In 2011, at the end of its fourth year of operation, FIMM has grown to an institute with 160 employees representing 27 nationalities, 13 research groups and an annual budget of about 14 M€. Every year since its launch in 2007—2008, the institute has grown at a rate of about 20—30% a year. FIMM is a member of the Nordic EMBL Partnership for Molecular Medicine, signed in 2007 between EMBL and representatives from Finland, Sweden and Norway. We are very thankful to the private foundations whose support made it possible to launch an EMBL partnership institute in Finland. How is the international EMBL model working at FIMM and how will the future look like after the FIMM start-up period, which will soon come to an end? In December 2011, the FIMM stakeholder meeting discussed these issues and challenges at length.

There are many similarities between the operations at FIMM and those of the parent EMBL. FIMM closely follows the EMBL practices for staff turnover, such as recruiting young group leaders globally for rotational 5+4 year contracts. As a unique international institute in Finland, FIMM is committed to attracting global talent at all levels. For example, FIMM PhD students are selected from a global pool of applicants in a major annual selection process, with 1—2% of the applicants accepted each year. All activities at FIMM are reviewed by outside international experts. The research groups at FIMM closely collaborate with one another, and increasingly with their Nordic and EMBL colleagues. Like the parent EMBL, FIMM develops and maintains cutting-edge technologies and infrastructures, including participation in national (Biocenter Finland) and international (ESFRI) infrastructure networks for genomics, bioinformatics, biobanking, chemical biology and translational research.

There are also some differences between operations at FIMM and those at the EMBL. In comparison with the basic research focus at EMBL, progress at FIMM is strongly dependent on local medical infrastructures, such as clinical contacts and expertise, biobanks and associated clinical data, which also take time to build. Fortunately, FIMM is located on the Meilahti Campus, which has been ranked among the top five in Europe in clinical medicine and provides plenty of opportunities for networking as well as access to unique clinical and...
epidemiological samples and data. In contrast to EMBL, which receives most of its funding from member state contributions, FIMM receives a continuously increasing fraction of its funding (now 65%) from project funding, which is often temporary in nature. Indeed, FIMM scientists have been very successful in raising outside support for science and infrastructures from the Academy of Finland, Tekes, EU and others. However, in order to sustain the EMBL partnership, continue pursue global recruitment and attack grand challenges for research, the level of basic funding at FIMM has now become critically important. International talent will not come to Finland based on the opportunity to compete for project funding. We will need to offer internationally competitive recruitment packages and funding, and make use of the brand name and recognition of EMBL. We will need our stakeholders’ continued support to ensure that the international EMBL model will continue to prosper after the first five years.

Overall, as the first five-year period for FIMM will soon come to an end, there has been enthusiastic support for what has been achieved so far. The EMBL partnership has been a cornerstone for the success of FIMM. In 2011, FIMM researchers published 118 papers and the FIMM National Network for Molecular Medicine another 73. FIMM researchers were prominently involved in the top networks in the university-wide evaluation, both in scientific quality and in society impact. We have helped dozens of research groups outside FIMM by offering cutting-edge technology services and built the first state-of-the-art biobank infrastructure in Finland. Most importantly, we have made breakthrough discoveries that are likely to have significant practical significance, such as the discovery of genes for migraine, pubertal growth and the risk of metabolic disorders, genetic risk factor scores for cardiovascular disease, a new gene mutated in leukaemias, personalized medicine approaches for cancer, emerging cellular targets for influenza antiviral agents, mobile microscopy for diagnostics, just to mention a few.

Indeed, this is where molecular medicine is special. We make discoveries which are exciting and of immediate human interest. People increasingly also expect concrete returns from investment in science, and researchers need to be engaged with the grand challenges in society. In the years ahead, we will ensure that benefits of FIMM research will flow to society, in the form of better health care, new diagnostics, treatments and individualized medicine. FIMM has launched grand challenge research programmes in “Finnish genomes and health” and “Individualized cancer treatments” which will pioneer new approaches for health care and medicine. These programmes are based on the unique strengths provided by the four host institutions of FIMM, the University of Helsinki, HUS, THL and VTT. We are also planning to capitalize on opportunities in Finland for collaboration across the different sectors of the society, and propose to place Finland in the global forefront in the adoption of individualized medicine in health care.
FIMM occupies – both physically and operationally – a central position at the “Meilahti Academic Medical Center” of Helsinki. Since the research activities started in 2008, FIMM has grown as a research institute with a distinct role within the academic environment of Finland. It combines knowledge in the rapidly growing field of genomic medicine, infrastructure needed for research utilizing a wide variety of biological samples of a varying nature, and all the prerequisites for pivotal translational research, thus transporting ideas in both ways between the patient’s bed and the laboratory. FIMM complements and reinforces the resources of its most important partners, the Faculty of Medicine and the University Hospital.

FIMM also responds to one of the biggest present-day challenges high level research and education in Finland must face, which is the urgent need for internationalization. As the Finnish node of the EMBL partnership, FIMM has built up a network of contacts with the top-class international research institutes. The Government and Ministry of Education and Culture should carefully consider the designation of a “national special mission” to this unique activity of the University of Helsinki, in order to improve the country’s threatened position in its recruitment of international scholars.

I wish to warmly thank the members of the Board of FIMM, representing many of the stakeholders of the institute, for their altruistic availability and activities toward the development of FIMM during 2011. In addition, I wish to express my sincerest gratitude to the Chair and Members of the Scientific Advisory Board; their continuous and constructive assessment of FIMM is an essential element to maintain its credibility.

Professor Kimmo Kontula, Chair of the Board of FIMM; Vice-Rector of the University of Helsinki

The Scientific Advisory Board (SAB) of FIMM had a meeting in Helsinki on 17 May 2011. Based on the presentations and meetings with the group leaders, postdoctoral researchers and PhD students as well as members of the FIMM National Network for Molecular Medicine, the SAB was impressed by the generally enthusiastic atmosphere within the different groupings of FIMM. Everyone seemed positive about their work and the progress that had been made. The SAB also noted with satisfaction that the research efforts are merging such that links are being formed between the different research groups, creating synergies essential for future success. These are still early days for FIMM but its productivity is already impressive. The level of external funding is also impressive and shows how capable FIMM researchers are in attracting competitive research grants.

Due to the big changes in the Finnish University system in 2010, new issues have arisen with respect to the funding of FIMM. The SAB emphasizes that FIMM indeed should have a role beyond being one research institute within the University of Helsinki framework. The reason for founding FIMM was to establish an international institute for molecular medicine. It is important for the success of FIMM to ensure continuity of the model adopted from EMBL: the young group leaders have 5+4 years before leaving FIMM. Only if this is the case can FIMM continue to attract international staff as it successfully does now. EMBL partnership institutes in Norway and Sweden receive direct support from their governments or the research councils. SAB recommended that discussions should be held between the government, the University of Helsinki and the other stakeholders to guarantee a future for FIMM. Rector Thomas Wilhelmsson of the University hosted the FIMM Stakeholder Meeting in December 2011 and the discussion, which was very positive, will continue in 2012.

Professor Kai Simons, Chair of the Scientific Advisory Board (SAB) of FIMM; Max-Planck-Institute of Molecular Cell Biology and Genetics, Germany
The Nordic EMBL Partnership for Molecular Medicine with Helsinki, Oslo and Umeå was established in 2007. We expect that a Danish node will be established and that it will join the Partnership in 2012. The requirements for EMBL Partnerships are scientific excellence, scientific complementarity to EMBL as well as scientific interaction and common initiatives. In addition, international recruitment, staff turnover system, regular external reviews and training are the core principles of EMBL; these are also followed in its partner institutes. Young group leaders are recruited internationally and they are initially offered posts for a five-year period with a possible extension of four years based on satisfactory performance. With staff turnover comes turnover in expertise and, therefore, renewal and the broadening of the research portfolio.

The Scientific Advisory Committee (SAC) of EMBL stated in its evaluation report in May 2011 that although still in its initial phase, the Nordic EMBL Partnership has developed successful scientific collaborations which attract significant local, national and European funding and has secured dissemination of the successful EMBL operational model and scientific standards. At least ten years of sustainable funding is required to secure scientific continuity and attract top European talents in a highly competitive market.

Professor Iain Mattaj, Director General of European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

The Centre for Molecular Medicine Norway (NCMM) and the Laboratory for Molecular Infection Medicine Sweden (MIMS), which were established in 2007, are young institutes like FIMM. The overall objective of NCMM is to facilitate translation of discoveries in basic medical research into clinical practice with a particular focus on disease mechanisms. There are altogether five NCMM-EMBL research groups and three founding groups at NCMM. At MIMS the molecular mechanisms of infectious diseases are in the research focus areas. MIMS has six full funded EMBL style group leaders and two partially funded MIMS group leaders together with six mentors/founding groups. Therefore, taken together with FIMM statistics, the Nordic EMBL Partnership for Molecular Medicine currently consists of 35 group leaders and a staff about 330.

During the first five-year period of the Nordic EMBL Partnership the three nodes have had joint recruitments for group leaders and PhD students. In addition, all the nodes have recruited postdoctoral researchers and other research staff as well as built up the infrastructure to be shared within the partnership. NCMM and MIMS are both funded by their host Universities (Oslo and Umeå). In addition both NCMM and MIMS receive governmental funding from the Norwegian Research Council and the Swedish Research Council for Infrastructure respectively.

The added value of the Nordic EMBL Partnership, to be completed with a Danish node in 2012 in the field of neurosciences, can be summarized as i) participation in an organised structure for collaboration with EMBL and inside the Nordic member countries; ii) organising a structure to effectively translate discoveries in molecular medicine to clinical practice; iii) capitalising on Nordic and European investments in molecular biology to extent applications to medicine; iv) attracting top international talent and v) educating specialists in molecular medicine, translational research and personalized medicine.

Professor Kjetil Taskén, Director of the Centre for Molecular Medicine Norway (NCMM), Oslo, Norway

Professor Bernt Eric, Director of the Laboratory for Molecular Infection Medicine Sweden (MIMS), Umeå, Sweden
The overall aim of our group is to build towards a more comprehensive understanding of the genomic landscape of common diseases utilizing the special opportunities provided by the Finnish population, the Finnish health care infrastructure and large national sample collections. This improved knowledge should provide us with new tools to develop more individualized health care. The recent development of high throughput genotyping and sequencing techniques has made this a realistic goal.

The unique setting provided by the Finnish infrastructure has stimulated several large whole exome and whole genome sequencing projects, which have organized themselves in a collaborative initiative called SiSu (Sequencing Initiative Suomi). This collaboration includes researchers from FIMM, THL, Lund University, the Broad Institute of MIT and Harvard, Michigan University, UCLA, NIH, Oxford University and the Wellcome Trust Sanger Institute. During 2012 the SiSu project will produce the complete genome or exome (coding areas of the genome) sequence of thousands of Finns. When this is combined with the existing genome wide genotyping (GWA) data from more than 47,000 Finns, we will have a rich resource that can be further expanded and used to facilitate more comprehensive understanding of the genome landscape associated with diseases that are major health burdens to the population.

Our group has a special interest in the genetics of neurological and neurodevelopmental traits. Also much of this work draws on the unique clinical and population-based samples collected from the Finnish founder population. These include such clinical collections as the Finnish Migraine Family sample (collected by Dr Mikko Kallela), the Finnish Schizophrenia family samples (collected by Dr Jouko Lönnqvist) and the Finnish Autism Sample collection (collected by Dr Lennart von Wendt) and such population cohorts as the Finrisk, Helsinki Birth Cohort, Northern Finnish Birth Cohort and Health 2000 cohorts (www.nationalbiobanks.fi). To combine different fields of expertise and to have sufficient power these studies are performed in collaboration with several international groups and high throughput platforms. The wealth of multiple large study samples enables the group to use different study designs for genome variant identification and verification and for the estimation of the size of the effect contributed by the variants. These studies include the UK10K study (www.UK10K.org) and GWA studies of the International Headache Genetics Consortium chaired by Dr Palotie.

Dr Palotie is a faculty member at the Wellcome Trust Sanger Institute in Cambridge UK and a visiting faculty member at the Broad Institute of MIT and Harvard.

**Key publications:**


**External research funding:** Academy of Finland: Center of Excellence and Academy Project; Helsinki Biomedical Graduate Program (HBCP), Sigrid Juselius Foundation, EU-FP7 SYNSYS
The Palmgren group has a strong biostatistics background coupled with more recent efforts to integrate data and the modeling process. Several of the ongoing projects are collaborations between Karolinska Institutet, where Palmgren has her Swedish base, and the FIMM human genomics group.

In 2011, our focus has been on:

1) Characterization of genetic structure. Swedish groups together with the FIMM Human Genomics groups investigated the genetic structure of the Swedish population. Using genome-wide data from more than 5,000 Swedes a strong difference was observed between northern counties compared to the rest of Sweden, challenging the view that the Swedish population is genetically homogenous.

2) Mediation of genetic effects on circulating metabolites. As a part of the work in the human genomics group on characterizing genetic effects on circulating metabolites we have contributed with aspects of how biological and environmental factors can act as mediators. In particular Alfredo Ortega-Alonso has carried out study on the heritability of a wide range of serum metabolites, how differences in sex and body adiposity mediates in the genetic regulation of serum metabolites, and the possibility to disentangle how habitual physical activity jointly with genes affects the development of adverse metabolic profiles. The results have relevance for prevention and treatment of metabolic disorders.

3) Data integration. As part of the SIMBioMS (System for Information Management in BioMedical Studies) project led by Dr Maria Krestyaninova we are pursuing a project to provide integrated information on data availability, facilitating project planning and integration of distributed data sources. This infrastructure project involves scientists across Europe. An ongoing pilot led by Ola Spjuth is to connect health care quality registries with biobanks in cancer research.

4) Integrated data-infrastructure for population biobanks and registries. Triggered by the ongoing revision of the EU Data Directive for personal data we have initiated discussions between THL, CSC and FIMM on integrating biobank data and population and health registers. Building on the revised legislation the ambition is to open up for closer harmonization of procedures within the Nordic countries.

Work will continue on contributing to general data infrastructures as well as more specific modeling tasks in human genetics.

FiDiPro Professor Juni Palmgren is also Professor of Biostatistics at the Department of Mathematics, Stockholm University and Guest Professor of Biostatistics at Karolinska Institutet, Sweden.

