

## **Interested in recruiting a Postdoc**

### **Project title**

Structural and metabolic pathways underlying enhanced CD8 T cell activation in cancer and viral infection.

### **Supervisor**

Adnane Achour, Professor of Molecular Immunology

Department of Medicine, Division of Infectious Diseases, Science for Life Laboratory, Karolinska

Institutet Email: [Adnane.achour@ki.se](mailto:Adnane.achour@ki.se) Phone: +46-70-3951023

### **Type of recruitment and qualifications of applicant**

Postdoc (24 months)

The applicant should have expertise in molecular and functional immunology.

### **Background**

Major histocompatibility complex class I molecules (MHC-I) play a crucial role in immune surveillance by selectively presenting intracellular peptides at the cell surface to CD8<sup>+</sup> T lymphocytes, including cytotoxic T lymphocytes (CTLs), via T cell receptors (TCRs). Recognition of MHC/peptide complexes by TCRs is a critical event in initiation of immune responses toward cancer and/or infections. A thorough molecular understanding of the TCR/pMHC interactions is essential for assessing how CD8 T cells are activated or not by different MHC-I-restricted epitopes, as well as for the development of new approaches that can complement already existing vaccine approaches or provide a template for entirely novel vaccines.

Using a combination of structural biology and immunology, we have defined a procedure that allows for the design of super-peptides that bind with high affinity to MHC-I molecules. This anti-dogmatic discovery provides a powerful and unique tool for improving cancer treatment and vaccines against viral infections. The highly immunogenic super-peptides act as mimotopes of disease-associated non-immunogenic epitopes, and display enhanced capacity to stabilize MHC-I molecules. Importantly, these modified super-peptides conserve a structural conformation similar to the wild-type epitopes. Their increased immunogenicity induces T cell responses of a magnitude never before observed, and the induced CD8<sup>+</sup> T cells cross-react with original peptides, resulting in enhanced in vitro and in vivo responses towards cancer targets (van Stipdonk et al, Cancer Research 2009; Hafstrand et al, JI 2016; Hafstrand et al, JI 2018; Doorduijn et al, J. Clin. Invest. 2016).

### **Project description**

The main aims of our research efforts are 1) to thoroughly understand the molecular bases for efficient induction of CD8 T cell responses; 2) transpose this knowledge to human cancer-associated antigens and neo-epitopes. We will achieve this by:

- 1) Using a large set of MHC-I-restricted peptides with well-established functional effects on specific TCR, reveal the molecular mechanisms underlying CD8 T cell activation.
- 2) Establish the metabolic pathways initiated by each designed altered peptide ligand compared to wild-type counterparts. This part of the study will be performed in close collaboration with the research group of Prof. Adil Mardinoglu (Royal Institute of Technology, Stockholm Sweden and Science of Life Laboratory).
- 3) Functional studies of the effects of super-peptide modifications on TCR recognition of the MHC-I allele HLA-A0201 in complex with the cancer-associated epitope NY-ESO1.
- 4) Developing a novel engineered modified mRNA-based human cancer vaccine using the targeted peptide modification strategy established in our research laboratory.

### **Research group**

<https://www.scilifelab.se/researchers/adnane-achour/>

<https://ki.se/en/meds/research-group-adnane-achour>

## **Interested in recruiting a visiting PhD student/postdoc/researcher**

### **Project title**

Multimorbidity of mental health conditions and somatic conditions.

### **Supervisor**

Zheng Chang, Assistant professor

Department of Medical Epidemiology and Biostatistics, Karolinska Institutet

Email: [zheng.chang@ki.se](mailto:zheng.chang@ki.se)

Phone: +46 8 524 82412

Home page: <http://ki.se/en/people/zhecha>

### **Type of recruitment and qualifications of applicant**

Visiting PhD student/postdoc/researcher (6-12 months).

We look for a highly motivated PhD graduate with a background in epidemiology, biostatistics, public health, psychiatry, biomedicine or other relevant field. Experience with statistical software (e.g., SAS, STATA, or R) or programming languages is preferred.

### **Background**

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

### **Project description**

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

### **Research group**

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

## Interested in recruiting a Postdoc

**Project title:** Microbiota contribution in diseases related to women health and potential treatment with bacteriophage

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

**Type of recruitment:** Postdoc (24 months)

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

**Aim:** In our group, we want to examine the diversity of genital microbiota and evaluate its influence for women health. We are also isolating phages target pathogens and investigating the potential for bacteriophage therapy in diseases, such as bacterial vaginosis.

**Work plan:** Samples are collected from collaboration of hospital. DNA is extracted and microbiome is analyzed with 16S rRNA sequencing using the IlluminaMiSeq machine. Bacteria pattern that related to diseases will be addressed. bacteriophages are isolated from the clinical samples and potential phage therapy will be analyzed in gut microbiota or vaginal microbiota culture platform.

**Significance:** The proposed projects compare microbiome distribution and biomarkers from patients, giving a comprehensive analysis of microbiome contribution on disease progression. In addition, bacteriophage is tested as potential therapy for infections.

## **Interested in recruiting a PhD student**

### **Project title**

Investigating the effects of anti-depressant/anti-psychotic drugs in in patient-derived cell models

### **Supervisor**

Sophie Erhardt, professor

Department of Physiology and Pharmacology, Karolinska Institutet

Email: [sophie.erhardt@ki.se](mailto:sophie.erhardt@ki.se). Phone: +46706296706

Home page: <https://ki.se/en/fyfa/neuropsychimmunology>

### **Type of recruitment and Qualifications of applicant:**

PhD student

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

### **Project description**

Psychiatric illnesses, such as major depressive disorder (MDD), schizophrenia (SZ) and bipolar disorder (BD), are leading causes of disability, affecting millions worldwide (Collins et al Nature, 2011;475: 27-30) and often causing chronic recurrent symptom and heightened risk of suicide. The unfavorable outcome of therapy in these disorders is related to our lack of insight into pathophysiological mechanisms, preventing treatment directed at causative targets. Furthermore, the absence of disease biomarkers hampers patient stratification as well as detection of patients early in the disease phase. We hypothesize that brain immune activation, leading to increased production of the NMDA receptor antagonist kynurenic acid (KYNA), is an underlying cause of schizophrenia and that increased synthesis of the NMDA receptor agonist, quinolinic acid (QUIN) is an underlying cause of depression and suicidality. In the present project, we will stimulate patient-derived fibroblasts with immune-stimulatory agents and analyzed how much KYNA and QUIN that are released. We will also investigate the efficacy of different anti-depressants and anti-psychotics to prevent KYNA/QUIN production.

### **Link to group home page:**

<http://ki.se/en/fyfa/neuropsychimmunology>

## **Interested in recruiting a postdoc**

### **Project title**

Impact of Immune Activity on Brain Energy Metabolism: Implication for Novel, Rapid Acting Pharmacologic Treatment of Treatment Resistant Depression

### **Supervisor**

Sophie Erhardt, professor

Department of Physiology and Pharmacology, Karolinska Institutet

Email: [sophie.erhardt@ki.se](mailto:sophie.erhardt@ki.se). Phone: +46706296706

Home page: <https://ki.se/en/fyfa/neuropsychimmunology>

### **Type of recruitment and**

Postdoc

### **Qualifications of applicant:**

We are looking for a highly motivated candidate with a PhD in neuroscience or other relevant area. Experience or interest in working with animals (rats and mice), cellular models, molecular biology with experimental experience from pre-clinical research as well as advanced statistics is significant merits. Excellent communication skills and an ability to interact socially and scientifically with other students and post docs in the laboratory and with collaborators in various networks are essential. Previous experience of laboratory supervision is a merit.

### **Project description**

The etiology of depression is still poorly understood but recent hypotheses suggest that its development involves the activation of the innate immune system as well as alterations in glutamate excitotoxicity. Increased circulating levels of interleukin (IL)-6 and C-reactive protein are the most frequently observed findings, but also increased central levels of IL-6 have been described. Studies have also pointed out that a dysfunctional mitochondrial activity could be of importance for the pathophysiology of major depression (MD). Reduced mitochondrial function has also been associated with treatment resistance to antidepressive drugs. Indeed, modulation of brain energy metabolism is critical to initiation of rapid antidepressant actions, by ketamine, a glutamate receptor antagonist, in treatment resistant depression. This appears to be due to a shift of neuronal function from 'survival' to 'growth', which functionally confers rapid upregulation of dendritic branching and enhancement of synaptic plasticity.

We here aim to elucidate the mechanistic link between immune activation and brain energy metabolism, within the context of antidepressant treatment resistance, suicidality and ketamine's rapid acting antidepressant actions. In a translational manner we will investigate the following: 1) Determine the effects of immune stimulation on brain energy metabolism (mitochondrial function and mTOR signaling). 2) Correlate immune activity (by measuring immune markers) and metabolic function with antidepressant response to ketamine in a preclinical model of treatment resistant depression. 3) Correlate immune activity and metabolic function with antidepressant response to ketamine in depressed patients with suicidality.

The present proposal has high potential to yield novel, clinically relevant mechanistic insight into the neurobiological mechanism contributing to treatment resistant depression and its reversal with ketamine.

