in computational analyses of RNA-seq data and OMICS data.

Interested in recruiting a PhD student

Project title: Evaluation of schizophrenia risk variants on synapse elimination in human cellular model system

Supervisor Carl Sellgren Majkowitz, MD, PhD, Psychiatrist
Dept. of Physiology & Pharmacology, Karolinska Institutet
Email carl.sellgren@ki.se Group homepage http://ki.se/en/fyfa/neuropsychoimmunology

Type of recruitment and qualifications of applicant:
PhD student. We welcome applications from highly motivated candidates who have a master's degree in molecular/cellular biology, molecular genetics, or other relevant area. Experience of working with cellular model systems, especially induced pluripotent stem cell (iPSC) models, is highly meriting. Communication skills and an ability to interact socially and scientifically within a team are also essential.

Project description
Schizophrenia is a disabling and strongly heritable illness. Recent studies implicate the selective engulfment of synapses by microglia in normal neurodevelopment, and preliminary data suggests a role for microglial synapse pruning in the pathogenesis of these psychotic disorders. Large-scale functional studies of human microglia in disease have been hampered by difficulties in obtaining live human cells amenable to rapid screening and quantitative functional assessments, particularly from individuals with severe psychiatric disorders. However, we have recently developed and validated patient-specific models of microglia-mediated pruning by reprogramming patient blood monocytes to induced microglial cells and assaying them with synaptosomes, i.e., isolated nerve terminals, derived from neurons differentiated from iPSCs (see Sellgren et al., *Mol Psychiatry*, 2017 Feb;22(2):170-177. doi: 10.1038/mp.2016.220).

The project is part of a larger research program aiming at applying large-scale cellular modeling of synaptic pruning to cells derived from schizophrenia patients and matched healthy controls. The specific project focus on defining the role of known genetic risk variants within the complement component 4 (*C4*) genes in synaptic pruning in human cellular models. For this purpose we will study naturally occurring copy numbers as well as using genetic engineering such as short hairpin RNA and CRISPR.

Interested in recruiting a Postdoc

Project title

Prevention of growth failure and osteoporosis in children treated with glucocorticoids and chemotherapy

Supervisor

Lars Sävendahl, MD,Ph.D, Professor, Group Leader
Farasat Zaman, Ph.D, Assistant Professor
Pediatric Endocrinology Lab, Department of Women´s and Children´s Health
Email: lars.savendahl@ki.se or farasat.zaman@ki.se
Home page: http://ki.se/people/larsav, http://ki.se/en/people/farzam

Type of recruitment and qualifications of applicant

Postdoc (24-48 months)
The applicant must hold a PhD in biomedical/biological sciences

Background

Lars Sävendahl and his team have developed new research models and have thereby managed to show how bone growth regulation takes place at the cellular level. The results have led to the forthcoming introduction of new treatment principles of different bone growth disorders (1, 2). Currently, the team is also focusing on the identification of new treatment strategies to prevent osteoporosis in chronic pediatric diseases.

Project description

Osteoporosis, and in children growth failure, are common health problems often linked to chronic disorders such as cancer and/or secondary to the treatment with glucocorticoids (GCs). Most often growth hormone therapy is ineffective as true growth hormone deficiency is rare in these patients. Therefore, it is an ultimate need for new treatment strategies to prevent and/or treat growth disorders and bone fractures caused by the long-term treatment with GCs in chronic disorders including different types of cancers such as acute lymphoblastic leukemia. Our previously reported data show that GCs increase apoptosis in growth plate chondrocytes by activating caspases and the pro-apoptotic protein Bax. Investigating underlying mechanisms, we recently reported that Wnt16 plays a key role in triggering osteoporosis (3) and an analogue (HNG) of a small mitochondrial peptide, humanin, was found to prevent growth retardation caused by bortezomib, a proteasome inhibitor belonging to a new promising class of anti-cancer drugs (4). It was also reported that HNG has an anti-cancer effect per se. The proposed project aims to explore small molecules/peptides specifically designed to prevent growth failure and osteoporosis. Our hypothesis is that HNG can prevent GC-induced growth failure and osteoporosis in mouse models of childhood cancer. An array of experimental model systems including mesenchymal stem cells (MSCs), bone organ culture, genetically modified mice models, and unique human growth plate cartilage biopsies will be applied. For more details of the project, please contact Prof Lars Sävendahl or Dr. Farasat Zaman.