Key publications:


External research funding: Biocenter Finland, Swedish Research Council, Swedish eScience Center, SeRC
Unprecedented amounts of new knowledge about the genetic architecture of common complex diseases have been accumulated over the past five years. Cataloguing common genetic variation in large well-phenotyped and population-based biobanks around the world has been the key factor for this success. Finnish cohorts and case-control samples have often been instrumental in these studies. Currently, the biobank samples are going to provide much more precise descriptions of our genomic, transcriptomic, metabolomics, proteomic and other high throughput variations.

Our research group studies these sources of variation and their relation to complex traits and diseases through adapting and further developing biostatistical and computational methods. With particular focus on cardiovascular diseases and metabolism, the aim is i) to identify genes modifying trait variation in populations, ii) to estimate the effect sizes of and joint effects of genes, biomarkers and lifestyle and iii) to predict the risk of future cases of clinical endpoints. To gain sufficient statistical power, the work often calls for national and international collaborations.

In the past year, the group took part in Global Lipid Genetics and ENGAGE consortiums to find genes modifying circulating lipid levels (Teslovich et al 2010; Surakka et al 2011). We also showed that the currently known lipid genes explain a much larger proportion of population level lipid variation in children than in adults (Tikkanen et al 2011).

The work on lipid modifying genes was also extended to the genetic architecture of a broad spectrum of serum metabolites. More than 30 loci were identified and shown to modify metabolite levels. We also showed that many of the previously known lipid loci associate not only with lipoproteins but also with a much more broad range of different metabolites (Kettunen et al 2012, Tukiainen et al 2012).

These studies are now being extended to describe genomic and metabolomic variations in a much greater detail. We are also evaluating how the new genomic and other high-throughput information helps to identify high-risk groups for cardiovascular diseases (Ripatti et al 2010).

Dr Ripatti is also an Honorary Faculty Member at Wellcome Trust Sanger Institute.

**Key publications:**


**External research funding:** Academy of Finland Center of Excellence and Academy Project, Helsinki Graduate School of Biotechnology and Molecular Biology (GSBM), Helsinki Biomedical Graduate Program (HBBGP), EU-FP7: ENGAGE and BioSHaRE
An autoimmune disease is a condition where the immune system mistakenly attacks and destroys healthy body tissue. The cause of most autoimmune diseases is unknown, but both genetic predisposition and environmental triggers are thought to contribute to the development of the diseases. With a typical onset in young adulthood, autoimmune diseases have severe economical and social impacts on the lives of the patients and their families.

Our goal is to improve understanding of the biological pathways and pathogenic mechanisms behind autoimmune diseases, especially multiple sclerosis (MS). We are also implementing and developing novel genomics and bioinformatics methods to investigate both autoimmune diseases and rare diseases with genetic causes. Our strategy is i) to identify predisposing genes for MS by genome-wide (GWA) and fine-mapping analysis of large international cohorts and by utilizing a specific high-risk MS subisolate originating from Southern Ostrobothnia with increased prevalence and familial occurrence of the disease, ii) to characterize the impact of the identified autoimmune disease predisposing variants in Finnish population cohorts, and iii) to implement novel genomics and bioinformatics tools for identifying causative mutations in MS and in rare, inherited diseases.

During 2011 we identified 29 novel MS susceptibility variants in a large international collaboration effort with the IMSGC and the WTCCC2, including nearly 10,000 MS cases from 15 different populations of European descent (IMSGC & WTCCC2, Nature 2011). All except two of the currently confirmed 50 MS loci map within or near genes with immune functions and many of them have been implicated also in other autoimmune diseases, which confirm that the critical disease mechanism in MS is primarily immune dysregulation. In 2011 we also conducted an extensive comparison of commercially available exome capture kits (Sulonen et al, Genome Biol. 2011), and developed a bioinformatics pipeline for NGS genome sequence analysis (Sulonen et al, Genome Biol. 2011) and for CNV analysis from the exome sequence data (EXO-CNV, Sulonen et al. manuscript in preparation) in close collaboration with the FIMM Technology Centre sequencing and bioinformatics units.

Our future research aims at identifying causative genetic variants for MS and rare inherited diseases, and characterizing their function in order to uncover the underlying disease mechanisms. This will allow improved diagnosis of the diseases and potentially offer clues on how to treat these patients.

Dr. Janna Saarela also acts as Research Director of the FIMM Technology Centre.

Key publications:


External research funding: Sigrid Jusélius Foundation, State funding for research to university hospitals (EVO), National Graduate School of Musculoskeletal Disorders and Biomaterials (TBGS), Helsinki Biomedical Graduate Program (HBCP)
Puberty is the last and very important developmental phase during which a child matures into an adult, attains fertility and the capacity to reproduce. Its timing varies quite substantially in the population, both due to mostly unknown genes and the environment. Accumulating epidemiological data suggests a link between early puberty and adult health outcomes, e.g. obesity, Type 2 diabetes, and hormone-dependent cancers, although the mediating mechanisms remain unclear, and the majority of the data are based on studies done only on females.

The goal of our research is to discover and characterize novel critical mechanisms influencing pubertal maturation and growth. The strategy is i) to identify the underlying genes by genome-wide association (GWA) mapping utilizing very large population cohorts with longitudinal growth data, and ii) to characterize their impact on adult health both in Finnish population-based cohorts and in targeted study populations manifesting puberty-associated diseases.

During 2011 we have characterized the link between puberty and adult disease risk, and performed genetic mapping studies to identify novel puberty-associated genes. Using a large Finnish birth cohort, with data on a wide spectrum of adult metabolic risk factors, we carried out detailed studies of the relationship between puberty and adult metabolic health. Our data showed that earlier pubertal timing is associated with adult metabolic syndrome-related derangements both in males and females. We also showed that this association is independent of preceding childhood growth events, thereby emphasizing that mechanisms advancing puberty also may contribute to adult metabolic disorders. To identify puberty-associated genes we lead a large international collaborative GWA meta-analysis project, including as many as 24,000 study subjects of both Finnish and European descent. The meta-analyses are still ongoing, but we have at present identified 10 loci showing significant association and 24 gene regions displaying suggestive evidence for association with pubertal growth. The preliminary analyses also indicate overlapping genetic architecture linking height growth, pubertal timing and childhood adiposity.

Our future research will aim at functional characterization of the genes pinpointed by our GWA study in order to uncover and elucidate the underlying causal pathways. We anticipate that these pathways may more accurately predict puberty-associated outcomes, of which some are health related, than any specific growth event.

**Key publications:**


**External research funding:** Academy of Finland
Making cancer care more individualized is a central aim for cancer researchers worldwide. To a large extent, this is being pursued via DNA sequencing-based efforts. Our focus is on individualized systems medicine, where we attempt to i) integrate genomic and proteomic data, along with tissue imaging and functional drug response data for individual cancer patients, ii) understand how these parameters change during the cancer progression and drug resistance, iii) develop means to guide patient treatments and study how the treatments help or why they fail, thus iv) creating a systems medicine opportunity to build and refine models.

In 2011, we applied drug sensitivity and resistance testing for the identification of novel efficacies of existing and emerging drugs in vitro, such as Disulfiram and Monensin in prostate cancer. We also developed new methods for individualized diagnostics, such as the classification of unknown primary tumours with the help of microarray reference databases (Ojala et al, 2011). We published one of the first next-generation RNA sequencing papers in breast cancer highlighting 24 novel fusion genes (Edgren et al., 2011) and reported on the identification of microRNAs regulating androgen receptor in prostate cancer (Östling et al., 2011). We also published an ultra-high-throughput method for RNAi screening using cell spot microarrays (Rantala et al., 2011).

Our current activities are strongly focusing on individualized medicine, as part of a "grand challenge" programme at FIMM to develop technologies for individualized cancer therapy. Using adult Acute Myeloid Leukaemia (AML) as a key model disease, we aim to: i) pioneer the combination of high-throughput ex-vivo functional drug sensitivity and resistance testing (DSRT) as well as molecular profiling for the identification of effective emerging and targeted drugs for AML, ii) identify molecular mechanisms of drug resistance, and iii) translate these data towards the clinic, for individualized treatment of AML patients. We are also undertaking similar studies in breast and prostate cancer, focusing on understanding drug resistance mechanisms in solid tumors. The complexity of solid tumours obviously provides more challenges for such applications.

The personalized medicine efforts are undertaken together with the groups of Wennberg, Heckman/Knowles, Aittokallio and Lundin, together with key clinical collaborators in haematology, urology, oncology and pathology at HUS as well as bioinformatics collaboration with Professor Samuel Kaski at the Helsinki Institute for Information Technology (HIIT).
Recent key publications:
External research funding: Academy of Finland, Biocentrum Helsinki, Cancer Society of Finland, Sigrid Jusélius Foundation, Helsinki Biomedical Graduate Program (HBGP), and DIANET graduate school, EU-FP7: Systems Microscopy Network of Excellence, Marie Curie Initial Training Network PRO-NEST: Innovative Medicine Initiative: PREDECT, ERDF: Biomarkers
The group is also involved in infrastructure programs: Biocenter Finland: Translational research and genome-wide networks; specifically Drug Discovery and Chemical Biology (DDCB) program, ESFRI programs: EU OpenScreen, BiomedInfra (ELIXIR, BBMRI and EATRIS collaboration), Tekes: Next-generation biobanking
One reason why the genetic basis of disease susceptibility has proven so difficult to identify is due to genetic interactions between genes: mutations that have no discernible individual effect on disease phenotypes may have strong synergistic effects leading to disease when combined. While such epistatic genetic interactions are prevalent and known to be involved in many disease phenotypes, such as in the development of cancers and cardiovascular diseases, they have remained extremely difficult to identify on a global scale because of the vast number of potential interactions and non-linear genotype-phenotype relationships.

Our FIMM-EMBL group was established in August 2011, with a focus on developing network-centric modeling frameworks for predicting and analyzing genetic interactions in the context of large-scale experiments, including i) ‘reverse-genetic’ approaches, in which the function of genes are systematically perturbed using e.g. high-throughput RNAi screening or chemical compounds; and ii) ‘forward-genetic’ approaches, such as genome-wide association or next-generation sequencing studies, where naturally occurring mutations pinpoint the loci that are associated with the trait of interest. Such experimental-computational approaches have the potential to identify key players and their interaction partners in disease networks, as well as to suggest targets for personalized therapies.

During 2011, two specific application cases were initiated: i) Modelling and prediction of synthetic lethal interactions in cancers, where we are applying a top-down modelling approach to predict synthetic lethal partners of individual cancer-causing mutations, the optimal targeting of which holds great promise of being a highly specific and selective means to kill the cancer cells without severe side-effects to normal cells; and ii) Exploring epistatic interactions among genetic loci in cardiovascular diseases and metabolic traits, where we are developing and exploiting computationally efficient statistical and predictive strategies for mining interactions among panels of genetic variants, environmental factors, and underlying pathways, which are most predictive of increased disease risk.

The future plan is to combine the information from the reverse and forward-genetic approaches to provide a more comprehensive view of the molecular mechanisms behind disease processes and system-level responses to genetic and chemical perturbations.

Key publications:

- Heiskanen MA, Aittokallio T. Mining high-throughput screens for cancer drug targets – lessons from yeast chemical-genomic profiling and synthetic lethality. Focus article, Wiley Interdisciplinary Reviews: Data Mining and Knowledge Discovery (in press).

External research funding: Academy of Finland, Biocenter Finland, and the Finnish Funding Agency for Technology and Innovation (Tekes).
Influenza A viruses (IAV) cause significant morbidity and mortality. Different prevention and treatment options (e.g. vaccinations and virus-directed drugs) have been developed. However, these are insufficient in the face of recent IAV epidemics and pandemics. Our mission is to improve human health using a new concept of controlling influenza infections. This concept includes assessment of risk of developing severe diseases in IAV-positive individuals and subsequent treatment of individuals at risk using next-generation antiviral drugs.

Our specific aims are: i) to identify genetic/environmental factors associated with severe forms of influenza infections, utilizing integrative omics profiling and genome sequencing of flu patients and associated IAV strains; ii) to identify and develop next-generation antiviral drugs. These drugs will create a barrier to viral drug resistance by targeting cellular factors that are essential for virus replication.

During 2011, we established a novel method of whole genomes sequencing of influenza isolates from Finnish patients. This method allows routine identification of drug-resistant strains and their attenuated/virulent variants. This method increases the resolution and accuracy of IAV investigations supporting surveillance and outbreak investigations. Towards the second aim, we identified two novel antiviral compounds and their cellular targets, providing an opportunity for future treatment of IAV infections and better understanding of virus-host cell interaction.

Our future focus from 2012 onwards is to launch a project on "Individual susceptibility to severe IAV infections" and continue to evaluate the novel antiviral compounds with in vivo and ex vivo assays, focusing on safety, broad-spectrum efficacy and delivery issues.

**Key Publications:**


**External Funding:** Academy of Finland, CIMO, Helsinki Biomedical Graduate Program (HBGP)
Group Knowles
Personalized Cancer Medicine

Advanced cancer treatment may now include the use of targeted therapies that have been developed to inhibit specific cellular pathways important for cancer cell function. However, in recent years there have been fewer approvals for novel agents largely due to their insufficient efficacy. While these new agents may target previously unmet mechanisms and pathways, the lack of efficacy may not necessarily be due to insufficient effect, but due more to patient and disease heterogeneity.

In order to improve clinical trial outcome and match patients with the correct therapies, it will become essential to better understand the genomic and molecular background of the patient and the disease.

The Personalized Cancer Medicine programme at FIMM is a cooperative study between basic and clinical investigators that uses cutting-edge technologies including next-gen whole genome and exome sequencing, transcriptome sequencing, proteomics and high-throughput drug sensitivity testing to screen clinical samples. Using these platforms, our group focuses on the discovery of biomarkers including novel genetic alterations and understanding their role in disease pathogenesis. We also aim to understand tumour heterogeneity, characterize resistant clones and further develop methodologies to improve our screening platforms. Our group, along with those of Olli Kallioniemi, Krister Wennerberg, Tero Aittokallio and members of the FIMM Technology Centre work in close collaboration with Professor Kimmo Porkka and Dr Satu Mustjoki of the HUS Hematology Clinic and Hematology Research Unit to screen leukaemia patient samples and analyze data from the various platforms, ultimately determining if viable therapeutic options exist for patients who have otherwise failed to respond to conventional therapeutics.

