

Good afternoon.

My name is Norm Rosenblum. I am Chair of the Faculty of Medicine Scientific Advisory Board. It has been my great pleasure to adjudicate the applications submitted by many of you for the 2018 research program competition. My colleagues on the SAB and I have been exposed to some great science that, without doubt, is going to shape our understanding of medicine and how we manage our patients.

During the presentations by the candidate research programs to the SAB time was short. Thus, there was no opportunity to introduce the members of the SAB beyond their names. My colleagues on the SAB are a distinguished group and I want to properly introduce them.

Professor Peter Lichter is Head of the Division of Molecular Genetics at the German Cancer Research Centre, and also Deputy Director of the National Centre for Tumor Disease in Heidelberg, Germany. Professor Lichter is an expert in molecular genetics and precision oncology.

Professor Kristina Schoonjans is Head of the Laboratory of Metabolic Signaling, and a Professor at the École polytechnique fédérale de Lausanne (*EPFL*). Professor Schoonjans is expert in metabolism, the gut-brain axis and bile acid signaling.

Professor Lars Farde is Professor of Psychiatry in the Department of Clinical Neuroscience at the Karolinska Institute in Stockholm and Chief Scientist in Precision Medicine and Genomics at AstraZenica. Professor

Farde is expert in central nervous system biology, brain imaging, major psychiatric disorders, brain function and translational neuroscience.

Not here, in person, today is Martin Blaser who is Professor of Internal Medicine and Microbiology at New York University, New York. Dr. Blaser is an expert in host-pathogen interactions, systems biology, the microbiome and inflammation.

I, myself, am a Professor of Paediatrics and Canada Research Chair in Developmental Nephrology at the University of Toronto and Scientific Director of the Canadian Institutes of Health Research Institute of Nutrition, Metabolism, and Diabetes. I am immediate past Associate Dean of Physician Scientist Training at the University of Toronto. My expertise resides in pediatric nephrology, developmental genetics of the kidney and urinary tract, and the training and career development of clinician scientists.

I want to express by sincere thanks to my colleagues on the SAB. Thank you for the energy, diligence, openness, inquisitiveness, wisdom, and good humor that you have brought to this process. May I ask you to join me in thanking Professors Schoonjans, Lichter, and Farde.

I also want to extend my appreciation to Dean Risto Renkonen and Vice Dean Hannu Sariola for asking me to undertake this role on the SAB and for working with me in such a constructive and collegial manner to introduce me to the Faculty of Medicine and to this application process. Your hospitality on-site has been second to none and we, the members of the SAB, are very appreciative.

Second to last, I want to extend a huge thank you to Riikka Palonkorpi. Riikka has arranged everything related to this competition and this visit. She has made sure that the SAB has everything needed to complete our tasks. Not only is Riikka really expert but she does everything with a smile. Thank you so much.

Finally, but not least by any means, I want to thank all of you who attended the Research Program presentations. Thank you who presented and who engaged the SAB in discussion. Thank you for presenting well and within the allotted time. It is so rare to not have to yank fellow investigators off the stage for going overtime – after all we are all so excited about our science and the programs within which we work – but you kept to time and got the message across in the time you were given. Bravo to all of you.

During our visit this week, the SAB has been presented with 12 Research Programs. Some represent re-development of previously successful programs; others are new. I expect that many if not all of you will not yet know the expanse of translational science ongoing in this Faculty. And thus, I want to briefly summarize each of these programs for you.

Program 1: Applied Tumor Genomics (ATG)

Group Leader: Lauri Aaltonen

ATG is divided into six interdependent workstreams or goals. It is translational, in nature, spanning basic science to clinical research, primarily focused on uterine leiomyomas and colorectal cancer. At the heart of this project is the professional establishment of data and material collections, including unique structures such as interconnecting registries, cancer morbidity as well as environmental exposure databases, and its combination with modern annotations of functional elements within tumor genomes and state-of-the-art OMICs data analysis and integration tools.

Program 2: Translational Cancer Medicine Program (CAN-PRO)

Group Leader: Kari Alitalo

The Translational Cancer Medicine Program (CAN-PRO) aims to develop a platform of translational cancer discovery. CAN-PRO seeks to: (1) develop new technologies by integrating genomics approaches with cancer cell biology, ex vivo living organoid biobanks and rodent tumor

models to improve cancer diagnostics, therapeutics, and patient quality of life; (2) discover novel targets and therapeutic modalities in cancer; (3) establish a platform for systematic evaluation of cancer gene function and drug testing in 3D ex vivo tumor organoids; (4) model human tumor pathogenesis in mice by establishing CRISPR/Cas9 gene edited tumor models; and (5) develop preclinical models of post-operative tumor recurrence, using mouse tumor models and patient-derived tumor xenografts, plus test peri- and post-operative therapies. Via these specific aims CAN-PRO seeks to integrate existing genomic, epidemiological, bioinformatic and pathological datasets with preclinical mechanistic validation and drug efficacy studies. It is projected that such an approach can lead to identification of new drug leads and intervention schemes harnessed for precision-based cancer therapies.

