Interested in recruiting postdocs, visiting researchers and PhD students

Adnane Achour, Prof. in Molecular Immunology
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Project 1, Determination of the crystal structures of Streptococcus pneumoniae-associated virulence factors

Streptococcus pneumoniae (pneumococcus) is a major human pathogen and the leading cause of pneumoniae, bacteremia and meningitis in adults. The increasing number of antibiotic-resistant strains and the suboptimal clinical efficacy of available vaccines hamper control of this pathogen. We focus on novel virulence-related pneumococcal proteins that could be used as potential targets for future drugs.

Representative publications from our laboratory:

1) Marc Panas *et al* (2015). ***Plos Pathogens***, 11(2):e1004659. doi: 10.1371/journal.ppat.1004659. eCollection 2015.

2) Miguel Angel Burguillos et al (2015). Cell Reports, pii: S2211-1247(15)00140-0. doi: 10.1016/j.celrep.2015.02.012

3) Tim Schulte *et al* (2014). ***Open Biology*** 4(1):130090.

4) Peter Mellroth *et al* (2014). ***mBio*** 5(1):e01120-13.

Project 2, Development of MHC class I-binding altered peptides for vaccines

Using a combination of structural biology and immunology, our research group has defined a procedure that allows for the design of altered peptide ligands (APLs) that bind with high affinity to MHC-I ligands. The immunogenic APLs act as mimotopes of disease-associated non-immunogenic epitopes, and enhance the stability of MHC-I molecules. Importantly, these modified peptides conserve a structural conformation similar to the wild-type infection-derived or non-immunogenic tumor-associated peptides. The induced immunogenic $CD8^+$ T cells cross-react with the original peptides, resulting in enhanced responses. Studies of consequences of substitutions in APLs on CD8 responses directed towards tumor associated antigens and viral immune escape variants are ongoing.

Within the frame of this project, we are looking for novel colleagues that would be interested into 1) functional cellular immunology or 2) X-ray crystallography.

Publications:

1) Marianne Van Stipdonk *et al* (2009). ***Cancer Research***, 69, 7784-7792.

2) Chaithanya Madhurantakam *et al* (2012). ***Plos One***, 7, 3, e32805.

3) Eva Allerbring, *et al* (2012). ***European Journal of Immunology,*** 42(11):2990-3000.

4) Hannes Uchtenhagen *et al* (2013). ***European Journal of Immunology***, 43(11):3051-3060.

5) Fermin Eduardo Gonzalez *et al* (2014). ***Immunobiology***, 219(3):189-97.

6) Levon Halabelian *et al* (2014). ***Journal of Biological Chemistry*** 7, 289(6): 3318-27.

7) Zeynep Hein *et al* (2014). ***Journal of Cell Science***, 127: 2885-2897.

Interested in applications from postdocs

Project title: "Cellular and molecular mechanisms of facial and organ shape development"

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Few words about the project:
"Shape-making, including the control over the precise 3D-geometries, size and scale of composite parts represents one of the most important questions in developmental biology and regenerative medicine. Building up skeletal elements has been extensively studied in the past. However, no understanding or consensus exist today about how embryos control precise and complex geometries of their cartilages, bones and joints.
Our hypothesis implies that specific molecular signals control allocation of individual skeletogenic clones and, through this, provide precise sculpting and scaling up cartilaginous and bony structures in development and during regeneration. WE WILL EXPLORE HOW GEOMETRY IS ENCODED IN GENES USING DEVELOPMENT OF CARTILAGE AS A MODEL. We will use state-of-the-art genetic tracing with multicolor reporters, novel type of mathematical modelling of 4D-cell dynamics, 3D-live imaging as well as revolutionizing know-how of micro X-ray computed tomography of soft embryonic tissues with special contrasting allowing for histological resolution. We will also apply multiple transgenic animals allowing for dissecting the role of different signaling pathways in shape-making. We will extensively use non-trivial ex vivo approaches including tissue and organoid cultures with microfluidics-based artificial gradients to understand the logic of induction and positioning of cartilaginous elements inside the body. This project is interdisciplinary and is interesting to a wide community of scientists because it addresses a novel and general logic of shape control in biological objects. The problem of shape is indeed very novel and crucial for understanding multiple life forms and organ designs. The MEDICAL IMPLICATION of this project will include better understanding of cartilage and bone regeneration providing new approaches to the recovery of the correct facial shape and other body parts following trauma. Technical advancements, generated resources and novel data gained through this project will help to bring a future when correctly designed skeletal elements will be induces in the tissues of the patients or transplanted after correct ex vivo growth."

Interested in recruiting PhD students and postdocs

Project title: **Deciphering regulatory T cell-mediated suppression to find new therapeutic targets for immunological diseases**

John Andersson, PhD
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Background and current projects: The immune system is the body's defense against infectious organisms. It is delicately regulated to allow responses against foreign- but not self-antigens. CD4+FOXP3+ regulatory T (Treg) cells comprise a subset of T cells that suppress immune activation. The importance of Treg cells is illustrated by the fact that mutations in Foxp3 lead to a fatal lymphoproliferative disorder in the scurfy mouse as well as the immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) in humans. Also, Treg cells modulate the progression and outcome of autoimmune diseases, allergy, infectious diseases and cancer, and are thus considered a therapeutic target in a large variety of diseases.

The transcription factor FOXP3 is essential for Treg function. FOXP3 exists in several distinct isoforms; however, the regulation and functional consequences of FOXP3 isoform expression remain poorly understood. We have found that FOXP3 isoforms have different or even opposing functions and that different diseases are characterized by distinct patterns of FOXP3 isoform expression. What factors induce alternative splicing of FOXP3 mRNA? What distinct functions do the different FOXP3 isoforms confer? How do FOXP3 isoforms confer their different functions? We are using a combination of genetic and biochemical approaches to answering these questions.

The exact mechanisms and cellular targets of Treg cell-mediated suppression remain controversial. In vitro studies suggest that Treg cells have the capacity to suppress directly a large number of cell types including T cells and dendritic cells (DCs). Many recent studies aiming to elucidate how Treg cells function have focused on Treg cells ability to suppress DCs as it is clear that Treg cells interact with DC in vivo. To define the exact mechanisms of suppression we have generated novel knockout mice and are now combining in vivo studies with global transcriptomic analysis of suppressed cells.

Methods currently used: Flow cytometry and cell sorting, magnetic bead-based cell isolation, primary cell culture, suppression assays, lentiviral transduction, oligonucleotide-mediated splice-shifting, western blot, immunoprecipitation and quantitative RT-PCR.

What we are looking for and what we can offer: We are interested in PhD students and postdoctoral fellows with a background in immunology, bioinformatics or cell biology. We greatly value social skills, an interest in learning new things and a drive to do good science. We can offer a friendly atmosphere in a well-functioning laboratory with state-of-the art equipment.

Interested in applications from PhD students

Project title ***Microparticles in hemophilia – friend or foe - to improve hemostasis or contribute to atherosclerosis?***

Jovan P. Antovic MD, PhD
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Consultant, Clinical Chemistry, Karolinska University Hospital
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Project description: Microparticles (MPs) are small membrane particles shed by activated or apoptotic cells, that can carry phosphatidylserine and tissue factor and thereby have an impact on coagulation. There are limited data on their role in haemophilia. Hemophilia A patients with similar factor levels can have different severity of clinical presentation. The mechanisms underlying these differences are not clear, but MPs could be of importance in this context. Procoagulant microparticles have been suggested to play a role in clot formation at sites of injury. In hemophilia mice, tissue factor-bearing MPs were shown to accumulate in the growing thrombus, to improve fibrin formation and normalize the bleeding phenotype. We have recently shown that in hemophilia A patients treated on demand, MP counts were shown to decrease after treatment, suggesting that MPs might be incorporated in the hemostatic plug formed at the site of injury.

We will in this study focus on the role of MPs in hemophilia. Specifically, we will visualize MP incorporation in fibrin clots and address the question whether there are differences in the extent of MP incorporation in patients treated prophylactically and on demand. Plasma from prophylactically treated patients will be collected in Stockholm, Sweden, while on demand treated patient samples are obtained from Belgrade, Serbia. The amount and phenotype of MPs will be analysed by flow cytometry. Fibrin gel preparations will be stained with antibodies and analysed by scanning electron microscopy in order to visualize and further characterize the MPs.

We also aim to study whether MPs injected into hemophilia A mice can improve hemostasis. We plan to inject mice with MPs, factor VIII concentrate, or the combination of the two treatments. After injection, we will perform tail bleeding in order to test how the bleeding phenotype is affected. To further investigate the hemostatic status, blood will be collected and the following global hemostatic assays will be performed: The Endogenous thrombin potential (ETP) assay and the Overall Hemostatic Potential (OHP).

The procoagulant potential of MPs is interesting for the management of hemophilia. However, elevated levels of circulating MPs have been shown in various atherothrombotic disorders and data suggesting a protective effect of hemophilia on atherosclerosis and atherothrombosis are somewhat controversial. This is of particular importance since adequately treated hemophilia patients reach old age and may potentially develop cardiovascular diseases. Therefore, we also plan to address the role of MPs in atherothrombosis by injection of MPs into ApoA/E/hemophilia A double knock-out mice.

This study will probably define if MPs exert potentially beneficial effects on clot formation in hemophilia, knowledge that could be useful for future treatment regimens. In this context, it is also of importance to know the role of MPs in atherothrombosis which also may contribute to common cardiovascular diseases in well treated hemophilia patients.

Interested in applications from PhD students

Project title: IMPACT OF UREMIC TOXICITY ON VASCULAR ENDOTHELIAL HEALTH: MECHANISMS AND TREATMENTS

Jonas Axelsson, MD PhD
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Project description: **Translational research into uremic toxicity**
We work with cell lines, primary cell cultures, transgenic animals (zebrafish and mice) and actual patient materials to discover novel pathophysiological pathways of relevance for patients with reduced renal function (kidney disease or uremia). Our data is generated using conventional and novel biomedical methods in combination with advanced imaging, proteomic analysis and transgenic animals.
This proposed 2-4 years project specifically aims to investigate key pathways of ER-stress in the vascular endothelium under uremic conditions.

Interested in recruiting a **Post Doc**

Project titel: **Translational studies of lipid mediators of inflammation and resolution in cardiovascular disease.**

Magnus Back, MD PhD, Associate Professor
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Magnus.Back@ki.se
Laboratory homepage: http://www.cmm.ki.se/group/translationell-kardiologi-back/

Project description:
Bioactive lipids, such as leukotrienes and lipoxins, may act both as proinflammatory mediators and promote the resolution of inflammation, respectively. This project explores the role of lipid mediators in cardiovascular disease from a translational perspective, from experimental molecular and cellular mechanisms to biomarker studies in patient cohorts.
In the present project, bioactive lipids will be studied in human cells and tissues, and mechanisms of signaling will be explored in cell cultures. Finally, inhibition and/or promotion of lipid mediator signaling will be examined mouse models of disease.
The candidate should have either a PhD or MD & PhD in cardiovascular research, preferably atherosclerosis research. Knowledge in molecular- and cellular biology as well as animal experimentation is required. Previous experience from the field of lipid mediators and bioinformatics is meriting.