During 2011, samples from 19 leukaemia patients were screened against a comprehensive oncology drug library with half of these analyzed by in-depth genomic and molecular profiling. These initial datasets not only allowed us to find new treatment ideas for these patients (Kontro et al 2010), but also identify important driving mechanisms for disease progression and drug resistance. In addition, exome and RNA sequencing studies led to the discovery of novel recurrent pathogenic mutations in rare leukaemias with previously unknown cause (Koskela et al 2010).

In future efforts, we will expand our study to include more patients focusing on understanding recurrent and resistance disease. Through these studies we will develop more targeted methodologies to follow the disease in the patient and eventually identify new treatment strategies.

Key publications:


External research funding: Tekes, Cancer Society of Finland, Sigrid Jusélius Foundation, Helsinki Biomedical Graduate Program (HBCP)
Breast cancer is the most common malignancy in women. At least four different subtypes of breast cancer can be recognized, among which basal-like breast cancers have the worst prognosis due to the lack of suitable molecular targets for therapeutic intervention.

The goal of our research is to identify essential pathogenic events involved in basal-like breast cancers that could be targeted therapeutically. For this purpose we aim to investigate molecular events associated with genetic mutations known to predispose individuals to basal-like breast cancers and how they contribute to cancer progression and therapy resistance.

During 2011 we evaluated existing therapeutic approaches in a panel of breast cancer cell lines carrying a mutant BRCA1 gene, one of the best known tumour suppressors predisposing to basal-like breast cancers. All these cell lines may be considered as a model of advanced breast cancer as they were resistant to the most common targeted therapeutics - cisplatin and PARP inhibitors. Interestingly, these cells were still sensitive to a well-known drug 6-thioguanine, recently shown to be active against BRCA2-deficient tumours. However, this sensitivity is affected by at least three different factors, which need to be considered before this therapy can be used on patients.

We also generated a mouse model, which showed that loss of Rad51c, another breast cancer predisposition gene, causes a mild differentiation defect in sebaceous glands but does not lead to tumours. Tumour progression required deletion of Rad51c together with p53. We expect that the ongoing gene expression profiling will provide insights into the molecular events underlying cancer progression and point towards possible therapeutic targets.

In the future we plan to identify modifiers of drug response in BRCA1-deficient tumour cells using high throughput siRNA screens. In addition, we will extend our analysis to novel tumour suppressors involved in basal-like breast cancers for which we are developing an in vivo validation system.

**Key publications:**


**External funding:** Academy of Finland, Cancer Society of Finland, Biocenter Finland, Helsinki Biomedical Graduate Program (HBCP), Helsinki Graduate School of Biotechnology and Molecular Biology (G5BM)
Our group develops methods for personalized prediction of disease outcome and image based diagnostics. Genetic and molecular information combined with clinical data using advanced informatics support will help identify patients at risk for disease recurrence and tailor individualized treatment, particularly in cancer. Our goal is to promote implementation of new decision-support technology, as well as improve the flow of information from basic research to the clinic.

We have developed an online risk calculator - “Prognomics” - for personalized prediction of cancer outcome. The calculator is an extension of our previously published “case-match” method and is connected to a database with molecular, as well as clinical and outcome data on more than 5 million cases from 15 countries. Survival estimates can be retrieved for all major cancers and the extensive database allows for estimation of risk even in rare subgroups. The case-match approach is also used for explorative analysis of novel biomarkers and is linked to our image analysis system described below.

The other major research area is image-based diagnostics, with special focus on microscopy images. In collaboration with the Machine Vision Group at the University of Oulu, we are exploring high-throughput computer assisted methods for automated analysis of digitized cancer tissue (breast, prostate and colorectal) and microbiological samples (e.g. malaria).

The webmicroscopy developed by our group (fimm.webmicroscope.net) enables digitization of entire microscope specimens and viewing as well as processing the virtual slides through a web interface. The technology is implemented as a research infrastructure on a national level within Biocenter Finland and on an international level via the EU funded EATRIS. Applications of the technology include analysis and management of tissue microarrays, laboratory quality assurance, consultation and education. The methods are implemented for remote diagnostics within global health in collaboration with Karolinska Institutet, Stockholm.

In 2011 a prognostic tool was developed for sarcoma patients (1) and the case-match method was applied for biomarkers XOR, PROX1 and FOXA1 (2-4). An automated computer vision method for segmenting tumour epithelium from stroma was developed (5) and a study regarding the effect of compression and scaling on automated IHC scorings (6) was published. A nationwide cohort study on breast cancer biological subtypes and metastasis sites (7) and a study concerning long-term prognosis of screen-detected breast cancer were published (8).
**Key publications:**


The aim of our research group is the discovery of new strategies for lung cancer intervention, the leading cause of cancer mortality. Personalised medicine approaches to lung cancer face big challenges: diagnoses are typically made when the disease is already metastatic, and cancer cell populations are notably heterogeneous, complicating molecular profiling. New methods to study the causes of lung cancer and inform the design of novel treatment options are therefore of crucial importance.

Our group studies cell biological and biochemical properties of key genes or pathways commonly altered in human lung disease, focusing on early initiation and metastasis. Our goal is to integrate expertise in both human and functional biology to create versatile mouse cancer models, matched with patient cohorts, for discovery of biomarkers or therapeutically targetable events. As an example, we identified functional inactivation of the EPHA3 receptor tyrosine kinase protein, which is mutated in six per cent of human cancers, and are creating in vivo models to study its physiological role in cancer susceptibility. Our approach uses pathological read-out of disease to comprehensively model complex pathway interplay and heterogeneity, with implications on drug response and drug resistance. We have successfully developed strategies for viral delivery to, and manipulation of, the mouse lung epithelium.

Increasing evidence suggests a crucial role for the cancer microenvironment and immune system in cancer surveillance and therapeutic responses. These are traditionally not accounted for in the drug discovery cascade, potentially explaining why many cancer drugs fail in patients. Within the EU public-private IMI-PREDECT project, coordinated by Emmy Verschuren on the academic side, complex models of the three most common solid tumours are systematically compared, to evaluate responses to inhibition of potential new targets. To this end, our lab has established organotypic lung explant models, enabling measurement of stem cell fate, viability, cell architecture and immune responses. These models also serve as an ultimate in vitro system to systematically validate lung cancer gene and pathway functions. We envision that PREDECT will shift paradigms in the preclinical pharmaceutical pipeline, guiding selection of optimal models representative of patient cohorts.

**Key publications:**


**External research funding:** Helsinki Biomedical Graduate Program (HBGP), CIMO, Marie Curie EU-FP7 IRG: SYSTUMS, FCT Portuguese Science Foundation, Biocenter Finland emerging technologies: LentiGEMM, Innovative Medicines Initiative Joint Undertaking (IMI-JU): PREDECT
Despite a tremendous progress in identifying mutations and genetic aberrations associated with different cancer types and an increasing number of targeted cancer-selective drugs in the clinic, we still lack targeted and safe and effective therapeutic strategies for the majority of cancers.

Our research aims to address the cancer undruggability problem both by screening for personalized and selective sensitivities to approved and investigational among primary cancer samples and cell lines as well as by the development of proof-of-principle small molecule inhibitors of promising novel molecular targets.

In 2011, our group at developed an ex vivo Drug Sensitivity and Resistance Testing (DSRT) platform together with the Chemical Biology Unit that measures the sensitivity of cancer cells to all approved cancer drugs and more than 150 clinically investigated cancer drugs. The platform has been used both on relapsed and AML patient cells and on cancer cell lines. Our clinical collaborators have already used the primary AML DSRT data in their clinical decisions with considerable success. Furthermore, we initiated the development of inhibitors against the MKLP1/MgcRacGAP/Ect2 protein complex and we began exploring a set of metabolic genes that are overexpressed in breast cancers where their expression is correlated with poor clinical outcome, and that are upregulated in response to chemotherapeutic agents.

Looking forward, we will continue to develop novel types of cancer-relevant small molecule inhibitor as well as the DSRT platform: refining the readouts, explore drug combination testing and together with Tero Aittokallio’s group develop analysis tools that allow for the identification of oncogenic driver signals based on the DSRT data and the target specificities of the inhibitors used and most importantly, link DSRT data to biomarkers that will allow clinical translation.

**Key publications:**


**External research funding:** Biocenter Finland, Helsinki Biomedical Graduate Program (HBGP)
Research Highlights

Group Ripatti: Genetic regulation of metabolomic biomarkers – paths to cardiovascular diseases and type 2 diabetes.

In a study of the genetic variances of human metabolism, we have identified 31 regions of the genome that associate with circulating metabolites, i.e., small molecules that take part in various chemical reactions in the human body. Many of the metabolites studied are biomarkers for cardiovascular disease or related disorders, thus the loci uncovered may provide valuable insight into the biological processes leading to common complex diseases.


Group Widén: Molecular mechanisms triggering early puberty may increase risk of metabolic syndrome in adults

Early puberty in females may correlate with increased risk for obesity, and type 2 diabetes, but the mediating mechanisms remain unclear. Utilizing unique longitudinal data from a large Finnish birth cohort we showed that earlier pubertal timing is associated with adult metabolic syndrome-related derangements both in males and females. We also showed that this association is independent of preceding childhood growth events, thereby emphasizing that mechanisms advancing puberty also may contribute to adult metabolic disorders.


Group Ripatti: Complex genetic and metabolic architecture underlies genetic loci affecting serum lipid levels.

We used a comprehensive metabolomic profiling and genotyping to uncover the strikingly complex and heterogeneous basis of the known lipid loci. The results also showed that commonly used laboratory lipid measures do not capture the complexity of the underlying lipoprotein metabolism, showing the advantages of the NMR metabolomics platform utilized in the study.

Group Palotie: A new approach for comprehensive understanding of disease risks associated with genes

Clinical decision making will soon move from a “one fits all” towards more personalized treatment, largely driven by the paradigm change facilitated by genomic and other omics techniques. These techniques provide an opportunity to classify diseases from a new angle. Typically scientists have searched for specific gene variants behind a predetermined phenotype. In contrast, we have developed new techniques to identify all phenotypic features that are overrepresented in individuals with particular genotypes. Such studies are ideally suited for studies of large, well characterized population cohorts, such as the national biobanks in Finland. We can now define subjects based on their genotype and ask what phenotypes are associated. Therefore, we can move from genes to phenotypes instead of the traditional way of using phenotype to define risk genotypes.

The first proof of principal study investigated what phenotypes would be associated with large genomic deletion in an unselected population cohort. We identified all individuals in the Northern Finnish Birth Cohort that had a deletion larger than 500 kb. Individuals carrying such deletions had an overrepresentation of neurodevelopmental related traits such as cognitive- and hearing impairments and poor school performance.


Group Kainov: New approaches towards combating deadly influenza epidemics

Our research is focusing on developing future personalized strategies for treatment of infection diseases. We have summarized current knowledge on influenza virus (IAV) replication, focusing on emerging cellular drug targets. Recent advances in understanding of IAV replication have revealed a number of cellular drug targets that counteract viral drug resistance. For many of these targets, compound safety testing in humans is available. Some of these compounds may be beneficial for the clinical therapy, especially in the case of severe infections, drug-resistant IAV strains and epidemics.

Group Palotie: Genome-wide association study reveals three susceptibility loci for common migraine in the general population.

We expanded our understanding of genes associated with the most common neurological trait migraine. We identified three gene regions associated to migraine in a population cohort, which represent a very different ascertainment than headache patients drawn from speciality clinics. These gene regions suggest both pain and glutamate pathways to be involved in migraine susceptibility.


Group Kallioniemi: miRNAs regulate the androgen receptor expression and provide potential therapeutic approaches to inhibit androgen-dependent growth of prostate cancer cells.

Despite the continuously increasing detection of small early-stage prostate cancers by PSA screening, the mortality associated with the disease has remained relatively stable. Androgen receptor signaling remains the central target of therapy for prostate cancer. Here, we show that expression of specific miRNAs provides a means to inhibit AR function in human prostate cancer and provide evidence of a previously unanticipated network structure regulating the AR at the post-transcriptional stage. Furthermore, the study highlights the role of UTRs in the regulation of gene activity.


Group Saarela: Genetic risk and a primary role for cell-mediated immune mechanisms in multiple sclerosis

FIMM researchers were involved in a large collaborative genome-wide association analysis with the International MS Genetics Consortium and the Wellcome Trust Case Control Consortium 2. This study involved almost 10,000 cases of European descent from 15 different countries. We identified 29 novel regions of the genome that associate with MS disease. We also confirmed the previously identified 20 loci. All except two of the loci mapped closest to an immunologically relevant gene. The results implicate T-helper-cell differentiation in the pathogenesis of multiple sclerosis.

Group Lundin: Identification of tumor epithelium and stroma in tissue microarrays using texture analysis

The aim was to assess whether texture analysis is feasible for automated identification of epithelium and stroma in digitized tumor tissue microarrays (TMAs). The results illustrate the capability of automated segmentation of epithelial and stromal tissue (accuracy 0.995; CI95% 0.991-0.998) in TMAs based on texture features and an SVM classifier. Applications include tissue specific assessment of gene and protein expression, as well as computerized analysis of the tumor microenvironment.


Group Lundin: Big size multitouch displays turned into microscopes

Researchers at the Institute for Molecular Medicine Finland (FIMM) have in collaboration with the Finnish company Multitouch Ltd created a hand and finger gesture controlled microscope. The method is a combination between two technologies: web-based virtual microscopy and giant size multitouch displays. The result is an entirely new way of performing microscopy: by touching a table- or even wall-sized screen the user can navigate and zoom within a microscope sample in the same way as in a conventional microscope. Using the touch control it is possible to move from the natural size of the sample to a 1000-fold magnification.

Biological samples are digitized using a microscopy scanner and stored on an image server. Samples displayed on the screen are then continuously read from a remote image server over the Internet and the size of a single sample can be more than 200 gigabytes.

The developers think that the method will revolutionize the way microscopy is being performed and the learning curve for using the multitouch microscope is practically zero. Microscopy at the same time changes from a private, single-user experience, to something social where groups of people can view, examine and learn from a same sample simultaneously.
**GRAND CHALLENGES**

FIMM research groups, Technology Centre and Biobank working together to solve major questions of importance to the society

**Finnish Genomes and the Future Health Care**
Palotie, Ripatti, Biobank, Technology Centre together with researchers at THL

Finland has a unique opportunity to make use of the national biobanks, specifically the unique THL collection of 200,000 DNA samples from the general population, not only to discover genes for diseases (as has been successfully done in the past 20 years), but to generate an important resource to guide health care decisions, and to enable intelligent targeted monitoring of health in people according to their individualized risk of diseases. This grand challenge project is therefore planning to genotype and eventually sequence, all the 200,000 DNA samples and connect this massive amount of data on the complete genetic variation with the excellent long term follow-up and health data. 8000 Finnish genomes will already be sequenced by the end of 2012, which forms a strong starting point for the project.

