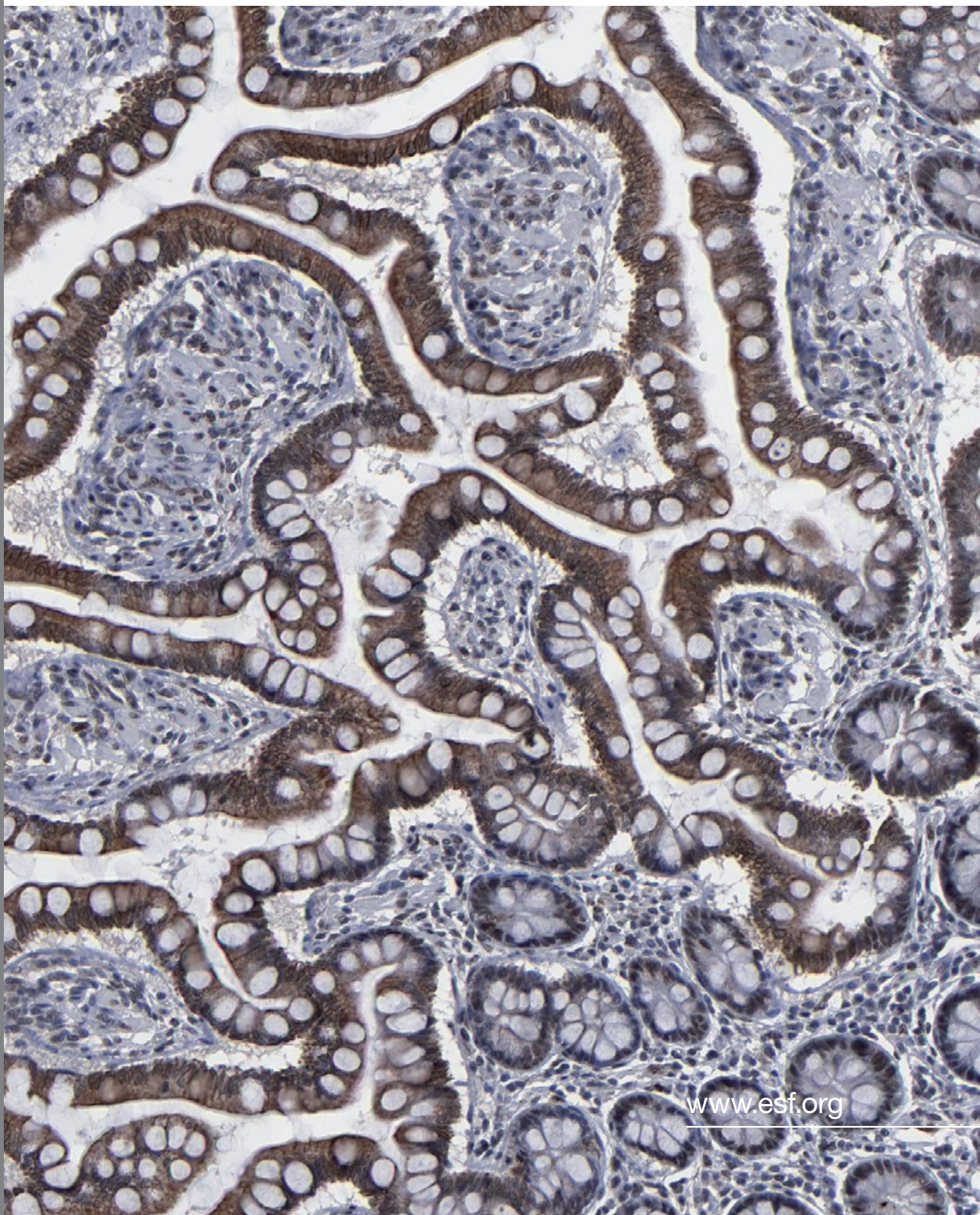
EUROPEAN SCIENCE FOUNDATION

SETTING SCIENCE AGENDAS FOR EUROPE

RESEARCH NETWORKING PROGRAMME

FRONTIERS OF FUNCTIONAL GENOMICS (FFG)

Standing Committee for Life, Earth and Environmental Sciences (LESC)
Standing Committee for the European Medical Research Councils (EMRC)



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Cover picture:
BAZ1A staining of human small intestine

Introduction

Following the sequencing of many genomes, genomics research has focused increasingly on elucidating the functions of gene products and their translation into the complex organisation of cells, tissues and organisms. These are the essential goals of functional genomics, the exploration of gene function on a global scale. Functional genomics investigations typically use large-scale assays in which many of the genes or proteins of an organism can be measured and tracked in parallel through space and time or under different environmental conditions. Revolutionary technologies, such as microarrays, are used, capable of high sample throughput and producing vast amounts of data requiring computational processing for interpretation. With the increasing assimilation of data by bioinformatics tools, integration into systems-level understanding has become a primary objective. Thus, functional genomics impacts in the most fundamental way on biological understanding, from individual molecules to cellular organisation and the physiology of whole organisms and their dysfunction in disease.