Program 3: Human Microbiome Research
Group Leader: Willem de Vos

This program will investigate causal links between microbiota and the risk of disease, mechanisms of host-microbe interactions, and microbiota-targeted therapeutics and diagnostics. The investigators, who span the range of fundamental sciences and clinical practice, will perform microbiome-wide studies in well-characterized, large cohorts, some of which feature clinical interventions that target diet and microbiota. Study cohorts cover the human life span from pre-conception to the old age, a range of microbiota niches, and a wide range of diseases from chronic inflammatory diseases, such as allergies

and inflammatory bowel disease (IBD) to metabolic and neurological diseases and infections.

Program 4: Systems Oncology (ONCOSYS)

Group Leader: Sampsa Hautaniemi

The overall strategy in this proposed new program is to apply computational algorithms to predict the biological and clinical behavior of tumors and to translate these predictions into clinical applications. Major aspects on the development of those algorithms are based on the concepts of deep learning and artificial intelligence (AI). Several AI approaches are used to harness big data to arrive at clinically useful information for diagnoses, prediction of response and tailored treatments. This program extends in its breadth from computational analyses to precision medicine solutions.

Program 5: Big Data for Lifelong Health (BigLIFE)

Group Leader: Jaakko Kaprio

The applicants aim to exploit numerous data registries that contain data as diverse as genetic, epidemiological, psychological, and environmental parameters, to predict morbidities due to health problems. Eventually, these studies are meant to lead to preventive measures and policies in order to improve lifelong health. Disorders to be included in the proposed analyses include, but are not limited to, cardiovascular, psychiatric, immunological and neurodegenerative.

Program 6: Program in Translational Immunology (TRIMM)

Group Leader: Satu Mustjoki

The mission of TRIMM is to create a center of excellence in translational immunology at the University of Helsinki. This program is based on harnessing advances in immunology for the treatment of diseases including immunodeficiency, auto-immunity and neoplasms. The investigators seek to: (1) explore the development and regulation of T cells and immune tolerance; (2) understand the aberrant immune responses in auto- and alloimmune diseases and cancer; and (3) translate discoveries into prevention, novel disease classifications, diagnostic tools and personalized treatment.

Program 7: Individualized Drug Therapy (INDIVIDRUG)

Group Leader: Mikko Niemi

This program focuses on the fundamental clinical challenge that not all patients respond to a certain medicine and that the sensitivity to adverse drug reactions is difficult to predict. This problem has over recent years been highlighted by the society (payers) and also forced industry to search for biomarkers supporting a Personalized Health Care (PHC) strategy ("right medicine in the right dose to the right patient"). Accordingly, this program aims to build capability for PHC or "individualized drug therapy". Besides understanding of classical PK and PD this program highlights the need for useful biomarkers of disease, disease progression, efficacy and sensitivity to adverse drug reactions, and develop novel drug treatments.

Program 8: Translational Stem Cell Biology and Metabolism (STEMM)
Group Leader: Timo Otonkoski

STEMM aims to elucidate the mechanisms of metabolic and endocrine diseases and to develop novel diagnostic and potentially therapeutic algorithms. Four themes will be interrogated: (1) alterations in cell-autonomous processes; (2) changes in cell-to-microenvironment interactions; (3) endocrine signaling between different tissues; and (4) diagnostics and therapeutic development. These aims will be pursued using stem cells, organoids in vitro, and in vivo experimental models using innovative cell manipulation approaches like cutting-edge genome editing.

Program 9: Cognitive, Systems, and Translational Neuroscience
(CoSTra)

Group Leaders: Satu Palva and Teija Kujala

This research program aims “to acquire a comprehensive understanding of the hierarchy and organization as well as the micro-scale and system-level neuronal basis of the brains perceptual, attention, memory, and language systems”. The program will elucidate basic cognitive functions and higher-level mental functions and their potentially predictive value in normal achievements in life, such as performance at work, in education or general intelligence. A second goal is the identification of neuronal dysfunctions that lead to cognitive deficits in brain diseases (neurodevelopmental and neurodegenerative disorders as well as traumatic) and following therapeutic interventions. A third and more

specific goal is to reveal the neural organization of language and music processing.

