

FUGE



An Evaluation of the Eleven National Technology Platforms founded by the Functional Genomics Programme in Norway (FUGE)

 The **Research Council** of Norway | Research programmes

The Norwegian Center for *Microarray* Technology (NMC)

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PREFACE

To strengthen research within functional genomics and to bring Norway to top international standard the Research Council of Norway (RNC) funded the large-scale research program FUGE – the National Program for Research in Functional Genomics. The program runs from 2002 until 2011.

During the period between March and June 2006 the technology platforms of FUGE were evaluated by international panels. This evaluation will reveal if the technology platforms have established the technology and competence nation wide that was stipulated in the original contract. The evaluation will also give an indication as to whether the platforms have contributed in bringing Norwegian research into a higher international level.

Prior to the evaluation material from the technology platforms was sent to the panel members. The material included original application, contract, annual reports 2003 and 2004 and 2005 and a midterm report 2005. The hearing took place at Losby Gods outside Oslo on the 3rd of May, 2006.

The participants from the Microarray platform during the panel's interview were:

Odd S. Gabrielsen, Eivind Hovig, Ola Myklebost, Arne Sandvik, Bjørn Skålhegg and Vidar M. Steen. There were no participants from FUGE present during the interview.

The panel acknowledges the vital importance of the FUGE

program for Norwegian research in the field of functional genomics, and was indeed pleased to find that the evaluated technology platforms overall demonstrate excellent performance at an international level. Among the three platforms evaluated, the panel found that the genotyping activity at CIGENE revealed the largest need for changes.

It should be noted that the panel had some problems in assessing the performance of the platforms as the written material from the platforms was produced approximately six months prior to the review, making the text somewhat outdated. The comments from the panel have therefore also largely been based on the more updated view provided in the presentations by the platform leaders, and from the subsequent discussion.

The panel would like to raise several issues that are of concern for the continuation of the FUGE program, issues which concern all three platforms:

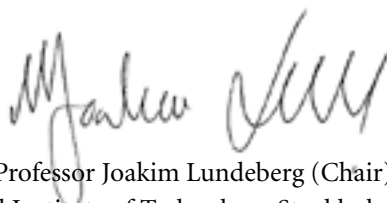
- › *Platform integration* – the panel suggests that the integration between the platforms (SNP, RNA, Protein etc) should be stimulated. A strategy for this could be to include a separate topic in the FUGE program that invites coordinated applications (cross-platform) in integrative system biology, *i.e.* that individual projects drive the system's biology efforts within FUGE rather than this being a platform activity.
- › *Platform personnel* – the panel urges FUGE to initiate the FUGE II process as early as possible in order to secure that trained personnel can remain without interruption in the platforms. It should be remembered that technical personnel will seek other positions if the funding for going forward is uncertain.
- › *New platform in DNA sequencing/transcript profiling* – new innovations in gene sequencing technology have recently changed the possibilities for performing massive sequencing projects at an affordable scale (whole genome sequencing, EST sequencing, mutation screening etc) with commercial alternatives (Roche/454 and Solexa). The panel recommends that such activity is initiated within FUGE, either as a separate platform or integrated into an existing platform. Strong interactions are envisioned between projects and current platforms with these new technologies.

STATEMENT FROM THE PANEL, WITH PANEL MEMBERS' SIGNATURES

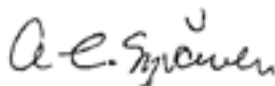
Statement:

This evaluation is based on the material provided by FUGE and the hearing at Losby Gods, the 3rd of May, 2006. There is consensus among the members of the evaluation panel about the views presented in this report. The panel members are in collective agreement with the assessments, recommendations and conclusions presented.

None of the panel members had any conflict of interest that would warrant disqualification from general participation in the evaluation.



Professor Joakim Lundeberg (Chair)
The Royal Institute of Technology, Stockholm, Sweden



Professor Ann-Christina Syvänen
Dept. of Medical Sciences,
Uppsala University, Sweden



Dr. Petri Auvinen
Institute of Biotechnology,
University of Helsinki, Finland



Professor Søren Brunak
Center of Biological Sequence Analysis,
Technical University of Denmark

Dr. Filippa Kull, Karolinska Institutet, Sweden, acted as scientific secretary of the evaluation panel.