Publications

1. Mårtensson K, Chrysis D, Sävendahl L. 2004. J Bone Miner Res .19(11):1805-12.
2. Fernandez-Vojvodich P, Zaman F, Sävendahl L. 2013. Ann Rheum Dis. 72(10)
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Interested in recruiting a PhD student

Project title

Role of chromatin modifiers and epigenome alterations in metabolic-inflammatory diseases

Supervisor

Eckardt Treuter, Professor
Department of Biosciences and Nutrition, Karolinska Institutet
Email: eckardt.treuter@ki.se Phone: +46852481060
Home page: http://cimed.ki.se/research/senior-researchers/eckardt-treuter/

Type of recruitment and qualifications of applicant

We seek a highly motivated individual with original thinking, team spirit and a background in molecular cell biology, molecular physiology, molecular medicine, metabolism, inflammation or endocrinology. Working with genetically modified mice is required for this position.

Background

Metabolic diseases including obesity, type 2 diabetes, and fatty liver disease are considered today also as metabolic-driven chronic inflammatory diseases, for which the term 'metaflammation' was coined. Epigenome alterations (not encoded by the genome) linked to gene expression are fundamental reprogramming processes known to be associated with these diseases. However, the underlying regulatory mechanisms, the critical components, and the causal relationship of these associations are currently poorly defined. In search for epigenomic modifiers involved in metaflammation our research identified a possible key role of a fundamental transcriptional corepressor complex linked to histone deacetylation and demethylation. We discovered that the anti-inflammatory function of the entire complex was compromised by loss of the GPS2 subunit in adipocytes and in macrophages of obese and diabetic humans and mice (see Fan et al. Nature Medicine 22, 2016, Treuter et al. FEBS letters 2017). Our hypothesis is that inappropriate complex function triggers epigenome reprogramming and thereby increases the susceptibility to metabolic-inflammatory disturbances and the progression of disease.

Project description

The Ph.D. project will aim to characterize the role of chromatin-modifying protein complexes, non-coding RNAs and epigenome alterations in different metabolic and inflammatory disease pathways. Particular emphasis will be on the generation and deep physiological and molecular characterization of novel mouse models that allow studying the role of cell type-specific epigenome alterations in the progression of obesity-associated inflammation, insulin resistance and atherosclerosis.

Research group

The team of Professor Eckardt Treuter at the Department of Biosciences and Nutrition is carrying out state-of-the-art preclinical research in molecular medicine. Research goal is to identify and understand transcriptional and epigenomic mechanisms that control metabolic-inflammatory pathways linked to human diseases, in particular to obesity, type 2 diabetes, fatty liver disease and atherosclerosis. The group currently utilizes experimental mouse models, genome-wide sequencing approaches, genome-editing using CRISPR/Cas9, biochemical/molecular methods and translational studies in collaboration with clinicians. For more information see http://cimed.ki.se/research/senior-researchers/eckardt-treuter/

Interested in recruiting a PhD student

Project title

Decoding the integration of spatial cues for a coordinated T cell response

Supervisor

Fredrik Wermeling, PhD. Rheumatology Unit, Department of Medicine Solna, KI
Email: Fredrik.wermeling@ki.se Home page: www.wermelinglab.com

Type of recruitment and qualifications of applicant

PhD student. We´re looking for a creative, hardworking and enthusiastic student with a background in biology or medicine. Experience with Immunology, T cells, animal models, molecular biology, next-generation sequencing, bioinformatics, and CRISPR is highly valued.

