

The FIMM SAB meeting took place on 26-27 May 2015 in Helsinki. The program of the meeting is enclosed. Present at the meeting were the following SAB members:

- Professor Kai Simons, Max-Planck-Institute of Molecular Cell Biology and Genetics, Germany (Chair)
- Professor Cornelia van Duijn, Erasmus University Medical School, the Netherlands
- Professor Carl-Henrik Heldin, Ludwig Institute for Cancer Research, Uppsala University, Sweden
- Professor Edison Liu, The Jackson Laboratory, USA
- Professor Nadia Rosenthal, The Jackson Laboratory, USA and EMBL Australia Partnership Laboratory, Australia

On the first day of the visit, the SAB heard presentations about FIMM, the Helsinki Life Science Center initiative and from the FIMM Group Leaders who were up for mid-term evaluation. We also had a meeting with the Vice Rector for Research, Professor Keijo Hämäläinen and the Dean of the Faculty of Medicine and the Chair of the FIMM Board, Risto Renkonen and met with the new director-candidate of FIMM, Academy Professor Jaakko Kaprio. The following day we had discussions with the FIMM staff and heard presentations about the FIMM infrastructure facilities.

Overview of FIMM and recommendations

FIMM has continued its successful build up to become a leading center worldwide in molecular medicine. FIMM is capitalizing from the Finnish investment in human genetics. We emphasized in the 5 year evaluation report in 2013 that “molecular medicine in Finland is now entering a most fruitful phase. After years of research and data collection, FIMM can now move Finnish population genetics into the clinic and into enterprises. Why is this? Because of the unique bottle neck history of the Finnish population, many potential disease-promoting genetic variants are at elevated frequency, so FIMM can pioneer studies with this smaller populations cohorts than is the case in all other countries with the know-how to tap this information. Therefore, the Evaluation Committee stresses that the situation is critical. With too little funding there is a risk that FIMM and Finland will be overrun. Well-funded leading institutions in the world can leave Finland behind by using approaches based on brute force to overcome the handicap that they have with their population cohorts. FIMM has structured its collaborations to ensure that the credit comes to Helsinki, but without the Institute this is unlikely to remain the case.

This is exactly what FIMM has been doing successfully in the 2 years since the report. It is also well documented in the outstanding publication record of the Institute. Another reflection of success is the capability of FIMM to procure external funding from national and international resources. The success is based both on the organizational skills of the Director, Olli Kallioniemi and the excellent staff and on the quality of the researchers recruited.

The SAB wants to emphasize that the area of research that FIMM is engaged in is central to the buildup of a future system of personalized diagnostics and treatment that will be the center piece of precision clinical care. This research

area will be fundamental for developing better and in the end more effective medical care for the future. A brilliant example at FIMM is the personalized drug-screening capability that Krister Wennerberg and his team have built up and is being used not only by FIMM scientists but also by several cancer units, such as the clinical hematologists at the Helsinki University Central Hospital Comprehensive Cancer Center.

Most importantly, FIMM has become a brand name internationally and thus a flagship for the University of Helsinki. However, brands are fragile entities that demand protection, especially in difficult times. The SAB therefore welcomes the initiative of the University Leadership to start a Helsinki Life Science Center with the Institute of Biotechnology (BI) and FIMM as central nodes. FIMM has built up an amazingly efficient research infrastructure that provides the internal and external user community with state-of-the-art technologies. Also BI has several excellent core facilities. The plan that we were informed about from the Vice Rector, Keijo Hämäläinen and the Dean of the Faculty of Medicine, Risto Renkonen, to place all the Life Sciences core facilities of the University of Helsinki in the Helsinki Life Science Center makes considerable sense and would enable the University of Helsinki and Finland to remain competitive in a shrinking funding scene. FIMM and BI would guarantee efficient organization and competent leadership for this difficult challenge. Everywhere in the world the increasing costs for infrastructure and core facilities is becoming a headache.

International networks

FIMM and BI have extensive international connections and are part of important networks. FIMM has excellent ties to the Broad Institute in Cambridge, USA and The Wellcome Trust Genome Campus in Hinxton, UK. These ties depend on the brand name of FIMM.

Moreover, FIMM is an EMBL partner in the Nordic network of institutes in molecular medicine. The SAB recommends that the FIMM Director-Designate Jaakko Kaprio visits the Director General of EMBL, Iain Mattaj to be informed what is required for FIMM to remain an EMBL partner after the establishment of the HLSC. The chair of the SAB has already informed Iain Mattaj of this proposal and he enthusiastically welcomes a visit.

Interim and next director

The SAB met with Academy Professor Jaakko Kaprio and found him an excellent candidate for an interim directorship, when Professor Olli Kallioniemi steps down in October 2015. Since Jaakko Kaprio only can take up a part-time directorship, the SAB recommends that the FIMM Board accepts the offer of Olli Kallioniemi to spend 25% of his time at FIMM.

The departure of Olli Kallioniemi is a great loss for FIMM and a great win for SciLifeLab in Sweden. On the positive side, there will now be a possibility to build bridges between the SciLifeLab and FIMM to share resources and facilities.

Important is to start a search for a new Director as soon as possible. To attract outstanding candidates it will be important to complete the organization of the

HLSC. Essential elements will be freedom of operation for FIMM within the HLSC. The SAB recommends that both BI and FIMM continue to have their own international Scientific Advisory Boards. Such boards are essential marketing and branding elements in a competitive international environment.