## **Interested in recruiting a PhD student**

### **Project title**

**Combining genetic risk scores and traditional risk factors to improve prediction and prevention of the frailty syndrome**

### **Supervisor**

Juulia Jylhävä, PhD, Assistant professor

Department of Medical Epidemiology and Biostatistics, Karolinska Institutet

Email: [juulia.jylhava@ki.se](mailto:juulia.jylhava@ki.se), Phone: 00358505351712,

Home page: <https://ki.se/en/people/juujyl>

### **Type of recruitment and qualifications of applicant**

PhD student (4 years)

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

### **Background**

Frailty has been described as the most problematic expression of aging. It is a state of increased vulnerability, resulting from decreases in physiological reserves and multisystem impairments, leading to susceptibility to adverse outcomes, such as hospitalization, disability and death. Although progress has been made in understanding its risk factors and precursors, the means to identify the individuals at the highest risk of becoming frail in old age are lacking. Genetic predisposition is likely to play a role, yet the genomics of frailty remain unknown.

### **Project description**

This project aims at identifying the genome-wide genetic and epigenetic (DNA methylation) markers that together with the traditional, i.e., lifestyle and environmental risk factors underlie longitudinally the development of frailty. We will assess if including the genetic and epigenetic markers to the models yields added predictive value beyond and above the traditional risk factors. The ultimate goal is to define a set of clinically useful predictors for individualized risk stratification and delineate new targets for prevention. Large samples consisting of the UK Biobank and the Swedish and Danish Twin Registries are used in the project. In the longitudinal analyses, we use latent growth curve modeling and co-twin control analysis to identify the most influential drivers of frailty. The proposed project has the advantage of using rich samples including phenotypic and genetic data, and through the existing collaborations, the project provides a unique opportunity toward answering the key questions regarding the frailty syndrome.

### **Research group**

The student will join Associate prof. Sara Hägg's and Prof. Nancy Pedersen's aging research groups, which constitute of about 15 researchers and PhD students with a large variety of backgrounds, research projects, and interests as well as different methods applied. The research environment is very pleasant and collaborative and the student will have access to in-house biostatistics support.

## **Interested in recruiting a Postdoc**

### **Project title**

**The role of checkpoint inhibitors for effective cellular immunity in HIV-related diseases and cancer**

### **Supervisor**

Annika Karlsson, PhD, Associate Professor, Group leader  
Division of Clinical Microbiology, Department of Laboratory Medicine  
Email: [Annika.karlsson@ki.se](mailto:Annika.karlsson@ki.se) Phone: + 46 70-467 01 30 Home page:  
<https://ki.se/en/labmed/research-group-annika-karlsson>  
[https://www.researchgate.net/profile/Annika\\_Karlsson](https://www.researchgate.net/profile/Annika_Karlsson)

### **Type of recruitment and qualifications of applicant**

I am seeking highly motivated Postdoc (12 - 24 months) with an interest in the interactions between HIV infection, immune regulation, and T cell effector function in human blood and tissue. Strong background in virology, human T cell immunology, single cell analysis, *In situ* visualization, gene expression analysis, and/or bioinformatics/proteomics is desirable. The applicant must have a Ph.D., possess superior communication skills in English, and have a demonstrated record of accomplishments.

### **Background**

Human immunodeficiency virus type 1 (HIV) is a chronic infection requiring life-long combinational antiretroviral treatment (ART). Effective ART with the ability to lower plasma viral load below the level of detection (20 copies/ml) was introduced in the mid 1990s. The access to ART has since changed the deadly HIV-infection into a chronic viral disease. With ART, an HIV-infected woman has a close to normal life-expectancy. Still, recent reports of the long-term consequences of ART for health in adults reveal an increased risk of cancer, autoimmunity, cardiovascular diseases, diabetes, and many other disorders. Subsequently, cancer is now the leading cause of death, primarily due to persistent immune activation and premature aging (exhaustion) of the immune system. Neither a cure or vaccine is available or currently within reach.

### **Project description**

Chronic infection and immunosuppression are important risk factors for many types of cancer. HIV is one chronic infection associated with severe immunosuppression that is only partly reversed by treatment. In Sweden the 400 newly identified HIV-infected individuals yearly are commonly late presenters, *i.e.* subjects with severe immunosuppression and frequently exhibiting cancer. The T cells which is an important part of the adaptive immune system in both cancer and chronic infection becomes highly dysfunctional during an HIV-infection. This process is usually known as T cell exhaustion and has been linked by us, and others, to the co-expression of several inhibitory receptors, *i.e.* checkpoint inhibitors. In this study, we aim to investigate co-inhibitory pathways of pathogen- and malignancy-specific T cell subpopulations in blood and tissue. Our goal is to gain insights into how to achieve optimized treatment of HIV in perinatally infected children, adults and in HIV-associated cancers. Thereby leading the way to better clinical outcomes in HIV infected and uninfected patients with cancer.

**Research group:** Annika Karlsson



## Interested in recruiting a PhD student or a postdoc

### Project title

Lineage decisions in early B cell activation

### Supervisor

Taras Kreslavskiy (Kreslavsky), Assistant Professor, Department of Medicine, Solna, Karolinska Institutet

Email: [taras.kreslavskiy@ki.se](mailto:taras.kreslavskiy@ki.se) Phone: +46 761 124 813

Home page: <https://ki.se/en/meds/team-taras-kreslavskiy>

### Type of recruitment and qualifications of applicant

PhD student or Postdoc

The candidate should be *passionate about science* and have a strong *background in immunology, molecular and cellular biology or developmental biology*. Candidates with computational biology background may also be considered.

### Background

Humoral immune responses to pathogens and vaccines are mediated by B lymphocytes. Upon encounter with cognate antigen, a naïve B cell has to choose between three mutually exclusive fates. First, it can enter germinal centre (GC) reaction – an iterative process of hypermutation of antibody genes and selection of clones with the highest affinity. This process will eventually result in generation of high affinity antibodies, but differentiation of these high affinity plasma cells and memory cells from GC B cells can take up to several weeks. Second, the activated B cells can give rise to an early wave of plasma cells that rapidly produce antibodies without increasing their affinity, thereby providing the first line of defence during the first days of an immune response. Finally, activated B cells can differentiate into early memory cells that can contribute to rapid recall responses to previously encountered pathogens. What determines the decision between these three alternative fates remains poorly understood. Moreover, it remains unclear at which point in time this decision is made and if a single naïve B cell has a potential to contribute to all branches of the response.

### Project description

In this project we aim to dissect lineage choices in early B cell activation by a combination of single cell transcriptomics and molecular barcoding. The ultimate goal of the project is to identify the branching point between GC B cells, early plasma cells and early memory B cells and to understand the molecular clockwork of this decision-making. Our recent results identified a novel factor that selectively restrains GC B cells but not the other two lineages. Intriguingly, this factor also negatively regulates T follicular helper cells – a specialized T cell subset that provides help to the GC B cells. Molecular function of this factor in activated B and T cells will be characterized. The project will involve experiments with mice and utilization of cutting edge methods of immunology and molecular biology (single cell RNA-seq, ChIP-seq, cellular barcoding).

### Research group

A successful applicant will be joining an enthusiastic international team of scientists that are passionate about basic immunology and biology in general. Our team currently consists of two postdocs, Annika Reinhardt and Josefine Dunst, a master student, Vassileios Glaros, and me. Working language of the group is English.

### Selected publications of the PI:

(1) Kreslavsky T., et al. 2017. Essential role for the transcription factor Bhlhe41 in regulating the development, self-renewal and BCR repertoire of B-1a cells. *Nat Immunol* 18:442-455.; (2) Mingueneau, M.#, T. Kreslavsky#, D. Gray#, T. Heng#, et al. 2013. The transcriptional landscape of  $\alpha\beta$  T cell differentiation. *Nat Immunol* 14:619-632. (# - equal contribution); (3) Kreslavsky, T., et al. 2012.  $\beta$ -Selection-induced proliferation is required for  $\alpha\beta$  T cell differentiation. *Immunity* 37:840-853.



## Interested in recruiting a Postdoc

### Project title

“Gene regulation and transcriptional control in liver metabolism”

### Supervisor

Claudia Kutter (PhD); Department of Microbiology, Tumor and Cell Biology, Karolinska Institute

Email: [Claudia.kutter@ki.se](mailto:Claudia.kutter@ki.se) Phone: +46 (0)704933896

Home page: [ki.se/en/mtc/claudia-kutter-group](http://ki.se/en/mtc/claudia-kutter-group), [scilifelab.se/researchers/claudia-kutter/](http://scilifelab.se/researchers/claudia-kutter/)

### Type of recruitment and qualifications of applicant

Postdoc (24 months) in Genomics, Chromatin and/or Transcriptomics

Requires strong background in genomics, computational biology, and/or statistics as well as experience in high-throughput genomic data analysis, extensive scripting and programming knowledge (Python, R/Bioconductor), data integration and regulatory network analysis, and data visualization. Candidates wishing to combine computational and experimental approaches should be proficient in methodologies related to functional genomics (e.g ChIP-seq, RNA-seq, ATAC-seq, GRO-seq, HiC or equivalent).