Background

This project deals with CD4+ T cells in the context of autoimmune disease with an emphasis of Rheumatoid Arthritis (RA). The Ph.D. student will identify genes affecting complex T cell behavior using relevant animal models and patient material. The student will learn to use CRISPR/Cas9 based screens as a major tool in these studies and also be part of developing a state of the art nanowire delivery system for rapid delivery of plasmid DNA to T cells.

Project description

The immune system is composed of a large collection of specialized cells that partake in complex coordinated behavioral patterns in response to environmental cues. CD4+ T cells are central coordinators of these behavioral patterns.
It is not known which exact signals influence CD4+ T cell decisions at different time points, and how these signals translate to the disease development in the context of RA.
In order to determine how T cells integrate different signals into a coordinated response, the Ph.D. student will use a mouse in vivo T cell transfer model and study localization and gene expression as T cells progress in discrete steps; from being transferred into the host, until they have coordinated the pathogenic immune response.
The descriptive gene expression data will be translated to fundamental understanding by using CRISPR-based in vivo screens. (See http://blog.addgene.org/custom-crispr-screens-the-green-listed-software for more details about our work with CRISPR). In this, identified genes will be disrupted and the consequence for T cell behavior will be studied. Furthermore, the student will also be involved in developing a novel precise vertical nanowire delivery system that will be used to introduce CRISPR constructs into T cells, which are generally resistant to many forms of genetic manipulation.

Central collaborators within the project include:

Dr. James J. Moon, MGH and Harvard Medical School, USA (MHC tetramer technology).
Dr. Jeffrey V. Ravetch, Rockefeller University, New York, USA (Animal models).
Dr. Brad Rosenberg, Icahn School of Medicine at Mount Sinai, New York, USA (Next gen. seq.).
Dr. Vivianne Malmström, Karolinska Institutet, Sweden (T cells in RA).
Dr. Lars Klareskog, Karolinska Institutet, Sweden (T cells in RA).
Dr. Zhen Zhang, Uppsala University, Sweden (Nanowire technology).

The lab is in close contact with the Rheumatology Clinic, Solna and thereby have great access to well define clinical material for translational studies.

Interested in recruiting a Postdoc or PhD student

Project title
Role of mitochondria in skin biology and disease

Supervisor
Jakob D. Wikstrom, MD PhD, Assistant professor
Department of Medicine Solna / Centre for Molecular Medicine Karolinska Institutet
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Home page: http://www.cmm.ki.se/en/team/jakob-wikstrom-team-2/

Type of recruitment and qualifications of applicant
Postdoc (24 months) or PhD student (48 months)
The applicant should be fluent in spoken and written English and proficient with at least some aspects of basic life science techniques (e.g. qPCR, cell culture, animal models, Western blot, bioinformatics, microscopy). We look for someone who is not only technically skilled but also creative and with good communications skills.

Background
Mitochondria is the powerhouse of the cell and produce 90 % of the body´s ATP. Recent years have shown mitochondrial involvement in a range of diseases including diabetes, neurodegeneration and heart disease. The skin is the body´s largest organ, comprising 15 % of the body weight, however thus far mitochondria have only been sporadically studied in both skin physiology and disease.

Project description
The main objective of the project will be to understand the role of mitochondria in skin physiology, with focus on their role in skin differentiation, and skin pathophysiology with focus on their role in wound healing though other conditions may also be studied. The project will involve characterizing clinical skin biopsies as well as in vitro and in vivo mechanistic studies.

Research group
Dr Wikstrom has recently established his own research group after completing an international posdoc and recruiting major national and international funding. Currently the group consists of 3 postdocs and 1 PhD student. The overall research focus of the group is to understand the role of mitochondria and ER in the skin. Dr Wikstrom has a close collaboration with Dr Ning Xu-Landéns research group as well as with Dr Orian Shirihai at UCLA (there may be opportunities to spend some time at UCLA). Dr Wikstrom´s clinical work as a dermatologist ensures good access to clinical samples.