'Frontiers of Functional Genomics' follows on from a previous ESF programme, 'Integrated Approaches to Functional Genomics', which was established in November 2000 for five years in order to foster communication and interactions among European researchers. The focus of Integrated Approaches was to unite experimental technologies and complementary informatics tools, facilitating discussion, networking, collaboration, common standards and training opportunities. It engaged a wide audience and through workshops, courses, major conferences on Functional Genomics and Disease in 2003 and 2005, an exchange fellowship scheme and a website, made a significant contribution to the genomics research environment.

Frontiers of Functional Genomics now aims to connect the most promising developments in functional genomics technologies with the expanding concept of systems biology, focusing particularly on applications in biomedicine, as well as the environment and implications for society at large. Frontier technology developments include high throughput array-based methods for analysis of genome variation, genome resequencing and protein detection, nanobiotechnology for single cell and single molecule analysis, and RNA interference, now the leading gene knockdown method. Through bioinformatics tools, data generated is integrated into the holistic systems biology approach, which complements the traditional study of genes and proteins as isolated entities by regarding biological systems as networks of complex relations, requiring high throughput experimental approaches together with mathematical simulation and modelling.

Central to the programme are the applications of functional genomics and systems biology in biomedicine, including epigenomics, neurogenomics, metabolomics, pharmacogenomics and predictive and personalised medicine, which will have a major impact on both understanding and treating disease in the future. Environmental issues include how post-genomic technologies and metagenomics can strengthen understanding of natural ecosystems. Consideration is also given to the social expectations that underlie European public funding of functional genomics research, including understanding of risks, ethical and legal issues, the implications of biobanking, and furthering of genomics-related biotechnology.

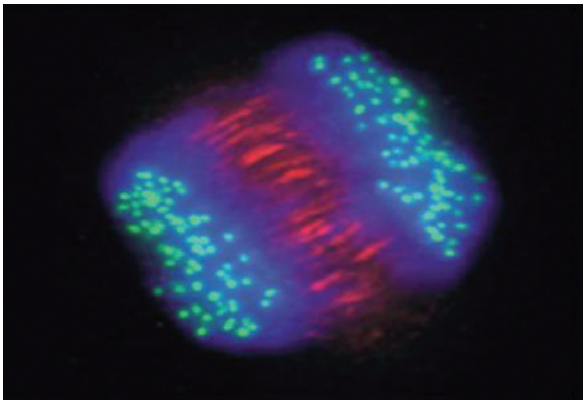

Figure 1 shows a dividing HeLa cell where the chromosomes are stained with DAPI (blue) and the two regulatory proteins, Hec1 (green) and Survivin (red), are labelled with specific antibodies, with kind permission of Marko Kallio.

The running period of the ESF Frontiers of Functional Genomics Research Networking Programme is for five years from June 2006 to May 2011.