**Systems Medicine for Individualized Therapy of the Cancer Patients**
Wennerberg, Heckman/Knowles, Kallioniemi, Aittokallio, Lundin groups, Biobank and the Technology Centre, and clinical collaborators at HUCH

This project advances the major unmet needs in the society for (i) better and more efficient treatments for cancer patients by the individualized combination of new targeted drugs, for (ii) the health care system to better individually optimize cancer treatments and for (ii) the global industry to derisk and clinically introduce new drugs to specific molecularly identified patient subgroups. The individualized systems medicine (ISM) project is a key clinical and translational study at the University of Helsinki, carried out in collaboration between FIMM, HUCH, along with national and international collaborators, both in the academia and in the industry. The unique part of the program is our Drug Sensitivity and Resistance Testing (DSRT) technology that has been developed at the Institute for Molecular Medicine Finland (FIMM) and piloted in Acute Myeloid Leukaemia (AML) diagnostics at the Helsinki University Central Hospital, Division of Hematology (HUCH). DSRT has already delivered groundbreaking results, especially when combined with other novel diagnostic modalities, such as next-generation sequencing (NGS).
DOCTORAL TRAINING

Research training continued to grow at FIMM during 2011. Several new PhD students joined FIMM research groups, bringing the total number of doctoral students at FIMM to over 40, with approximately 40% international students and 60% Finnish students. In the autumn, FIMM celebrated the admission of many of these new students into Finnish doctoral programmes including the Helsinki Biomedical Graduate Program (HBGP), the National Doctoral Programme of Advanced Diagnostic Technologies and Applications (DIA-NET), and FinPharma Doctoral Programme (FPDP).

The year 2011 was the second year of the FIMM-EMBL International PhD Training Initiative, bringing two new outstanding doctoral students to the institute. Naga Poojitha Kota Venkata and Himanshu Chheda, both from India, were selected from a strong and large international applicant pool. These two successful candidates represent only 1% of the total applicant pool. Poojitha and Himanshu joined FIMM in late August and after a few days of orientation began their first research rotation. All of the FIMM-EMBL PhD students participated in the EMBL International PhD Symposium, an annual training session at the EMBL (Heidelberg, Germany), in November 2011.

The rigorous FIMM-EMBL recruitment began with an international call announced jointly with NCMM and MIMS in early 2011. Students selected through the institute level evaluation process spend the first 6—9 months engaged in research rotations with the aims of diversifying individual research training and building connections within FIMM. At the end of the rotational period, students then select a research group, in mutual agreement with the group leader, in which to complete their PhD studies. Based on the continued success of this training plan, a third joint call was initiated at the end of 2011.

In addition to the FIMM-EMBL PhD training initiative, FIMM was engaged in several other aspects of doctoral training. For example, the EU FP7 Marie Curie Initial Training Network (ITN) PRO-NEST continued and a new ITN proposal was filed in late 2011. In addition, through the Biocenter Finland International Visitor Program, FIMM recruited several doctoral students and postdoctoral researchers from abroad to drive research activities in eight different groups at FIMM.
FIMM researchers offered several courses and lectures for doctoral and masters students, including courses in chemical biology, functional genomics, disease genomics, next generation sequencing, and cancer. There are future plans for multiple courses on topics such as molecular and personalized medicine, DNA repair, molecular pathology and imaging, biostatistics, and biobanking to be developed and offered in the upcoming year.

FIMM joined the EU-, Finnish-, and City of Helsinki-funded PhDs to Business Life project coordinated by Culminatum Innovation, Ltd. This project aims to train PhD students and postdoctoral researchers in business principles, career coaching, and project management with the ultimate goals of enhancing collaborations between doctoral programmes and business as well as readying doctoral students for careers in industry.

FIMM Scientific Coffee Breaks are arranged twice a month. Students, postdoctoral researchers, as well as senior researchers and group leaders present their work for FIMM staff.

Finally, FIMM celebrated the completion of the two doctoral dissertations in 2011 at the University of Helsinki:

**Anu Kemppinen:**
"Studies on Causes of Multiple Sclerosis: From Genes to Transcriptome" Supervisors: Leena Peltonen-Palotie and Janna Saarela

**Sami Kilpinen:**
"Studies of the Human Transcriptome" Supervisor: Olli Kallioniemi

In addition, the following dissertations were completed at the University of Turku and VTT Technical Research Centre of Finland:

**Santosh K. Gupta:**
"Functional Study of Oncogenic Transcription Factor ERG and its Signaling in Prostate Cancer" (supervised by Olli Kallioniemi)

**Juha K. Rantala:**
"A cell spot microarray method for high-throughput biology" (supervised by Olli Kallioniemi and Johanna Ivaska)

**Paula Vainio:**
"High-Throughput Screening for Novel Prostate Cancer Drug Targets – Getting Personal" (supervised by Kristiina Iljin and Olli Kallioniemi)

**Kirsi Ketola:**
"Chemical Biology Screen for Prostate Cancer Therapeutics" (supervised by Kristiina Iljin and Olli Kallioniemi)
Technology Centre

Research Director Janna Saarela

Overview

The FIMM Technology Centre is a national and international research core unit providing an extensive spectrum of biomedical research services. FIMM Technology Centre operates seven core units with a total of 41 technology experts from diverse educational backgrounds being involved in the operations. Technology Centre develops methods and offers services in the areas of genomics (sequencing, genotyping, expression, methylation and CNV profiling), high throughput screening (chemical compounds, approved drugs, and siRNA), bioinformatics and IT services using state-of-the-art technologies. During 2011 we also started setting up metabolomics and translational research (serum and oligonucleotide arrays) technologies. FIMM Technology Centre operates in close collaboration with the Biocenter Finland infrastructure networks and is strongly involved in the European Research Infrastructure (ESFRI) networks.

In 2011 we completed altogether over 150 projects serving or collaborating with tens of research groups from over 10 national and international universities and research institutes, including all Biocenter Finland universities, as well as from a few companies. Technology Centre played a key role in the development of personalized medicine activities at FIMM by setting up fast-track services for exome, transcriptome and drug sensitivity and resistance profiling of leukemia samples. Further development of clinical profiling services and efficient integration of the comprehensive profiling data will be our next major challenges.

<table>
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<tr>
<th>Services</th>
<th>Samples/Cell lines</th>
<th>User Groups</th>
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<tr>
<td>Genome sequencing</td>
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<tr>
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<tr>
<td>Custom targeted sequencing</td>
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<td>Amplicon sequencing</td>
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<td>Targeted SNP genotyping</td>
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<tr>
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<tr>
<td><strong>High through-put screening</strong></td>
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<tr>
<td>siRNA screens</td>
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<tr>
<td>Chemical screens</td>
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<tr>
<td>Drug sensitivity and resistance screens</td>
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<td><strong>Bioinformatics</strong></td>
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<td>RNA seq analyses</td>
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<tr>
<td><strong>Translational research</strong></td>
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<td></td>
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<tr>
<td>Serum printing</td>
<td>18 000</td>
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The Genomics Unit of the FIMM Technology Centre is the only nationwide centre that offers high-throughput genotyping, gene expression, and DNA methylation analysis services in Finland. These services were provided on several platforms in year 2011: Illumina’s iScan and BeadStation, Sequenom MassArray, Roche Light Cycler 480, Affymetrix GeneChip, and ABI 3730XL. The Unit produced approximately 572 million genotypes or gene expression and methylation analysis results this year for over 21 000 DNA or RNA samples. This included whole genome SNP genotyping with nine different microarray types, fine mapping genotyping with three platforms, and gene expression analysis of three different organisms. Our first custom DNA methylation project was also performed. As a new service for year 2011 we provided genotyping for cell line authentication. The genotyping unit was involved in nearly 70 service and/or collaborative projects from eight national and three international universities or other research institutes, as well as one commercial customer. In addition to high quality and high-throughput laboratory services, the Genomics Unit offered expertise in project planning, data handling, and analysis. The focus in our internal development was placed on further strengthening our database tools and management of laboratory processes. Besides research collaborations, the staff of the Genomics Unit is also active in their own research projects, especially on genetics of complex traits, including e.g. migraine and genetic structure of populations.

**Personnel:**
Contact Person, Senior Researcher: Päivi Lahermo
Postdoctoral Researcher: Mari Kaunisto
Senior Laboratory Technicians: Sirkka Ekström, Anni Korvenpää, Anu Yliperttula
Research Assistant: Mikko Siurala (until December 2011)

**Statistics on 2011 services**
- No of genotypes or expression/methylation data points produced: 572 million
- No of samples genotyped with Genome-wide SNP arrays: 992
- No of samples genotyped with targeted SNP assay: 20,093
- No of samples profiled with genome wide expression arrays: 174
- No of cell line genotyped for identification: 2

**Services provided by the Genomics Unit**
- targeted and genome-wide SNP genotyping
- targeted and genome-wide microsatellite genotyping
- expression profiling on microarrays
- targeted and genome-wide methylation profiling
- cell line authentication

**Publications utilizing genomics services in 2011:**


Sequencing Unit

The Sequencing Unit is a national and international service provider for next generation sequencing (NGS) and capillary sequencing services. The Sequencing Unit has been operating in the NGS field with Illumina sequencing-by-synthesis technology since early 2008. The Unit receives support from Biocenter Finland as a part of the Genome-Wide Methods network and participates in EATRIS, The European Advanced Translational Research Infrastructure in Medicine, activities. Year 2011 was once again an era of rapid growth and development in terms of personnel, technology, capacity and number of scientific projects. Sequencing unit successfully recruited three professionals to better respond to the demands of the scientific community.

During March 2011 the Sequencing Unit moved to new lab facilities. As a part of the move sequencing capacity was upgraded through installation of Illumina HiSeq2000 platform. Platform was rapidly adapted to laboratory’s workflow. HiSeq2000 platform is capable of producing sequence data in genome scale volumes. Since March 2011 over 4.4 Terabases of sequence data could be obtained, equivalent to amount of sequence of about 1 460 human genomes, was produced for scientific projects with NGS platforms. In addition, we operate a capillary sequencing service, where request increased by 24 % exceeding 200 000 capillary sequencing reactions per year.

Altogether 51 new service projects were initiated (+45 %) and a total of 914 libraries were processed (+228 %) for various applications. The most used services were exome analysis (n=286) and custom targeted genome sequencing (n=325). Transcriptome sequencing services were set up at first quarter of the year and gained immediate interest (n=116). Bioinformatics analysis pipelines were further developed in collaboration with the Bioinformatics Unit and research groups towards more in-depth analysis of structural and copy number variation of the genome and Sequencing unit’s research collaboration with its clientele lead to a highly accessible publication comparing available exome sequencing methods. Scientists of the sequencing unit were co-authors in four peer reviewed articles during 2011.

The Sequencing Unit played also an important role in the development of personalized medicine activities in FIMM by setting up fast-track services for PM projects and processing 48 exomes and 27 transcriptomes for molecular profiling of leukaemia patients. Additionally a new development was launched towards ultra-deep amplicon sequencing where the goal is to validate low quantity somatic mutations, provide disease marker follow up tool and enable the study of clonal evolution in cancers. Growing interest towards clinical sequencing has led to initiation of several studies where exome sequencing will be used to identify causative mutation in cases where the genetic basis of the disease is unclear.

Publications, where the sequencing unit contributed:


Contact Person, Head of Laboratory: Pekka Ellonen
Senior Researcher: Pirkko Mattila
Senior Laboratory Technicians: Maija Leppistö, Sari Hannula, Sonja Langström
Laboratory Analysts: Tiilni Hannunen, Anna Kossila, Aino Palva.

Statistics on 2011 services

Amount of sequence produced: >4.4 Terabases
No of genome sequenced samples: 35
No of exome sequenced samples: 286
No of custom targeted samples sequenced: 325
No of sequenced transcriptomes: 116
No of amplicon sequenced samples: 81

Services provided by the Sequencing unit

- Targeted re-sequencing (exomes, custom targets)
- Transcriptome sequencing (RNA-seq, small RNA-seq)
- Genomic sequencing
- Ultra-deep amplicon sequencing
- Metagenomics
- Capillary sequencing, fragment analysis

Personnel:

Contact Person, Head of Laboratory: Pekka Ellonen
Senior Researcher: Pirkko Mattila
Senior Laboratory Technicians: Maija Leppistö, Sari Hannula, Sonja Langström
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- Transcriptome sequencing (RNA-seq, small RNA-seq)
- Genomic sequencing
- Ultra-deep amplicon sequencing
- Metagenomics
- Capillary sequencing, fragment analysis
The main goal of the FIMM Technology Centre RNAi Unit is to facilitate the application of high-throughput screening approaches, primarily small interfering RNA (siRNA) screening, to basic biomedical research by providing up-to-date instrumentation and adequate expertise to the research community. The RNAi Unit receives support from Biocenter Finland as a part of the “Genome-Wide Methods” network.

The RNAi Unit maintains a genome-wide collection of siRNAs and houses instruments needed to process a large amount of samples in high-throughput fashion. Our platforms include both plate-based and cell-spot microarray-based screening, currently enabling screens of targeted libraries. We are constantly developing our platforms to enable genome-wide siRNA screening. We support both plate reader assays and high-content microscopy. We also provide expertise in assay development and optimization, and are further developing our image and data analysis capabilities.

Besides siRNA screening, we also offer array printing services, such as serum and oligonucleotide array printing. A pilot project to set up serum microarrays was initiated in 2011.

During the year 2011, the Unit became fully operational. Altogether six projects were initiated and transfection conditions of 10 cell lines were optimized. Our first screening project with 2688 siRNAs on the 384 well-platform was completed. Most of the initiated screens were solely siRNA screens whereas a few were combining siRNAs and drugs in a screen. Three serum printing projects were completed during the past year including over 18000 serum samples in total.