Senior Scientists

The SAB was immensely impressed by the quality of the Senior Scientists. A number of essential activities depend on this group of experienced scientists within FIMM. This includes the operation of technology infrastructures, running multi-center studies, industrial and international collaborations, writing and acquiring grants. This feature of having flexible and knowledgeable staff scientists engaged in running institute key functions, is completely unique to FIMM. We have never seen such an amazing organizational innovation anywhere else. The SAB is convinced that the Senior Scientists, as now organized, are a substantial contributor to the success of FIMM.

The SAB recommends that the outstanding contribution of Senior Scientists is incorporated into the planning of HLSC. The SAB recommends the establishment of a committee that comes up with a proposal to give this flexible group of scientists a career perspective.

PhD Students and Postdocs

The SAB was impressed by the activities to update the FIMM Doctoral Training Program and to establish a FIMMPOD postdoctoral research program by Senior Researcher Gretchen Repasky, who works both as a Coordinator at the Doctoral School of Health at the UH as well as a Coordinator of research training at FIMM.

FIMM has close to 60 PhD students, about half of whom come from abroad. They are admitted through a centralized FIMM-EMBL PhD program (20%) or through direct recruitment by the individual PIs. The size of the FIMM-EMBL Program will be enlarged, a plan that is endorsed by the SAB. Since the last SAB meeting two years ago, the procedure for the direct recruitment into the research groups at FIMM has been formalized through the establishment of an Admission Committee, to assure a high quality of all the accepted PhD students. The SAB endorses also this reform.

At its last meeting, the SAB recommended to abandon the rule that a PhD thesis needs to contain a certain number of papers, since this leads to publication of small incomplete papers of low impact. In response to this recommendation, Gretchen Repasky has made a survey among several universities in different countries. The survey showed that the University of Helsinki stands out with more formal requirements with regard to number of papers in a PhD thesis compared to other European universities. This survey will now be used in order to persuade the leadership of the University of Helsinki to change these obsolete rules.

During the visit, the SAB met with the PhD students and the postdocs and listened to their opinions. Overall, they were very satisfied with their working conditions at FIMM. In particular, the international atmosphere, the

collaborative spirit and the support from the Coordinator of Research Training were emphasized.

The SAB was very impressed by the well thought through organization of the graduate training and the establishment of a new postdoc programme, FIMMPOD at FIMM, and with the progress made during the last 2 years. FIMM is a very attractive training site and is actively spreading good practices on the campus and within the University of Helsinki system.

Infrastructures at FIMM

The SAB listened to a presentation of the FIMM Tecnology Center. This included presentations of the IT, DNA sequencing, Genomics, Bioinformatics, Metabolomics, HighThroughput Biomedicine and Molecular Pathology and Imaging Units. The SAB was very impressed by the quality of these essential services. It is obvious that the success of FIMM relies on the outstanding performance of these Units. The SAB had been asked to evaluate the FIMM infrastructure and technology services. We declined to do this because with the establishment of HLSC, this task should be done for the whole life science sector. The task would be to come up with a concept where the life science core facilities are concentrated in the HLSC. Thus, the SAB recommends the Rector of the University of Helsinki to initiate an evaluation of Life Science research infrastructure and core facilities to be able to decide which facilities are essential and which are not e.g. to avoid duplication of scarce resources and weed out obsolete ones.

Assessment of clinical genomics integration at FIMM.

FIMM has as an institutional goal to have an impact in personalized medicine. A number of FIMM faculty (Kallioniemi, Wennerberg, Heckman, and Aittokallio) have developed an excellent moderate throughput cell based drug screening program with a focus on primary cancer cells. The results based on drug response were intriguing and potentially significant. For each cancer, they have also obtained sequence information in terms of exome sequencing and RNA seq on each cancer. However, little of the sequence analysis was discussed. Upon questioning, the junior faculty did not seem to have a clear view as to how this cancer genome data could be integrated with the response data, and seemed to focus on the use of the empirical response output from the AML screens as the major goal.

We believe that the major impact of this platform is to uncover the underlying genetic determinates for drug response and for drug selection. Predictive genomics is an achievable goal if a concerted effort with strategic thinking could be enunciated. Assessing the mutational and expression profiles of the tumors and correlation with response is a first step. As the data accumulates, then genetic models for drug responsiveness can be constructed. The network models by Dr. Aittokallio give a higher order assessment of the affected gene networks. Armed with kind of data, there should be a concerted effort to find genetic principles behind drug tolerance and sensitivity. These principles can be tested experimentally using their cell screening technologies.

Thus far, FIMM has done well to establish the individual experimental platforms, but the construction of predictive models of therapeutic response is still rather nascent. Given the potential of their platform to have such an impact, we recommend that the investigators place more focus on the analysis of the genomic data towards predictive models for drug responsiveness.

Lastly, we also recommend that FIMM look at their sequencing operations to determine whether their protocols are sufficiently reproducible to be utilized in clinical decision making. Genomic sequencing for clinical applications has to have stringent quality control measures that most research laboratories do not embrace. This may lead to misdiagnosis or missed diagnoses. We recommend that FIMM consider CAP (College of American Pathologists) certification for their genomic diagnostic functions.

Participation in teaching

With the establishment of HLSC it will be important to integrate the skills of the FIMM staff in the teaching at all levels in University courses. Both Master and PhD programs would profit from vibrant input from FIMM staff.

Conclusion

Because of the serious funding situation, the University of Helsinki needs to protect its flagships and assure that excellence in the Life Sciences remains the pillar that the University of Helsinki will build on, to move up the ranking ladder of the world's best universities.



Kai Simons
Chair of FIMM SAB