Scope and Objectives

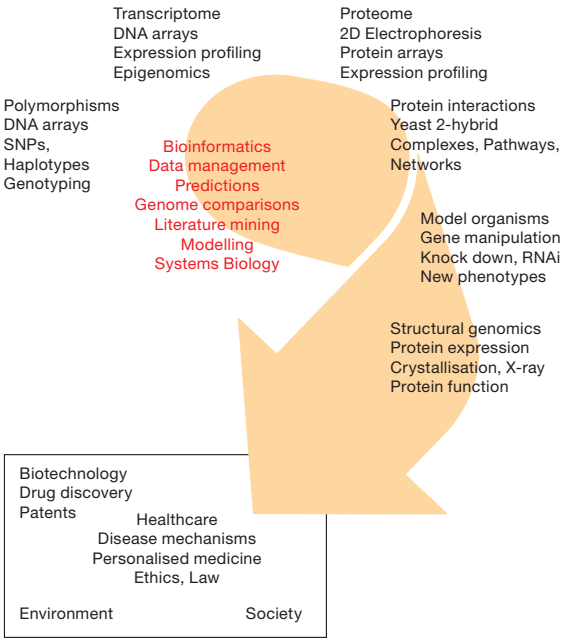

Figure 2: Areas of Functional Genomics

Figure 2 shows an overview of the major areas of functional genomics which come into the scope of the programme, illustrating their integration through bioinformatics and systems biology, and indicating that they impinge directly on human health, environment, industry and society. High throughput data for genome-wide analysis are obtained using a variety of technologies, followed by computer-based analysis and then integration. Key data areas include: genome-wide variation; gene expression at the mRNA and protein levels; protein interactions and organisation in networked pathways; and the effects of modification of gene structure and expression in model organisms. Bioinformatics tools identify function through genome comparisons, predictions, literature mining and modelling, while integration enables interpretation and understanding at the whole-cell and organism levels (systems biology). The implications of functional genomics research are particularly important in healthcare, from greater disease understanding to predictions, novel therapies and new opportunities for industry; in addition there are environmental implications, while ethical and legal issues are of increasing public interest and concern. These different aspects define specific areas of focus for the programme. Building on the success of the Integrated Approaches programme, the Frontiers programme takes functional genomics a stage further into systems biology and explores key areas of its applications, particularly in biomedicine.

Programme Areas

The first area of focus is on **emerging technologies** including arrays, nanosystems, and gene silencing. Highly sensitive array systems (biochips) are being developed for genotyping, resequencing, transcriptome analysis, protein detection and function, and cell and tissue analysis, while nanosystems allow for detection and analysis down to the single molecule and single cell levels. Mutational and knockdown strategies, particularly the powerful RNA interference (RNAi), can specifically silence individual genes, the phenotypic effects of which can be observed on a global scale in genetically amenable model organisms or cells.

A second focus is on **bioinformatics**, without which the data cannot be made accessible, organised and understood, and **systems biology**. The latter, one of the most far-reaching developments in recent years, attempts to understand function not on individual genes or proteins but on multimolecular modules and ever more complex systems. Three levels of genomic analysis – the mRNA level, the protein level, and the level of low molecular weight intermediates (metabolites) – combine to provide an understanding of whole organism functioning. Systems biology aims to describe how the molecular properties of the cell the predictable development of organs and the organism as a whole.

There is great potential for the human genome sequence information, through the application of new technologies and systems biology, to yield new insights into the pathogenesis of human diseases and new strategies for prevention or treatment. **Biomedicine** is therefore a third major focus for this programme, from disease understanding to predictive and personalised approaches to treatment and responses to drugs. Functional genomics will increase the understanding of disease mechanisms and guide the development of new drugs and therapeutic procedures. Areas coming to the fore where technologies are key include:

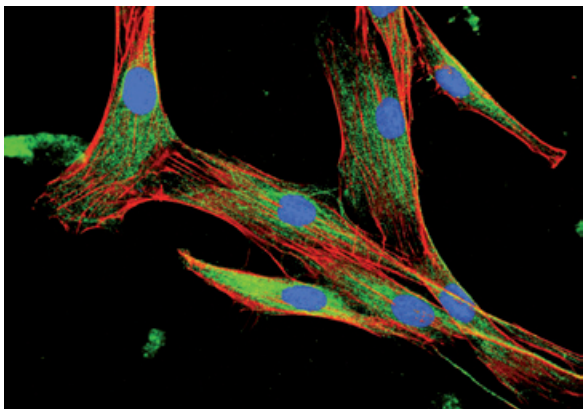

Figure 3: Staining with llama single chain anti-muscle actin A1
© Silvere van der Maarel

Figure 4: An antibody microarray upon incubation with a labelled sample of serum proteins from a single patient © Joerg Hoheisel

- **epigenetics** and **epigenomics** describe heritable chromatin and DNA modifications that alter gene expression without altering the DNA sequence. The study of epigenomics will greatly expand the understanding of gene regulation and disease, especially in oncology;
- **neurogenomics**, which is leading to the assembly of gene expression and function maps in the brain and relating them to neurological disease;
- **metabolomics**, in which comprehensive knowledge of metabolic pathways has applications in biomarker discovery and toxicology;
- **pharmacogenomics** examines the influence of genetic variation on drug response and has enormous implications for personalised medical interventions.

Other emerging biomedical topics are stem cell genomics and cardiogenomics. In addition, population genomics and epidemiology are a particular European strength which will continue to be an important part of identifying disease genes. Therapeutic as well as economic benefits accrue through the biotechnology and pharmaceutical industries, which use the new methods and knowledge to identify novel drug targets.