Two new senior researchers were recruited to the RNAi Unit in 2011, bringing with them expertise on cell biology, imaging, miRNA and protein lysate array screening. We also continued developing new technologies for the unit. The first microRNA screens were initiated already during year 2011 whereas development of the protein lysate microarray platform has just begun.
Chemical Biology Unit

Chemical Biology Unit of the Technology Centre is focused on assay development and high throughput screening in plate-based formats. It is designed to operate as a local, national and eventually as an international research infrastructure. The Chemical Biology unit receives support from Biocenter Finland for and coordinates the “Drug Discovery and Chemical Biology” platform of the national Translational Technologies research infrastructure platform and participates as the Finnish partner in the preparatory phase of EU-OPENSCREEN, a European strategic research infrastructure initiative that aims at building up a pan-European open access chemical biology research infrastructure.

The Unit provides screening services of many types, including molecular probe discovery, screening of large chemically diverse libraries, biological profiling screening using libraries of known bioactives, drug repositioning and personalized medicine screening using approved and investigational drugs, and combining compound screening with genetic screens using siRNA libraries. The Unit manages two screening laboratories, one self-service facility that contains the equipment to perform small chemical and genetic screens on a largely manual basis and one fully automated state-of-the-art HTS system that can process more than 100,000 data points per day. Both facilities are set up to handle cell-based and biochemical screens. To support the use of the screening facilities, the Unit maintains a chemical collection of 120,000 compounds and together with the RNAi Unit, a genome-wide collection of siRNAs.

In 2011, the Unit handled a wide array of projects all the way from small-scale cherry-picking of a handful of compounds for directed screens, up to screening of tens of thousands of compounds in a day. A total of 93 screens in 16 different user-driven projects were handled. An important direction the Unit took was to work very actively within the personalized medicine program and run more than 80 oncology compound screens on both patient samples and cancer cell lines. Several combined chemical and siRNA-based screens were initiated together with the RNAi Unit and the establishment of a system for distributing small-scale amounts of bioactive compounds to researchers in Finland was begun.

Statistics on 2011 services
No of data points produced: XXXXX
No of chemical screens completed: 7
No of drug sensitivity and resistance screens completed: 84

Services provided by the Chemical biology unit:
- Maintenance, support and user training for High Throughput Centre 1 in BMH 1
- HTS assay development and optimization
- High throughput screening in 96-, 384 and 1536-well formats
- DSRT and other small molecule bioprofiling screens
- Virtual screening and follow-up confirmatory screening together with collaborators in national DDCB network
- Batch as well as custom compound and siRNA delivery in assay plates
- Development and running of nanoliter scale bioassays with the Labcyte Echo
- Distribution of proof of concept scale bioactive compound aliquots
- Providing assay plates and HTS reagents in small scales at big batch prices as well as batch-controlled FBS for researchers at FIMM
The Metabolomics Unit of the Technology Centre focuses on targeted quantitative analyses of endogenous metabolites in a high throughput manner. A list of different classes of metabolites that will be targeted by the analysis includes sugars, nucleotides, nucleosides, nucleobases, organic compounds, bile acids, amino acids, central carbon metabolites, TCA cycle, urea cycle, and neurotransmitter metabolic intermediates, enzyme cofactors, etc. During 2011 all the available information about these metabolites was retrieved from the Human Metabolome Database (HMDB, www.hmdb.ca) and collected into an in-house developed database covering the details of HMDB ID, chemical formula, molecular weight, structure, CAS, KEGG, METLIN & pubchem IDs, water solubility, concentration ranges etc for about 150 polar metabolites.

A Waters Xevo TQ-S triple quadrupole mass spectrometer (UPLC-MS/MS system) used in the analysis was installed in 2011. Further, an analytical method for the extraction of most of the endogenous polar metabolites was developed. It includes fast and simple preparation techniques (protein precipitation), separation of a mixture of basic, neutral and acidic molecules within a single chromatographic run (Hydrophilic interaction liquid chromatography, Hilic separation) and short run times (15 minutes/run, i.e., 96 samples in 24 h). A pilot study with human plasma samples was run in December 2011 to assess the performance of the developed method. Sample extraction method for the rest (1/3rd) of the compounds is still being developed and optimized.

We also acquired a liquid handling platform, MicroLab Star, from Hamilton in 2011. The currently developed sample extraction protocol has been programmed into the software and already successfully implemented. The liquid handling system is also used to make serial dilutions of pure compounds for calibration curves.
Bioinformatics and IT Unit

Information and communication systems are as vital an infrastructure as heating, plumbing, ventilation and electrical systems for a biomedical research institute - hardly appreciated when working as intended but causing misery and suffering when not. FIMM has continued investing in both equipment as well as the people to implement solutions to make modern science happen.

FIMM’s computing infrastructure has been designed for scalability and flexibility utilizing the latest virtualization and scale-out storage technologies, to enable us to meet the rapidly increasing capacity and performance demands of data-intensive research. In 2011, we expanded the capacity of the EMC CX4-480 storage system by 60TB. That and the additional 20TB storage pool hosted at CSC-IT Center for Science Ltd. increased the total storage capacity by roughly 35% in 2011 (30% growth in 2010 and 2009).

During 2011 FIMM’s computing cluster, partly hosted at CSC, was also expanded by 20% to 1200 processors and the total amount of computation done in the cluster was 570 cpu years ($5 million cpu hours). In addition to the cluster the IT infrastructure of FIMM consists of more than hundred virtual and physical servers hosting various bioinformatics applications and databases. In December we further installed an experimental fast 1.2TB flash memory file system to facilitate reading and writing of large amounts of data.

Bioinformatics and data management activities served mainly the needs of the users of FIMM’s largest data producers next generation sequencing (NGS) and genotyping units. The most often used analysis in 2011 was sequence variant identification and annotation in the context of the universal reference sequence. This was performed on 497 samples from 29 research groups. We also have tools for identifying possible disease causing mutations by comparing the genome sequences of affected individuals and healthy relatives as well as for comparing sequences from tumor tissue and normal tissue from the same individual. This analysis was performed on 217 samples from 9 research groups. All of these tools have also been used to analyse NGS data from patients with the aim to understand, and help clinicians to treat, their disease better.

In the next year, we will streamline and further automate our NGS pipelines so that they can be applied with minimal human intervention and be executed fast. We will also refine the output. On one hand we will have to add more in-depth information to the variants identified for the researcher or physician to be able to better and more easily evaluate the significance of the findings and how to use them. On the other hand we need to remove (or hide) the information that just clutters the reports and causes more confusion than helps. We can only achieve these improvements by working closely with our clients, listening their feedback and understanding their needs.

During 2011 the unit received support from Biocenter Finland as part of the nationwide bioinformatics network as well as from the Academy of Finland to the build-up phase of the EATRIS translational research infrastructure in Finland.
Statistics on 2011 services
No of genome sequence analyses completed: 497
No of transcriptome analyses completed: 79

Services provided by the Bioinformatics and IT units
- Variant calling and annotation
- Comparative variant identification from cases and controls, e.g. affected and healthy relatives or tumor and normal tissue
- Gene expression quantification from RNA sequence data
- Identification of fusion transcripts from RNA sequence data
- Server and application hosting
- High performance computing and bioinformatics environment
- End-user support for the computing cluster and bioinformatics applications
- Custom software development

Publications utilizing bioinformatics services:


Biobanks of human biological samples with associated medical data represent a vital resource in unraveling the etiology of diseases, identification and validation of new diagnostic methods as well as advancing personalized medicine. Biobanking can bridge basic, translational and clinical research, life-science industry, and help in the assessment of health care outcomes and efficiency. Today, biobanking is not only about collecting and storing samples. It is all about building a comprehensive and systematic approach to managing samples, patient data and data generated by deep molecular profiling.

Finnish researchers have been in the global front-line in the application of biobanks for decades. Especially the Meilahti campus is in the position to benefit from the largest patient pool in Finland, as well as decades long tradition and experience in collecting both clinical and population sample cohorts. For example, the DNA sample archives of the National Institute for Health and Welfare (THL), FIMM partner institution on the Meilahti campus, cover samples from >200,000 individuals, all linked with detailed demographic and comprehensive long-term follow-up information (www.nationalbiobanks.fi).

Meilahti Integrated Biobank Infrastructure (MIBI): A leading national centre for next-generation biobanking

In 2009—2011, FIMM and THL joined forces with other stakeholders (HUCH, HUSLAB) on the campus to create a state-of-the-art biobanking facility, the Meilahti Integrated Biobanking Infrastructure (MIBI). FIMM and THL also serve as the coordinating node for the national BBMRI biobanking infrastructure in Finland.

Already, MIBI can currently provide access to samples from nearly 200,000 subjects (see tables below), and has a capacity to store over a million more. As described below, new prospective clinical biobanking projects were launched in 2011. The MIBI infrastructure also provides several capabilities for sample processing and analysis by state-of-the-art technologies, such as exosome isolation, iPS cell preparation, sample microarrays, multi-spectral imaging for molecular pathology, web microscopy, clinical informatics and databases.

Contact at FIMM:
Head of Development: Kimmo Pitkänen
Research Director: Johan Lundin
Research Director: Janna Saarela

Contact at THL:
Head of Public Health Genomics Unit (THL), Senior Scientist (FIMM): Anu Jalanko

FIMM personnel:
Project Coordinator: Tiina Vesterinen
Laboratory Engineer: Niina Eklund
IT specialist: Askar Ibragimov
Senior Laboratory Technicians: Siv Knaappila, Minna Suvela
IT Designer: Timo Miettinen
Senior Researchers: Juha Muli, Kaisa Silander
Bioinformatician: Teemu Perheentupa
Information Systems Specialist: Kyösti Sutinen
Systems Analyst: Hannu Turunen

THL personnel:
Head of Laboratory: Päivi Laiho
Senior Scientist: Aija Kyttälä
Systems architect: Markku Laukkanen
Research Technicians: Sini Lähteenmäki, Eilina Mäkinen, Anne Nyberg, Seija Puomilahti
Laboratory Coordinator: Minttu Saaristo, Tuuli Sistonen
Research Technician: Arja Terola, Regis Wong, Anne Vikman
Integrated full-service biobanking

A wide range of biobanking related capabilities has been set up in close collaboration with FIMM Technology Centre and the Translational unit of FIMM.

MIBI experts can offer consultation help on how to build a biobank (ethical, consent, legal, technological, informatics, funding and scientific advice) as well as give an overview of the wide technological capabilities that can make use of the sample collection projects.

Sample storage services

MIBI has a liquid nitrogen based sample storage facility which provides secure and controlled storage of samples in liquid nitrogen vapor phase. In 2011, the system was expanded with one additional freezer tank and currently has the capacity to store 480,000 samples with a capacity upgrade available to 1.7 million.

The LN2 based sample storage is available to all research groups on the campus and elsewhere. Over 180,000 samples were stored in the facility during 2011.

Automated DNA, RNA and protein extraction and aliquoting

MIBI offers automated DNA extraction service from whole blood, buffy coats, cell and tissue samples, saliva and buccal swabs, as well as automated DNA aliquoting including normalization and quality control. During 2012, we will also implement automatic RNA extraction and set up protein extraction methods for tissue samples. High-quality sample logistics is guaranteed by SamWise database/LIMS system specifically developed in-house for biobanking.

Towards full automated next-gen sample management

In 2011 MIBI performed a tendering process for a fully automated sample storage and retrieval system for “cherry picking” and processing of samples. The sample automation line will be completed with -20C and -80C storage modules with a capacity to store 200,000 samples (in 0.5 ml vials). The system will be fully operational in 2012 and will facilitate sample logistics of large biobanking projects.

Contact for automated sample storage and management services:

Head of Laboratory: Päivi Laiho

Biobank informatics

Biobanking informatics provides a range of critical services to facilitate biobank activities, from standardized annotation ontologies, to methods for handling large, multidimensional datasets. Biobank integration brings along the deep challenge of managing the sensitive nature of the data at the individual level. The IT group at FIMM is building a national biobanking IT infrastructure as part of the BBMRI.FI network, with THL, hospital districts and CSC. This infrastructure will pool national sample data and facilitate information on their availability for research. The data management group has also been working on harmonizing THL’s population cohorts like Finrisk studies, containing hundreds of variables.

Services:
- Development of in-house software for biobanks, research programs and consortia.
- Database services for hosting, management and curation of clinical and research data associated with biobanks.
- Data collection and federation services for research programs across multiple institutions.

Contact:
Senior Researcher: Juha Muilu
Tissue biobanking, molecular pathology and imaging services

Tissue processing, histology and immunohistochemistry:

FIMM molecular pathology laboratory provides routine services for tissue embedding, sectioning, immunohistochemical staining, quantification and analysis.

Complete Tissue Microarray (TMA) workflow

Tissue microarray technology (TMA) allows simultaneous analysis of large number of cases under standardized laboratory and evaluation conditions without significant damage to the original tissue block. The TMA and molecular pathology services can be coupled with digital microscopy and image analysis.

The image analysis facility provides brightfield scanning of slides and the WebMicroscope platform to researchers, as well as the new multi-spectral microscopy imaging platform. Multi-spectral microscopy is used for imaging several different markers in the same tissue slide. Images of formalin-fixed paraffin-embedded tissue stained with multiple antibodies can be acquired to provide substantially more information on the heterogenous nature of the cancer tissue. Both conventional chromogenic and fluorescent staining approaches are being used for multicolor tissue staining.

Services:

– Designing and preparation of TMA blocks from paraffin embedded tissues
– Sectioning of TMA and other paraffin embedded tissue blocks
– Staining of the sectioned slides histochemically and/or by using immunohistochemical techniques

Microscopy sample digitization:

Whole slide tissue samples and TMAs can be digitized with an automated high capacity microscopy scanner. The scanner captures images at high magnification (resolution approx. 0.25 micrometer) and generates a gigapixel-sized digital copy of the microscopy sample.

Webmicroscopy:

Scanned whole-slide images are automatically transferred to a digital whole-slide management platform (fimm.webmicroscope.net). The scanned images are accessible for web-based viewing, annotation and processing with image analysis algorithms using a standard web browser interface. The webmicroscope platform allows research groups to have password protected accounts with project specific digital slide series. Digitized slides can be shared with other users or become part of a common tissue image repository according to agreement with the researchers.

Visual and automated microscopy image analysis:

The webmicroscope platform allows tissue and cell samples to be assessed visually and results can be entered by the use of a graphical user interface into a database. Tissue spots in a TMA can be linked to corresponding clinical data and displayed one at a time for visual scoring. Results of both visual and automated analysis are stored on a web server or downloaded by the user in a spreadsheet format.