### Background/Project description

Liver cells ensure metabolic homeostasis by regulating synthesis and breakdown of nutrients. Activating specific gene regulation programs facilitates homeostasis. Deregulation of genes has been observed upon increased and unbalanced food consumption and is linked to developing liver diseases<sup>1-4</sup>. Hormonal treatment strategies have been effective to prevent liver diseases but the underlying molecular mechanisms that facilitate this outcome remain unknown. The aim of this project is to:

- i. identify how transcriptional programs are regulated to maintain cellular plasticity by using state-of-the-art ChIP- and RNA-sequencing in human and mouse primary hepatocytes and multiple liver cancer cell lines (comprehensive dataset already available)
- ii. investigate how gene regulatory programs get unhinged during high- and low-fat diet and measure the effect upon applying hormonal treatments in human and mouse by using comparative genomics
- iii. determine predictive measurements in gene deregulation by using machine learning approaches

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

The work will be conducted in collaboration with Cecilia Williams (KI, KTH) whose expertise will complement the success of this project.

### Research group

The Kutter lab has a strong track record in deciphering molecular mechanism by which noncoding RNAs (i.e. long noncoding, transfer and small RNA) regulate genes and genome structure in mammalian somatic tissue and in the germline (Ernst NatComm 2017; Rudolph PLoS Genetics 2016; Schmitt Genome Research 2014; Kutter PLoS Genetics 2012; Kutter Nature Genetics 2011). We investigate the roles of noncoding RNAs genome- and transcriptome-wide by employing a combination of next generation sequencing technologies and high-throughput genetic screening approaches, developing computational methods, along with applying experimental techniques. Our interdisciplinary and multi-national team is located at the newly established SciLifeLab on the Karolinska Institute campus in Stockholm, which offers an attractive research environment.

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

## Interested in recruiting a Postdoc

### **Project title**

“Molecular signatures controlling developmental and cancerogenesis”

### **Supervisor**

Claudia Kutter (PhD); Department of Microbiology, Tumor and Cell Biology, Karolinska Institute

Email: [Claudia.kutter@ki.se](mailto:Claudia.kutter@ki.se) Phone: +46 (0)704933896

Home page: [ki.se/en/mtc/claudia-kutter-group](http://ki.se/en/mtc/claudia-kutter-group), [scilifelab.se/researchers/claudia-kutter/](http://scilifelab.se/researchers/claudia-kutter/)

### **Type of recruitment and qualifications of applicant**

Postdoc (24 months) in Chromatin and RNA biology

Requires strong background in chromatin and RNA biology, genomic approaches (e.g. ChIP-seq, RNA-seq, ATAC-seq, ChIRP-seq, GRO-seq, HiC or equivalent), molecular biology, genetics, and/or biochemistry as well as expertise with mammalian model systems (mouse and human tissues and cell lines) is highly valued. Familiarity with computational tools to analyze sequencing data and/or R programming for statistical computing and graphics is an asset.

### **Background/Project description**

Liver cancer is the sixth most common form of cancer and incidences are increasing world-wide.

Recent studies suggest that cancer cells reactivate developmental programs to drive cancer progression. However, the molecular mechanism that control how the genome is deployed to define genome plasticity and cell functionality in normal liver development remain elusive. We observed that long noncoding RNAs (lncRNAs) are important components that regulate chromatin and allow protein-coding gene activation. By using high-resolution genome-wide sequencing technologies and functional assays, this study will identify genomic and transcriptional key regulators that dictate normal liver development and become reactivated in liver cancer cells.

The aim of this project is to:

- i. Characterize chromatin and gene expression signatures across liver development and liver cancer by working with mouse models and human patient samples using state-of-the-art ChIP- and RNA-sequencing methodologies. A particular focus will be on lncRNAs (including long intergenic, antisense and enhancer RNAs) due to their well-described roles in development and cancer (Kutter PLoS Gen 2012).
- ii. Test regulatory mechanisms of lncRNA transcription and functionality by using genome-engineering methods (CRISPR interference and activation) followed by functional assays in mouse and human liver cancer cell lines.

Understanding tumour progression by studying liver development will aid in the refinement of therapeutic strategies. The focused project addresses original research questions is designed for a two-year postdoctoral study and is based on the experimental and computational expertise in the group.

### **Research group**

The Kutter lab has a strong track record in deciphering molecular mechanism by which noncoding RNAs (i.e. long noncoding, transfer and small RNA) regulate genes and genome structure in mammalian somatic tissue and in the germline (Ernst NatComm 2017; Rudolph PLoS Genetics 2016; Schmitt Genome Research 2014; Kutter PLoS Genetics 2012; Kutter Nature Genetics 2011). We investigate the roles of noncoding RNAs genome- and transcriptome-wide by employing a combination of next generation sequencing technologies and high-throughput genetic screening approaches, developing computational methods, along with applying experimental techniques. Our interdisciplinary and multi-national team is located at the newly established SciLifeLab on the Karolinska Institute campus in Stockholm, which offers an attractive research environment.

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

**Platelet-regulated inflammatory mechanisms in atherosclerosis**

### **Supervisor**

Nailin Li, associate professor

Karolinska Institutet, Department of Medicine-Solna, Clinical Pharmacology Group

Email: Nailin.Li@ki.se Phone: +46-8-517 739 96

### **Type of recruitment and qualifications of applicant**

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

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

### **Project description**

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

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

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

### **Supervisor**

Nailin Li, associate professor

Karolinska Institutet, Department of Medicine-Solna, Clinical Pharmacology Group

Email: Nailin.Li@ki.se Phone: +46-8-517 739 96

### **Type of recruitment and qualifications of applicant**

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

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

### **Project description**

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

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

## **Interested in recruiting a PhD student/Postdoc**

### **Project title**

**High Resolution Immunological Studies of the Responses to mRNA vaccines**

### **Supervisor**

Karin Loré, professor

Department of Medicine Solna, Karolinska Institutet

Email: [Karin.lore@ki.se](mailto:Karin.lore@ki.se) Phone: +46 73 712 1551

Home page: <https://ki.se/en/meds/research-group-karin-lore>

### **Type of recruitment and qualifications of applicant**

Postdoc (24 months) or PhD student 48 months

### **Background**

The development of vaccines based on mRNA encoding for pathogen antigens has recently emerged as a new era in vaccinology. The first clinical studies indicate that mRNA vaccines are extremely promising because of the high immunogenicity and safe administration, in combination with the potential for rapid and low-cost manufacturing. This makes them particularly relevant for emerging infections or pandemic influenza strains where vaccine production is urgently needed after the pathogen sequence has been identified. Yet, fundamental understanding of the cells targeted by mRNA vaccines and the induction and maintenance of long-term immunological memory is largely lacking.

### **Project description**

In the PhD project outlined here, we aim to build on our recent studies in this area and explore in further detail some of the key immune functions by which mRNA vaccines interact with the immune system.

### **Methods and Studies planned**

We recently published original findings that mRNA vaccines target key antigen presenting cells at the site of vaccine administration *in vivo*. This PhD project will further the analyses on the mechanisms by which mRNA vaccine-targeted cells induce and polarize vaccine responses. We have an established collaborative agreement with one of the companies that has pioneered the mRNA vaccine technology from which we receive mRNA vaccines for our studies. The studies will involve *in vitro* cell culture systems as well as immunogenicity studies in non-human primates prior to clinical testing.

### **Significance of the doctoral education**

The project is unique in its opportunity to combine mechanistic studies *in vivo* using a clinically relevant animal model with analyses of human samples after vaccination to address central questions in basic immunology and vaccinology. This project also gives a unique possibility to perform functional studies in academia while collaborating with the leading vaccine industry in this area.

### **Research group**

Supervisor Loré has more than 15 years of experience working with preclinical vaccine studies. The applicant will work in an active group with other PhD students and post doc.

## **Interested in recruiting a PhD student**

### **Project title**

**Improved immunotherapy against renal cell carcinoma**

### **Supervisor**

Andreas Lundqvist, Assoc. Prof.

Department of, Oncology-Pathology Karolinska Institutet

Email: [Andreas.lundqvist@ki.se](mailto:Andreas.lundqvist@ki.se) Phone: +46851776859 Home page: xxxxx

### **Type of recruitment and qualifications of applicant**

PhD student (48 months)

The applicant should be familiar with cell-based assays including flow cytometry, primary cell culture techniques, molecular techniques including PCR, Western blot, Real-time PCR, Co-IP, CRISPR/Cas9.

### **Background and Project description**

Due to spontaneous regression and its sensitivity immunotherapy, renal cell carcinoma (RCC) is considered to be an immunogenic tumor. Although clinical responses to immune-checkpoint therapy, in particular anti-PD1 treatment is promising, the majority of patients do not respond to this therapy. In order to increase clinical responses to immunotherapy a better understanding of the immune contexture in RCC is needed. We will therefore perform a detailed analysis of the immune landscape in patients with RCC before and after treatment with anti-PD1 inhibitors.

Patients that respond to immunotherapy can develop acquired resistance to the therapy. Acquired resistance is often associated with loss of antigen processing and presentation. Such tumor cells become sensitive to targeting by NK cells. However, NK cells are very sensitive to immunosuppressive features and therefore rarely populate tumors. We will dissect role of hypoxia-related metabolic immune pathways in NK cells, and develop strategies to overcome inhibition by these pathways.

These studies will identify important biomarkers for disease progression and relapse prediction. We furthermore anticipate to uncover several differences in immunological parameters in patients that have clinical benefit from treatment with anti-PD1. With this knowledge, we can develop novel therapeutic targets to increase NK cell activity and thereby improve clinical responses.

### **Research group**

At present, the group consists of four PhD students and one postdoctoral fellow.