Genomic analysis also leads to increased appreciation and understanding of the diversity **of the environment**. The programme will explore means of strengthening efforts to apply post-genomics technologies (e.g. metagenomics) to improving understanding of natural ecosystems and to exploit their capabilities to degrade xenobiotic chemicals and other pollutant products of human activities.

Finally, we propose to take into account the interface between advances in **functional genomics research and society**. Biobanks and populations are now major resources for genome research; the use of both sources has raised significant ethical and legal questions. The programme will aid the understanding of risks and promote discussion of the ethical and legal issues to be confronted through public and governmental debate.

Frontiers of Functional Genomics encourages collaboration and interaction through a series of small- and medium-scale **workshops**. Following on from three very successful conferences, the fourth biennial **Functional Genomics and Disease conference** is being held 14-17th April 2010 in Dresden, Germany. **Training courses** help to train a new generation of young researchers and technicians in emerging technologies. **Bursaries** are available through science meeting organisers to facilitate the attendance of young scientists. **Exchange grants** promote mobility of researchers between laboratories in different European counties and hence contribute both to training and to advancing basic research projects. Programme information is disseminated through the **website** where there is also an opportunity to sign up to an email information service. These instruments provide opportunities for communication and outreach, dissemination of research information and data, and training. The programme also actively interacts with other international organisations and initiatives, particularly the increasing range of EC Framework projects and networks related to the genomics area.

Funding Opportunities There are usually two calls for proposals for both science meetings and short visit and exchange grants per year with deadlines in spring and autumn. To apply for these funds and for further information please go to the programme website: www.functionalgenomics.org.uk.

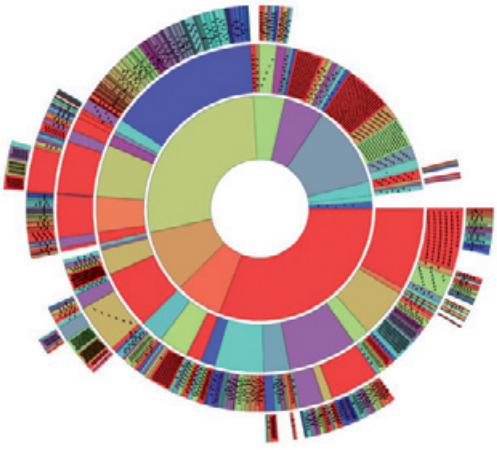

Figure 5: image from the GNOM project
© www.moebio.com/santiago/gnom/

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FFG Steering Committee

Dr. Michael Taussig (Chair)
Technology Research Group
Babraham Bioscience Technologies • Babraham Campus
Cambridge CB22 3AT • United Kingdom
Tel: +44 1223 496557 • Fax: +44 1223 496045
Email: mike.taussig@bbsrc.ac.uk

Professor Siv Andersson
Head
Department of Evolution, Genomics and Systematics
Uppsala University
Norbyvägen 18C • 752 36 Uppsala • Sweden
Tel: +46 18 471 43 79
Email: Siv.Andersson@ebc.uu.se

Dr. Christiane Branlant
UMR 7567 CNRS
Maturation des ARN et Enzymologie Moléculaire
Faculté des Sciences
Bld des Aiguillettes • B.P. 239
54506 Vandœuvre-les-Nancy Cedex • France
Tel: +33 3 83 68 43 05 • Fax: +33 3 83 91 20 93
Email: christiane.branlant@maem.uhp-nancy.fr

Professor Søren Brunak
Center for Biological Sequence Analysis
BioCentrum
Building 208
Kemitorvet • 2800 Lyngby • Denmark
Tel: +45 45 25 24 77 • Fax: +45 45 93 15 85
Email: brunak@cbs.dtu.dk

Professor Christoph Dehio
Department of Molecular Microbiology
Biozentrum
Klingelbergstrasse 50-70 • 4056 Basel • Switzerland
Tel: +41 61 267 2140 • Fax: +41 61 267 2118
Email: christoph.dehio@unibas.ch

Professor Joachim Engels
Institute of Organic Chemistry and Chemical Biology
Faculty of Chemistry and Pharmacy
Marie-Curie-Strasse 11 • 60439 Frankfurt/Main • Germany
Tel: +49 69 798 29150 • Fax: +49 69 798 29148
Email: joachim.engels@chemie.uni-frankfurt.de

Professor Evelyne Friederich
Life Sciences Reserach Unit
Cytoskeleton and Cell Plasticity Lab
162A, Avenue de la Faïencerie
1511 Luxembourg • Luxembourg
Tel: +352 46 66446448 • Fax: +352 621 541354
Email: evelyne.friederich@uni.lu