Interested in recruiting postdocs, PhD students, visiting researchers

Project title: **Novel epigenetic biomarkers of hepatocellular carcinoma**

Isabel Barragan, PhD, Assistant Professor
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Group of Pharmacoepigenetics in Health and Disease
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Project description:
Hepatocellular carcinoma (HCC), the most common type of liver cancer, causes more than half a million deaths every year and has a 5-year survival rate of only 0-10%. There is an urgent need for clinically reliable biomarkers, and a limiting factor for the development of screening tools and novel drugs has been the lack of good models for liver diseases.
In addition to the genetic factors that contribute to the carcinogenesis of HCC, epigenetic changes, such as DNA methylation (5mC), also play an important role.
This project aims to identify novel epigenetic biomarkers of HCC with an innovative approach for their whole genome assessment. Specific differences in those biomarkers between tumor and adjacent healthy tissues in HCC patients will be identified at base-pair resolution, and then validated and studied mechanistically in unique 3D liver cultures derived from patients. The project provides with a pioneering workflow to identify epigenetic polymorphisms relevant to the diagnosis and treatment of HCC.

Interested in recruiting PhD students and postdocs

Project title: **Identification of Microbial and Dietary Metabolites with Effects on Innate Immunity**

Peter Bergman, MD, PhD
Associate Professor, Consultant Physician
Birgitta Agerberth, Professor
Department of Laboratory Medicine, Karolinska Institutet
Clinical Microbiology, Karolinska University Hospital, Huddinge
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Homepage: http://ki.se/en/labmed/research-group-bergmanagerberth-the-amp-group

Project description: Antimicrobial peptides (AMPs) constitute the first line defense of mucosal surfaces and are abundant in human immune-cells. AMPs can be upregulated by inflammatory stimuli and by exogenous compounds, including vitamin D and phenylbutyrate. In addition, microbial metabolites, such as butyrate and litocholic acid, induces AMP-expression in epithelial cells. In fact, emerging evidence suggest that bacterial as well as dietary metabolites have profound impact on host immunity both at the local site of infection, but also in distal organs via the circulation. In this project we will use a novel cell-based reporter-system to screen libraries of microbial and dietary metabolites for AMP-inducing properties. Selected candidates will be further subjected to in-depth studies of mechanism, target effects and relevance for human disease. Finally, the results from the molecular screen will be validated in clinical cohorts of patients with inflammatory and infectious disorders, where microbial metabolites may play important roles. The results of this project could be of great importance for understanding how AMPs are regulated by microbial and dietary metabolites, which could have major implications for interventional strategies in human disease.

Interested in recruiting PhD students

Project title: The role of antibiotic use on the development of upper-gastrointestinal cancer and other diseases.

Nele Brusselaers, Associate professor of clinical epidemiology, MD MSc PhD.
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Project description: *Helicobacter pylori (H. pylori)* is a known risk factor for gastric cancer, and may be protective for oesophageal cancer (through the reduction of gastro-oesophageal reflux). We are currently investigating the role of *H. pylori* eradication (with proton pump inhibitors and a combination treatment of 2 or more antibiotics) on the risk of upper-gastrointestinal cancer. So basically we are evaluating if *H.pylori* eradication really reduces the risk of gastric cancer, and increases the risk of oesophageal cancer (and maybe also influences the risk of other types of cancer).

Yet, an increasing body of evidence suggests that *H. pylori* is only a part of the puzzle, and that antibiotic use for other indications may already influence our gastrointestinal flora (or microbiome). Therefore, we want to assess the use of antibiotic treatment on the occurrence of cancer, mainly based on the Swedish Health Registries, in particular the Swedish prescribed drug registry. This population-based epidemiologic design enables to investigate large cohorts of individuals, basically everyone residing in Sweden who is exposed to any of the selected antibiotics, adjusting for confounding by many variables such as comorbidities or other medication use.

For this project we look for an enthusiastic and talented person with suitable medical education at basic and advanced level with experience and interest in clinical cancer research and infectious diseases. Experience with pharmaco-epidemiology and diseases of the upper gastro-intestinal tract are important merits. Some knowledge and experience in epidemiology, data management and statistical analyses are pre-requisites

Interested in applications from postdocs, visiting researchers and PhD students for our collaboration with Nanjing Medical Univer regarding evaluation of the health care reform.

Kristina Burström, Associate Professor of Health Economics
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Interested in applications from postdocs and PhD students

Yihai Cao Professor, MD, PhD
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Project 1. Mechanistic study of antiangiogenic drug resistance and optimizing antiangiogenic cancer therapy
One of the key issues of antiangiogenic cancer therapy is to overcome the drug resistance, which occurs in most cancer patients. A majority of cancer patients are intrinsic resistant to antiangiogenic drugs. Additionally, for the minority of patients who initially responded to antiangiogenic therapy often develop resistant when therapy persists. Therefore understanding mechanisms underlying antiangiogenic drug resistance is essential for improvement of current antiangiogenic therapy and for optimization of antiangiogenic therapy. In response to anti-VEGF therapy, tumors often employ other non-VEGF factors to grow blood vessels. This mechanism is referred to as the compensatory mechanism of drug resistance. With our current available tumor models in mice, we would like to study antiangiogenic drug sensitivity in tumors that express different factors. To overcome the antiangiogenic drug resistance, we plan to use antiangiogenic agents with different principles such as anti-VEGF, anti-integrin, endogenous angiogenesis inhibitors, and vascular destructive agents. This organizing principle of antiangiogenic therapy in combination of chemotherapeutic drugs will be studied in preclinical tumor models.

Project 2. Off-tumor targets as potential beneficial sites of antiangiogenic therapy
Clinical experiences with antiangiogenic therapy shows that survival benefits of these drugs do not always correlate with reduction of tumor sizes, which cannot be used as a reliable surrogate marker to predict survival benefits. In clinical settings, the antiangiogenic drugs are given systemically to cancer patients but not the local tumor tissue. In one of our mouse tumor models, we have found that tumor–derived VEGF enters into the circulation and results in systemic destruction of multiple tissues and organs including impaired bone marrow hematopoiesis, splenohepatomegaly, and endocrine dysfunctions. These VEGF-induced systemic syndromes resemble the paraneoplastic syndrome in cancer patients, suggesting that VEGF induces cancer-associated systemic syndrome. Based on this model, our further findings show that treatment of these tumor-bearing mice with anti-VEGF drugs significantly improves tolerance to chemotherapy-induced systemic toxicity. Therefore, reduction of chemotoxicity by antiangiogenic drugs may provide a novel mechanism underlying combination therapy. These findings may lead us to design new therapies in order to improve the therapeutic efficacies.

Project 3. Modulation of angiogenesis in adipose tissue: a new concept of treatment of obesity and metabolic disease
Pathological angiogenesis also significantly contributes to the onset, development and progression of many human diseases. We proposed that angiogenesis is essential for adipose tissue expansion and modulates adipose metabolism. The initial evidence from obese models in mice demonstrated that angiogenesis inhibitors significantly modulate adipose tissue growth and metabolism. At the international leading position, we would like

to further extend our study toward molecular mechanisms underlying angiogenesis in regulation of obesity, metabolism, and insulin sensitivity. We are particularly interested in translational aspects of our study toward therapeutic implications of obesity, diabetes and their related complications by targeting angiogenesis.

Project 4. Activation of BAT-mediated lipolysis by angiogenesis modulators or cold in development of atherosclerosis-related cardiovascular disease.
Atherosclerosis-associated coronary heart disease (CHD) including myocardial infarction is the leading cause of mortality in the Western society. Obesity and its associated alteration of metabolism is probably one of the most common causal bases of development of CHD. We have recently shown in mice that cold exposure induces transition of white adipose tissue (WAT) into a brown adipose tissue (BAT)-like phenotype, leading to increased rates of thermogenesis and lipolysis. The cold-induced transition from WAT into BAT also triggers an angiogenic switch in the adipose tissue in association of upregulation of VEGF. Although the cold-induced BAT activation is in general beneficial for obese individuals, BAT activation also increases lipolysis, leading to increased levels of blood lipids. Based on these initial findings in mouse models, we hypothesize that cold-induced lipolysis and angiogenesis might alter development and stability of atherosclerotic plaques leading to accelerated development of CHD. We've found that ApoE knockout mice in the cold environment showed markedly increase of the atherosclerotic plague growth. In addition to increased plaque growth, these cold-ApoE mice also show instability of plaques with increased levels of inflammatory cells and angiogenesis. We plan to further study the mechanisms underlying cold-associated increase of CHD, to develop novel therapeutics for the treatment of CHD by targeting adipose metabolism and angiogenesis, to associate our findings to clinical relevance in human patients.

Interested in applications from PhD students, postdocs and visiting researchers

Project title: **Renal and Islet Microcirculation in Cardiovascular Disease and Type 2 Diabetes – Role of oxidative stress and nitric oxide deficiency**

Mattias Carlstrom, PhD, PharmD, Docent
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Link: http://ki.se/en/fyfa/reactive-oxygen-species-and-nitric-oxide-signaling-in-renal-and-cardiovascular-function

Project description:
Adequate minute-to-minute regulation of blood perfusion within a given organ is obtained by modulation of microcirculation. In the kidney, the afferent arterioles importantly contribute to the overall renal autoregulation, and hence control glomerular filtration and blood pressure. In the pancreas, the arterioles are regulating islet perfusion and hence ß-cell glucose metabolism and insulin release. The mechanisms for microcirculatory regulation are multifactorial, but are influenced by metabolism- and endothelium-derived factors including adenosine, angiotensin II (ANG II) and nitric oxide (NO). Impaired renal and islet arteriolar functions have been suggested in aging and obesity-related disorder including cardiovascular disease (CVD), kidney disease and type 2 diabetes (T2D). Further mechanistic understandings are necessary to develop new and cost-efficient treatment strategies against these global health problems. We aim to investigate the role and interaction between adenosine and ANG II receptors in regulation of renal, cardiovascular and metabolic functions. In particular, studies address how receptor interaction influences oxidative stress and NO signaling. This translational project includes *in vivo* animal studies, sophisticated *ex vivo* vascular studies, cellular and molecular analysis, and also human studies. Novel insight from this project may have both nutritional and therapeutic implications in the treatment of CVD andT2D.