Interested in recruiting a PhD student

Project title

Reprogrammed human stem cells as a model for childhood cancer development

Supervisor

Margareta Wilhelm, PhD, Associated Professor
Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet
Email: margareta.wilhelm@ki.se Phone: +46 8 52487474
Home page: http://ki.se/en/mtc/margareta-wilhelm-group

Type of recruitment and qualifications of applicant

We are looking for a very motivated and creative PhD student with a strong interest in tumor biology. Proficiency in cell culture techniques and mouse models are a requirement. Skills in bioinformatics and R/BioConductor, are an advantage. The candidate should be self-motivated, have good communication skills and ability to interact effectively and work productively in a team. Emphasis will be placed on personal suitability.

Background

Medulloblastoma (MB) is the most common malignant brain tumor in children. Compared to adult tumors, pediatric tumors generally have a dramatically shortened latency period and harbor fewer genetic aberrations causing oncogene activation or loss of apoptotic regulators. The reason for these differences is that these malignancies arise from stem or progenitor cells, which already possess proliferative capacity as a part of the normal developmental process. In collaboration with the Falk lab and iPS core facility at KI, we have generated iPS cells and subsequent disease-relevant cells from skin cells of patients with cancer-driving germline mutations, focusing on medulloblastoma (MB). Orthotopic transplantation into mice show that patient cells, but not control cells, form tumors that closely mimics human MB. Our models offer a way to recapitulate all stages of tumor development, from initiation to late stages, thus providing novel models for studying cancer processes in relevant human cells. The aim of this PhD-project is to gain a greater understanding in molecular mechanisms operating during MB development, and identify new therapeutic targets.

Project description

The student will use our human stem cell models for both in vitro and in vivo studies to investigate how MB develops and progress. Potential targets will be identified using high throughput genomics. The student will be involved in drug screens to identify new potential therapeutic target drug. The project is based on mouse models of cancer and advanced human stem cell culturing. Analyses include molecular biology methods such as RNA and DNA preparations, western blotting, qRT-PCR, CRISPR/Cas9, flow cytometry, and microscopy, RNA and DNA seq, Bioinformatics.

Research group

The Wilhelm lab consists of 1 PI, 2 postdocs and 3 PhD students

Interested in recruiting a PhD student

Project title

Elucidate the preventive role of estrogen receptors and lncRNAs in colorectal cancer development

Supervisor

Cecilia Williams, Professor
Department of BioNut, Karolinska Institutet
Email: cecilia.williams@ki.se Phone: 08-790 9891 Home page:
http://ki.se/en/bionut/hormone-signaling-and-non-coding-rnas-in-cancer-cecilia-williams

Type of recruitment and qualifications of applicant

PhD student (48 months)
The applicant should have a strong interest in cancer research and have previous experience form a molecular biology lab. Research experience of nuclear receptors and/or contribution to a peer-reviewed scientific publication is seen as a merit.

Background

Colorectal cancer is the third most common cause of cancer-related death in the Western world, but a truly preventive or targeted therapy against colon cancer does not yet exist. However, estrogen has been shown to reduce the formation of colorectal cancer. Estrogen receptor beta (ERbeta) and G-coupled estrogen receptor 1 (GPER1) can both mediate estrogenic effects in the colonic epithelium, and both can be selectively activated or inactivated by ligands and are ideal candidates for therapeutic targeting. It is essential to understand the basic mechanistic background of their activity in colorectal cancer and its development in order to identify biomarkers of its activity and design future therapies.

Project description

In this project we want to clarify the impact on estrogen receptor-regulated lncRNAs in the development and characteristics of colorectal cancer. The project uses cell lines, large-scale molecular analysis (transcriptomics, ChIP-seq, proteomics), mechanistic assays (chIP, co-IP, qPCR, Western blot, 3'UTR luciferase assay, ERE luciferase assay), functional assays (proliferation, migration, adhesion, and apoptosis assays), clinical samples and ex vivo cultures, and in vivo animal studies (tissue-specific knock-out mice). We collaborate with research groups at KTH the Royal Institute of Technology (www.kth.se), the Texas Medical Center) and the Human Protein Atlas (www.proteinatlas.org) and we use exceptional facilities at SciLifeLab (www.scilifelab.se). The overall goal of the research is to provide a mechanistic background in order to provide new colon cancer biomarkers and treatments.