Custom image analysis development: Custom image analysis algorithms can be developed to perform automated tissue and cell segmentation, staining quantification (IHC, FISH) and quantitative microscopy in general.

Clinical informatics and online statistical tools:

Clinical and phenotypic data related to tissue and cell samples can be linked to the image analysis results and stored in the webmicroscope database. An online tool that uses novel adaptive informatics allows statistical analysis, correlation of image analysis results with clinical data and generates graphical reports of results.

A prototype information management system that allows large-scale data pooling of results from tissue biomarker studies is under development. Prognostic and predictive models (i.e. for personalized outcome estimation) can be constructed and shared with other researchers or clinicians online. The system also allows researchers to match and compare biomarker and tissue analysis results with results stored in a pooled reference database. According to agreement with FIMM, researchers can decide to add their study specific data to the common reference database.

Services in 2011:

Number of TMA spots processed: 11500
Number of slides digitized: 2570
Amount of server space needed for storing images: 27 terabytes

Contact:

Research Director: Johan Lundin
Project Coordinator: Tiina Vesterinen
Population cohorts available for researchers

Through the collaboration between FIMM and THL, MIBI can offer access to the DNA sample sets available as part of the THL national biobanking cohorts. The ability to combine the DNA sample sets with the services offered by MIBI and the FIMM Technology Center creates a unique and powerful research infrastructure for translational research. The available DNA sample sets are listed below.

<table>
<thead>
<tr>
<th>Name of cohort</th>
<th>Participants with blood/DNA</th>
<th>Plasma or serum available</th>
<th>Participants with GWA data</th>
<th>Participants with cardio-metabochip data</th>
<th>Participants with Exome or Genome Sequencing in progress</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population cohorts</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATBC study</td>
<td>28000</td>
<td>Yes</td>
<td>5000</td>
<td>1911</td>
<td>100</td>
</tr>
<tr>
<td>Health 2000 (£2011)</td>
<td>8087</td>
<td>Yes</td>
<td>2603</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helsinki Birth Cohort Study</td>
<td>2500</td>
<td>Yes</td>
<td>1676</td>
<td></td>
<td></td>
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<tr>
<td>Helsinki Sudden Death Study</td>
<td>693</td>
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<td>693</td>
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<tr>
<td>Northern Finland Birth Cohort 1966. NFBC66</td>
<td>5987</td>
<td>Yes</td>
<td>5253</td>
<td></td>
<td></td>
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<tr>
<td>Northern Finland Birth Cohort 1986. NFBC86</td>
<td>7342</td>
<td>Yes</td>
<td></td>
<td>6500</td>
<td></td>
</tr>
<tr>
<td>1000 genomes</td>
<td>200</td>
<td>No</td>
<td>110</td>
<td></td>
<td>180</td>
</tr>
<tr>
<td>Twins study</td>
<td>15535</td>
<td>Yes</td>
<td>2661</td>
<td></td>
<td></td>
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<tr>
<td><strong>Disease cohorts</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corogene</td>
<td>5367</td>
<td>Yes</td>
<td>2400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eufam study</td>
<td>3046</td>
<td>Yes</td>
<td>184</td>
<td></td>
<td></td>
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<tr>
<td>Intracerebral aneurysm</td>
<td>3862</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraine family study</td>
<td>8500</td>
<td>No</td>
<td>1123</td>
<td></td>
<td>1000</td>
</tr>
<tr>
<td>Multiple sclerosis family study</td>
<td>2586</td>
<td>Yes</td>
<td>525</td>
<td></td>
<td></td>
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<tr>
<td>Mental health family studies</td>
<td>6508</td>
<td>Yes</td>
<td>625</td>
<td></td>
<td>560</td>
</tr>
<tr>
<td>Smaller misc. projects</td>
<td>52319</td>
<td>Yes (partial)</td>
<td>6743</td>
<td>1850</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>188132</td>
<td></td>
<td>34519</td>
<td>15182</td>
<td>6913</td>
</tr>
</tbody>
</table>
**Access principles:**
The cohorts, samples and data are accessible through applications to the cohorts’ steering committees (see www.nationalbiobanks.fi for contact details). A short study plan (1-2 pages) is reviewed by cohorts’ key individuals and if the plan is agreeable with the original ethical statements and consents and also seen as scientifically valid, aliquots of samples and data can be transferred to identified scientists. A material and data transfer agreement will be signed before the transfer by all sides.

**Contact:**
Research Professor, THL, and Senior Scientist, FIMM: Markus Perola
Senior Scientist: Kaisa Silander

**Examples of major biobanking projects involving population cohorts**

During the year 2011 we have utilized the large prospective Finnish cohorts for >10 large international collaboration projects, as part of consortia such as ENGAGE, CHARGE, GIANT, MAGIC, and SUMMIT. The cohorts most often utilized include Finrisk, Health 2000, Northern Finland Birth Cohorts and the Schizophrenia Family Collection. These international collaborations included

- a genome-wide association study (GWAS) of adiponectin (ADIPGen);
- a gene-smoking interaction analysis in coronary artery disease (CARDioGRAMPlus);
- GWAS of leukocyte telomere length, an ENGAGE flagship project;
- genetic prediction of type 2 diabetes, an ENGAGE study;
- a CHARGE study, which used a multi-stage design in 200,000 individuals of European descent, that identified sixteen novel loci for systolic and diastolic blood pressure, including 10 novel genes that provide new clues to blood pressure physiology; various GIANT GWAS for traits such as BMI, waist circumference, height, weight and extreme obesity;
- MAGIC GWAS for gender specific effects on fasting insulin and glucose, and gene-BMI interaction affecting fasting insulin, glucose and HOMA-indexes;
- a SUMMIT GWAS of complications of type 1 and type 2 diabetes;
- early repolarization pattern (ERP) GWAS meta-analysis and replication in Health 2000 cohort.

Genome-wide SNP data is currently available for >30 000 Finnish individuals with rich phenotype data and with linkage to national registers, forming the basis of a second generation biobank where the samples are being transformed into data. These data are complemented by several other large Finnish cohorts managed elsewhere.

During 2011 we have also been involved in a new international collaborative effort to sequence the whole genome or exome of 8000 Finnish individuals, which is being carried out in large scale sequencing centers including the Broad Institute, the Sanger Institute and the Genome Institute at Washington University. These studies aim at constructing a Finnish haplotype catalogue, and providing a minimal set of informative SNPs that would allow sampling nearly all the genomic variation in Finnish individuals. This new resource is expected to have a major impact in future disease prediction studies by forming the basis for the Finnish Genomes and the Future Health Care initiative, described on page 25.

MIBI has also been actively involved in the collection of a new cohort of newborns and their parents from the Tampere area, to study the relationship between sleep, family environment, and genetic factors (the Child-Sleep project). The collection is continuing in 2012, and will include approximately 2000 families with DNA samples, and >1000 variables from each participant. A venous blood sample is collected from both parents, and an umbilical cord blood sample is collected from the newborns.

Together with Folkhälsan, MIBI has performed a saliva DNA isolation pilot for the project Finnish Health in Teens (Fin-HIT). The aim of Fin-HIT is to recruit a new cohort including 40,000 Finnish preadolescents. This will enable a study of a series of etiological hypotheses regarding the role of exposures and mediating factors, including genetic susceptibility, on the development of overweight, obesity and disordered eating.

**Contact:**
Research Professor, THL and Senior Researcher, FIMM: Markus Perola
Senior Scientist: Kaisa Silander
Major ongoing clinical biobanking projects

In order to serve the future needs of personalized medicine and translational research in cancer, FIMM has been active in promoting the establishment of modern biobanks with samples and long-term clinical follow-up data. Utilizing the integrated biobanking services of MIBI, two comprehensive new clinical biobanking projects were launched in 2011.

**Finnish Hematology Registry and Biobank (FHRB)**

FHRB is a national collaborative project for collecting samples from patients with hematological disorders (e.g. acute and chronic leukaemias, myelomas). It is operated by The Finnish Association of Hematology (FAH), Finnish Red Cross Blood Service (FRCBS) and FIMM. The consortium offers the sample processing, storage and management service for all the hospitals/clinics treating hematological patients. Hospital District of Helsinki and Uusimaa (HUS) is the first hospital district to utilize the service (prof. Kimmo Porkka), and new hospital districts are expected to join during 2012.

Based on informed consent and after insuring the needs of routine diagnosis and treatment, FHRB collects bone marrow and blood samples coupled with skin biopsies and a broad range of clinical information at the time of diagnosis and/or at follow-up visits.

FHRB is an open biorepository and the access rights will be granted by the FHRB Steering Group, based on prepublished criteria and scientific evaluation of the proposals. Approximately 500 newly diagnosed patients with a hematological disorder are expected to be enrolled yearly.

**Contact:**
Head of Development: Kimmo Pitkän

**Helsinki Urological Biobank (HUB)**

In 2011, we designed and launched a Tekes funded Helsinki Urological Biobank (HUB) which is a joint project undertaking of FIMM and HUS. HUB is a regional development project of diagnostics and treatment of urological cancers in the area of HUS. Peijas and Meilahti Hospitals are the main clinical centers, whereas FIMM and HUSLAB are responsible for sample logistics, processing and storing. The FIMM data management group has been responsible for the IT connections between the data management systems at FIMM and the Peijas hospital, as well as Finnish Red Cross Blood Service and FIMM for FHRB. The main clinical collaborator is Docent Antti Rannikko, Department of Urology, HUCH.

HUB collects a comprehensive set of sample material from each patient: fresh frozen and formalin fixed paraffin embedded tissue samples combined with blood and urine samples and wide clinical information.

Every year, there are about 900 urological operations performed in the Peijas Hospital. HUB aims to enroll at least 80% of these patients. The HUB biorepository will be open for research and R&D studies fulfilling predefined criteria.

**Contact:**
Senior Researcher, Pathologist, FIMM/HUSLAB: Tuomas Mirtti
Project Coordinator: Tiina Vesterinen

**Personnel:**
Postdoctoral Researcher: Andrey Golubtsov
Senior Researcher: Taija af Hällström
Senior Laboratory Technician: Reija Randen-Brady
Prostatectomy cohorts with long-term follow-up on tmas

Formalin-fixed paraffin-embedded (FFPE) samples from 452 prostate cancer patients treated with total prostatectomy between 1982 and 1998 at the Helsinki University Central Hospital were organized as tissue microarray blocks (TMA). The information on treatment, follow-up and survival, has been retrieved from the medical records. All the immunohistochemical stainings done on the TMAs thus far have been digitized and made available through the WebMicroscope platform. The project is coordinated by the Prostate Cancer Research Group Helsinki whose principal investigator is Docent Antti Rannikko, Department of Urology, HUCH. The TMAs are available for research upon request and approval.

Built in close collaboration with FIMM, FinnProstata IX is a retrospective clinical study with a collection of TMAs and detailed preoperative and follow-up information with survival data on 1,870 prostatectomies in four university hospital districts in Finland, including HUS. As a reference cohort, the study also consists of the survival information on all prostate cancer patients treated with radical prostatectomy in Finland during the years 1969 to 2010 (n>11,400). In these patient series, a systems pathology approach is developed, combining clinical, pathological, biomarker and imaging data to achieve a personalized assessment of the disease. With this clinical data collection and TMA repository, FIMM participates in international collaborative prostate cancer research, such as Movember prostate biomarker global action plan.

Contact:
Research Director: Johan Lundin
Senior Researcher, Pathologist FIMM/HUSLAB: Tuomas Mirtti

Technology development and emerging mibi services

Development of biobanking services at MIBI is progressing towards integrated, comprehensive service packages addressing the state-of-the-art and future needs of translational research. Some biobanking technology development projects are highlighted below.

iPS cell technologies
Production of induced pluripotent stem (iPS) cells from somatic cell samples is a novel technique under development at MIBI. The aim is to establish iPS techniques for utilization of previously stored samples as well as to collect novel cell samples that are optimized for the iPS-technology. The iPS cell technique has enormous potential for utilization of cells stored in the biobanks, as the samples can be differentiated into various lineages. Last year, iPS optimized mononuclear blood cells were collected from 260 individuals from Kuusamo as a pilot study for the large Finrisk 2012 cohort study.

Contact:
Senior Scientist: Aija Kyttälä

Tissue slice culture technologies
MIBI has established tissue slice cultures (TSCs) to facilitate short-term functional studies of both benign and malignant prostate tissues ex-vivo. TSCs are thin sections of tissues that are maintained alive in culture for several days. TSCs are perhaps the most representative model of the human prostate cancer and tissues available, containing almost all of the cells typically present in the body, and maintaining essential epithelial-stromal interactions as well as the differentiated cells, which are typically lost in long-term primary cultures or cell-line models. TSCs can be used for functional genomic studies, cellular and tumor biology as well as for drug response testing.

Contact:
Senior Researcher: Taija af Häggström
Exosome technologies
Extracellular circulating microvesicles represent an emerging and rapidly growing field of biomedical research, which strongly promises diagnostic and therapeutic possibilities. Exosomes represent a particular type of microvesicle with about 100 nm in size originating from early endocytic compartment of cells. Exosomes serve as vehicles for regulatory signaling molecules, such as miRNA, mRNA and proteins, and are generally regarded as an important mechanism of intercellular communication. Exosomal cargo is believed to reflect the biological status and wellbeing of specific tissues and this can be helpful for diagnostics and monitoring of disease. We are developing the exosome-related technologies for reliable analysis, fractionation and preservation of microvesicles from human blood and urine. Importantly, exosomes require special sample processing (plasma) and will not tolerate repeated freeze-thaw cycles, providing a challenge that underlies the importance of biobaking infras.

Contact:
Postdoctoral Researcher: Andrey Golubtsov

Integration of mibi with the European Biobanking Infrastructure BBMRI
MIBI is the national core site of the BBMRI.fi infrastructure and FIMM and THL act as the national coordinators of the BBMRI activities in Finland. The activities are organized as part of the Biomedinfra consortium, with support from the Ministry of Education and Culture and links to biobanking activities in all medical campuses and University Hospital sites in Finland. In September 2011, representatives of 13 EU countries approved the principles of operation, access, funding and governance of BBMRI (Biobanking and Biomolecular Resources Research Infrastructure).