Professor Michel Georges
Service de Génétique Factorielle et Moléculaire
Faculté de Médicine Vétérinaire
Bld de Colonster 20 B 43/3
4000 Sart Tilman (Liège 1º) • Belgium
Tel: +32 4 366 41 57 • Fax: +32 4 366 41 98
Email: Michel.Georges@ulg.ac.be

Professor Lukas A. Huber
Division für Zellbiologie
Medizinische Universität Innsbruck
Christoph-Probst-Platz
Innrain 52 • 6020 Innsbruck • Austria
Tel: +43 512 9003 70170
Fax: +43 512 9003 73100
Email: Lukas.A.Huber@i-med.ac.at

Dr. Hana Kovarova
Institute of Animal Physiology and Genetics
Rumburská 89 • 22721 Libechov • Czech Republic
Tel: +420 3 156 395 66 • Fax: +420 3 156 971 86
Email: kovarova@iapg.cas.cz

Professor Andres Metspalu
Estonian Biocentre
Department of Biotechnology
Institute of Molecular and Cell Biology
Riia 23 • 51010 Tartu • Estonia
Tel: +372 7 375 066 • Fax: +372 7 420 286
Email: andres@ebc.ee

Professor Aarno Palotie
Director
Finnish Genome Centre
PO Box 63 • Haartmaninkatu 8 • 00014 Helsinki • Finland
Tel: +358 9 1912 5470 • Fax: +358 9 1912 5478
Email: palotie@mappi.helsinki.fi

Professor Joanna Rytka
Department of Genetics
Institute of Biophysics and Biochemistry
Polish Academy of Sciences
ul. A. Pawinskiego 5a • 02-106 Warsaw • Poland
Tel: +48 22 592 12 21 • Fax: +48 22 658 46 36
Email: rytka@psd.ibb.waw.pl

Professor Kjetil Taskén
The Biotechnology Centre of Oslo
Department of Medical Biochemistry
PO Box 1125 Blindern • 0317 Oslo • Norway
Tel: +47 228 40505 • Fax: +47 228 40506
Email: Kjetil.tasken@biotek.uio.no

Professor Alfonso Valencia
Structural and Computational Biology Programme
(S-CompBio)
Fundación Centro Nacional de Investigaciones Oncológicas
c/ Sinesio Delgado 6 • 28029 Madrid • Spain
Tel: +34 91 732 80 59 • Fax: +34 91 224 69 76
Email: valencia@cnio.es

Professor Christine Van Broeckhoven
Scientific Director
Department of Molecular Genetics VIB8
Flanders Interuniversity Institute for Biotechnology/Institute
Born-Bunge
Parking P4, Building V, Room 0.10
Universiteitsplein 1 • 2610 Antwerpen • Belgium
Tel: +32 3 265 1001 • Fax: +32 3 265 1012
Email: christine.vanbroeckhoven@ua.ac.be

Professor Gertjan B. van Ommen
Head
Center for Human and Clinical Genetics and Center for
Medical Systems Biology
Department of Human Genetics
LUMC, zone S-4-P
P.O. Box 9600 • 2300 RC Leiden • Netherlands
Tel: +31 71 526 9400 • Fax: +31 71 526 8285
Email: gjvo@lumc.nl

Dr. Isik Yulug
Department of Molecular Biology and Genetics
Faculty of Science
B. Building • 06800 Ankara • Turkey
Tel: +90 312 290 25 06 • Fax: +90 312 266 50 97
Email: yulug@fen.bilkent.edu.tr

Programme Coordinator:

Dr. Cheryl Smythe
Babraham Bioscience Technologies
Babraham Research Campus
Cambridge CB22 3AT • United Kingdom
Tel: +44 1223 496246 • Fax: +44 1223 496045
Email: cheryl.smythe@bbsrc.ac.uk

ESF Liaison

Dr. Lars Kristiansen
Science Officer
Ms. Céline Seewald
Administration

Life, Earth and Environmental Sciences Unit
European Science Foundation
1 quai Lezay-Marnésia • BP 90015
67080 Strasbourg cedex • France
Tel: +33 (0)3 88 76 71 58 • Fax: +33 (0)3 88 37 05 32
Email: cseewald@esf.org

For the latest information on this Research Networking Programme consult the FFG websites:
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EUROPEAN SCIENCE FOUNDATION
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1 quai Lezay-Marnésia | BP 90015
67080 Strasbourg cedex | France
Tel: +33 (0)3 88 76 71 00 | Fax: +33 (0)3 88 37 05 32
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