Research group: Renal, Cardiovascular and Metabolic Research

Interested in applications from postdocs

Project title: **Regulation of the epigenetic state of oligodendrocyte precursor cells**

Gonçalo Castelo-Branco, Ph.D., Senior Research Fellow/Associate Professor
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Our research group is interested in the molecular mechanisms defining the epigenetic state of stem/progenitor cells, such as pluripotent cells and oligodendrocyte precursor cells. We are particularly focused on how interplay between transcription factors, non-coding RNAs and chromatin modifying enzymes contributes to the transition between epigenetic states in oligodendrocyte precursor cells, with the aim to design epigenetic based-therapies to induce regeneration (remyelination) in demyelinating diseases, such as multiple sclerosis.

Interested in recruiting postdocs

Project title: **Neurophysiological dysfunctions in Parkinson's disease**

Karima Chergui, Ph.D., Associate Professor
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Link to group home page: http://ki.se/ki/jsp/polopoly.jsp?l=en&d=9426

Project description: Our group examines dysfunctions of glutamatergic neurotransmission in the brain of mouse models of Parkinson's disease. The focus is on the subunit composition of the NMDA type of glutamate receptor and the development of novel strategies to identify dysfunctions in neurotransmission and plasticity in Parkinson's disease. The laboratory uses electrophysiological and electrochemical approaches to measure, in acute brain slices, neuronal activity and neurotransmitter release. These methods are combined with pharmacological tools, western blotting, histochemistry and behavioral approaches.

Interested in recruiting from all the categories, PhD student, postdoc and visiting researcher.

Project title: **Estrogen signaling in metabolic disease, particularly type 2 diabetes and breast cancer**

Karin Dahlman-Wright, Professor
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The group is approaching the molecular mechanism of estrogen signaling in metabolic disease and breast cancer combining phenotypic and functional genomics data with the ultimate goal to identify novel diagnostic criteria and drug targets. Specifically, 1) we investigate metabolism-related phenotypes and underlying mechanisms in tissue-specific estrogen receptor alpha knockout mice; 2) we explore functional genomics technologies to explore estrogen signaling in breast cancer, in particular tamoxifen-resistant breast cancer.

Interested in recruiting postdocs

Project title: **Contribution of interactions between polycyclic aromatic hydrocarbons to the carcinogenicity of polluted air**

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Link: http://ki.se/en/imm/project-interactions-between-pahs-in-complex-mixtures-and-cellular-effects

Project description:
The methods commonly used for assessing the toxicity of complex environmental mixtures probably significantly underestimate the risk of exposure to human health since they do not take into account interactions which potentially give rise to synergistic effects. One major group of environmental pollutants is the polycyclic aromatic hydrocarbons (PAHs) which have been linked with numerous adverse health effects including cancer, cardiovascular and respiratory diseases and most strongly so because of its association with air particulate matter and air pollution. The goal of this project is to investigate the harmful effects of exposure to complex mixtures of PAHs and to improve the scientific base for risk assessment of human exposure to PAHs in urban air and industrially-contaminated soil.

In the project we study the effects of complex mixtures of PAHs in environmental samples on DNA damage and repair, and inflammation using mammalian cells. Our published data indicate that complex PAH mixtures induce unexpected and persistent DNA damage signaling responses. Our hypothesis is that synergistic effects between different PAHs in complex mixtures represent a major carcinogenic effect and there is an urgent need to include these interactions in the health risk assessment

Interested in applications from PhD students, postdocs and visiting researchers

Project title: **Opioid related toxicities and their potential alternatives**

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Project description:
Opioids are still considered to be the most effective analgesics for moderate to severe pain. Although, in addition to their serious side effects (respiratory depression), there are major concerns about their use include the potential addiction, abuse, misuse, and diversion. Understanding the precise mechanisms of tolerance/addiction development is thus important for the development of potent analgesics devoid of this side effect. In this study we address the molecules involved in the tolerance setting and test the hypothesis that inhibiting those molecules will abolish or at least diminish tolerance and, in turn, the addiction risk. Herein, we focus on microRNAs, matrix metalloproteinase (MMP), peroxynitrite ($ONOO^-$), aquaporins (AQP), glycogen synthase kinase (GSK) and elucidate the interaction between those molecules leading to tolerance development. As, a novel promising painkiller to be devoid of the opioid side effects, we are testing the opioid chimeras (which induce much more potent analgesia) for those tolerance markers. Comparing them to the regular opioids will furnish a base for new drug with no/less such side effects. Our preliminary data indicate that opioid chimeras show less tolerance linked molecules induction.

Interested in recruiting PhD students and postdocs

Project1 Epigenomic signatures of transposable elements (Bioinformatics)
Project 2 Testing the histone code using synthetic acetylation
Project 3 Viral delivery systems for amber suppression technology

Simon Elsasser, PhD Fellow, SciLifeLab Stockholm
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Department of Medical Biochemistry and Biophysics
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1. Epigenomic signatures of transposable elements (Bioinformatics)
Studying the epigenetic silencing of transposable elements (TE), we are aiming to understand one of the most prominent examples of epigenetic gene control throughout evolution.The project will use the vast collection of epigenomic data available through the NIH Epigenome Roadmap project, developing a pipeline for large-scale, automated and integrated analysis of chromatin signatures at repetitive sequences. We are looking for a highly motivated student or researcher with programming skills and knowledge in next-gen sequencing analysis.

2. Testing the histone code using synthetic acetylation
The project applies amber suppression technology to a 'real' biological problem, for which our lab is at the front edge of the field. Chromatin is known to control gene expression, in part through modification of the histone tails. Deciphering the code of modifications has been challenging in the past. Site-specific acetylation/crotonylation/propionylation sites will be installed on histone proteins in living cells using genetic code expansion, and the effect of these modifications on the transcriptional outcome of a reporter locus and endogenous genes are studied.

3. Viral delivery systems for amber suppression technology
Expanding the scope of unnatural amino acid mutagenesis to primary cells and living animals, we are looking for novel delivery methods for the synthetic biology modules, such as amber suppression systems.

Interested in recruiting PhD students and postdocs

Project title: **Function and regulation of the alarmin HMGB1 in inflammatory conditions such as arthritis**

Helena Erlandsson Harris, Professor in rheumatological inflammation research
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Our research aims at improving the knowledge regarding disease-causing mechanisms active during chronic inflammatory joint disease (arthritis). The obtained knowledge forms a basis for the development of new, targeted anti-inflammatory therapy. We are especially interested in the alarmin HMGB1. Alarmins are molecules with defined functions inside cells and a common function outside of cells; to alert the body to danger, cell death or cell stress due to infection or trauma, and induce an inflammatory response. We are studying features and regulation of HMGB1s inflammation-inducing functions, its role in arthritis pathogenesis and its potential as a target for anti-inflammatory therapy. Our research programme can be divided in three related projects:

1. Studies of the proinflammatory functions of HMGB1 and their regulation
2. Development of HMGB1-targeted therapies
3. The role of HMGB1 in juvenile arthritis disease mechanisms and the use of HMGB1 measurement as prognostic and diagnostic marker of disease

Our projects encompass molecular biology techniques, in vitro cellular immunology techniques, in vivo disease models and analysis of patient samples.

Interested in recruiting a post-doctoral fellow

Title of project: Characterization of the role of bacterial genotoxin in infection and cancer development

Teresa Frisan, Assoc. Prof.
Dept Cell and Molecular Biology (CMB), Karolinska Institutet
Email: Teresa.Frisan@ki.se , http://ki.se/en/cmb/teresa-frisans-group

Project description

The research team studies the effect of acute and chronic infection/intoxication in vitro and in vivo with bacteria expressing a novel family of bacterial toxins, known as genotoxins, which cause DNA damage in mammalian cells.
The project aims at characterizing the effects of the genotoxins on the tissue architecture (e.g. intestinal tract and liver), the host response (special focus on the immune response), induction of DNA damage and genomic instability caused by short term and long term infections/intoxication in *ex vivo* organoids models as well as in *in vivo* models.

Qualifications of applicant
Prior experience of work with laboratory animal models as well as a certified FELASA C level education will be considered as a merit

Interested in applications from postdocs and PhD students

Project title: **Novel approach for cancer treatment: Biasing Receptor Tyrosine Kinase (RTK) Signaling through G-protein coupled receptors (GPCR)**

Leonard Girnita M.D., Ph.D.
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Department of Oncology-Pathology, Karolinska Institutet, Karolinska University Hospital
leonard.girnita@ki.se webpage

Short description of the project: Our overall objective is to investigate the function and determine potential utility of the signaling complexes involved in the GPCR/RTK cross-talk as potential biomarkers or molecular targets in cancer. This is based on the underlying hypothesis that the signaling complexes coordinated by β-arrestins (β-arr) and involving kinases, non-coding RNAs (ncRNA), ubiquitin ligases and/or deubiquitinating enzymes, contributes to tumorigenesis and the progression of cancer, and could be targeted therapeutically.

Specific Objectives:

1. Investigate the molecular mechanism of β-Arrestin/GRK-biased agonism at the IGF-1R

2. Model validation: Investigate the utility of the β-arr signaling complex as a potential diagnostic or prognostic biomarker.

3. Clinical applications: Un-biasing β-arr/GRK signaling through GPCR as a novel approach for cancer treatment

Key publications:
1. Huiyuan Zheng, Claire Worrall, Shen Hongchang, Tarik Issad, Stefan Seregard, Ada Girnita and **Girnita L.** Selective recruitment of G protein coupled receptor kinases (GRKs) controls signaling and trafficking of the Insulin-like Growth Factor 1 Receptor. Proc Natl Acad Sci U S A. 2012 May 1;109(18):7055-60.

2. Zheng H, Shen H, Oprea I, Worrall C, Stefanescu R, Girnita A**, Girnita L.** β-Arrestin-biased agonism as the central mechanism of action for insulin-like growth factor 1 receptor-targeting antibodies in Ewing's sarcoma. Proc Natl Acad Sci U S A. 2012 Dec 11;109(50):20620-5.

3. Girnita L, Worrall C, Takahashi SI, Seregard S, Girnita A. Something old, something new and something borrowed: Emerging paradigm of insulin-like growth factor type 1 receptor (IGF-1R) signaling regulation. Cell Mol Life Sci. 2013 Nov 26.

Interested in applications from postdocs for a two year project

Project title **BIOGERONTOLOGY: AN OMICS APPROACH TO DISCOVER NEW BIOMARKERS OF NEURODEGENERATION**

Sara Hagg, Associate Professor
Department of Medical Epidemiology and Biostatistics (MEB)
Sara.Hagg@ki.se
(http://ki.se/en/people/sarhag)

The world's population is growing older and a large proportion of the elderly develop Alzheimer´s Disease (AD) and related neurodegenerative disorders. The aim of this project is to find new biomarkers associated with neurodegeneration by using whole blood samples collected in TwinGene (n=12,614), a prospective cohort of elderly twins within the Swedish Twin Registry. The biomarkers to be used are measures of telomere length, metabolites and proteins which will be associated with AD. The project is intended to be a two-year postdoc project at Department for Medical Epidemiology and Biostatistics [MEB] (http://ki.se/en/meb) with Associate Professor Sara Hägg as advisor; she has been conducting many studies using different *omics* approaches with focus on aging conditions. Many of the research projects are done in national and international collaboration, providing a great network of researchers and MEB will support by in-house statisticians, IT and administration.