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

Molecular epidemiology and pathogenesis mechanism of Shiga toxin-producing *Escherichia coli* (STEC) infection

### **Supervisor**

Andreas Matussek, Associate Professor

Department of Laboratory Medicine, Karolinska Institutet

Email: andreas.matussek@ki.se Phone: +46 725978889

Home page: [https://ki.se/en/labmed/christian-giske-group-0?\\_ga=2.153334648.1515769113.1538379269-1319237637.1537452357](https://ki.se/en/labmed/christian-giske-group-0?_ga=2.153334648.1515769113.1538379269-1319237637.1537452357)

### **Type of recruitment and qualifications of applicant**

Postdoc (6-24 months)

The applicant should be highly motivated, independent, inventive and communicative with good English skills and with a PhD in microbiology, molecular biology or related discipline, and should have solid knowledge in bacteriology, more specifically on enteropathogenic bacteria. In addition, experience in bioinformatics and omics analysis is considered as a significant advantage.

Applicants must have completed their PhD by the start of the appointment and within the last 3 years.

Applicants should submit their curriculum vitae, including date of the thesis defence, title of the thesis, previous and current academic positions, academic title, academic distinctions, field experience, publication list, and e-mail address of two references.

### **Background**

STEC can cause a spectrum of clinical manifestations ranging from diarrhoea, haemorrhagic colitis (HC) to life-threatening complication haemorrhagic uremic syndrome (HUS). In Nordic countries, STEC are widely spread and usually associated with gastrointestinal symptoms and HUS. The pathogenesis mechanism of STEC infection is complicated as various bacterial and host-related factors contribute to the pathogenicity.

### **Project description**

The project will focus on molecular epidemiology and pathogenesis study of Shiga toxin-producing *Escherichia coli* (STEC) infection. The objective is to ascertain the virulence spectrum of clinical STEC strains, to find genetic markers that can be used to predict high pathogenicity and long duration of bacterial shedding, to investigate the transmission route among populations, and to explore pathogen-host interactions in STEC pathogenesis by using whole genome sequencing, microarray analysis, proteomics, cell culture, and *in vitro* models.

### **Research group**

The research group conducts basic and translational studies of *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, and consists of two research teams:

Antimicrobial Resistance (AMR) team, headed by the research group leader Professor Christian Giske MD/PhD and the intestinal pathogen team, headed by Associate professor Andreas Matussek, MD/PhD. The successful applicant will join Dr. Andreas Matussek's team consisting of several PhD-students and one postdoctoral researcher who focus on pathogenomic analysis of clinical Shiga toxin-producing *Escherichia coli* (STEC) strains and clinical STEC diagnostics enhancement.



## **Interested in recruiting a Postdoc**

### **Project title**

**SOX21 protein stabilization – strategy to target glioma stem cells**

### **Supervisor**

Jonas Muhr, Professor

Department of Cell and Molecular Biology, Karolinska Institutet

Email: [Jonas.muhr@ki.se](mailto:Jonas.muhr@ki.se) Phone: +46-70-6805017

Home page: <https://ki.se/en/people/jonmuh>

### **Type of recruitment and qualifications of applicant**

Postdoc (24 months). The applicant we are looking for should be highly motivated and well experienced in performing functional studies in brain- and cancer stem cells. A successful candidate has a broad knowledge base in cell biology and molecular/protein biology. The person we are looking for should keep a PhD in neurobiology, cancer biology or equivalent.

### **Background**

An important mechanism by which stem cells evade malignant transformation is the activation of tumor suppressor cascades. How organ-specific stem cells execute these antitumorigenic programs is however not well understood. To address this issue, the aim of this project is to examine how tumor suppressor mechanisms are activated in brain stem cells in response to genotoxic stimuli. In addition, I aim to identify means to re-activate anti-tumorigenic pathways in malignant brain stem cells.

### **Project description**

Stable expression of the transcription factor SOX21 is essential and sufficient for the activation of tumor suppressor responses in healthy and malignant brain stem cells. To address the significance of this protein in activating these protective mechanisms we aim to: **1)** Use genome-wide techniques (RNA-Seq and ChIP-Seq) to examine the regulatory roles of SOX21 in human neural stem cells exposed to genotoxic insults. **2)** Use HPLC-based proteomics to characterize post-translational processes involved in SOX21 modification and stabilization following DNA damage. **3)** Identify therapeutically-relevant molecules that promote SOX21 stability in glioma stem cells using a drug discovery platform. To understand the mechanisms by which stem cells evade tumorigenic transformation and unravel how tumor suppressor response programs can be reactivated in cancer stem cells, will be significant for the development of more efficient therapeutic approaches for the treatment of brain cancer.

### **Research group**

Jonas Muhr's group currently consists of five members. The main focus of the group is to examine how stem cells are regulated in the brain and its derived tumors. One important aim is to understand how healthy stem cells are controlled to avoid excessive proliferation, but also how these regulatory mechanisms are circumvented in malignant cells. The Muhr group is addressing these questions at the gene regulatory and protein levels using mice and human cells as model systems.

## Postdoc/Visiting Researcher/ PhD student in Immunogenetics or Cancer genetics

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

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

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

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

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

### **Type of recruitment and qualifications of applicants**

#### **Postdoc or Visiting Scientist (12-24 months)**

The applicant is eligible to apply if he or she has obtained a PhD in the fields of Medicine, Biology, Genetics, Oncology, and Immunology, or related fields.

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

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

#### **PhD students (4 years)**

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

### **Research group**

Our group currently consists of two lab managers, 4 postdocs, 2 PhD students and several visiting students and scientists. For details please visit our website: <https://ki.se/en/bionut/research-group-qiang-pan-hammarstrom>.

## **Interested in recruiting a postdoc**

**Project title:** Genome-wide study of transcription complexity in human disease.

**Supervisor:** Vicente Jose Pelechano Garcia, PhD. Assistant Professor. Karolinska Institutet. Department of Microbiology, Tumor and Cell Biology. Science for Life Laboratory and Wallenberg Fellow. Email: [vicente.pelechano.garcia@ki.se](mailto:vicente.pelechano.garcia@ki.se) Group home page: <http://pelechanolab.com/>

**Type of recruitment:** Postdoctoral Fellow

### **Qualifications of applicant:**

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

### **Project description:**

One of the biggest challenges in biology is to understand how identical genetic information encoded in the genome generates diversity between cells and tissues. Gene expression is the fundamental process whereby genetic information is expressed to control cellular identity and plasticity; defects in this process have been associated with numerous diseases. To adapt to changes in the environment cells and organism must alter their gene expression program, often involving changes in RNA abundance. However, in recent years, our view of RNA has markedly changed, from regarding these molecules solely as intermediates of genetic information to appreciating their variety of functions that are independent of their protein-coding potential. The development of high-throughput approaches has revealed pervasive transcription in all genomes that have been investigated so far. This has uncovered a highly interleaved transcriptome organization that involves thousands of coding and non-coding RNAs and has challenged our traditional definitions of genes and functional regions of the genome.

We will use novel computational and genome-wide approaches to investigate the transcriptional basis of the non-genetic heterogeneity driving divergent gene expression in human cells. We will combine the use of Transcriptom-Isoform Sequencing (TIF-Seq) with long read sequencing approaches. This project will be performed in the context of a long-term collaboration with Prof. Wei Wu (CAS Key Laboratory of Computational Biology and Shanghai Institutes for Biological Sciences). In the context of this collaboration we will investigate the functional consequences of alternative transcript isoform usage in cancer persistent cells and dilated cardiomyopathy. Once we identify potential mechanisms implicated in the appearance of phenotypically divergent cells, we will characterize selected targets using biochemical and molecular biology tools.

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

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

Characterization of human midbrain radial glia cells

### **Supervisor**

Thomas Perlmann, professor

Department of Cell and Molecular Biology, Karolinska Institutet

Email: [thomas.perlmann@ki.se](mailto:thomas.perlmann@ki.se) Phone: +46 70 680 5057

Home page: [perlmannlab.org](http://perlmannlab.org)

### **Type of recruitment and qualifications of applicant**

Postdoc (24 months)

The applicant should be a highly motivated individual who can collaborate, communicate and function well in a team. We are looking for an individual with a PhD in neuroscience, stem cells or developmental biology, and with good theoretical knowledge and practical skills on working with human or mouse embryonic stem cells. In addition, skills preferably in more than one of the following areas are considered an advantage: mouse genetics and hands-on experience on using mouse as a research model, bioinformatics, using and making virus vectors, and histological methods.

### **Background**

Cell loss in many adult tissues triggers resident stem cells to proliferate, ultimately leading to replacement of lost cells and tissue repair. However, in the adult mammalian CNS almost all neurons generated during embryogenesis are stably maintained without any generation of new nerve cells. In our lab we investigate how midbrain dopamine neurons – cells that degenerate in Parkinson's disease – are generated during embryonic development from radial glia. We aim to use this knowledge to develop strategies to regenerate dopamine neurons in the adult mammalian brain.