Research group

The Williams group has generated significant data using in vivo, ex vivo, and in vitro models and by applying omics and focused mechanistic research. We have identified clear roles of ERbeta and GPER1 and have generated a list of lncRNAs candidates associated with colorectal cancer development that are regulated by these receptors. Questions can be directed to PI Cecilia Williams (cecilia.williams@ki.se) or lab manager Amena Archer (amena.archer@scilifelab.se)

Interested in recruiting a Postdoc

Project title

Human Innate Lymphoid Cells in Lung Inflammation

Supervisor

Tim Willinger, M.D., Ph.D.
Senior Researcher/Group Leader
Center for Infectious Medicine, Department of Medicine Huddinge, Karolinska Institutet
Email: tim.willinger@ki.se, Phone: +46760987082

Type of recruitment and qualifications of applicant

Postdoc (24 months)
The applicant must have a PhD in immunology or equivalent with publications in internationally renowned peer-reviewed journals. Merit is given to applicants who are experienced in multicolor flow cytometry and functional immunological assays. Great advantage is experience in performing animal experiments and previous work with genetically-modified mice. The candidate should be a talented and highly motivated researcher, have good communication skills, and the ability to work productively in a team.

Background

Innate lymphoid cells (ILC) are a recently discovered immune cell type that carries out tissue repair, lymphoid tissue formation, and host defence in mice. Human counterparts of ILC have been described, but the in-vivo function of human ILC is poorly understood due to the lack of suitable experimental systems. To overcome this limitation, we have developed a novel humanized mouse model to study human ILC in vivo. This cutting-edge model expresses human cytokines through gene knock-in (Trends Immunol 32:321, 2011), which allows the reconstitution of a complete human innate immune system in the mouse (Nat Biotechnol 32:364, 2014).

Project description

All types of human ILC develop in our unique model, which allows us to study their function in vivo, with a particular focus on the lung. Specifically, we aim to understand how ILC migrate during inflammation, how they are maintained in the inflamed lung, and how they contribute to lung inflammation.
This exciting project will give the postdoc the opportunity to carry out cutting-edge research in the field of lung immunology. The projects aim to lead to fundamental new insights that are relevant to common and important lung diseases in humans, such as asthma, chronic obstructive airways disease, and influenza infection.

Research group

The research group is based in the Center for Infectious Medicine, which has excellent expertise in human immunology and provides a stimulating and collaborative environment. Dr. Willinger's group studies immune responses in mucosal tissues in health and disease (http://ki.se/en/medh/tim-willinger-group). Recently, we have been investigating the link between ILC migration and function (Immunity 2017, in revision).

Interested in recruiting a PhD student

Project title
Investigation of the oxidative control of regulatory T cells

Supervisors
Name, title Kajsa Wing, assistant professor, and Rikard Holmdahl, professor
Department of Medical Biochemistry and Biophysics, Karolinska Institutet
Email: Kajsa.Wing@ki.se Phone: + +46 (0) 70-43 31 86 Home
page: http://ki.se/en/mbb/research-division-of-medical-inflammation-research

Type of recruitment and qualifications of applicant
PhD student (48 months)
The applicant must have successfully passed an education in medicine or biological science including a master education, which also shows scientific ability. Laboratory experience and excellence is a requirement, in particular in immunology and biochemistry. Experience in experimental animal research is needed. Computer skills and bioinformatic knowledge are needed. Fluent English is a requirement.

Background
The Ncf1 gene codes for a component essential for the development of induced oxidative burst in phagocytes and in antigen presenting cells. Our group originally cloned the genetic polymorphism and could demonstrate its important in autoimmune diseases in both experimental animals and in humans with autoimmune disease. One important biological effect is that it affects T cell activation including the activation of regulatory T cells. This could be of critical importance not only in autoimmune disease but also in tumors.