Interested in recruiting PhD students/postdocs/researchers

Project title :**Genetics of primary immunodeficiency diseases**

Lennart Hammarstrom, Professor
Head of division, Division of Clinical Immunology and Transfusion Medicine, Department of Laboratory Medicine, Karolinska Institutet
Lennart.Hammarstrom@ki.se

Project description:
More than 200 different forms of primary immunodeficiency diseases have been recognized to date, varying markedly in clinical severity. In some of the disorders, the gene (and mutation(s)) associated with the defect has been identified (monogenic diseases). However, these can only explain the etiology in a minority of patients. We are using state of the art technologies (including whole exome sequencing and whole genome sequencing, epigenetics, transcriptome sequencing and protein profiling) in order to identify novel genes associated with primary immunodeficiency and new mutations in previously recognized genes. Patients are recruited from Sweden (from our own clinic and our recently initiated newborn screening program for primary immunodeficiency), China (where we already have an ongoing collaboration in Shanghai, Shenzhen and Guangzhou) and countries with a high consanguinity rate (the latter most often resulting in homozygous mutations), including Iran and Saudi Arabia. Publications in the past few years in this project include papers in Nature Communications, Science, JACI, Nature Genetics, J Exp Medicine and two manuscripts currently under review in Nature Genetics.

Interested in recruiting a PhD student or Post doc

Moustapha Hassan, Prof. of transplantation research, Director of preclinical laboratory, Karolinska Institutet
Epost moustapha.hassan@ki.se

Personalized Medicine
Our aim is to improve the clinical outcome and minimize transplantation related complications for children treated with hematopoietic stem cell transplantation (HSCT) as the only cure from their cancer through personalized/individualized medicine based on the patient's genetic constitution and mutations.

Background
HSCT is a curative therapy, if not the only treatment, for many children with cancer. Conditioning regimen facilitates the engraftment of stem cells and pursues a curative treatment. After HSCT, children suffer from a number of acute and late complications including: graft-versus-host disease (GVHD), liver toxicity, pulmonary complications, hemorrhagic cystitis, cardiotoxicity, growth, diminished fertility and others. Despite increasing knowledge of mechanisms implicated in HSCT-related complications, these mechanisms are not fully elucidated.

This project consists of 4 studies:
1. To study the basic mechanisms of GVHD following chemotherapy-based conditioning compared to radiation based therapy.
2. To use gene array profiling to map the pharmacogenetics in correlation to treatment efficacy in order to personalize chemotherapy based conditioning
3. To investigate the effect of HSCT on functional properties of the arterial system and endothelial cells in order to minimize long term cardiovascular complications
4. To study minimal residual disease of AML after HSCT in mouse model to enhance treatment strategies

Methods
We will use quantitative RT-PCR, Western blot, IHC, 4-chamber Danish Myotechnology, FACS, FISH and IVIS.

SIGNIFICANCE FOR CHILDHOOD CANCER
Personalized treatment with chemotherapy in combination with knowledge of GVHD caused by cytostatics will enable physicians to choose a treatment strategy that provides maximum treatment efficacy and minimum treatment related complications. We hope that the results of this project will lead to a better quality of life for pediatric patients.

Interested in recruiting a Postdoc in Translational Medicine

Thomas Helleday, Professor, Division of Translational Medicine and Chemical Biology, Department of Medical Biochemistry and Biophysics, Karolinska Institutet
thomas.helleday@scilifelab.se
Group website http://www.helleday.org

Our vision, in the Helleday Laboratory, is to use the discoveries from our basic research programmes on DNA repair and survival mechanisms within cancer cells, to help identify and validate novel anticancer targets and facilitate the discovery of new anticancer drugs. We previously developed a novel concept to target tumour suppressors in cancer using the concept of synthetic lethality (Nature 2005), and a PARP inhibitor was recently FDA and EMA approved for treatment of BRCA1 and 2 mutated ovarian cancers. Recently we described a small molecule inhibitor for a novel target; MTH1, which selectively eradicates cancer, based on its lost redox potential (Gad et al., Nature 2014, Hubert et al., Nature 2014).

Our goal is to develop our hypotheses first in preclinical models, then proceed to study the effect and underlying mechanisms of new cancer treatments in patients. To do this, we have created an integrated translational strategy, with teams of scientists from a variety of disciplines taking our basic findings all the way from bench to bedside. We are based at SciLifeLab, Karolinska Institutet, where we perform high-throughput screening, basic molecular and cell biology, biochemistry, systems biology, pharmacology and medicinal chemistry.

We are looking for a highly motivated and skilled postdoctoral fellow to work individually as well as in a team to discover novel biology within DNA repair and the cancer field leading to new potential anticancer treatments. You will be performing productive, innovative and high quality research to the highest standards, including target validation, mechanism of action studies and efficacy studies both in vitro and in vivo in relevant disease models.

Interested in applications from: Visiting researchers, postdocs and PhD students

Rikard Holmdahl, professor, MD, PhD.
Division of Medical Inflammation Research, Department of Medical Biochemistry and Biophysics (MBB), Karolinska Institutet,
email: Rikard.Holmdahl@ki.se, web address: www.inflam.mbb.ki.se

Projects:

1) **Developing a vaccine preventing rheumatoid arthritis addressing the precise autoimmune mechanisms.** To analyze the mechanisms of induced T cell regulation using a specific vaccine protecting against arthritis. The work will be done in both experimental mouse systems and with human cells. We have made unique mouse strains with physiologic expression of the Asian (0405) as well as the Caucasian (0401) MHC class II alleles associated with rheumatoid arthritis along with humanization of other interacting MHC molecules. Together with relevant TCR and BCR knockins this will be a unique setting for the project. In addition we have access to clinical samples to translate findings in human RA.

2) **The precise oxidative regulation of T cells studied with designed conditional and mutated mouse strains.** To address new discoveries that NOX2 generated reactive oxidative species (ROS) profoundly regulate T and B cell activation. Mouse strains with conditional expression of NOX2 in T cell, B cells and antigen-presenting cells are available. We have also replaced selected regulatory cysteins with serins in proteins that are critically redox regulated in the T and B cell activation signaling. The project aim to identify the precise mechanism for redox regulation of immune activation, with these in vivo and in vitro tools.

Interested in recruiting PhD students, postdocs and visiting researchers

Lars Holmgren, Professor
Department of Oncology and Pathology, Karolinska Institutet
Karolinska Hospital
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https://se.linkedin.com/pub/lars-holmgren/b/48b/746

In this project we aim at deciphering the cellular signaling pathways that relay mechanical force and apply this knowledge in a clinical setting. In the last decades the scientific community has acquired an impressive amount of knowledge regarding how cells communicate using diffusible factors such as hormones and growth factors. This has been to the gain of the patient as it has been used to target signaling pathways associated with disease. How cells communicate by exerting or responding to mechanical force remains an unexplored and relatively unexploited territory. Cells and tissues are exposed to mechanical forces during organogenesis, homeostasis that control shape and elastic properties. Defects in how cells perceive mechanical forces, mechanotransduction, are implicated in various diseases ranging from cancer, atherosclerosis and cardiomyopathies.

References: Mojallal et al Nature Comm, 2014, Hultin et al Nature Comm 2014.

Interested in applications from PhD students

Project title: Utilization of whole-genome sequencing to identify markers to aid in diagnosis, prognosis and treatment of thyroid cancer

Carl Christofer Juhlin, MD, PhD, BSc
Department of Oncology-Pathology, Karolinska Institutet. Stockholm, Sweden
Christofer.Juhlin@ki.se
Link to group home page: http://ki.se/en/onkpat/research-team-christofer-juhlin

Project description: We propose to use a combination of tumor tissues from various subtypes of thyroid cancer to be subjected to whole-genome sequencing, to aid in the identification of driving events which could help us pinpoint 1) benign from malignant thyroid nodules pre-operatively, 2) highly aggressive tumor variants which could mandate adjuvant treatment options and 3) potential molecular aberrancies in cases with utterly dismal prognosis which could be targeted for treatment purposes.

Interested in recruiting PhD students and postdocs

Henrik Larsson, Associate professor
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http://ki.se/en/people/henlar
http://www.impactadhdgenomics.com/sv/researchers/sweden-henrik-larsson

I Henrik Larsson am an associate professor of psychiatric epidemiology and research group leader for a team that focus on ADHD epidemiology. I have a strong track-record in supervising international PhD students. I am currently the main supervisor of one PhD student supported by the China Scholarship Council (Shuyang Yao awarded in 2013) and I have been the main supervisor of two PhD students (Zheng Chang, and Qi Chen) that have received the "Chinese government award for outstanding self-financed students abroad".

My research group explores how genes and environments influence ADHD across the life span. We also study the developmental consequences of ADHD and try to identify the benefits and risks associated with ADHD treatment interventions.

The research group use large ADHD cohorts identified from national health registers, the Swedish twin register and clinical cohorts. These datasets contains valid diagnoses of ADHD, prospective measures of environmental risks, high throughput genotyping, longitudinal information on prescribed ADHD medications and assessments of serious medical (cardiovascular, neurological, and psychiatric problems) and functional outcomes.

Interested in recruiting postdocs

Project title: **Gene-environment interactions behind coronary heart disease – meta-analyses of genome wide association studies.**

Karin Leander, Associate Professor of Epidemiology
Unit of Cardiovascular Epidemiology, Institute of Environmental Medicine
Karolinska Institutet
Email: Karin.Leander@ki.se
Link to group homepage: http://ki.se/imm/enheten-for-kardiovaskular-epidemiologi

Background

Studies of gene-environment interactions may reveal associations that will guide research towards as yet unknown mechanisms giving rise to CHD. Surprisingly few studies have explored such gene-environment interactions.

Aim

The aim of the project is to increase knowledge about how individual genetic makeup can be coupled with specific alterations in life style factors to reduce risk of CHD. The life style factors to be considered are smoking, physical inactivity and dietary habits as they pertain to fat intake (type and amount). The gene-environment interactions will be explored with no specific hypothesis of which genes may be involved.

Materials and methods

The studies will use combined material from the Stockholm Heart Epidemiology Program (SHEEP) and the Stockholm Coronary Atherosclerosis Risk Factor study (SCARF), two case-control studies encompassing in total 1560 individuals aged 45-70 years who suffered a first time myocardial infarction and 1939 control individuals. Data on 200,000 genetic variants included in the Cardiometabochip are available. Gene-environment interactions in relation to incident myocardial infarction will be analyzed. A software program developed in our group (the GEIRA program) specifically designed to identify such synergisms and antagonisms, will be used. A possible continuation of the project will be to perform corresponding studies based on material from cohorts included in the CARDIOoGAM and C4D consortia. Each cohort agreeing to participate will run interaction analyses locally. Combined estimates will be calculated and reported using forest plots along with study specific interaction results.