### **Project description**

The project will focus on using human embryonic stem cells in different strategies to reconstruct the developmental process that gives rise to ventral midbrain radial glial cells in cultures in vitro. This may involve regular cell cultures and/or formation of organoids. The aim is to develop a method for characterization of human ventral midbrain radial glia. By using such a method it will be possible to understand and characterize the human counterparts to the radial glia we have characterized in mouse, and it will be possible to analyse their potential for neurogenesis. We are using state-of-the-art technologies for our studies, including in vitro cell culture, in vivo studies in genetically modified mice and single cell RNA sequencing. The project has major relevance both for basic understanding of how the CNS is generated and for the potential of new regenerative strategies.

### **Research group**

Thomas Perlmann

## **Interested in recruiting a PhD student**

### **Project title**

Investigation of the role of non-coding RNAs in skin cancer

### **Supervisor**

Andor Pivarcsi, Associate professor, Department of Medicine Solna, Karolinska Institutet

Email: andor-pivarcsi@ki.se

Phone: +46 73 833 0057

Home page: <https://www.cmm.ki.se/sv/andor-pivarsci-group>

### **Type of recruitment and qualifications of applicant**

A PhD student position is open at our laboratory for a motivated student with interest in understanding the molecular alterations in one of the most common human malignancy, skin cancer. The applicant should possess a master degree in molecular biology or medicine or equivalent field. The applicant should be a team player, interested in increasing our knowledge about the molecular mechanisms of cancer and proficient in English.

### **Background**

Skin cancers are the most common human cancers with increasing incidence. Although the somatic mutations driving skin cancers have been mapped, much less is known about the contribution of regulatory RNAs, short and long non-coding RNAs such as microRNAs (miRNAs) and long intergenic non-coding RNAs (lincRNAs) in cancer initiation and progression. Our group investigates the altered expression of ncRNAs using human skin cancer samples and studies their roles in cancer in *in vitro* and *in vivo* disease models. Our preliminary results suggest that a large number of lincRNAs have altered expression in skin cancer and in the next years we aim to understand their roles in the disease using a translational approach that combined the use of human patient material with mechanistic investigation in *in vitro* and *in vivo* disease models.

### **Project description**

The student will work as a part of a team consisting of postdocs, physicians and PhD students who have experience with *in vitro* and *in vivo* cancer models. The student will have opportunity to learn a wide range of molecular biology methods related to cancer biology during his/her PhD project. The PhD student will study the role of skin cancer-associated lincRNAs using human cancer cell lines *in vitro* (e.g. cancer cell survival, proliferation, invasiveness and stemness) and *in vivo* (tumor xenograft model). The student will study the effect of oncogenic pathways on the altered expression of skin-cancer-associated ncRNAs. Results from the project will contribute to the better understanding of the function of non-coding RNAs in the initiation and progression of skin cancer.

### **Research group**

The student will work as a part of a team active at the Centre for Molecular Medicine (CMM) at Karolinska Institutet, Stockholm, Sweden. The group belongs to the Dermatology and Venerology Section, which is an independent section within the Department of Medicine Solna, Karolinska Institutet.

## Interested in recruiting a PhD student

### Project title

**Late-life blood pressure instability and cognitive phenotypes in aging: a population-based study**

### Supervision

*Main supervisor:* Chengxuan Qiu, PhD, Associate Professor and Senior Lecturer, Aging Research Center (ARC), Department of Neurobiology, Care Sciences and Society (NVS), Karolinska Institutet, Widerströmska Huset, Tomtebodavägen 18A, 171 65 Solna, Sweden. Email: [chengxuan.qiu@ki.se](mailto:chengxuan.qiu@ki.se).

*Co-supervisors:* Erika J. Laukka, PhD, Associate Professor & Rui Wang, PhD, ARC, NVS, Karolinska Institutet.

### Type of recruitment

A four-year full-time doctoral (PhD) position in the major of medicine/geriatric epidemiology, supported by the CSC scholarship (50%) and project grants (50%).

### Qualifications of the applicant

General requirements for the applicant: (1) a bachelor degree or equivalent in medicine in general and a master degree in epidemiology or neurology (e.g., brain imaging analysis); (2) experiences of using statistical software such as SPSS, Stata or SAS; (3) documents/certificates to demonstrate the proficiency in English language; and (4) good communication skills and ability to interact effectively and work productively with others in a multidisciplinary research group.

### Brief information of the doctoral project

**BACKGROUND:** The age-dependent relationship between blood pressure and risk of dementia has been well established, such that midlife high blood pressure and low blood pressure in very old age both are associated with an increased risk of dementia later in life. However, the greater variability or instability of blood pressure, which is a risk factor for cardiovascular events, in association with dementia risk remains to be elucidated. **PURPOSES:** The overall aim of this doctoral project is to elucidate the relationships of blood pressure variations with cognitive decline and dementia among older adults. Specific aims will be addressed in four individual studies: *Study I* aims to investigate the relationship of orthostatic hypotension with global cognitive decline and dementia; *Study II* seeks to explore associations of various patterns of blood pressure trajectory in late-life with cognitive phenotypes in aging (e.g., global cognitive decline and dementia); *Study III* aims to characterize the cognitive profile (e.g., memory, speed, and executive function) associated with blood pressure instability; *Study IV* seeks to explore how measures of blood pressure instability can interact with markers of cerebral small vessel to affect cognitive phenotypes in aging. **METHODS:** The overall goal and specific aims will be fully addressed in a series of studies based on the population-based Swedish National study on Aging and Care in Kungsholmen (SNAC-K, n=3363) in central Stockholm, and the embedded SNAC-K magnetic resonance imaging study (SNAC-K/MRI, n=555). At baseline (2001-2004) and subsequent follow-ups until 2016, data on demographics, lifestyle and behaviors, blood pressure, health history, use of medications, cognitive function, and dementia were collected following a standardized procedure. Markers of cerebrovascular and neurodegenerative lesions were assessed in the SNAC-K/MRI sample. Different statistical approaches will be utilized to address those specific research questions. **RELEVANCE:** Clarifying the relationships of late-life blood pressure instability or variability with cognitive dysfunction in aging as well as potential neuropathological mechanisms may help achieve not only healthy brain and cognitive aging but also a longer and healthier life.

**Aging Research Center (ARC) at Karolinska Institutet (KI)** (<http://ki-su-arc.se/>; <http://ki.se/en/>)

ARC at NVS/KI is a multidisciplinary center devoted to studying health in aging. Researchers at ARC conduct scientific research, educate the next generation of aging researchers, and disseminate information about our research findings within and outside the scientific communities. Our research group includes senior researchers, postdocs, doctoral students, and visiting scientists. We study the transitional process of health in aging from biomedical and psychosocial perspectives.

## Interested in recruiting a Postdoc or Visiting Researcher

### Project title

Analysis of world-wide prevalent *Pseudomonas aeruginosa* clone C

### Supervisor

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

### Type of recruitment and qualifications of applicant

Postdoc (24 months) or visiting scholar (24 months)

The applicant should have a profound background in molecular microbiology, infection biology and/or chemical biology.

### Background

*Pseudomonas aeruginosa* is the 4<sup>th</sup> most frequent nosocomial pathogen, but also an environmental organism. The population structure of *P. aeruginosa* is endemic with the occasional emergence of highly successful clones. We have previously identified the *P. aeruginosa* clone C strain cluster, which has been found to be world-wide prevalent in acute and chronic infections in patients as well as in the aquatic habitat.

### Project description

This project aims to characterize the molecular mechanisms of persistence and transmission of the world-wide distributed highly successful clone C of *P. aeruginosa* found in aquatic habitats and patients. The specific aim of this project is the systematic characterization of the contribution of genes on the clone C specific genomic island PACGI-1 towards enhanced stress resistance such as temperature tolerance and other features of clone C required for successful infection. The project includes state-of-the-art microbiology techniques such as molecular biology approaches including cloning and genome manipulation through the construction of deletion and point mutants. The functional characterization of selected gene products by protein expression and subsequent functional characterization of the purified proteins by biochemical and biophysical approaches will complement the impact of the gene products on microbial physiology. In addition, profound knowledge of the candidate in bioinformatics analyses of genome sequences and proteins and/or knowledge in infection biology such as cell culture is a major advantage.

### References

Lee CH, Kim H, Mansour Kamal S, Lünsdorf H, Nimtz M, Jänsch L, Treck J, Bukau B, Mogk A, **Römling U** (2018) Stand-alone ClpG disaggregase confers superior heat tolerance to bacteria, *Proc Natl Acad Sci USA*, 115: E273-E282.  
Lee CH, Wigren E., Trček J, Peters V, Kim J, Sharif Hasni M, Nimtz M, Lindqvist Y, Park C, Curth U, Lünsdorf H, and **Römling U** (2015) A novel protein quality control mechanism contributes to heat shock resistance of world-wide distributed *Pseudomonas aeruginosa* clone C strains, *Environ Microbiol*, 17, 4511-4526.

### Research group

Ute Römling group, Karolinska Institutet



## Interested in recruiting a Postdoc or Visiting Researcher

### Project title

Regulation of biofilm formation in *Salmonella typhimurium*

### Supervisor

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

### Type of recruitment and qualifications of applicant

Postdoc (24 months) or visiting scholar (24 months)

The applicant should have a profound background in molecular microbiology, infection biology and/or chemical biology.

### Background

Biofilm formation is the natural model of growth of most, if not all microorganisms. *Salmonella typhimurium* and *Escherichia coli* form characteristic RDAR biofilms on agar plates.