Project description
The project aims to investigate the role of the Ncf1 genes and the NOX2 complex in regulating T cell activation and in particular the role of regulatory T cells. We will use already established conditional floxed mice together with relevant Cre strains to determine the role in different lymphocyte subsets and on specific antigen presenting cells. Of particular importance will be the impact on development of autoimmune disease and tumors in the experimental animal models.

Research group
Medical Inflammation Research, MBB, Wing/Holmdahl

Recruitment of a PhD student

Project title
Investigation of the regulatory role of antibodies to cartilage specific proteins

Supervisor
Bingze Xu, scientist, and Rikard Holmdahl, professor
Department of Medical Biochemistry and Biophysics, Karolinska Institute
Email: Bingze.Xu@ki.se, Rikard.Holmdahl@ki.se
Phone: +46705424607
Home page: http://www.inflam.mbb.ki.se

Type of recruitment and qualification of the applicant
PhD student (48 months)
The applicant must have successfully passed an education in medicine or biological science including a master degree, which also shows scientific ability. Experience and excellence in immunological and biochemical laboratory work is a requirement. Experience in experimental animal research, computer skills and knowledge in bioinformatics are needed. Fluent English is a requirement.

Background
Rheumatoid arthritis (RA) is an autoimmune disease, which starts many years before disease symptoms appear. Before the onset of clinical symptoms and during the chronic phase of the disease the activation of antibody secreting plasma cells is unique to this disease. The function of these antibodies are unknown and the aim of the current project is to investigate the function of monoclonal antibodies isolated from RA patients.

Project description
The project aim is to investigate the function of antibodies that cross-react with the joint cartilage, and which occur during the development of RA. The project includes analysis and validation of antibody epitopes exposed on the joint cartilage that are of relevance for rheumatoid arthritis as well as studies of the function of cloned antibodies. A new preliminary diagnostic test has been developed which contain the major epitopes defined from joint proteins. This first test will be validated in both animal models and in human RA cohorts. The project will focus on epitope-specific antibodies that are associated with protection against the disease. These antibodies have been shown to also protect against experimental models of arthritis. The project will analyse the therapeutic mechanisms of such antibodies in both experimental models and in patients with RA and individuals at risk of developing RA.

Research group
Medical Inflammation Research, MBB, Holmdahl

Interested in recruiting a PhD student, Postdoc or Visiting Researcher

Project title

Investigation of the role of regulatory RNAs in skin wound healing

Supervisor

Ning Xu Landén, PhD, Associate Professor, Group leader
Unit of Dermatology and Venerology, Department of Medicine Solna, Karolinska Institutet
Email: ning.xu@ki.se Phone: +46 8 51772158
Home page: www.xulandenlab.com or http://ki.se/en/people/ningxu

Type of recruitment and qualifications of applicant

1. Visiting researcher and post-doctoral fellow (longer than 1 year):
The candidate should have obtained a PhD degree within the area of molecular or cell biology and have deep interest in medical and biological problems. The applicant is preferred to have documented previous experience with RNA research or skin biology. Previous experience with tissue culture, molecular and biochemical techniques is desired. A high level of English, spoken and written, is a requirement.

2. Doctoral student:
The candidate should have a master degree within the area of medicine or molecular or cell biology and have deep interest in medical and biological problems. A high level of English documented by an internationally recognized test e.g. TOEFL or IELTS, is a requirement. The successful candidate need to be very motivated and able to work independently, and at the same time interact with scientists from other areas to coordinate complex projects. Previous experience with RNA research, tissue culture, molecular and biochemical techniques is a merit.

Project description

The immense economic and social impact of deficient wound healing e.g. chronic ulcers, post-surgical wounds care and skin scarring, calls for attention and allocation of resources to understand biological mechanisms underlying wound complications. Due to the complex nature of wounds, efficient targeted approach to enhance healing are essentially lacking today. The recent discovery of non-coding RNAs (ncRNAs) as powerful gene regulators provides hope to develop novel RNA-based treatments for a wide variety of diseases. However, the role of ncRNAs in human skin wound healing remains largely unexplored**.** The objective of our study is to reveal the role(s) of ncRNAs in skin wound healing and to explore the potential of RNA-based therapy for chronic wounds.