Interested in recruiting post-docs, PhD students, and visiting researchers

Nailin Li, MD, PhD, associate professor
Department of Medicine-Solna, Clinical Pharmacology Group, Karolinska Institutet,
Karolinska University Hospital-Solna
Email: Nailin.Li@ki.se Tel: +46-8-51773996;

Project I: **Platelet-regulated CD4$^+$ T effector cell responses and their impact on atherosclerosis**

Atherosclerosis is an inflammatory and thrombotic disease, in which both CD4 T cells and platelets play critical roles. We have recently shown that platelets distinctly regulate immune responses of different CD4$^+$ T cell subsets. Aim of the project is thus to elucidate the impact of platelet-regulated CD4$^+$ T effector cell responses 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. Using murine models of platelet-specific deficiency of CD4$^+$ T cell regulators, we will study how platelet deficiency affects CD4$^+$ T effector responses 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.

Project II: **Platelet angiogenic activity and its role in cancer metastasis**

Platelets are closely engaged in angiogenesis, apart from exerting their principal functions in thrombosis and haemostasis. We and others have recently shown that platelets differently release pro-angiogenic and anti-angiogenic factors upon different stimuli. We are therefore investigating the mechanisms underlying the distinct packaging of pro-angiogenic and anti-angiogenic factors into separate alpha-granules, the storage pool of proteins in platelets, and the signalling mechanisms controlling selective release of pro-angiogenic and anti-angiogenic factors. Through intervention of the signalling mechanisms, we will study how pro-angiogenic and anti-angiogenic activities of platelets can modulate angiogenesis in cancer, and subsequently regulate cancer growth and metastasis.

Interested in recruiting postdocs

Project title: **Identification of biomarkers and molecular mechanisms for periodontitis**

Tülay Yucel-Lindberg, Associate professor
Department of Dental Medicine, Karolinska Institutet
Tulay.Lindberg@ki.se

Project description: Periodontitis is a chronic inflammatory disease resulting in destruction of tissue and bone supporting the teeth, which ultimately leads to tooth loss. Our group has investigated the gene expression profile of periodontitis in a large number of biopsies from patients with periodontitis and healthy subjects using RNA-sequencing. We have identified numerous up-regulated and down-regulated genes and aim to further explore the most highly up-regulated/down-regulated genes in saliva, gingival fluid and serum in order to identify biomarkers for periodontitis.

Interested in recruiting postdocs

Project title: **Genetic variance in androgen metabolism in Chinese and Swedish women**

Angelica Lindén Hirschberg, professor at the Department of Women's and Children's Health, Karolinska Institutet
angelica.linden-hirschberg@karolinska.se
http://ki.se/kbh/endokrinologi-och-metabolism

Project description: The genetic variance in the metabolism of sex steroid hormones in Asian and Caucasian women is of great interest in view of large differences in reproductive and metabolic disorders, as well as in breast cancer rate. The objective of the present project is to investigate interethnic variation of androgen metabolism and excretion in about 100 Chinese women and 100 Swedish women of Caucasian origin of fertile age. Urine and blood samples will be collected in a standardized manner for analysis of steroid hormone profiles (endogenous androgens and their metabolites) by LC-MSMS and genetic polymorphisms of importance for androgen metabolism (e.g. UGT2B7, UGT2B17, CYP17) by real time PCR. Finger measurements of the second and fourth digit, and the ratio 2D:4D is calculated as a measure of prenatal androgen activity. The results will be compared between ethnic groups and related to clinical symptoms of hyperandrogenism (acne and hirsutism).

Interested in recruiting a PhD student or a postdoc

Project title "**Myositis specific autoantibodies, muscle biopsy features and clinical outcome in patients with myositis**

Ingrid Lundberg, M.D., Ph.D. Professor in Rheumatology,
Rheumatology Unit, Department of Medicine, Karolinska University Hospital, Solna
Karolinska Institutet,
Ingrid.Lundberg@ki.se webb: http://www.cmm.ki.se/en/group/myositis/

Project description: Myositis is a chronic, rheumatic muscle inflammation leading to muscle weakness and muscle fatigue. Some patients also have inflammation in the skin or in the lungs. Immunosuppressive treatment is often disappointing with a high degree of morbidity and mortality. Subphenoyping patients according to newly identified autoantibodies may be a new way forward to identify prognostic biomarkers and molecular pathways that eventually could lead to new therapies. Limited information is available on the pattern of inflammatory changes in muscle biopsies from patients with different autoantibodies. To be able to test the hypothesis that autoantibodies may identify subgroups of patients that share some pathophysiology and that myositis specific autoantibodies predict treatment response and prognosis, large cohorts of well-characterized patients with longitudinal follow-up are needed.

Objectives: In this project we aim as a first step to investigate muscle biopsy features in patients with different myositis specific autoantibodies. A second step will be to link biopsy features and autoantibodies to clinical outcome measures. As a third step patients with Caucasian ancestry will be compared to patients with Chinese ancestry for these variables and clinical outcome.

Project strategy
The first part of the project will be performed on patients from Karolinska University hospital, where we have one of the largest cohort of patients with myositis and longitudinal follow up in the world. This will include training in the use of the Euromyositis registry, use of the international validated outcome measures and in standardization of muscle biopsy assessment. In a second part of the project, myositis patients from Chinese centers will be included in the project and be assessed in a similar way and compared with the Swedish and the European cohorts. For this type of multicenter project training on how to use the outcome measures is essential to avoid systematic bias from different centers.

Investigations of pathways of specific interest based on results from gene expression and proteomics data from muscle biopsies such as the type I interferon pathway will be investigated in relation to clinical outcome.

Importance of the project: This project is likely to reveal novel information concerning muscle biopsy features in relation to myositis specific autoantibody profiles. The results from this study will form the basis for extended studies in the larger European cohort and in a Chinese patient population. We anticipate to achieve novel information that will be important to perform functional molecular studies to get a better understanding on the immune specificities in the myositis subsets. We also expect to find that autoantibody profiles may disclose differences in treatment response and outcome. As a final result we expect to identify prognostic biomarkers.

Interested in recruiting a post-doctoral fellow

Title of project: Mechanisms of viral-mediated oncogenesis

Maria G. Masucci, Prof.
Dept Cell and Molecular Biology (CMB), Karolinska Institutet
Email: Maria.Masucci@ki.se , http://ki.se/en/cmb/maria-g-masuccis-group

Project description

The research team is studying the biology of tumor virus infections with special focus on the induction of DNA damage and telomere dysfunction and their contribution to tumor initiation and progression.
The objective is to applying fundamental knowledge of cell biology and biochemistry to understand the pathogenesis of infection-associated cancers, and identify new targets for interfering in pro-inflammatory and regulatory pathways.

Qualifications of applicant

Prior experience of work on the regulation of DNA damage response and telomere homeostasis will be considered as a merit.

Interested in recruiting a postdoc or a visiting researcher

Project title: **A glioblastoma model in genetically modified mice; studies of stem cell phenotypes in the pre-neoplastic brain**

Monica Nistér, Professor, MD, PhD
Department of Oncology – Pathology, Karolinska Institutet
Monica.Nister@ki.se
http://ki.se/en/onkpat/monica-nisters-group

We have generated a transgenic mouse glioma model, based on combined platelet derived factor B (PDGF-B) signaling and loss of p53 function (Hede *et al. Glia* ***57,*** 1143, 2009). In these mice, the human glial fibrillary acidic protein (GFAP) promoter directs expression of PDGF-B to the lateral ventricular wall – subventricular zone neural stem cell (LVW-SVZ NSC) niche and to different astrocytic cells of the mouse brain. While forced PDGF-B expression only resulted in a normal adult brain phenotype, concurrent loss of p53, a known regulator of stem cell self-renewal and pluripotency, resulted in GBM-like tumors. This system is particularly well suited to elucidate the earliest molecular changes in the pre-neoplastic brain, in mice with the tumor permissive genotype (PDGFB/p53 null) compared to in the control p53null, PDGF-B, and WT mice, which do not develop tumors. The fact that PDGF-B/p53 null mice develop brain tumors first at 3-6 months of age provides a window of time in which to monitor cellular and biochemical changes in the tumor-permissive brain, before tumors occur.

Further work is required to understand how the wild type tissue differ from the pre-neoplastic environment in the (PDGFB/p53 null) mouse and what further alterations that may have occurred in cells that progress to form tumors. This will be performed by neural stem cell culture, proteomic analysis, gene expression analysis, sequencing and tumor formation experiments.

SIGNIFICANCE: This project will provide novel information on key stem cell regulatory mechanisms involved in brain cancer development.

For this work, we search for a postdoc/researcher experienced in working with mouse models of cancer and/or genetically modified mice.

Interested in recruiting Post-docs and PhD-students

Project positions in angiogenesis with focus on cellular signaling and imaging

Daniel Nyqvist, PhD, Assistant Professor – Group Leader
Dept. of Medical Biochemistry and Biophysics
Division of Vascular Biology, Karolinska Institutet
E-mail: Daniel.Nyqvist@ki.se
Website: http://ki.se/en/mbb/daniel-nyqvist-group

Research interests

The research group of Dr. Daniel Nyqvist is investigating molecular mechanisms regulating blood vessel growth and barrier function in health and disease. We study angiogenesis during developmental processes and in pathophysiological conditions such as CNS angiogenesis, BBB formation and tumor growth. We are a young, dynamic and very enthusiastic research team with a well-established collaborative network and strong funding.

Project description: The project will focus on elucidating the role of canonical Wnt/ catenin signaling for blood vessel growth and barrier function. The work will take advantage of a repertoire of genetically modified mouse models, including inducible gain- and loss-of-function mutations, applied onto both developmental and disease models. We use a wide range of cell and molecular biological techniques, as well as biochemical assays and gene arrays. To understand the dynamic processes of vessel growth at the cellular level we are currently developing new applications for both live cell imaging and non-invasive *in vivo* confocal imaging. Two new state-of-the-art confocal imaging systems will be available for these applications.

Lab references: Nyqvist et al., Diabetes 2011, Corada et al., Dev Cell 2010, Speier, Nyqvist et al., Nat Med 2008.

Qualifications of the applicant

We are seeking highly motivated researchers with a good team spirit and deep curiosity for science on all entry levels; Post-docs and PhD-students. The applicant should be fluent in English with good communication and writing. Emphasis will be put on laboratory practical skills and personal attitude in the evaluation process. Furthermore, experience with animal work, vascular biology and imaging is highly valued.