### Project description

The overall aim of this project is to analyze regulation of expression of the RDAR biofilm type and its major biofilm regulator CsgD with a focus on the cyclic di-GMP signaling system. In addition, we investigate the interactions of biofilms with host cells and the immune system. The project includes state-of-the-art microbiology techniques such as molecular biology approaches including cloning and genome manipulation through the construction of deletion and point mutants. The functional characterization of selected gene products by protein expression and subsequent functional characterization of the purified proteins by biochemical and biophysical approaches will complement the impact of the gene products on microbial physiology and in microbial host interaction. In addition, profound knowledge of the candidate in bioinformatics analyses of genome sequences and proteins and/or knowledge in infection biology such as cell culture is a major advantage.

### Recent references

Sun L, Vella P, Schnell R, Polyakova A, Bourenkov G, Li F, Cimdins A, Schneider TR, Lindqvist Y, Galperin MY, Schneider G, and **Römling U** (2018) Structural and functional characterization of the BcsG subunit of the cellulose synthase in *Salmonella typhimurium* J Mol Biol, pii: S0022-2836(18)30758-7.

Cimdins A, Simm R, Li F, Lühje P, Sjöling Å, Brauner A, **Römling U** (2017) Alterations of c-di-GMP turnover proteins modulate semi-constitutive rdar biofilm formation in commensal and uropathogenic *Escherichia coli*, MicrobiologyOpen, 6, doi: 10.1002/mbo3.508.

El Mouali Y, Kim H, Ahmad I, Brauner A, Liu Y, Skurnik M, Galperin MY, and **Römling U**. (2017) Stand-alone EAL domain proteins form a distinct subclass of EAL proteins involved in regulation of cell motility and biofilm formation in enterobacteria, J Bacteriol, 199, pii: e00179-17.

### Research group

Ute Römling group

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

**Dissecting the mechanisms behind the inadequate hypoxia signalling in diabetes**

### **Supervisor**

Sergiu-Bogdan Catrina, M.D., Ph.D., Associate Professor  
Department of Molecular Medicine and Surgery, Karolinska Institutet  
Email: Sergiu-Bogdan.Catrina@ki.se Phone: xxxxxx  
Home page: <https://ki.se/en/mmk/growth-and-metabolism>

### **Type of recruitment and qualifications of applicant**

The applicant must be talented, well-organized, highly motivated and enthusiastic for science, have good communication skills and the ability to interact in an international and dynamic team. The applicant should have innovative thinking and be eager to solve problems. A documented practical experience in animal studies, cell culture, molecular biology and biochemistry is meritorious. Good knowledge in written and spoken English is a requirement.

### **Background**

Diabetes is reaching epidemic proportions and is predicted to affect 300 million people worldwide by 2025. Chronic complications of diabetes represent the main concern for modern diabetes therapy, and it has become a priority to further characterise the pathophysiological mechanisms of these complications to ensure the development of novel rational therapeutic strategies.

Although the prolonged exposure of tissues to hyperglycaemia is the primary causative factor for chronic diabetes complications, it has recently become increasingly evident that hypoxia also plays an important role in all diabetes complications. Compelling evidence has accumulated over the last decade indicating that the cellular reaction to hypoxia is impaired in diabetes, and is a central pathogenic mechanism for diabetes complications. It is represented by a complex repression of hypoxia-inducible factor (HIF), which is the main regulator of the adaptive response to hypoxia. The exact mechanisms by which hyperglycaemia has a repressing effect on HIF are still not completely unravelled.

### **Project description**

The project proposes to investigate the pathways that are relevant for this repression in order to identify new potential therapeutic targets for complications of diabetes. The work will involve investigation *in vitro* but also confirmation *in vivo* in animal models for diabetes complications. Unique patient material that can generate hypothesis to be confirmed experimentally is available. If successful the work will provide the chance to tailor new therapy for complications of diabetes.

### **Research group**

Sergiu-Bogdan Catrina's research group

## **Interested in recruiting a PhD student**

### **Project title**

**Deciphering the role of mononuclear phagocytes in sarcoidosis.**

### **Supervisor**

Dr. Anna Smed Sørensen, Associate Professor (docent)

Division of Immunology and Allergy, Department of Medicine Solna, Karolinska Institutet

Email: [anna.smed.sorensen@ki.se](mailto:anna.smed.sorensen@ki.se) Phone: +46 73 712 1641

Home page: <http://ki.se/en/meds/research-group-anna-smed-sorensen>

### **Type of recruitment and qualifications of applicant**

PhD student (4 years).

The applicant should hold a Master degree in immunology, medicine, cell biology or equivalent. A suitable applicant should have experience with cell culture work, immunological and molecular biological methods, flow cytometry and cell sorting. An additional qualification is experience with bioinformatics and programming in R.

### **Background**

The overall goal of this research is to allow early identification of sarcoidosis patients that develop severe disease and to provide them with effective treatment options. Specifically, the projects evolve around mononuclear phagocytes (MNPs) - macrophages, monocytes and dendritic cells (DCs) - immune cells that are critical in sarcoidosis as they produce granuloma-promoting cytokines and activate T cells that drive the disease. Sarcoidosis is an inflammatory disease of unknown aetiology affecting multiple organs with non-caseating granulomas. 90% of sarcoidosis patients have granulomas in the lungs and lung-draining lymph nodes.

### **Project description**

An important originality of our studies is that they are based on longitudinal, clinically well-characterized patient samples from sarcoidosis patients with different clinical phenotypes, and healthy controls, that we study with state-of-the-art methodology. Our specific aims are:

1. To perform functional analyses of respiratory MNPs from bronchoalveolar lavage, lung tissue, lung-draining lymph nodes and peripheral blood, from the same sarcoidosis patient comparing patient groups with different clinical phenotypes over time and correlate immunological findings with disease progression.
2. To evaluate the effect of anti-TNF treatment of sarcoidosis patients on the capacity of MNPs to produce TNF at the single cell level, in different anatomical compartments.
3. To perform transcriptional and epigenetic analyses of sorted subsets of blood and respiratory MNPs from sarcoidosis patients with different clinical phenotypes.

### **Research group**

The Smed Sørensen lab consists of 4 PhD students and 2 postdocs. We do immunological studies and omics to understand the role of dendritic cells and monocytes in respiratory diseases such as sarcoidosis as well as respiratory viral infection. We work closely with clinical colleagues at the Karolinska University Hospital to obtain unique patient samples to conduct our studies.

## **Interested in recruiting a PhD student**

### **Project title**

Investigation of non-coding RNAs in chronic skin inflammation

### **Supervisor**

Enikő Sonkoly, MD PhD, senior lecturer

Department of Medicine Solna, Karolinska Institutet

Email: [eniko.sonkoly@ki.se](mailto:eniko.sonkoly@ki.se) Phone: +46730770374

Home page: <https://www.cmm.ki.se/web/guest/eniko-sonkoly-group1>  
<https://ki.se/en/people/enison>

### **Type of recruitment and qualifications of applicant**

The applicant should have an MS degree in molecular biology, medicine or equivalent.

We are looking for a highly motivated student with a strong, genuine interest in medical research.

The student should speak excellent English and should be able to work in a team.

The prospective PhD student will work with studies on basic disease mechanisms underlying chronic inflammatory skin diseases, focusing on the role of non-coding RNAs in skin inflammation. The projects will include in vitro and in vivo studies, bioinformatic analyses, and clinical samples will be utilized. The student will be responsible for designing and performing experiments, analyzing data, and presenting data in manuscripts and on national/ international meetings.

### **Background**

Chronic skin inflammatory diseases such as psoriasis and atopic dermatitis belong to the most common inflammatory diseases and affect patients' quality of life significantly. These diseases can also serve as model diseases for understanding general mechanisms of inflammation. Non-coding RNAs have emerged as a new layer of gene regulation with roles in nearly all biological processes. Our research focuses on understanding the roles on non-coding RNAs (microRNAs and long non-coding RNAs) in chronic inflammatory skin diseases, and skin biology.

### **Project description**

The aim of this PhD project is to explore the function and therapeutic potential of non-coding RNAs in the inflammatory skin disease psoriasis, focusing on keratinocytes, the epithelial cells of the skin. We have identified changes in coding (mRNA) and non-coding (miRNA and long non-coding RNA) transcriptome of psoriasis keratinocytes using our cell-type specific approach. In this project, the role of non-coding RNAs will be characterized in keratinocytes and the therapeutic potential of their modulation in psoriasis will be explored using in vitro and in vivo disease models. The regulation of non-coding RNAs will be characterized in cell culture and 3D epidermal models. The student will overexpress/inhibit non-coding RNAs and perform relevant functional assays (proliferation, differentiation, cytokine production etc) to explore the functions of the non-coding RNAs. The function of non-coding RNAs in vivo will be explored using skin inflammation models on genetically modified animals. The methods included in the project are well established in the laboratory.

### **Research group**

The Sonkoly group focuses on exploring the roles of non-coding RNAs in skin inflammation, and to explore their potential as biomarkers and therapeutic targets. The group has several years of experience in non-coding RNA research. The research activities are located at the Center for Molecular Medicine (CMM), which is at the Karolinska Hospital area, in proximity to the New Karolinska Hospital, which allows a close interaction. The research group belongs to the Dermatology and Venereology Section which is an independent section within the Department of Medicine, Solna, Karolinska Institutet, where a broad range of experimental and clinical dermatological research is conducted.