Research group

Research Group N Xu Landén

Interested in recruiting a PhD student or a Postdoc

Project title

Deciphering the estrogen receptor-associated interactome on chromatin: towards understanding endocrine resistance in breast cancer

Supervisor

Chunyan Zhao, Associate Professor
Department of Biosciences and Nutrition, Karolinska Institutet
Email: chunyan.zhao@ki.se Phone: 46-8-52481126 Home page: http://ki.se/en/bionut/esr-estrogen-signaling-research-group-chunyan-zhao

Type of recruitment and qualifications of applicant

One Postdoc (24 months) or one PhD student
The applicant should be highly motivated and has good communication skills in spoken and written English.

Background

Patients with estrogen receptor (ER)-positive breast cancer are usually treated with anti-hormone therapies such as tamoxifen or aromatase inhibitors. However, many of these patients are resistant to these drugs at diagnosis or develop resistance during treatment resulting in treatment failure. In addition, patients with triple-negative breast cancer (TNBC) have limited treatment options.

Project description

Our group is using functional genomics approaches towards unravelling mechanisms of drug resistance in estrogen receptor (ER)-positive breast cancer and understanding molecular determinants of malignant cell behaviors in triple-negative breast cancer (TNBC). The ultimate goal is to develop novel and improved prognostic tools and therapies for patients with invasive breast tumors.
Specifically, 1) we focus on global identification of the ER-associated interactome on chromatin in response to different ER ligands in breast cancer cells. For this, an approach termed RIME (rapid immunoprecipitation mass spectrometry of endogenous proteins) will be used. The major goal is to provide a novel and valuable resource to further complement the knowledge of ER mediated gene transcription and ultimately its role in physiology and disease; 2) Identification of the ER-associated interactome on chromatin in tamoxifen resistant compared to tamoxifen sensitive breast cancer. We aim to identify proteins that are specifically associated with chromatin-bound ER in tamoxifen resistant cells and breast tumors. These proteins could represent potential targets for inhibition by novel compounds; 3) we also focus on functional genomics analysis of transcription factor AP-1 in regulating the invasive phenotype of triple-negative breast cancer.

Research group

Two senior researchers, one lecturer, one postdoc, one bioinformatician, two PhD students

Relevant publications

- Jia M, Andreassen T, Jensen L, Bathen TF, Sinha I, Gao H, **ZHAO C**, Haldosén LA, Cao Y, Girnita L, Moestue SA, Dahlman-Wright K. (2016) Estrogen receptor α promotes breast cancer by reprogramming choline metabolism. *Cancer Res.* 2016 Oct 1;76(19):5634-5646.
- Qiao Y, He H, Jonsson P, Sinha I, **ZHAO C** and Dahlman-Wright K. (2016) AP-1 is a key regulator of proinflammatory cytokine TNFα-mediated triple-negative breast cancer progression. J Biol Chem. 2016 Mar 4;291(10):5068-79.
- **ZHAO C**, Qiao Y, Jonsson P, Wang J, Xu L, Rouhi P, Sinha I, Cao Y, Williams C and Dahlman-Wright K. (2014) Genome-wide profiling of AP-1-regulated transcription provides insights into the invasiveness of triple-negative breast cancer. Cancer Res. 2014; 74(14):3983-3994.

Interested in recruiting a PhD student

Project title
Multimorbidity of mental health conditions and somatic conditions.