Interested in applications from postdocs and PhD students

Sam Okret, Professor of Molecular Endocrinology
Vice Chairman, Dept. of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden.
sam.okret@ki.se

Are you a Ph.D candidate or postdoc interested in the impact of sex hormones on lymphomas?

Lymphomas are not considered as endocrine-related cancers despite the fact that most lymphoma subtypes show a clear gender difference with a higher incidence and poorer prognosis in men. In addition, epidemiological data implies a role for reproductive factors in this gender difference. We are interested in elucidating the molecular mechanisms underlying this gender difference and to translate this into the clinic to see if it can be used therapeutically and to identify biomarkers that can be used to predict prognosis. Based on already achieved results we are addressing the following aspects.

- How do sex hormones affect lymphoma growth?
- Can sex hormones explain the gender difference in incidence and prognosis?
- What are the molecular mechanisms involved in estrogen (particularly estrogen receptor □ (ER □ agonist) inhibition of lymphoma growth, vascularization and dissemination?
- What is the role of the lymphoma microenvironment on drug response?
- What is the impact of environmental compounds with estrogenic activity on lymphoma growth?
- How does ER □ expression in clinical lymphoma material correlate to lymphoma subtype, gender, prognosis etc.

A large part of our experiments utilize mouse models and are performed in house in a newly established animal facility with up-to date leading technology and equipment including small animal *in vivo* imaging tools. We use several cell biological and molecular techniques, like immunostaining, cell co-culture systems, lentivirus infections, CRISPR/Cas9, flow cytometry and cell sorting. We also do gene expression and signaling pathway analysis by performing microarray, Western blotting, Q-PCR and immunoprecipitations.

We have a broad collaboration with clinicians and biobanks to analyze clinical material, aiming to translate basic scientific ideas or findings into clinical applications.

The Department (totally around 250 scientists) is equipped with a lot of basic instruments and most of the more sophisticated equipment required to performed modern research incl. core facilities for imaging, sequencing, gene expression profiling, bioinformatics and high throughput platforms.

If you are interested, feel free to contact me. Please provide a CV, previous lab experience, your level of English knowledge and contact information for 2-3 references.

Some Key references:

1. Yakimchuk, K., Iravani, M., Sharif Hasni, M., Rhönnstad, P., Nilsson, S., Jondal, M. and Okret, S. Effect of ligand-activated estrogen receptor β on lymphoma growth *in vitro* and *in vivo. Leukemia* 25, 1103-1110, 2011 (Leading Article).
2. Yakimchuk, K., Jondal, M. and Okret, S. Estrogen receptor□□ and □and effects on normal immune system and lymphoid malignant malignancies. *Mol Cell Endocrinol*., 375, 121-129, 2013.
3. Yakimchuk, K., Hasni, M.S., Guan, J., Chao, M., Sander, B. and Okret, S. Inhibition of lymphoma vascularization and dissemination by estrogen receptor □□agonists. *Blood*, 123, 2054-2061, 2014. Accompanied in the same issue with Editorial comments, pp. 1980-1981.

Interested in applications from PhD students/postdocs/ researchers

Research area: Clinical Immunology, Immunogenetics, Cancer Genetics

Qiang Pan Hammarström, MD, PhD, Professor
Div of Clinical Immunology
Dept of Laboratory Medicine, Karolinska Institutet
Karolinska University Hospital Huddinge
Qiang.Pan-Hammarstrom@ki.se
Website: http://ki.se/en/labmed/research-group-qiang-pan-hammarstrom

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 by next generation sequencing*

The project is aimed at identifying potentially treatable molecular targets in mature B cell lymphomas (with focus on diffuse large B cell lymphomas and mantle cell lymphomas) by high-throughput, next generation-sequencing omic- technologies such as whole genome and exome sequencing and RNA-seq.

Interested in recruiting postdoc or PhD student

Project title: Statistical and bioinformatics analysis of high-throughput molecular data in medicine

Yudi Pawitan, Professor
Department of Medical Epidemiology and Biostatistics
Email: yudi.pawitan@ki.se

Project description: Since the publication of the human genome in 2001, the past 15 years of medical research have been driven by a technological revolution in measurement of genome-wide molecular and cellular components. It is now routine to measure millions of features from each person. However, while promising major discoveries and useful translation to the clinic, the data volume has also generated substantial challenges in analyses and interpretation. The goals of our research are to develop statistical and bioinformatics methodologies to exploit high-throughput molecular data at DNA, RNA, protein and metabolite levels, and, in close collaboration with medical researchers, to apply these methodologies to clinical problems in cancer or other diseases. Our recent projects include, for example, development of methods to analyse RNA sequencing data and to integrate various omics data in order to identify cancer drivers. My last PhD student received the *2014 National Award for Outstanding Self-financed Chinese Students Study Abroad* from China Scholarship Council.

Interested in applications from PhD students and postdocs

Project title: "**Dynamics of regulatory RNA by NMR**"

Katja Petzold, PhD, Assistant Professor, Group Leader,
Department of Medical Biochemistry and Biophysics, Karolinska Institutet
katja.petzold@ki.se
homepage: http://petzoldlab.com & http://ki.se/en/mbb/petzold-group

Description: "Structural Biology is perceived as a single picture of a molecule, we have shown that many other structures are present and influencing the molecules function. This is especially relevant for regulatory RNAs, in cancer, aging, infectious disease or brain development. In a project in my lab, an RNA system will be evaluated using latest biophysics method (NMR, CD, UV, ITC…) and functional outcome will be tested with collaborations."

Interested in recruiting a postdoc

Project title: **Deciphering the role of *spv* virulence genes in systemic salmonellosis using probabilistic modeling**

Mikael Rhen, Professor
Department of Microbiology, Tumor and Cell Biology
Mikael.Rhen@ki.se
Link to group home page http://ki.se/en/mtc/mikael-rhen-group

Project description:
While many virulence genes have been identified in *Salmonella* their actual input on the infection dynamics often remain unclear. In this, the *Salmonella spv* genes represent a prime example, being essential for *Salmonella* virulence in mice but completely dispensable for bacterial growth *in vitro* or in cell cultures. We have recently developed a murine infection model based on a genetically barcoded isogenic library of salmonella bacteria (PLOS Pathogens (2014)10: e1004270). This model allows quantification of the actual number of bacteria initiating visceral infection, as well as modeling of the dynamics of the infection and concomitant inter-organ spread. The project proposal, intended for a postdoctoral fellow, utilizes this new infection model to gain more information regarding the role of the *spv* virulence genes in the infection dynamics in mice, and in the transition from acute to chronic salmonellosis.

Interested in applications from: postdocs and PhD students

Project title: "**Clinical and translational research to increase the efficacy and safety of fertility preservation for young people with cancer**".

Kenny A. Rodriguez-Wallberg MD, PhD
Senior Consultant, Associate Professor
Clinical responsible of Programme for Fertility Preservation
Karolinska Institutet Department of Oncology Pathology
Karolinska University Hospital, Obstetrics and Gynecology and Reproductive Medicine
kenny.rodriguez-wallberg@ki.se; kenny.rodriguez-wallberg@karolinska.se

My research projects in Fertility Preservation encompasse both clinical research and experimental work. The projects are conducted at the Department of Oncology-Pathology at Karolinska Institutet.

My research group is composed by two PhD students, both MD, residents in Obstetrics and Gynecology. I have three postdocs, two of them are MD specialists in Ob/Gyn and one postdoc is a molecular biologist, who is currently conducting experiments on in vitro follicle culture of ovarian follicles.

In my group, there is the possibility to work with clinical data and large databases, as well as to perform experimental research which includes the use of animal models.

Interested in recruiting a postdoc

Title of Project: **Novel Mechanims in the Growth and Rupture of Abdominal Aneurysms**

Joy Roy, Associate Professor, Consultant Surgeon
Vascular Surgery Section, Department of Molecular Medicine and Surgery
CMM, Karolinska Institutet
Joy.Roy@ki.se

In our research group at the Department of Vascular Surgery, Karolinska University Hospital and Institute we have access to large vascular tissue biobanks which are used to study the molecular mechanisms, find biomarkers and develop potential therapies for vascular disease. The research facilities are localized at the Center for Molecular Medicine (cmm.ki.se) where we have state of the art laboratories with advanced invitro and invivo imaging and molecular biological techniques. This specify project targets Abdominal aortic aneurysms (http://ki.se/en/mmk/star) where we will analyze aortic tissue and subject them to analysis including modern transcriptomics, proteomics and bioinformatic analyses. In addition, we have a close collaboration with the Royal Institute of Technology to perform Advanced computational finite element modeling and biomechanics testing.

Interested in applications from postdocs

Matti Sallberg, DDS, PhD, professor

Head of Department of Laboratory Medicine, Clinical Microbiology

Karolinska Institutet at Karolinska University Hospital Huddinge

matti.sallberg@ki.se

Projects:

1. Hepatitis C virus replication in mouse models
2. Therapeutic vaccine development against hepatitis B and D viruses

Interested in recruiting PhD students

Project titel: **Prevention of growth failure and osteoporosis caused by glucocorticoids**

Lars Savendahl, MD, Ph.D Professor and **Farasat Zaman**, Ph.D
Pediatric Endocrinology, Astrid Lindgren Children's Hospital,
Karolinska Institute University Hospital, Stockholm, Sweden.
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Project description: Osteoporosis, and in children growth failure, are common health problems often linked to chronic inflammatory disorders 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 osteoporosis caused by the long-term treatment with GCs. We have previously shown that GCs increase apoptosis in growth plate chondrocytes and cause growth failure in treated rats. Mechanistic studies revealed that GCs induce apoptosis in proliferative chondrocytes by activating caspases and suppressing the PI3K-signaling pathway. Recent data from our group have demonstrated that suppression of this undesired apoptosis has the potential to rescue from GC-induced bone growth failure. The overall scientific objective is to identify new drug targets allowing the prevention of growth failure and osteoporosis caused by long-term treatment with GCs. We'll use an array of experimental model systems including mesenchymal stem cells (MSCs), bone organ culture, genetically modified mice models, and human growth plate cartilage biopsies. We recently reported that the humanin can prevent growth retardation caused by bortezomib, a novel class of anti-cancer drugs. It was also reported that HNG has an anti-cancer effect *per se*.