SUMMARY OF RECOMMENDATIONS FROM THE PANEL

- › **Service:** Continue and expand the excellent service which is based on active involvement of the nodes. Furthermore, the monitoring of customer needs by the excellent evaluation forms should also be continued. The panel supports additional bioinformatics support at the nodes to facilitate the increasing demand from customers for array analysis.
- › **Research.** To secure the development of the platform new microarray applications should be pursued. It is likely that a platform without any technology development will stagnate. Projects that are planning to expand from array analysis into other areas should be supported given the future needs within systems biology.
- › **Training.** The excellent training possibilities provided by the nodes should be continued and can be ‘upgraded’ locally through the proposed bioinformaticians. It is the panel’s belief that this will further improve the communication between external users and the Microarray platform.
- › **Collaboration with other platforms.** The platform collaborates mainly with the bioinformatics platform. This should be continued and expanded with integration with other large data sets (FUGE generated or public domain) as a common goal for the platforms involved.
- › **International collaboration.** Increase the number of international collaborations and promote Nordic initiatives that may open possibilities of platform access with new emerging technologies for transcript mapping.

THE PANEL’S DESCRIPTION OF THE MICROARRAY TECHNOLOGY PLATFORM

The Microarray technology platform consists of groups from the University of Oslo (UiO), the Norwegian Radium Hospital (DNR), the Norwegian University of Science and Technology in Trondheim (NTNU) and the University of Bergen (UiB). Together they form a consortium called the Norwegian Microarray Consortium (NMC) which was initiated already before the FUGE program started.

The consortium offers a wide variety of services ranging from custom spotting to RNA-in-DATA-out services. The nodes cover most of the main commercial platforms available and in addition they are also producing several custom-made arrays covering species like human, mouse, rat and zebra fish. Support for basic bioinformatics is provided for the users. A common web portal has been built which distributes all necessary information concerning the platform activities, from news to courses, in a very effective manner. Additionally, a Microarray Newsletter is published twice a year that highlights recent activities.

This platform is well connected to the research community in Norway and is also a participant in international projects.

EVALUATION OF THE PLATFORM

Achievements

The microarray platform consists of three nodes forming the Norwegian Microarray Consortium (NMC), and is a good example of a joint national initiative established already before the first FUGE funding was in place. Within the FUGE program the technology platforms have established many of the available commercial platforms in combination with in-house spotting activities. The commercial technologies are not present in all the nodes, but wisely divided across the regional nodes. Already in the early phase of the program, the production of microarrays and/or hybridization of arrays have been connected to the

bioinformatics analysis. It is the panel's opinion that the demonstrated close interaction between wet-lab activities and development and use of bioinformatics tools is critical to the success of the platform and supports increased interaction in order to keep the research at an international level.

After evaluation of the written report and the material presented to the panel during the hearing, it is clear that most of the milestones listed in the original plan have been achieved. This has been accomplished although only about 50% of the applied funding was delivered to the platform. This accomplishment is mainly due to the concerted effort of the three nodes together with additional funding provided by the host institutes. This has obviously demanded a firm commitment from and achievement of the groups involved in developing the platform.

The microarray technology platform has an effective process for feed-back from the users. Most of the users are clearly satisfied with the service provided by the nodes. It is the panel's impression that NMC has made it possible for the majority of researchers in Norway to utilize array technology optimal for their experiments. The microarray nodes are also adapting their activities according to the feed-back from the customer questionnaires.

The service they provide can compete with the commercial platforms regarding price and, more importantly, also regarding the partial bioinformatics support that can be further improved. In-house produced arrays are of good quality but, as also mentioned by themselves, will be discontinued if the need for them is declining. The panel still believes that there will be a need for array production even in the future, if the platform considers new array-based applications.

The microarray technology platform has trained hundreds of researchers through courses and seminars. Furthermore, they have arranged several meetings for a national audience and some major international meetings within the field of functional genomics. The groups of the NMC nodes have associated research activities at an international level, but its relation to the FUGE program is somewhat unclear. This platform has good international

contacts also outside Scandinavia. Still, there is room for improvement in the cross-platform activities and the visions of the scientific goals of the platform.