Program 10: Sleep and stress in health and in transition from acute to chronic diseases (SLEEPWELL)

Group Leader: Tiina Paunio

SLEEPWELL is a new program that is based on the emerging hypothesis that insufficient sleep is a central underlying factor of metabolic and neuropsychological disorders. SLEEPWELL aims to: (1) understand characteristics of sleep from early life to adulthood and its impact on health and disease; (2) identify determinants for sleep disturbance and transition from occasional symptoms of disturbed sleep to chronic disease and to sleep-related secondary disorders (depression, anxiety and chronic pain); and (3) apply and develop novel evidence-based interventions for prevention and treatment of sleep disturbances, and to promote testing of new imaging and sleep-related health technologies.

Program 11: Clinical and Molecular Metabolism (CAMM)

Group Leader: Kirsi Pietiläinen

CAMM aims to understand the pathophysiology and advance the management of diabetes and other cardiometabolic diseases. The investigators will study key physiological functions and cross-talk between multiple peripheral organs during the development of metabolic diseases. This program combines deep clinical analysis with state-of-the-art genetics in large patient samples of the Finnish population and combines it with multi-omics analytical strategies

(epigenomics /metabolomics/microbiome...) as well as preclinical models for interrogation of pathobiologic mechanisms and analysis of therapeutic targets.

Program 12: Inflammation in cardiovascular diseases

Group Leader: Juha Sinisalo

The main focus of this program is the role of inflammation in cardiovascular diseases. Three specific aims are proposed: (i) to investigate inflammation in atherosclerosis with a goal to develop new biomarkers and therapies, (ii) to investigate the pathobiology of giant cell and sarcoid myocarditis, and (iii) to develop new regenerative therapies for cardiovascular disease.

So, colleagues, there you have the rich tapestry of research being performed within the Faculty of Medicine. The SAB congratulates you on your work to date and wishes you great success going forward. There seems little doubt that clinical medicine and medical science will continue to reap the benefits of your efforts.

Without commenting specifically on any one Research Program at this particular time, I want to highlight certain themes that have impressed the SAB in our review of your written applications and during your presentations and subsequent discussion. Herein, I discuss a few issues, highlighted by some applications, but relevant to many applications and worthy of your considerations as you reflect on your efforts moving forward.

The attention to translational science is impressive. You have very seriously embraced the challenge of joining discovery research to application to human beings. This, of course, is very difficult and fraught by failure. But this endeavor is greatly strengthened by the careful collection, annotation and analysis of human data. This is a fantastic strength in this country and you take great advantage of your long-term investments. Moreover, we were impressed by how human data is interrogated in preclinical models and then forward tested in humans. We were pleased to see that ethical considerations were sometimes included in your applications; in an era of big data and human investigation, this is extremely important, not only for the performance of research but also for the training of early career investigators.

Of course, translational medicine requires, by its very nature, an interaction between academia and industry. Some of you have already created spin-off companies or are planning to do so or are attempting to build companies in house in collaboration with government programs that would fund such enterprises. These efforts are clearly important for the sake of your research and its translation. These activities also have important implications for the education and career development of junior scientists. The translation medicine pathway has important distinctions when compared to the typical academic itinerary. As such care must be taken for junior scientists in translational programs to be exposed to the ways of thinking and doing that characterize this pathway.

Building a bridge between fundamental scientists and clinicians and clinical scientists is key to success in the translational space. We were impressed with examples of how teams are integrating at the professional level and finding ways to build bridges between these two distinct domains.

Implicit, if not explicit, in this Research Program exercise, is the aim to renew research efforts with a new generation of investigators. This requires purposeful attention to recruitment and development of junior investigators and great care to the issue of diversity, particularly gender diversity within our ranks. We applaud examples in which early career investigators and women constitute a major proportion of research programs and are taking on leadership roles within these teams. Renewal of leadership is inevitable and critical to success.

In their composite, your programs feature, a large number of successful scientists, whether fundamental or clinical. In some applications the marriage between individual research plans and the program is clear; in others individual plans are not so obviously integrated into program strategies. Demonstrating the relationship between individual investigator efforts and a program is critical, not only for reviewers, but also for your ongoing efforts in building cohesive programs that add real value.

Finally, a word about training and career development planning. Research Program applications routinely featured scientific training towards excellence and productivity using, what we might call the apprenticeship type modeling and supervision. This has worked for

decades. Mentorship, even multi-interdisciplinary mentorship teams, was featured by some; this has added value for trainees as has been shown by published studies. Understanding the needs of trainees through needs assessments was also observed – this is a strong strategy to demonstrate attention to trainees’ needs and also to educate and support in a way that addresses these needs. As science has changed from ‘boutique science’ to ‘team science’ and has become more and more interdisciplinary, the skills needed to lead science and manage programs have expanded. Programs will do well to feature the learning and practice of so called 21st Century skills including skills in critical thinking and problem solving, communication, creativity and innovation, collaboration, and contextual learning.

To close, on behalf of the SAB, I thank you again for this opportunity and thank you for your attention.