Selected Publications:

- Combined treatment with GH and IGF-I: additive effect on cortical bone mass but not on linear bone growth in female rats. Sundstrom K et al. Endocrinology 2014;155(12):4798-807
- Dexamethasone differentially regulates Bcl-2 family proteins in human proliferative chondrocytes: role of pro-apoptotic Bid. Zaman F. *et al*. Toxicology letters 2014;224(2):196-200. Osteoblast-derived WNT16 represses osteoclastogenesis and prevents cortical bone fragility fractures. Moverare-skrtic S *et al*. Nature medicine. 2014;20(11):1279-88
- Protective role of humanin on bortezomib-induced bone growth impairment in anticancer treatment. Eriksson E, *et al*. Journal of the National Cancer Institute 2014;106(3).
- Recent research on the growth plate: Impact of inflammatory cytokines on longitudinal bone growth. Sederquist B, *et al*. Journal of molecular endocrinology 2014;53(1):T35-44

Interested in recruiting a Postdoc

Title of project: Studies on resolution of inflammation in Alzheimer's disease

Marianne Schultzberg, Professor
Dept of Neurobiology, Care Sciences & Society
Section for Neurodegeneration, Karolinska Institutet
Email: Marianne.Schultzberg@ki.se

Project description:
Dementia in the form of Alzheimer's disease (AD) is costly in terms of human suffering and healthcare expenses. Since no cure or effective treatment exists, research efforts focused on finding new pathogenic mechanisms and treatment targets are highly motivated. It is established that the neurodegeneration in the AD brain is accompanied by an inflammatory process that appears to be chronic and to contribute to the neuronal injury and impairment that is the primary cause of the cognitive impairment.

The mechanisms of restoration/healing after an injury are still poorly understood, and even less is known with regard to the central nervous system. It may not be possible to reach the more or less complete restoration of tissue that can be seen in non-nervous tissue, but there are activities and signals related to restoration present in the brain that hypothetically can be modulated and utilized in treatments for AD and other neurodegenerative disorders. The process of restoration is intimately related to the immune response, since these occur in the final stage of inflammation, the ***resolution*** phase. In this phase, the inflammation is halted and the tissue returned to homeostasis and normal function, and phagocytosis of debris and trophic activity are therefore prominent in this process. Thus, to stimulate the resolution of inflammation would be a novel strategy for treating AD, by down-regulating inflammation while promoting restoration. A family of fatty acids, so called specialized pro-resolving mediators (SPMs), has been discovered to play a vital role in resolving inflammation and tissue restoration. The pathway of SPMs constitutes a potential target for treating AD and other neurodegenerative disorders. The project will involve 1) exploration of the beneficial and neuroprotective effects of SPMs in *in vitro* models of AD, as well as characterising the intracellular mechanisms of these activities, and 2) testing the possibility of using SPMs to stop or ameliorate the cognitive decline that occurs in a transgenic mouse model of AD.

Qualifications of applicant:
Emphasis will be put on experience with animal behavioural experiments, and having attended courses on this subject. We will also emphasize laboratory practical skills and personal attitude, in the evaluation process.

Interested in recruiting PhD student or postdoc

Project title: **Influenza A virus perturbation of human dendritic cell function**

Anna Smed Sorensen, PhD, assistant professor
Clinical Immunology and Allergy, Dep. of Medicine Solna, Karolinska Institutet
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http://ki.se/en/meds/research-group-anna-smed-sorensen

Brief project description: Dendritic cells (DCs) are rare innate immune cells with the unique capacity to activate naive T cells for the initiation of adaptive immune responses often required to control and clear viral infections such as those caused by Influenza A virus (IAV). We have previously shown that IAV infection of human DCs impairs their ability to present antigen to and activate CD8 T cell. This project focuses on identifying the underlying mechanism of this virus-induced perturbation in DCs using immunological and cellbiological tools.

Interested in applications from Postdocs

Project title: **Normalizing alterations in glutamatergic neurotransmission in Parkinson´s disease**

Per Svenningsson, Professor in Neurology
Department of Clinical Neuroscience, Karolinska Institutet
Per.Svenningsson@ki.se
http://www.cmm.ki.se/group/translationell-neurofarmakologi/

Abstract: Parkinsons disease (PD) is the second most frequent neurodegenerative disorder. PD is pathologically characterized by the progressive appearance of intracytoplasmic protein inclusions, called Lewy bodies, in dopamine neurons of the substantia nigra and in several other brain regions. Both in sporadic and in familial cases of PD, the major component of Lewy bodies is aggregated α-synuclein (α-syn). Native α-syn is an abundant 14kDa protein mainly located in presynaptic nerve terminals, associated with the SNARE complex close to synaptic vesicles. It is plausible that glutamate receptors are altered by α-syn overexpression. Of particular importance are alterations in NMDA receptor as overactivation of these receptors cause excitotoxicity, a mechanism which has been implicated in the progression of PD. Excessive activation of NMDA receptors enhance calcium influx leading to calcium-dependent enzymatic processes, including production of free radicals and nitric oxide, contributing to cell death. This project will use biosensor to measure glutamate levels in real time in animal models of PD including α-syn overexpressing rodents. It will intervene with pharmacological agents targeting specific subunits of glutamate receptors.

Interested in recruiting in PhD students

Project title: Genetic events and cellular senescence in testicular cancer secondary to cryptorchidism

Olle Söder, Professor, MD
Department of Women´s and Children´s Health, Karolinska Institutet and University Hospital in Solna
e-mail: Olle.Soder@ki.se

Project description: Infertility due to disrupted spermatogenesis and testicular cancer has long been associated with undescended testes/cryptorchidism. The mechanisms behind testicular cancer secondary to this congenital condition are currently unknown. This study aims to identify the genetic factors responsible for cryptorchidism and testicular cancer associated with the disorder, and to define the cellular and molecular mechanisms involved in the malignant transformation of the cryptorchid testis.

Interested in: A four-year CSC supported PhD student. Preferable background with medicine or biomedicine and laboratory experience).

Interested in recruiting postdoc or visiting researcher

Project title: **Statin modulate T cell function via lipid raft?**
-with application in autoimmune disease and cancer.

Jesper Tegnér, Strategic Professor (MSc Mathematics, MK Med School, BSc Philosophy, PhD Medicine)
Department of Medicine Solna (KI) and the Clinical Epidemiology unit in the hospital (KUH)
Email: jesper.tegner@ki.se
Group home page:http://compmed.se/

Backgrounds: Pharmacological lipid lowering using statins provided the original rationale for treating cardiovascular disease, however, it has become increasingly apparent, however, that the beneficial effects of statins in cardiovascular medicine cannot be ascribed solely to their lipid-lowering properties, the accompanied reduction of inflammatory phenotype of disease had been demonstrated both in clinical and preclinical studies. It is not known if the reduction of inflammatory response is due to direct effect of cholesterol lowering or due to pleiotropic effects of statins. Based on our preliminary data, we hypotheses that the lipid reduction change the membrane cholesterol content, then subsequently lead to the lipid raft architecture re-organization, since a lipid raft can co-ordinate various signaling pathways, which play key role in lymphocytes activation, proliferation, differentiation and function.

Project plans: In this project, **we aim to elucidate the lipid raft change by statin treatment**, which lead to proliferation and activation inhibition. We use human primary T lymphocytes purified from healthy donors, then stimulate the cells with plate-binding anti-CD3 antibody and soluble anti-CD28 antibody, apply statins on the cells, using flow cytometer to access the changes on lipid raft architecture and T cell activation markers at single cell level after different period exposure to statins, laser confocal microscope will be used to validate the findings (some receptor will change along with lipid raft re-organization) in cells *in situ*. Total cellular cholesterol and unesterifyed free cholesterol will be measured with Amplex Red cholesterol kits to correlate with the lipid lowering effect.

Significance: Elevated circulating cholesterol level had been reported in many malignancy such as prostate cancer, breast cancer and colon cancer. Recent research had suggested there are two subsets of lipid raft, one is enriched with cholesterol–sphingomyeline–ganglioside–cav-1/Src/EGFR (“chol-raft”), that is involved in normal cell signaling, upon dysregulated promotes cell transformation and tumor progression, another subset is enriched with ceramide–sphingomyeline–ganglioside–FAS/Ezrin (“cer-raft”) that generally promotes apoptosis. Statin most likely target chol-raft due to cholesterol lowering, which indicate the potential using in treating malignancy.

Interested in applications from Visiting researchers, postdocs and PhD students

Project title: **Lymphocyte dynamics during inflammation and re-establishment of intestinal homeostasis.**

Eduardo J. Villablanca, PhD, Assistant Professor
Laboratory of Leukocyte trafficking and intestinal immune homeostasis
Department of Medicine, Translational Immunology Unit | Karolinska Institutet
Karolinska Sjukhuset,
eduardo.villablanca@ki.se
Villablanca lab webpage: http://ejvillablanca.wix.com/villablancalab

Description: Lymphocytes cells are essential for maintaining peripheral tolerance as well as modulating the progression and outcome of autoimmune diseases, allergy, infectious diseases and cancer, and are thus considered a therapeutical target in a variety of diseases. Our aim is to determine the cellular and molecular mechanisms involved in migration of lymphocytes from the bone marrow to the gut, their imprinting to exert specific functions and their dynamics during steady state and inflammatory conditions. Our methods are in vivo models, FACS analysis, FACS sorting and single cell RNA sequencing (RNA-seq)

Interested in recruiting PhD student/Postdoc/Researcher

Title of project: Dynamic nanotechnology for the study of cells and biosurfaces

Vladana Vukojevic, Department of Clinical Neuroscience, Karolinska Institutet
Email: vladana.vukojevic@ki.se; http://ki.se/en/cns/lars-terenius-and-vladana-vukojevics-research-group

Project description

Our research focuses on quantitative characterization of the kinetics of molecular interactions in live cells [1,2] and the development of new imaging modalities [3,4]. Our mission is to understand how reaction-diffusion processes are integrated in live cells/tissues to form dynamical biochemical networks and how the functional dynamics of these regulatory networks is impaired in common diseases of the Central Nervous System (CNS). To this aim, we use advanced fluorescence microscopy and fluorescence correlation spectroscopy based techniques with high spatio-temporal resolution and single-molecule sensitivity. These methods are particularly suited for non-destructive quantitative characterization of molecular trafficking and interactions in live cells, which is a prerequisite for understanding the function of biological molecules.

Quantitative study of synthetic Hox transcription factor-DNA interactions in live cells.
Vukojevic V, Papadopoulos D, Terenius L, Gehring W, Rigler R
Proc. Natl. Acad. Sci. U.S.A. 2010 Mar;107(9):4093-8
Lipoprotein complex of equine lysozyme with oleic acid (ELOA) interactions with the plasma membrane of live cells.
Vukojević V, Bowen A, Wilhelm K, Ming Y, Ce Z, Schleucher J, *et al*
Langmuir 2010 Sep;26(18):14782-7
Quantitative single-molecule imaging by confocal laser scanning microscopy.
Vukojevic V, Heidkamp M, Ming Y, Johansson B, Terenius L, Rigler R
Proc. Natl. Acad. Sci. U.S.A. 2008 Nov;105(47):18176-81
A single-photon avalanche camera for fluorescence lifetime imaging microscopy and correlation spectroscopy
Vitali *et al. IEEE J. Sel. Top. Quantum Electron. 2014 20:1-10*

Qualifications of applicant

We are looking for a highly motivated individual with a strong interest in multidisciplinary approaches to biomedical research. The candidate should have a degree in molecular life sciences, biomedicine, biotechnology or biophysics. Previous experience in molecular biology, cell culture, fluorescence microscopy and fluorescence spectroscopy techniques, are advantageous for this project.