Organizational and Administrative Aspects

This consortium has a clear and effective administration with a rotating chairmanship between the three sites, which is well suited for the current tasks with complementary technologies at the nodes. Going forward, a new generation of platform leaders is considered to replace the founders of the consortium. The future challenge will probably be to adjust the organization from a spotting facility to a more hybridization and post-analysis oriented facility given the possibilities for outsourcing spotting activities or commercial arrays. Yet spotting activities will probably remain at some level for special purposes, *i.e.* less characterized species, as well as for other biomolecules such as protein and carbohydrates. At some point the spotting activities should be concentrated to a single site taking the national responsibility to reduce costs related to the upgrading of instruments, such as introduction of second generation inkjet technology. It appears that the microarray consortium is well connected to the host universities, but the nodes are concerned that a delay in the process of the continuation of the FUGE program will result in loss of key personnel. The panel did acknowledge this concern.

Plans for the Future

This platform demonstrates excellent performance with impressive numbers of users and course participants. Furthermore, the spotting activities appear to fully occupy the available instruments. Yet the panel found that the platform can improve its visions for the future, *i.e.* beyond longer spotting projects. Some activities using protein arrays and miRNA have been initiated. However, to secure the platform, a more focused technology development program should be considered. Cell arrays, antibody arrays, etc., are examples of efforts that could be of national interest as resource and that would also bridge over to the proteomics platforms.

Tag counting methods may also come into practice in the near future as a means of monitoring transcript levels with the access of massive sequencing technology. The panel suggests that this platform considers such complementary technology as part of the future strategy. This may also have implications for the genotyping field as well as bacterial/parasite whole genome sequencing, and it would clearly strengthen the interactions between platforms and make a foundation for an additional type of large scale data set used for systems biology within Norwegian projects. This should also be considered to be a national interest that will require additional bioinformatics expertise.

There are some experiences of product commercialization within the platform and the panel supports such efforts, and it is anticipated that this platform may contribute to new biomarkers and classifiers that have a commercial interest.

CURRICULUM VITAE FOR MEMBERS OF PANEL 2

Joakim Lundeberg

Present position: Head of Department, Gene Technology, Royal Institute of Technology (KTH), Stockholm, Sweden.

Education:

- › 1988: Master of Science in Chemical Engineering, Royal Institute of Technology (KTH), Stockholm
- › 1993: Ph. D. in Biotechnology (M.Uhlen, supervisor), Royal Institute of Technology (KTH), Stockholm
- › 1996: Associate Professor, Royal Institute of Technology (KTH), Stockholm
- › 2002: Professor, Royal Institute of Technology (KTH), Stockholm

Comissions of trust:

- › Member of the Appointment Board at the Faculty at KTH (2003-present).
- › Member of the Steering Board of the Department of

Biotechnology, KTH (2003-2006).

- › Member of the program committee for nanoscience, biotechnology and IT, NABIIT (DSF, Denmark, 2004-present).
- › Faculty opponent for three doctoral dissertations (UU and Oslo Univ).
- › Member of the evaluation committee for >25 doctoral or licentitate theses (1998-2006).
- › Evaluator of application for academic positions: Karolinska Hospital, Karolinska Institute, Lund University.
- › Evaluator of application for research grants: Wellcome Trust, Academy of Finland, Genome Canada, Finnish Microarray Consortium, Karolinska Institute/Hospital, INSERM/Biotox, the Radiumhospital (Stockholm), Högteknologifonden (Denmark), the Swedish Research Council (Stockholm).

Networks in academia and industry:

- › Director KTH Genome Center (1998-present),
- › Coordinator for the Wallenberg Consortium North - Expression platform (2001-2005),
- › Member of the WCN Coordinating Group (2006-present),
- › Member of the EMBnet Sweden board (1997-2000),
- › Member of Reference Council for Stockholm Bioscience(2002-present),
- › Member of HUGO (Human Genome Organization) (1997-present),
- › Member of the Swedish Biochemical and Mol. Biology Society (1996-present),
- › Member of Advisory Board for the Swedish Pharmaceutical Society (2003-present),
- › Member of the EU- IMAGE consortium,
- › Member of the board Center for Biomembrane Research (2006-present),
- › Advisory Board of Stockholm Bioinformatics Center (2006-present),
- › Scientific adviser: Dynal AS (1994-2000), AstraZeneca Ltd(1999-2002,), Neuronova AB (2001-2003), Qiagen (2003).