Supervisor
Zheng Chang, PhD
Department of Medical Epidemiology and Biostatistics, Karolinska Institutet
Email: zheng.chang@ki.se
Phone: +46 8 524 82412
Home page: http://ki.se/en/people/zhecha

Type of recruitment and qualifications of applicant
PhD student (4 years)
We look for a highly motivated student with a background in epidemiology, biostatistics, public health, psychiatry, biomedicine or other relevant field. Experience with statistical software (e.g., SAS, STATA, or R) or programming languages is preferred. The successful candidate needs to have the ability to work independently and at the same time to work in a research team. For more information regarding general and specific entry requirements: http://ki.se/en/education/entry-requirements-eligibility-for-doctoral-education

Background
Management of the rising prevalence of chronic disorders is the main challenge facing health-care systems worldwide. Mental disorders often coexist with chronic somatic conditions, leading to mental-somatic multimorbidity. Despite the growing evidence that multimorbidity was associated with greater symptom burden and functional impairment, poorer quality of life, and excess mortality, very few studies have investigated the how preventable these outcomes are and how to intervene to minimise them.

Project description
The aim of the PhD project is to investigate the multimorbidity patterns between common mental disorders (e.g., mood disorders, ADHD) and chronic somatic conditions, and the effects of pharmacotherapy on health outcomes. Data are available through linkage of national registers in Sweden, which provide longitudinal information on disease diagnoses, drug prescriptions, and assessments of medical and functional outcomes. We will conduct population-based cohort studies to quantify the health outcomes associated with mental-somatic multimorbidity, and to evaluate the effectiveness and safety of polypharmacy treatments.

Research group
Our research group is interested in understanding the causes and consequences of psychiatric disorders, as well as the risks and benefits associated with pharmacological treatments for these disorders. Together with Professors Paul Lichtenstein and Henrik Larsson, we have an interdisciplinary research team from various backgrounds, including epidemiology, biostatistics, sociology, and psychiatry. To keep up with new research perspectives, we also collaborate with a number of Swedish and international research groups.

Interested in recruiting a Postdoc

Project title

Studying Mechanisms of **F**unctional **I**dentification of drug **T**arget by **Ex**pression **P**roteomics

Supervisor

Roman Zubarev, professor
Department of Medical Biochemistry & Biophysics (MBB), Karolinska Institutet
Email: Roman.zubarev@ki.se Phone: +468 524 87594
Home page: http://ki.se/en/mbb/research-division-of-physiological-chemistry-i
http://ki.se/en/mbb/roman-zubarev-group

Type of recruitment and qualifications of applicant

Postdoc (24 months)
The applicant must possess basic knowledge of mass spectrometry and have experience in cell biology, with a PhD in a relevant discipline

Background

Functional **I**dentification of drug **T**arget by **Ex**pression **P**roteomics (FITExP) is a novel method of chemical proteomics developed in our lab (Nat Sci Rep **2015,** *5,* art. 11176). FITExP allows one to determine the target and the mechanism of action of small-molecule anticancer drugs, which can significantly shorten time of drug development. In FITExP, the test molecules are applied to cancer cells at LC50 concentrations, causing death of half of the cells within 48 h. The proteomes of the remaining cells are analyzed, and the most regulated proteins showing specific response to a given drug are taken as target candidates. FITExP has a very high success rate, and yet the molecular mechanisms behind the exceptionally strong regulation of drug targets remain largely unknown.

Project description

Here we will test different hypotheses of the FITExP mechanism. Hypothesis I suggests that strong upregulation may be caused by overexpression of the target proteins, while hypothesis II, on the contrary, postulates their lower rate of degradation. Hypothesis III suggests selection of the cells with naturally high level of target expression. As for downregulation which is also frequently observed for target proteins, it may be caused by protein translocation. These hypotheses will be tested by cell experiments combined with proteomics analyses. A high-profile publication (e.g., *Nature Methods*) is expected.

Research group

Roman Zubarev's Division of Physiological Chemistry I of MBB has broad scientific interests, with one of the important focuses on developing new methods for chemical proteomics. The lab is equipped with the latest mass spectrometric instrumentation, including 6 Orbitrap MS instruments. The Division includes two proteomics core facilities, one of which (Chemical proteomics) is part of the Swedish national BioMS facility. There are ca. 20 researchers and students in the Division from all over the world.