Interested in applications from PhD students and postdocs

Project title: **Psychosocial factors and neurodegenerative diseases and brain structural changes**

Hui-Xin Wang, PhD, Associate Professor of Aging Research
Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet
huixin.wang@ki.se
http://ki-su-arc.se/about-us/staff/hui-xin-wang/

My major research field is epidemiology of neurodegenerative diseases in the elderly and have also research experience in epidemiological studies on cardiovascular disease. My major contribution to research concerns the following topics:

1. *Lifestyle factors and risk of dementia*. My research findings have provided evidence of the influence of lifestyle factors (social network, lifestyle, participation in leisure activities, B12 or folate, smoking) on risk of dementia and cognitive decline.

2. *Psychosocial factors and risk of dementia*. From the life-course perspective, my research have been focus on the effects of early-life school performance and education, mid-life occupation-related psychosocial stress and work complexity, late-life personality, psychological stress, sleep disturbances, depression, and the life course negative life events, on risk of dementia, cognitive impairment, and brain structural changes.

3. *Psychosocial factors and progression of coronary heart disease*. My research concerned the influence of emotional support, social isolation, depressive symptoms, and stress from family or work life in relation to risk of coronary disease progression.

Interested in receiving applications from Phd students and postdocs

Project title: **Antibodies in health and disease**

Fredrik Wermeling, Assistant Professor
Department of Medicine, Solna, Rheumatology unit
Karolinska Institutet
fredrik.wermeling@ki.se
http://ki.se/en/meds/autoimmune-and-inflammatory-diseases-novel-treatment-strategies.

Project description

My lab is interested in the immune system with a focus on antibodies. We're interested in how antibodies mediates their effector functions and how this can be controlled; decreased in patients with disease causing antibodies (e.g. patients with autoimmune diseases like rheumatoid arthritis and ITP), or increased in patients where therapeutic antibodies are used to e.g. deplete tumors.

We do this by combining animal models, patient material and also put a lot of effort into CRISPR/Cas9 based screens to identify druggable targets.

Currently we are three postdocs, one lab manager and one master student. Find more information through http://ki.se/en/meds/autoimmune-and-inflammatory-diseases-novel-treatment-strategies.

Interested in recruiting a post-doctoral fellow (24 months)

Title of the project: **'Cognitive impairment, cognitive restoration and early diagnosis in Alzheimer's disease: a multimodal study of the cholinergic system'**

Main applicant
Eric Westman, Associate Professor Eric.Westman@ki.se

Co-applicants
Lars-Olof Wahlund, Professor Lars-Olof.Wahlund@ki.se

Maria Eriksdotter, Professor Maria.Eriksdotter@ki.se

Daniel Ferreira, PhD daniel.ferreira.padilla@ki.se

Division of Clinical Geriatrics; Center for Alzheimer Research; Department of Neurobiology, Care Sciences and Society; Karolinska Institutet.

Home page of the group
Division: http://ki.se/en/nvs/division-of-clinical-geriatrics
Group: http://ki.se/en/nvs/imaging-research

Brief description of the project
The overall aim of this project is to investigate the role of the cholinergic system in cognition by using novel neuroimaging and molecular techniques. The basal forebrain is composed of cholinergic cells with their neuronal bodies located at the basal forebrain. We will use a novel method based on structural magnetic resonance imaging (sMRI) to reconstruct separated parts of this region. Then we will model cholinergic projections to the hippocampus and different neocortical regions using diffusion tensor imaging (DTI) and functional magnetic resonance - resting state (fMRI-RS). We will also investigate other novel cholinergic markers such as ChAT activity and the Ach index based on electroencephalography (EEG). We will study associations with cerebrospinal fluid markers of amyloid burden and neurodegeneration, as well as genetic factors (ApoE e4). Finally, we will try to translate findings and knowledge acquired in this project to the clinical benefit. We will try to generate and will investigate the utility of a diagnostic index for early diagnosis of AD and differential diagnosis with other dementias and depression. The study sample includes healthy controls, individuals with subjective cognitive decline, mild cognitive impairment and pacients with Alzheimer's disease and other dementias. Around 2150 individuals will be included by combining five unique international cohorts already available at our group.

The fellow will work together with four co-supervisors with different expertise (neuropsychology, medicine, geriatrics, engineering). The fellow will also be in contact with many other researchers and students at our group and NVS Department, and will be able to attend numerous scientific activities at Karolinska Institutet.

Interested in applications from: postdocs and visiting researchers

Project title: **The role and function of CTLA-4 in immune tolerance**

Kajsa Wing, PhD, Assistant Professor
Karolinska Institute, Department of Medical Biophysics and Biochemistry, Section of Medical Inflammation Research
Kajsa.Wing@ki.se
http://ki.se/en/people/kajwin
http://www.inflam.mbb.ki.se/

Project description:

CTLA-4 is an immune inhibitory molecule that is vital for T cell homeostasis and tolerance. It is expressed by all activated T cells but constitutively expressed by Foxp3+ regulatory T cells (Tregs). Mice that lack CTLA-4 expression from birth will die before 4 weeks of age from lymphoproliferative disease while mice that lack CTLA-4 specifically on Tregs will live twice as long before succumbing to fatal myocarditis (Wing et al, Science 2008). Thus CTLA-4 plays different but vital parts in different cell types. Moreover the protein exists in several different isoforms complicating the biology further.

We are using genetically modified mice and inducible deletion to investigate how CTLA-4 expression contributes to immune regulation. This means that we can do both cell specific and time specific studies and we apply this to different models of autoimmune disease such as EAE (experimental encephalomyelitis), arthritis models such as CIA (collagen induced arthritis) as well as the spontaneous organ specific autoimmunity that occur after CTLA-4 deletion. It is important to understand the multiple ways that CTLA-4 is operating and the effects that CTLA-4 manipulation can have on the immune system since CTLA-4 is currently used to treat both cancer and rheumatoid arthritis patients.

Interest in recruiting a PhD student

Project title: The role of telomere/telomerase in cancer and aging

Dawei Xu, associate prof.
Dept. of Medicine Solna, Karolinska Institutet
e-mail: Dawei.Xu@ki.se

Project description: My study is focused on telomere/telomerase biology in aging and cancer. More specifically, I want to define how exactly telomere/telomerase contributes to aging and cancer development, and how they are regulated during aging and malignant transformation.

Interested in applications from PhD Students and Postdocs

Project title: **Can cognitive reserve counteract the risk effect of cardiometabolic disorders on dementia**?

Weili Xu, MD, PhD, Associate professor
Aging Research Center, Dept. of Neurobiology, Care Sciences and Society

The purpose of this project is to investigate whether higher education and stimulating lifestyles may counteract the deleterious effects of cardiometablic diseases (diabetes, obesity and CVD) on cognitive impairment and dementia.
This project will use two large population-based studies: the Swedish National study of Aging and Care in Kungsholmen - SNAC-K on aging and care and the HARMONY study, a nationwide study on dementia in Swedish twins.

More information about us at ARC can be found at: http://ki-su-arc.se/

Interested in applications from PhD students, postdocs and visiting researchers

Project title: **The role of non-coding RNAs in human skin wound healing**

Ning Xu Landén, Assistant professor

Group M Ståhle, Department of Medicine, Solna, Karolinska Institutet

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Group homepage: http://ki.se/en/people/ningxu

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.

Interested in applications from Visiting researchers, postdocs and PhD students

Project title **Manipulation of p53 family members to target p53 deficient and mutant tumors**

Joanna Zawacka-Pankau, PhD, PI
Department of Microbiology, Tumor and Cell biology, Karolinska Institutet
E-mail: jonna.zawacka-pankau@ki.se,
http://ki.se/en/mtc/joanna-zawacka-pankau-project

Project description: The primary goal of my research group is to explore the roles of p53 family members TAp73 and TAp63 in tumor suppression. To address this, we apply both genetic and pharmacological approach to reinstate TAp73 and TAp63 in tumors that are deficient in p53 or have an inactivating p53 mutation. In particular, we focus on tumors of poor clinical outcomes including lung and pancreatic cancers. Our results show that activation of TAp73/TAp63 in p53-deficient and mutant background stimulates potent cancer cell death. To achieve our goal, we will build on these findings by further characterizing the outcome of TAp73 and TAp63 restoration in tumor suppression. In particular, we investigate the roles of p53 family members in regulation of oncogenic pathways triggering evasion of apoptosis and metabolic switch in cancer cell. Our approach will significantly improve the understanding of the fundamental mechanisms leading to efficient ablation of tumors in which p53 is lost or mutated. The long-term goal is to identify novel therapeutic targets, which act in concert with p53 family members to establish new drug-combination regimes to treat aggressive tumors deficient in p53 or containing mutant p53.

Interested in applications from Visiting researchers, postdocs and PhD students

Project title: **Identification of drug target and mechanism of action of anticancer molecules using advanced proteomics**

Roman A. Zubarev, PhD, professor
Division of Chemistry I, Head
Department of Medical Biochemistry & Biophysics, Karolinska Institutet
roman.zubarev@ki.se
Link to group home page: http://chem1.mbb.ki.se

Project description: Recently we have developed a novel proteomics-based method for identification of the drug target and mechanism of action of anticancer molecules (Scientific Reports, 2015, 5, Article Number: 11176). Together with the complementary thermal-shift assay approach, this method allows one to solve mysteries of action of many novel drugs. The project will consist of application of the new methods to a variety of novel molecules, with the goal of identifying their targets as well as deciphering the death-inducing pathways.

Interested in recruiting PhD students or postdocs

Project title: Novel immunotherapies in chronic neurological diseases – reducing pathogenesis and improving healing

Xingmei Zhang, MD, PhD, Assistant Professor
Department of Clinical Neuroscience, Center for Molecular Medicine
Email: xingmei.zhang@ki.se, http://www.cmm.ki.se/en/group/applied-immunology/

Project description: Multiple Sclerosis (MS) is an inflammatory autoimmune disease of the central nervous system (CNS) for which there is no current treatment for chronic disease states. Glioblastoma multiforme (GBM) is a common and lethal brain tumour with a median patient survival time of just 14.6 months. Alzheimers Disease (AD) is a chronic neurodegenerative condition in which loss of nerve cell function leads to progressive cognitive impairment. Effective treatments for these neurological conditions represents a currently unmet medical need. The general research aim of our research programme is to develop novel immunotherapies for treatment of these neurological diseases, which we address using a multifaceted approach including myeloid cell therapy, vaccination and tolerance induction.