Joakim Lundeberg's research program has focused on development and application of technologies and bioinformatics tools for identification of differentially expressed genes, characterization of single nucleotide polymorphisms, and identification of genetic alterations in pathological conditions. The aims with these technologies are to contribute to an improved understanding of gene function in the studied biological systems. Previous research achievements include the development of new technologies such as Solid-phase representational difference analysis, cDNA Microarrays, Transcriptome amplification technologies, single cell analysis in histological tissues sections, Magnetic bead capture of nucleic acids, pyrosequencing of cDNA libraries and other genomic targets, and SNP genotyping by protease mediated allele specific extension. Joakim Lundeberg is currently director of the KTH Genome Center (www.biotech.kth.se/mol-bio/genome_center.html) and was previously coordinator for the Expression platform of the Wallenberg Consortium North program (www.wcn.se) in functional genomics.

Sören Brunak

Present position: Professor, Center Director, Center for Biological Sequence Analysis, Bocentrum-DTU, Technical University of Denmark.

Education:

- › 1987: M.Sc. in Physics, Niels Bohr Institute, University of Copenhagen, Denmark.
- › 1991: Ph.D. in Computational Biology, Department of Structural Properties of Materials, Technical University of Denmark.
- › 2002: Dr.phil. (honoris causa), Natural Science Faculty, Stockholm University.

Professor Brunak works on integrative approaches for elucidation of complex biological mechanisms, where experimental and predicted data on coding and non-coding sequence, structure, localization, modification, function, expression, pathways and interaction are combined in new

ways. A particular aim of his work is to reveal systemic aspects of cellular function, often using integrative tools from the machine learning area in combination with advanced data warehouse structures.

Currently Professor Brunak's research group is doing work on:

- › Protein-protein interaction networks and their dynamics
- › Systems biology of genetic diseases
- › Reverse engineering of gene regulatory networks from microarray data
- › Feature based prediction and characterization of protein function
- › Classification of cancer types from "omics" data

Professor Brunak has published more than 120 papers with peer-review; he has co-authored four books, three proceedings and he has edited books. Most recent high-impact publication: "Dynamic protein complex formation during the yeast cell cycle", de Lichtenberg, Jensen, Brunak and Bork, *Science*, Jan 28, 2005. Several papers have been on the Institute for Scientific Information Red Hot List.

Honors and awards:

- › 1993-present: Member of the Danish Academy for the Natural Sciences (DNA)
- › 1997-2003: Board of Directors, BioCentrum-DTU
- › 1998: Bjerrum-Brøndsted-Lang Award from the Royal Danish Academy of Sciences and Letters
- › 2000-present: Board of Directors, Selskabet for Naturlærens Udbredelse
- › 2000-present: Nordic Bioinformatics Network Program Board
- › 2001- 2004: Board of Directors, International Society for Computational Biology
- › 2001-present: Member of the Danish Academy of Technical Sciences
- › 2002: Dir. Ib Henriksens Price for Outstanding Science Achievement

- › 2004-present: Member of the Royal Danish Academy of Science and Letters
- › 2006: Receives the Villum Kaan Rasmussen Prize for Technical Research
- › 2000, 2004, 2005: Swedish Research Council (VR-NT) Biotechnology review committee.
- › 2000-present: Reviewer of grant applications, incl. Academy of Finland, NWO, the Netherlands, Wellcome Trust, UK, Genome Canada, 3-5 applications annually.