Contact:
BBMRI-ERIC preparation and BBMRI.fi National Coordination: Anu Jalanko, Head of Public Health Genomics Unit, THL and Senior Scientist, FIMM
BBMRI.fi National IT-infrastructure: Juha Muilu, Senior Scientist, FIMM

Personnel:
Laboratory Engineer: Niina Eklund
Systems Architect: Askar Ibragimov
Senior Scientist: Kaisa Silander
The FIMM Administration Unit is composed of eight people, who support the Director in the management and development of the Institute. The Administrative Manager of FIMM is Reetta Niemelä, who is the Secretary of the Board of FIMM. The Unit includes staff responsible for financial and personnel issues as well as other institutional functions, such as the research infrastructure build up. The Unit is also involved in the planning and implementation of the many events mentioned in this report. A new initiative was launched in 2011 together with the Research Sector of the University of Helsinki: joint appointment of Senior Advisor Mika Frederiksen brought project funding services closer to FIMM researchers. When applying for external funding, researchers have support services in planning and preparation of the applications, contract negotiations and reporting of the projects. Senior Researcher Gretchen Repasky, Project Coordinators Sari Kivikko and Huei-Yi Shen, Coordinator Imre Västrik and Laboratory Engineer Jouko Siro contributed to the work of the Unit.

The Steering Group of the Institute meets every month and is composed of all the principal investigators and the people responsible for the Technology Centre’s Units and the Biobank, as well as key administrative personnel. The Steering Group discusses important issues that need opinions such as equipment, joint initiatives, training and recruitments.

The current Board of FIMM chaired by Vice Rector, Professor Kimmo Kontula started its term on 1 July 2010. The Board of FIMM steers and supervises the Institute’s activities by approving the finances, strategic plans and objectives.

The Scientific Advisory Board (SAB) comprised of six internationally recognised experts assesses the Institute’s activities and quality of research and provides the Board with recommendations on these matters. The Chair of the SAB is Professor Kai Simons.

Administration Unit:
Director, Professor Olli Kallioniemi
Administrative Manager Reetta Niemelä
Human Resources Coordinator Riitta Alatalo
Senior Advisor Mika Frederiksen
Department Secretary Sanni Hyppönen
Financial Planning Officer Riitta Koskinen
Financial Manager Marja Medina
Personal Assistant to Director Kallioniemi Susanna Rosas
Laboratory Coordinator Virve Tiusanen
Board 1 July 2010—31 March 2014:

Chair of the Board: Vice Rector, Professor Kimmo Kontula, University of Helsinki

Members (Deputy Members of the Board):
Dean, Professor Risto Renkonen, Faculty of Medicine, University of Helsinki
(Professor Kalle Sakala, Haartman Institute, Faculty of Medicine, University of Helsinki)
Research Director, Professor Anna-Elina Lehesjoki, Neuroscience Center, University of Helsinki
(Research Director, Professor Irma Thesleff, Institute of Biotechnology, University of Helsinki)
Professor Kimmo Porkka, Institute of Clinical Medicine, Faculty of Medicine, University of Helsinki
(Professor Annamari Ranki, Institute of Clinical Medicine, Faculty of Medicine, University of Helsinki)
Chief Research Officer, Professor Lasse Viinikka, HUS
(Chief Administrative Physician, M.D., Ph.D., LL.D., MFPM, Assistant Professor Lasse Lehtonen, HUS)
Deputy Director General, Professor Juhani Eskola, National Institute for Health and Welfare, THL
(Senior Researcher, Head of Public Health Genomics Unit, Anu Jalanko, THL)
Vice President, Professor, R&D Biotechnology, Anu Kaukovirta-Norja, VTT
(Technology Manager Kirsli-Marja Oksman-Caldentey, VTT, until 31 December 2011; Technology Manager Richard Fagerström, VTT, as of 1 January 2012)
Chief Executive Officer Pekka Mattila, Desentum Oy, industry
(CEO Saara Hassinen, Strategic Centre for Health and Well-being, SalWe Oy, industry)
Director, Professor Eero Vuorio, Biocenter Finland, BF
(Chair of the Board, Academy Professor Seppo Ylä-Herttuala, Biocenter Finland, BF)
IT Designer Anne Leinonen, FIMM Technology Centre, personnel)
(Laboratory Manager Pekka Ellonen, FIMM Technology Centre, personnel)

Permanent Experts of the Board:
Director, Professor Olli A. Jänne, Biomedicum Helsinki, University of Helsinki

Scientific Advisory Board (SAB) 1 May 2007–30 April 2012:
Professor Kai Simons (Chair) Max-Planck-Institute of Molecular Cell Biology and Genetics (Germany)
Professor Cornelia van Duijn, Erasmus University Medical Center (the Netherlands)
Professor Carl-Henrik Heldin, Ludwig Institute for Cancer Research, Uppsala University (Sweden)
Professor Eric S. Lander, The Broad Institute of MIT and Harvard (USA)
Professor Edson Liu, Genome Institute of Singapore (Singapore)
Professor Nadia Rosenthal, EMBL Monterotondo (Italy) and EMBL Australia Partnership Laboratory (Australia)
Examples of Ongoing Projects

Eu’s 7th Framework Programme, Research Projects

**BIOSHARE-EU (2010—2015)**

BioSHaRE-EU (Biobank Standardisation and Harmonisation for Research Excellence in the European Union) is a consortium of leading biobanks and international researchers from all domains of biobanking science. The overall aim of the project is to build upon tools and methods available to achieve solutions for researchers to use pooled data from different cohort and biobank studies. This, in order to obtain the very large sample sizes needed to investigate current questions in multifactorial diseases, notably on gene-environment interactions. This aim will be achieved through the development of harmonization and standardization tools, implementation of these tools and demonstration of their applicability. The project involves 16 participating organizations, three of them from Canada. FIMM has played a key role and led two work packages in this project. Contact Persons at FIMM: Group Leader Samuli Ripatti, Professor Aarno Palotie and Senior Researcher Markus Perola, Research Professor at THL. http://www.bioshare.eu/

**ENGAGE (2008—2012)**

ENGAGE (European Network for Genetic and Genomic Epidemiology) aims to translate the wealth of data emerging from large-scale research in genetic and genomic epidemiology from European (and other) population cohorts into information relevant to future clinical applications. The concept of ENGAGE is to enable European researchers to identify large numbers of novel susceptibility genes that influence metabolic, behavioural and cardiovascular traits, and to study the interactions between genes and life style factors. The ENGAGE Consortium has brought together 24 leading research organizations and two biotechnology and pharmaceutical companies across Europe and in Canada and Australia. The project was led by the world-leading human geneticist Academician of Science, Professor Leena Peltonen from FIMM, University of Helsinki for its first 26 months, until March 2010. The project co-coordinator, Professor Mark McCarthy from the University of Oxford has assumed the leadership as Scientific Coordinator since March 2010. FIMM, University of Helsinki continues as EC contractual Coordinator. In addition to its active involvement in ENGAGE scientific activities, FIMM also hosts the Coordination Office in charge of day-to-day consortium management and coordination tasks. Contact Persons at FIMM: Professor Jaakko Kaprio, Professor Aarno Palotie and Group Leader Samuli Ripatti. http://www.euengage.org/

**GEN2PHEN (2008—2012)**

GEN2PHEN (Genotype-To-Phenotype Databases: A Holistic Solution). The project aims to unify human and model organism genetic variation databases towards increasingly holistic views into Genotype-To-Phenotype (G2P) data, and to link this system into other biomedical knowledge sources via genome browser functionality. The five-year project (2008-2012) is funded with 12 million euros and has 20 participating institutions from Europe as well as India and South Africa. Contact Person at FIMM: Dr Juha Muilu. http://www.gen2phen.org/

**SYNSYS (2010—2014)**

SynSys (Synaptic Systems: dissecting brain function in health and disease) aims at molecular analysis of synapse function and dynamic modeling. The perspective is to generate a blueprint for the discovery of novel pathways and targets that enable rational strategies to design therapies for human brain disease. There are altogether 16 participating institutions and the funding is for four years (2010—2014). Contact Person at FIMM: Professor Aarno Palotie. http://www.synsys.eu/

**SYSTEMS MICROSCOPY NETWORK OF EXCELLENCE (2011—2015)**

The research network SYSMIC NoE (Systems Microscopy Network of Excellence) unites 15 multidisciplinary laboratories located throughout Europe. The joint research plan spans over five years (2011—2015) and is supported with 12 million euros. The aim is to develop next-generation systems biology tools and strategies on live cell imaging and to make them available to the wider research community. The advances in automated fluorescence microscopy, cell microarray platforms, highly specific probes, quantitative image analysis and data mining provide a powerful emerging technology platform to enable “Systems Microscopy” of the living cell. The core cellular processes analyzed within this NoE, cell division and cell migra-
tion, are highly relevant to human cancer. Through close collaboration between biologists, physicians and mathematicians, this NoE will create mathematical models of biological processes in time and space and test them experimentally. This NoE will develop a powerful enabling platform for next-generation systems biology and will apply these tools to understand cellular systems underlying human cancer. Contact Person at FIMM: Professor Olli Kallioniemi. http://www.systemsmicroscopy.eu/network-excellence

PREDECT (2010—2015)

PREDECT is an IMI-funded partnership between nine academic, three SME (Small and Medium Enterprise) and eight EU pharmaceutical partners, aiming to develop novel, advanced, complex in vitro and in vivo models for breast, prostate and lung cancers. Three-dimensional complex cell cultures, attempting to closely mimic in vivo tumours, will be investigated for their improved potential to validate therapeutic targets, applying molecular pathology and systems biology methods to compare the circuitry of resting and perturbed states. The project is expected to shift paradigms in cell biology as well as preclinical target validation, permitting greater predictivity of drug efficacy in patient cohorts. FIMM/University of Helsinki is the academic coordinator of the project, which consists of 26 principal investigators. Contact persons at FIMM: Group Leader Emmy Verschuren (academic coordinator of PREDECT), Professor Olli Kallioniemi and Research Director Johan Lundin. http://www.predect.eu/

ESFRI Projects (European Strategy Forum on Research Infrastructures)

BIOMEDBRIDGES (2012—2015)

BioMedBridges is a four-year project (2012—2015) addressing a call to implement common solutions for a cluster of ESFRI infrastructures in the field of life sciences. It brings together partners from 21 institutions from 9 countries and is lead by Professor Janet Thornton from EMBL-EBI (European Bioinformatics Institute). It will provide the computational ‘data and service’ bridges between the individual biological and medical sciences research infrastructures, clustering them together and linking the basic biological research and data to the clinical research and associated data. FIMM is leading the use of case work packages on personalised medicine and participating in another use case work package on large scale image datasets. These use case work packages provide input and test-beds for designing and testing the ‘data and service’ bridges. Contact persons at FIMM: Professor Olli Kallioniemi and Dr Imre Västrik.

EU-OPENSCREEN PREPARATORY PHASE (2010—2013)

EU-OPENSCREEN (European Infrastructure of Open Screening Platforms for Chemical Biology) integrates high-throughput screening platforms, chemical libraries, chemical resources for hit discovery and optimisation, bio- and cheminformatics support, and a database containing screening results, assay protocols, and chemical information. In the current preparatory phase (2010—2013), the network contains 13 partner institutes/institutions representing 12 European countries. FIMM is the partner representing Finland in the network. Contact persons at FIMM: Group Leader Krister Wennerberg, Senior Researcher Heidi Virtanen and Professor Olli Kallioniemi. www.eu-openscreen.eu

EU-OPENSCREEN (2012—2013)

Europian Infrastructure of Open Screening Platforms for Chemical Biology
Marie Curie Actions

PRO-NEST (2009—2013)

PRO-NEST (Prostate Research Organizations-Network of Early Stage Training) is a Marie Curie Initial Training Network that offers training on all aspects of prostate cancer research, ranging from the molecular basis of this disease to the translation of biomarkers into the clinic, to 24 PhD students and starting post-docs. The ultimate scientific aim of PRO-NEST is to understand the molecular basis of prostate cancer to address prevention, and to provide novel biomarkers and therapeutic targets for monitoring and treatment of this major European health problem. PRO-NEST has started in 2009 for a period of 4 years until 2013. http://www.pro-nest.org/

SYSTUMS (2010—2014)

SYSTUMS (Systems Biology Approaches to Novel Tumour Suppressors) is a project funded by a Marie Curie International Reintegration Grant aiming to study protein networks and molecular functions regulated by the candidate tumour suppressor protein EphA3. This action funds individual projects presented by experienced researchers returning to Europe after having worked in a non-associated third country for at least three years, to assist in reintegration and promote transfer of knowledge into EU Member States or Associated Countries. Grantee at FIMM: Group Leader Emmy Verschuren, for reintegration period 2010—2014.

European Regional Development Fund

LEUKAEMIA BIOMARKERS (2011—2013)

The Leukaemia Biomarkers project (“Elämän merkit” in Finnish) aims at developing diagnostic services based on biomarkers. The project is funded for three years (2011—2013) by the Regional Council of Päijät-Häme from the Southern Finland ERDF programme. The project is coordinated by Turku Science Park and also includes the VTT Technical Research Centre of Finland, the Hospital District of Varsinais-Suomi, the University of Turku as well as Culminatum Innovation Oy. FIMM is developing a service which would enable the use of personalized biomarkers for measuring treatment efficacy and early detection of relapse in leukaemia patients. Contact persons at FIMM: Professor Olli Kallioniemi and Dr Imre Västrik.
Juni Palmgren’s Inauguration Lecture

FiDiPro Professor Juni Palmgren’s (Stockholm University and Karolinska Institute, Sweden) Inauguration Lecture entitled “The Nordic Lead in e-Science and Health” on 21 March 2011 was given in Biomedicum Helsinki 1 lecture hall. The Chancellor of the University of Helsinki, Professor Ilkka Niiniluoto appointed Juni Palmgren to the post of Finland Distinguished Professor in Biostatistics. Professor Jaakko Kaprio is the Finnish host. “The data and competence of tFIMM and Karolinska Institute supplement each other in a brilliant way, and I hope that we also can somehow involve the Department of Mathematics and Statistics of the University of Helsinki in the cooperation,” says Juni Palmgren. She also states that “Most people do not appreciate that molecular medicine processes amounts of data comparable in size to particle physics, but with a more complex structure. Therefore, immense data storage and processing capacity is required, as well as new algorithms and models able to extract meaningful information from this avalanche of data.”