## **Interested in recruiting a Postdoc**

### **Project title**

New gene immunotherapies for chronic hepatitis B and D virus infections

### **Supervisor**

Matti Sällberg, professor

Department of Laboratory Medicine, Karolinska Institutet

Email: [matti.sallberg@ki.se](mailto:matti.sallberg@ki.se)

Phone: +46706082101

Home page:

<https://ki.se/labmed/forskargruppen-inom-viral-hepatit>

### **Type of recruitment and qualifications of applicant** Postdoc (24 months)

The applicant should hold a PhD in molecular biology, immunology, virology or gastroenterology. The applicant should know techniques in molecular immunology and biology, and be proficient in English. Experience with animal studies is an advantage.

### **Background**

Chronic hepatitis caused by the hepatitis B and D viruses (HBV/HDV) are major causes for severe liver disease and cancer. Current therapies for chronic HBV with reversed transcriptase inhibitors block viral maturation and infectivity, but are unable to block production of viral proteins or clear the infection. More than 10 years of therapy fails to induce off therapy responses in more than 5-10% of treated patients. Thus, therapy is life long in the majority of patients. HDV can only replicate productively in cells coinfecting by HBV. For chronic HDV infections, a two year therapy with alfa-interferon can cure only 25% of patients. Thus, new immunotherapies are needed for chronic HBV and HDV infections

### **Project description**

The project aims at developing new immunotherapies for chronic HBV infections. We have previously developed a therapeutic vaccine for chronic HCV infections that was tested in patients. We are now well under way to take a therapeutic vaccine for chronic HBV to clinical testing. The project involves optimizing the delivery of the vaccine and the final selection of a vaccine candidate. Vaccine candidates are developed in house or in collaboration with partners such as the Mayo Clinic, USA. This involves immunization studies in mice, rabbits and possibly macaques. The responses are analysed by EIA, ELISpot, and multi color flow cytometry. Antibodies are tested for in vitro neutralization of HBV and HDV in collaboration with University of Heidelberg. In vivo neutralization in humanized mice is tested in collaboration with University of Gent. For both HBV and HDV specific T HLA-A2 restricted T cell receptors are cloned from immunized HLA-A2 transgenic mice. These are then evaluated in vitro as potential T cell therapies for chronic HBV and HDV and HBV positive cancers.

### **Research group**

The group is headed by Prof Sällberg and assoc prof Frelin. The HBV vaccine project is run in collaboration with MSc Panagiota Maravelia. Dr Ahlen is clinical trial manager for a large EU project on vaccine development. Dr Caro Perez is heading studies on HCV. Dr Pasetto recently joined the group from Dr Steve Rosenbergs group at the NIH. The group holds grants from EU Horizon 2020, Vinnova, Cancerfoundation, Science Council, and the County Council.

## **Interested in recruiting a PhD student**

A project on the molecular basis of drug resistance in malaria

### **Project title**

The mechanism of artemisinin-resistance in *Plasmodium falciparum*

### **Supervisor**

Mats Wahlgren, MD, PhD, Professor

Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet

Email: mats.wahlgren@ki.se

Home page: <https://ki.se/en/mtc/the-mats-wahlgren-group>

### **Type of recruitment and qualifications of applicant**

A full-time PhD student.

To be eligible for doctoral education, the applicant should meet the general entry requirements for doctoral study at Karolinska Institutet. The applicant must have an educational background and experimental experience in molecular and cell biology. Previous experience in work with *Plasmodium falciparum*, post-transcriptional gene regulation, non-coding RNAs or OMICS study is a strong merit. The applicant must have the ability to work independently and bring in new ideas to drive the project forward. Furthermore, good communication skills are expected to work collaboratively in a group.

### **Background**

Artemisinin-resistance in *P. falciparum* has recently emerged and is stalling the progress of global malaria control. The spread of resistant parasites to the African continent is projected to cause an additional 100,000 deaths in excess of the present 450,000 annual deaths. The mechanism of artemisinin resistance is atypical and remains poorly understood, but resistant parasites exhibit similar phenotypic characteristics of cellular stress response and misbalanced proteome homeostasis. The PhD project aims to unravel the molecular mechanism of artemisinin resistance by focusing on the unique features of the parasite genome and its translation machinery, which could be potentially utilized as mechanisms for stress response and drug resistance.

### **Project description**

The student will perform routine *in vitro* culturing of *P. falciparum* parasites and generate mutant parasites using relevant genomic manipulation techniques such as the CRISPR/ Cas system and *in vitro* evolution to screen and study potential genes important for drug resistance. The student will employ genome-wide transcriptomics, proteomics and reporter assay methodologies to study the regulation and the regulatory role of non-coding RNAs; the importance of genomic arrangements and translational regulation in relation to the parasites' ability to respond to acute cellular stresses and the generation of drug resistance.

### **Research group**

The Mats Wahlgren lab focuses on the understanding of the molecular pathogenesis of *P. falciparum* infection and has been actively working towards the development of next generation drugs and vaccine to avert the most severe consequences of malaria infection. The group is comprised of a highly international team of skilled scientists. Furthermore, the group has very strong national and international collaborations as well as previous publications in Nature Med, Nature Micro etc. The doctoral students are encouraged to participate in short research visits to collaborators' lab in Europe or in malaria endemic areas, so that the student may experience working in a different environment and establish a strong research network.

## **Interested in recruiting a Postdoc**

### **Project title**

**Neural stem cells derived from reprogrammed patient cells as novel models for childhood cancer**

### **Supervisor**

Margareta Wilhelm, PhD, Associated Professor

Department of Microbiology, Tumor and Cell biology (MTC), Karolinska Institutet

Email: [margareta.wilhelm@ki.se](mailto:margareta.wilhelm@ki.se) , Phone: +46737075707

Home page: <https://ki.se/en/mtc/margareta-wilhelm-group>

### **Type of recruitment and qualifications of applicant – Postdoc (48months)**

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

Please include in the application;

- 1) Curriculum vitae
- 2) A complete list of publications
- 3) A short summary of current work (no more than one page)

### **Background**

Neuroblastoma (NB) is the one of the most common extracranial solid tumors in children. It manifests in the peripheral nervous system and is thought to originate from a sympathoblast derived from neural crest during development. We have generated iPS cells and neural crest cells from non-cancerous skin cells of NB patients with cancer-driving germline mutations. Orthotopic transplantation into mice shows that patient cells can form tumors resembling human NB. Our models offer a way to recapitulate all stages of tumor development, from initiation to late stages, thus providing novel models for studying cancer processes in relevant human cells. The project will involve advanced cell culturing techniques and in vivo modeling to identify at which developmental stage from neural crest to sympathoadrenal cells driver mutations are activated and induce cellular transformation. Our approach will lead to a greater understanding in the molecular mechanisms operating during NB development, with the ultimate goal to identify new therapeutic targets.

### **Project description**

The Postdoc will use our human stem cell models for both in vitro and in vivo studies to investigate how NB develops and progress. The candidate will develop neural crest to sympathoadrenal cells differentiation protocols to study the tumor initiation stage. Potential targets will be identified using high throughput genomics. The project is based on in vivo modeling and advanced human stem cell culturing and neural differentiation assays. Analyses include molecular biology methods such as RNA and DNA preparations, western blotting, qRT-PCR, CRISPR/Cas9, flow cytometry, and microscopy, RNA and DNA seq, Bioinformatics.

### **Research group**

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



## **Interested in recruiting a PhD student**

### **Project title**

**Liver X Receptor (LXR) role in immune-mediated gastrointestinal tumorigenesis**

### **Supervisor**

Eduardo J. Villablanca, Associate professor

Department of Medicine, Solna, Karolinska Institutet

Email: [Eduardo.villablanca@ki.se](mailto:Eduardo.villablanca@ki.se) Phone: 073-628-2289

Home page: <https://ki.se/en/meds/research-group-eduardo-villablanca>

### **Type of recruitment and qualifications of applicant**

PhD student (48 months)

The applicant (to be determined) will be required to have experience in mucosal immunology

### **Background**

Based on statistic carried out by the GLOBOCAN project ([http:// globocan.iarc.fr/Default.aspx](http://globocan.iarc.fr/Default.aspx)), colorectal cancer is the third most common cancer worldwide and is the second leading cause of cancer deaths. Interestingly, chronic intestinal inflammation is associated with a significantly increased risk of developing colorectal cancer. Cholesterol, comprises an important component of our diet particularly in the western diet and deregulation of cholesterol metabolism has been associated with various metabolic and inflammatory diseases. By sensing hydroxylated derivatives of cholesterol (i.e. oxysterols) the nuclear receptor LXR regulates cholesterol homeostasis and promotes anti-inflammatory immune responses. We and others have shown that the oxysterol-LXR axis modulate the function of immune cells.

### **Project description**

During the last years, we have generated preliminary data and new tools (see below) to investigate the role of the oxysterol-LXR axis in intestinal immune homeostasis. Using complete LXR-deficient mice as well as conditional KO mice, in which both LXR isoforms have been depleted in specific cell types (e.g. intestinal epithelial cells) we have provided insights into the role of oxysterols in regulating intestinal immune responses, such as oral tolerance and humoral responses. We will now investigate the role of LXR in colorectal cancer.