Ann-Christine Syvänen

Present position: Professor in Molecular Medicine, Dept of Medical Sciences, Uppsala University, Sweden

Education:

- › 1987: Doctor of Philosophy (Biochemistry), University of Helsinki, Supervisor prof. Hans Söderlund, Institute of Biotechnology, University of Helsinki, Finland
- › 1989: Appointed “Docent” in Biochemistry, University of Helsinki
- › 1993: Visiting scientist, Department of Molecular Biology, Uppsala University
- › 1999: Appointed “Docent” in Molecular Medicine, Uppsala University

Positions of trust:

- › 2002-present: Vice prefect (dean) of the Department of Medical Sciences, UU
- › 2001-present: Council member, Uppsala Graduate School for Biomedical Research
- › 2000-2005: Coordinator of WCN national technology platform for SNP/DNA analyses
- › 2000-2005: Council member, Human Genome Organization (HUGO International)
- › 2005 -present: Scientific advisory board, Quebec Genome and Innovation Center, Montreal, CA
- › 2002-present: Scientific advisory board, Centre National de Génotypage (CNG), Evry, France
- › 2005-present: Scientific adviser, Beckman Coulter, Krefeld, Germany
- › 2003-present: Editorial Board, Hum Genetics, Hum Mutation, Cancer Genomics and Proteomics, BMC Biotechnol.

Ann-Christine Syvänen’s research group at Uppsala University has ~ 20 members and was established in 1998 (www.medsci.uu.se/molmed). Currently, she is responsible for the graduate studies at the department, and for the SNP technology platform in Uppsala that offers SNP genotyping services to academic research projects (www.genotyping.se).

Ann-Christine Syvänen’s major research interests are the development of technology for analysis of genetic variation, as well as the application of the technology in medical and biological studies. Her most important scientific contribution is that she pioneered the “minsequencing” primer extension method which is the reaction principle underlying many SNP genotyping methods used today. She is the author of more than 180 scientific publications, she has supervised 8 PhD theses and she has been a co-organizer of several international (EMBO, HUGO) and national (WCN) conferences and practical courses in the SNP and mutation detection field.

Ann-Christine Syvänen has produced 183 publications (102 original articles, 46 review articles or book chapters, 21 articles in congress proceedings, 3 patent families, 11 miscellaneous).

Petri Olli Viljami Auvinen

Present position: Group leader, Institute of Biotechnology, University of Helsinki

Education:

- › 1987: M. Sc., genetics, University of Turku, Finland.
- › 1990: Ph. D., genetics, University of Turku, Finland.
- › 1998: Docent, virology, University of Helsinki, Finland.

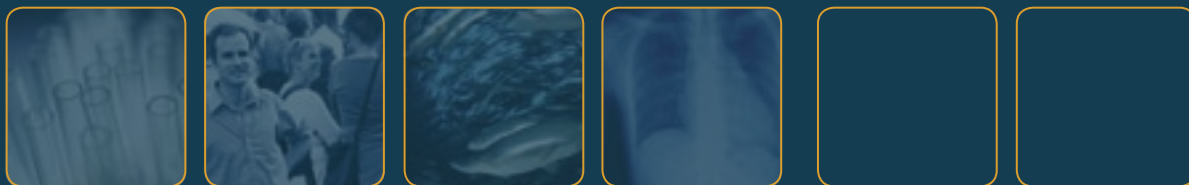
Petri Auvinen has studied genetics enteroviruses during his Ph.D. thesis project. After his Ph.D. thesis he spent the first post doctoral period in Turku working on the structure and function of the syndecan-1 gene. He spent his second postdoctoral period in EMBL Germany working on cell biology aspects of the regulation of the polarity of mammalian cells. After the period in Heidelberg he returned to Finland where he worked as a staff scientist at the Institute of Biotechnology. During this time he was involved in many projects concerning replication strategies and mechanism of mammalian and plant RNA viruses belonging to the group of alphaviruses. Since 2000 he has lead the DNA microarray group at the Institute of Biotechnology, University of Helsinki. He has been involved in many projects dealing with EST library sequencing, whole genome sequencing projects and DNA microarray production including the bioinformatics connected to these kinds of approaches.

Scientific expert functions:

1999-2002: Member of the Board of the Institute of Biotechnology, University of Helsinki; External reviewer for 4 M.Sc. theses and 5 Ph.D. theses; Member of 5 graduate school doctoral thesis follow-up groups at the University of Helsinki.



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