SAB Visit

The SAB visited FIMM on 17 May 2011. Present were Professors Cornelia van Duijn, Carl-Henrik Heldin, Edison Liu, Nadia Rosenthal and Kai Simons (Chair of the SAB). The SAB concluded in its report that they noted with satisfaction that the FIMM build-up is proceeding in an outstanding way. The SAB also recommended that the funding FIMM had received in the start-up phase should be extended.

Leena Peltonen-Palotie Symposium

Together with the Academy of Finland, University of Helsinki and THL, FIMM arranged in May 2011 in Helsinki the symposium entitled: ‘A Global View of Disease Genomics’ as a tribute to Academician of Science, Professor Leena Peltonen-Palotie. There were altogether over 30 distinguished speakers, including Members of the Scientific Advisory Board of...
FIMM, and almost 500 registered participants from all over the world. In addition, about 300 participants attended the public lectures.

Leena Peltonen-Palotie’s legacy is immense: “She was a visionary in the field of science, creating an infrastructure for research needs that weren’t even on the horizon yet,” said Richard Durbin of the Wellcome Trust Sanger Institute in England.

“Right now we’re in a situation where genetics research has progressed faster than the methods it requires. We must find a way to bridge this gap. Leena was the one who said, ‘don’t just rely on one method—use all the tools available,'” remembered David Altshuler of the Broad Institute of MIT and Harvard and Massachusetts General Hospital.

Leena Peltonen-Palotie, who passed away in March 2010, built an international research network to which many of the symposium’s 35 speakers belong. They discussed their own research projects and shared memories of Leena: “Exceptionally intelligent, warm, supportive and demanding. She inspired her colleagues to strive for better results and helped fellow scientists see beyond the challenges they faced. She believed that researchers should work together instead of competing with each other.”

Second meeting of the Nordic Molecular Medicine Network

Nordic Molecular Medicine Network (NMMN) promotes collaboration between EMBL (European Molecular Biology Laboratory) and its Nordic nodes FIMM, NCMM and MIMS, as well as among the three Nordic nodes themselves. The second joint meeting of the NMMN, bringing together almost 140 participants from the three nodes and the EMBL, was hosted by FIMM in Helsinki, Finland from 29 to 30 of September 2011. The meeting provided a highly stimulating environment for the researchers of all three institutes and the parent organization EMBL to share their research and explore facilities and infrastructure within the partner institutes. Group leaders, postdoctoral researchers and PhD students presented their research in short talks and posters providing an overview of ongoing projects. An interactive ‘Meet the Experts’-session, organized by FIMM technology platforms, provided an opportunity to address technological challenges and practical suggestions to all levels of researchers. A common initiative was forged to encourage exchange of knowledge, technologies and personnel. In addition to scientific interest, PhD students and postdoctoral researchers agreed to make a common platform for communication and a Facebook group named ‘Nordic Molecular Medicine Network (NMMN)’ was created thereof. The success of the meeting in respect to collaboration and networking was clearly apparent even in informal meetings during coffee breaks, dinner and social events organized by the FIMM students. The next meeting of the NMMN will be held in conjunction with the Centre for Genomic Regulation (CRG), an EMBL Partnership institute located in Barcelona, Spain, in September 2012.

2nd annual FIMM retreat

The second annual FIMM Scientific Retreat was held on 7—8 June 2011 at Hotel Rantasipi Sveitsi in Hyvinkää. The FIMM staff was almost completely present with 133 persons attending the event. The first day programme started with a very interesting scientific highlight from translational research and personalized medicine. The scientific highlight was directed by Professor Olli Kallioniemi and FiDiPro Professor Jonathan Knowles and it included a case study presented by Professor Kimmo Porkka. It was also largely appreciated that a patient was present speaking about his personal case. It brought the topic to a concrete level. In the afternoon FIMM research and technology highlights were presented by several persons from different areas and a poster session was held which included 49 posters. The official programme was brought to an end on the first day by the keynote speaker Professor Juha Siltala, who gave a lecture about changing working life and work motivation. The second day consisted of group discussions.
FIMM Stakeholder Meeting, 8 December 2011, participating organisations

Predec Consortium Meeting
In September 2011 FIMM and the University of Helsinki hosted the annual IMI-PREDECT consortium meeting, which included a scientific meeting at the Biomedicum Helsinki premises. The meeting gathered over 50 participants from its 20 European partner institutions, including representatives of seven major pharma industries, to discuss early partnering strategies on novel cancer target validation models.

FIMM Stakeholder Meeting
A FIMM Stakeholder Meeting was arranged on 8 December 2011. The purpose of the meeting, chaired by Rector Thomas Wilhelmsson, was to discuss the funding of FIMM and to secure sustainable and sufficient basic funding for it in the coming years as part of the Nordic EMBL Partnership, since the university system in Finland has changed dramatically after the establishment of FIMM in 2006.

The meeting gathered altogether 42 participants e.g. from the Nordic EMBL Partnership, Ministries, founding organisations and supporters of FIMM as well as from national research funding agencies. The discussion at the meeting was very positive. All supporters of FIMM stated that FIMM has fulfilled the expectations set out at its establishment and that FIMM’s role in the Nordic EMBL Partnership for Molecular Medicine has to be secured. Follow-up actions and further discussions with the ministries as well as other founding organisations and current supporters of FIMM will take place in 2012.
FIMM Scientific Coffee Breaks and Seminars

The FIMM research community was strengthened in the FIMM Scientific Coffee Breaks. In short talks arranged twice a month students, postdoctoral researchers, as well as senior researchers presented their work for FIMM staff. In addition, group leaders and invited guest speakers have given presentations in seminars open to wider researcher community on Meilahti Campus.

Christmas Party

The annual get together for all FIMM personnel, was arranged on 18 November 2011. For the second time, Poliisien kesäkoti in Lauttasaari was chosen to be the venue for this yearly event. Approximately 95 people attended the event where dinner was served and a band, “Steppin Peanuts”, entertained the partygoers.

Entertainment Committee 2011:

Diana Cousminer
Yuexi Gu
Jani Heikkinen
Siv Knaappila
Anna Lehto
Muntasir Mamun Majumder
Minna Suvela
Laura Turunen
Anu Yliperttula

Visits

In addition to the events mentioned above, FIMM was also involved in the Meilahti Campus Day by providing lectures and guided tours at FIMM for the general public. FIMM also hosted amongst other things:

• Visits of representatives of the Japan Science and Technology Agency (JST) in March and December 2011, latter in connection to a symposium arranged by the Academy of Finland, Tekes and JST.

• Visit of representatives of the Joint Committee of the Nordic Medical Research Councils (NOS-M) in October 2011. NOS-M works to promote Nordic cooperation among research councils, discusses research policy and disseminates information on national and international science policy actions and initiatives of topical interest.

• Visits to the FIMM Biobank Infrastructure by experts from the University of Jyväskylä, Lisbon Institute of Molecular Medicine, Portugal as well as Facultad de Medicina, Universidad de Chile, Chile. The purposes of these visits were to get a better knowledge of the FIMM Biobank system, including administrative, scientific and technical aspects.

• Visits of representatives of the Embassy of Chile and Embassy of France.

• Visits of several groups of students from high schools from Southern Finland.
FIMM IN FIGURES
Personnel Statistics

Figure 1. Total number of FIMM employees 2007-2011, estimate 2012

Figure 2. Number of FIMM personnel 2008-2011 according to the type of employment

Figure 3. Number of FIMM personnel in 2011 according to the type of employment

Figure 4. Distribution of FIMM personnel by category of employment
Nationalities represented among FIMM personnel:
(December 2011)

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**Financial Report**

**Figure 5.** Total funding of FIMM in 2011 (13.1 M€) divided based on the source of income. The basic funding refers to the support from the University of Helsinki. External funding refers to competitive research and infrastructure funding.

**Figure 6.** Distribution of FIMM external funding 2011 (8.8 M€) according to source.

**Figure 7.** FIMM expenditure 2011

- Basic funding (including University of Helsinki fund) 23%
- Strategic funding 2%
- Competitive external funding 65%
- Service revenue (external) 3%
- Service revenue (internal) 7%
- Biocenter Finland
- Academy of Finland (including ESFRI)
- TEKES
- Other public funding (including THL, HUS, City of Helsinki)
- Foundations
- EU funding
- Other international funding
- Service revenue (external)
- Personnel cost
- Facilities
- Consumables
- Equipment
- Depreciation
- Services and other costs
Personnel including researchers and students with grants and members of the FIMM National Network for Molecular Medicine

Research groups

**Tero Aittokallio**
Petteri Hintsenan
Agnieszka Szwajda
Ing Tang
Bhagwan Yadav

**Denis Kainov**
Maria Anastasina
Oxana Denisova
Laura Kakkolii
Minttu Kaloinen

**Olli Kallioniemi**
Anna Aakula
Marilillä Arjama
Sam Blom
Oscar Brück
Henrik Edgren
Akira Hirasawa
Susanne Hultsch
Taija aJ Hällström
Sara Kangaspeska
Sam Kilpiäinen
Disha Malani
John Patrick Mpindi
Astrid Murumägi
Petrá Mäki-Teeri
Kalle Ojala
Teijö Pellinen
Vilja Pietiläinen
Khalid Saeed
Jenni Säilä
Johan Lundin
Maija Tumiati
Annabrita Schoonenberg
Pauliina Munne
Sonja Koopal
Sharif Iqbal
Yuexi Gu
Daria Bulanova
Yuexi Gu
Sharif Iqbal
Sonja Koopal
Pauliina Munne
Annabrita Schoonenberg
Manuela Tumiati

**Sergey Kuznetsov**
Daria Bulanova
Yuexi Gu
Sharif Iqbal
Sonja Koopal
Pauliina Munne
Annabrita Schoonenberg
Manuela Tumiati

**Johan Lundin**
Juho Konsti
Tiina Lehtimäki
Nina Linder
Mikael Lundin
Ville Ojansivu
Riku Turkki
Margarita Walliander

**Aarno Palotie**
Verner Anttila
William Hannen

**Eija Hämäläinen**
Carita Jussila
Elläi Kemptas
Sari Kivikko
Leena Leikas
Tiia Liuukonen
Mikko Muona
Anne Nyrhinen
Mari Rossi
Olli Pietiläinen
Kaisa Silander
Minna Suvela
Maija Wessman

**Juni Palmgren**
Martin Eklund
Alfredo Ortega-Alonso
Ola Sjphutz

**Samuli Ripatti**
Johannes Kettunen
Maria Krestyaninova
Marine Largeau1
Pirkka-Pekka Laurila
Alfredo Ortega-Alonso
Karola Rehnström
Pietari Ripatti
Mari Rossi
Antti-Pekka Sarin
Huei-Yi Shen
Jarkko Soronen1
Ida Surakka
Emmi Tikkannen
Taru Tukiainen
Peter Würzt

**Janna Saarela**
Himanshu Chheda
Evelinä Jakkula
Virpi Leppä
Annu Nääkö
Ann-Maja Sulonen

**Emmy Verschuren**
Danielle Bansfield1
Sonja Koopal
Jenni Lahtelä
Rita Matos
Ashwini Nagaraj
Dat Nguyen
Katja Närh1
Nitaï Peled
Annabrita Schoonenberg
Merja Särkioja1

**Kristin Wennerberg**
Arjan van Adrichem
Tonge Ebai1
Leena Karhinen
Sawan Kumar
Muntari Marnam Majumder
Tea Pemovska
Gretchen Repasky
Amy Sessions1

**Elisabeth Widén**
Diana Cousminer
Jaakko Leinonen

**FIMM Technology Centre, including infrastructure projects**
Henrikki Almusa
Maxim Bespalov1
Myles Byrne
Henrik Edgren
Sirkka Ekström
Samuli Eldfors
Pekka Ellonen
Sari Hannula
Tiina Hannunen
Jani Heikkinen
Vasudev Kantee
Mari Kaunisto
Anna Korvenpää
Anna Kossila
Evgeny Kuleshkiy
Suvi Kyttyän
Sonja Lagström
Paivi Lahermo
Anna Lehto
Anne Leinonen
Maija Lepistö
Jesús María López Martí1
Pirkko Mattila
Ruusu-Maria Merivirta
Timo Miettinen
Juha Muilu
Daniel Nicorici1
Aino Palva
Teemu Perheentupa
Vilja Pietiläinen
Paivi Rosenström1
Jani Saarela
Janna Saarela
Tomi Simonen
Jouko Siro
Mikko Siurala1
Kyösti Sutinen
Kari Tuomainen
Hanno Tunuren
Lauri Tunuren
Carina von Schantz-Fant
Imre Västrik
Vidya Velagapudi
Kristin Wennerberg
Anu Vipertutula
Jean-Christophe Yorke
Päivi Östling

**Biobank Infrastructure**
Niina Eklund
Andrew Golubtsov
Taija aJ Hällström
Askar Ibraqimov
Siv Knaappila
Aija Kyttälä
Paivi Lahimo
Tuomas Mirtti
Juha Muilu
Kimo Pitkänen
Reija Randen-Brady
Kaisa Silander
Kyösti Sutinen
Tiina Vesterinen

**Biobank Infrastructure/THL personnel:**
Anu Jalanko (THL/FIMM)
Aija Kyttälä
Paivi Lahimo1
Sini Lähteenmäki
Elina Mäkinen
Anne Nyberg
Seija Puomilahti
Minttu Sauramo
(leave of absence)
Tuuli Sistonen
Minna Suvela
Arja Terola
Regis Wong

**FIMM Administration**
Olli Kallioniemi
Riitta Alatalo
Mika Frederiksen
Sanni Hyppönen
Riitta Koskinen
Maija Medina
Reetta Niemelä
Susanna Rosas
Virve Tiisanen
Kari Pitkänen

**FIMM Clinical Collaborators**
Tuomas Mirtti
Kirsí Pietiläinen
Jakob Stenman

**Members of the FIMM National Network for Molecular Medicine**
Lauri A. Aaltonen
Kari Alatalo
Akseli Hemminki
Iliris Hovatta
Elina Ikonen
Sirpa Jalkanen
Heikki Joensuu
Jaakko Kaprio
Heli Nevanlinna
Matej Orešič
Taina Pihlajaniemi
Jussi Taipale
Willem de Vos
Anu Wartiovaara
Jukka Westermarck

**Adjunct Personnel**
Tero Hiekkanilann
Taru Murenann
Markus Perola
Juba Raj Pokharel
Antti Posto
Päivi Tuomaala
1 until 2011
2 started in 2012

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