### **Research group**

Our research program seeks to dissect the complex dynamics of host-environment interactions required to sustain intestinal immune homeostasis and how breakdown in these interactions may lead to inflammatory bowel diseases (IBD) and colorectal cancer (CRC). In particular we are trying to understand how deregulation of intestinal immune homeostasis might lead to IBD and CRC. To do so, we focus in immunological processes that are involved at the initiation (priming of adaptive immune responses), progression (chronic inflammation) or resolution (tissue repair) of IBD and CRC.

## **Interested in recruiting a Postdoc**

### **Project title**

**Discovery of cell-level somatic mutation from single-cell RNA-sequencing**

### **Supervisor**

Trung Nghia Vu, assistant professor

Department of Medical Epidemiology and Biostatistics, Karolinska Institutet

Email: [TrungNghia.Vu@ki.se](mailto:TrungNghia.Vu@ki.se) Phone: +46 (0) 8-524 822 68

Home page: <https://ki.se/en/people/nghvu>

### **Type of recruitment and qualifications of applicant**

Postdoc (12 months, extendable up to 02 years)

The applicant is expected to have a PhD degree in bioinformatics, biostatistics or computer science. Programming skills at least one of languages R/Python/C++ are required. Experiences in data analysis of next-generation-sequencing data are advantage.

### **Background**

Mutation is a key event to study mutational cell-to-cell heterogeneity from single cells. To study genomic mutations of a cell, single-cell DNA-sequencing (scDNA-seq) is the method of choice. However, the task is still challenging due to very low input materials (only two copies of DNA in a cell) and technical artefacts, amplification bias, allelic drop-out, etc. To overcome these issues, we will identify cell-level exonic mutation from single-cell RNA-sequencing (scRNA-seq) data. It is a potential approach because: 1) RNA has many more copies than DNA in a cell; 2) recently scRNA-seq achieves a great improvement of technology to reduce the noises and bias; 3) it was demonstrated that bulk-cell RNA-seq can identify over 70% of all expressed coding variants (PMID:24075185).

### **Project description**

Although there exists various methods for detecting mutation from DNA bulk-cell sequencing, these conventional approaches are not suitable for scRNA-seq because 1) methods are designed for bulk-cell sequencing data from average signals of a population of cells and 2) single-cell sequencing data have a significant level of noises and biases. To address these issues, we will attempt different robust statistical methods such as quantile regression, two-dimensional local false discovery rate and etc... to address the noisy signals. With experiences in method development and analysis of single-cell sequencing data (PMID:27153638, PMID:29490015), we believe having sufficient expertise to overcome these issues.

The method of this project will be applied to the single-cell data from 400 Acute Myeloid Leukemia (AML) patients to characterise heterogeneous cell populations. We expect discover rare but malignant mutational cell subgroup, e.g., Leukemia stem cells which are one of reasons causing relapse. The data are collected from an AML project in a collaboration with Professor Yudi Pawitan, MEB, KI. Each AML patient consists of RNA-seq data of up to 96 single cells generated using Fluidigm C1 platforms. Available public datasets such as breast cancer scRNA-seq dataset (PMID:28474673) are used for pilot tests.

### **Research group**

This project is under supervision by Dr. Trung Nghia Vu experienced in statistical and computational methods for cancer genomics data and Prof. Yudi Pawitan, an expert in biostatistics, bioinformatics and high-throughput molecular data modelling.

## **Interested in recruiting a Postdoc/Visiting Researcher**

### **Project title**

Investigation of the role of regulatory RNAs in skin wound healing

### **Supervisor**

Ning Xu Landén, PhD, Associate Professor, Group leader

Unit of Dermatology and Venerology, Department of Medicine Solna, Karolinska Institutet

Email: [ning.xu@ki.se](mailto:ning.xu@ki.se) Phone: +46 8 51772158

Home page: [www.xulandenlab.com](http://www.xulandenlab.com) or <http://ki.se/en/people/ningxu>

### **Type of recruitment and qualifications of applicant**

Visiting researcher and post-doctoral fellow (longer than 12 months):

The candidate should have obtained a PhD degree within the area of molecular or cell biology and have deep interest in medical and biological problems. The applicant is preferred to have documented previous experience with RNA research or skin biology. Previous experience with tissue culture, molecular and biochemical techniques is desired. A high level of English, spoken and written, is a requirement.

### **Project description**

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

### **Research group**

Research Group N Xu Landén

## **Interested in recruiting a PhD student**

### **Project title**

Oral microbiome and cancer

### **Supervisor**

Tülay Yucel-Lindberg, Associate professor  
Department of Dental Medicine, Karolinska Institutet  
Email: [tulay.lindberg@ki.se](mailto:tulay.lindberg@ki.se)  
Phone: +46-70-5088126  
Home page: <https://ki.se/en/people/tullin>

### **Type of recruitment and qualifications of applicant**

PhD student (4 years)  
Master's degree in Molecular and Cell Biology, Immunology or Biotechnology  
Dentists and specialist in periodontology

### **Project description**

Infection and inflammation play a key role in carcinogenesis. In addition to the clearly infection-driven cancers like *Helicobacter*-induced stomach cancer, infection-caused systemic inflammation associates with malignancies. For example, the chronic inflammatory disease periodontitis associates statistically to over-all cancer prevalence and moreover candida, the opportunistic pathogen, has been implicated in oral and oesophageal cancers (Meurman & Bascones-Martinez 2011; Alnuaimi et al. 2015). In addition, Söder et al. 2011 and Virtanen et al. 2014, reported that periodontitis is associated with breast and prostate cancer in the long-term epidemiological cohort study. Furthermore, periodontal pathogens have been linked to oral and gastrointestinal carcinogenesis although the specific mechanisms are unknown. We have also recently reported that *treponema denticola*, which is associated with severe periodontitis, may contribute to orodigestive carcinogenesis via its chymotrypsin-like proteinase (Nieminen et al. 2018).

Recent research has emphasized the importance of holistic microbiome approach instead of focusing on individual microbial species in the pathogenesis of cancer. Various mechanisms have been suggested to mediate the interaction between microbiota and host that, when pathological, it may lead to malignant transformation (Pang et al. 2018). Similarly, in oral cancer the microbiome seems to add to cancer risk in persons with poor oral hygiene (Hsiao et al. 2018). The hypothesis with this project is that pathogens in oral microbiota associate with cancer, both locally and systemically, and that microbiome profiling (using 16s rRNA gene analysis in our long-term epidemiological cohort study) will be beneficial in assessing the risk of cancer. We expect that results of this study will help the clinician in future diagnosis, treatment and prognosis assessment of patients with cancer with special emphasis on oral health.

### **Research group**

|   |  |
|---|--|
| Tülay Yucel-Lindberg (PI) – Associate professor | Anna Kats – Postdoc, affiliated group member |
| Natalija Gerasimcik – Postdoc                   | Caroline Lindström – Graduate Student        |
| Kaja Eriksson – Postdoc, associated             | Martina Ericson – Graduate Student           |
| Anna Lundmark – Postdoc, associated             | Caroline Åwall Blom – Graduate Student       |
| Birgitta Söder – Professor em, associated       | Shigufta Syed – Master Student               |

## **Interested in recruiting a Postdoc**

### **Project title**

Regulatory mechanisms that impact Hedgehog signaling, a pathway implicated in many cancers.

### **Supervisor**

Peter Zaphiropoulos, Professor of Molecular Biology

Department of Biosciences and Nutrition, Karolinska Institutet

Email: [peter.zaphiropoulos@ki.se](mailto:peter.zaphiropoulos@ki.se) Phone: +46 8 52481052 Home page:

<https://ki.se/en/bionut/hedgehog-signalling-role-of-rna-based-mechanisms-peter-zaphiropoulos>

### **Type of recruitment and qualifications of applicant**

Postdoc (12 months, with the possibility of extension for additional 12 months).

The applicant should have experience in modern molecular biology approaches, including cell culture, RNA isolation, cDNA synthesis, qPCR, Western blot. Familiarity with the analysis of RNAseq data and with mouse models of tumor development will be considered a plus. Good knowledge of both written and spoken English, good communications skills and willingness to effectively work in a group are required.

### **Background**

Hedgehog signaling is a major developmental pathway, whose dysregulation can result in a variety of human cancers, including basal cell carcinoma, medulloblastoma and rhabdomyosarcoma. It is estimated that about 25% of human cancer deaths may be related to this signaling pathway. Activation of the pathway initiates when extracellular Hedgehog ligands interact to Patched transmembrane receptors, with this event relieving the inhibition of Patched on the signaling molecule Smoothened. Smoothened, relieved from Patched inhibition, translocates to the primary cilium and elicits activation of the effectors of the pathway, the GLI transcription factors. However, the genes that are regulated by the activated GLI factors are poorly understood.

### **Project description**

Recently, we identified a signature of 29 target genes of the GLI1 transcription factor, the terminal effector of the pathway. Among these genes is FOXS1, a transcription factor that blocks the capacity of the GLI1 oncogene to activate target gene expression and is a marker of good prognosis in breast cancer.

The project aims to further address the impact of FOXS1 in tumorigenesis using mouse models and also dissect the role of non-coding RNAs, including circular RNAs, in mediating the transduction of the Hedgehog signal.

### **Research group**

The research group currently consists of a Ph.D. student, who is in the process of finalizing her studies and a postdoc, who obtained the Ph.D. degree within our group and stayed on in order to complete projects already initiated.