



EuroMouse
Understanding human disease through mouse genetics
The European dimension

14th October 2005, Venice

Draft Agenda

Introduction

09:00 – 09:10 **Meeting aims**
Steve Brown, MRC Mammalian Genetics Unit, UK

CHAIR: Glauco Tocchini-Valentini

Session 1: Mutation and gene expression

09:10 – 09:30 **EUMORPHIA, European Union Mouse Research for Public Health and Industrial Applications**
Steve Brown, MRC Mammalian Genetics Unit, UK

09:30 – 09:50 **FunGenES, Functional genomics in Engineered mouse ES Cells**
Jürgen Hescheler, Institute of Neurophysiology, University of Cologne, Germany

09:50 -10:10 **EurExpress, A European consortium to generate a web-based gene expression atlas by RNA *in situ* hybridisation**
Andrea Ballabio, TIGEM, Italy

10:10 – 10:30 **BioSapiens, A European Network for Integrated Genome Annotation**
Ewan Birney, EMBL-EBI, UK

10:30 – 11:00 ***TEA AND COFFEE***

11:00 – 11:20 **FLPFLEX, A flexible toolkit for controlling gene expression in mouse**
Nadia Rosenthal, EMBL, Monterotondo, Italy

11:20 – 11:40 **EUCOMM, European Conditional Mouse Mutagenesis Program**
Allan Bradley, The Wellcome Trust Sanger Institute, UK

CHAIR: Steve Brown

Session 3: Use of mouse models to investigate disease

11:40 – 12:00 **MUGEN, Integrated functional genomics in mutant mouse models as tools to investigate the complexity of human immunological disease**
Georgios Kollias, Biomedical Sciences Research Centre "Alexander Fleming", Greece



- 12:00 – 12:20 **Lymphangiogenomics, Genome-Wide Discovery and Functional Analysis of Novel Genes in Lymphangiogenesis**
Kari Alitalo, University of Helsinki
- 12:20 – 12:40 **EUROHEAR, Advances in hearing science: from functional genomics to therapies**
Karen Avraham, Tel Aviv University, Israel
- 12:40 – 13:00 **EuReGene, European Renal Genome Project**
Thomas E Willnow, Max-Delbrueck-Center for Molecular Medicine, Germany
- 13:00 – 14:00 **LUNCH**
- 14:00 – 14:20 **MYORES, Multi-Organismic approach to study normal and aberrant muscle development, functions and repair**
Krzysztof Jagla, INSERM U384, France

CHAIR: Georgios Kollias

Session 4: Imaging

- 14:20 – 14:40 **MolecularImaging: integrated technologies for in-vivo molecular imaging**
Jorge Ripoll, University of Crete, Greece
- 14:40 – 15:00 **Pathbase, European Mutant Mouse Pathology Database**
Paul Schofield, University of Cambridge, UK

CHAIR: Nadia Rosenthal

Session 5:

- 15:00 – 15:30 **PRIME, Priorities for Mouse Functional Genomic Research in Europe**
Steve Brown, MRC Mammalian Genetics Unit, UK
- 15:30 – 16:00 **TEA AND COFFEE**
- 16:00 – 16:30 **EMMA, European Mouse Mutant Archive**
Martin Hrabé de Angelis, GSF-IEG, Germany
- 16:30 – 17:30 **Open discussion**
Priorities for mouse research for presentation to Research Councils, Funders and Policy Makers at the EC Funders' Forum at December 2006



**PRIME 1st Open Scientific Meeting
Priorities for mouse functional genomics research**

15th October 2005, Venice

Draft agenda

CHAIR: Andrea Ballabio

- 09:00 – 09:05 **Introduction of the aims of PRIME**
Steve Brown, MRC Mammalian Genetics Unit, Harwell
- 09:05 – 09:20 **EC Perspective on research funding**
Jacques Remacle, DG Research, European Commission
- 09:20 – 09:35 **Systematic production of mutant mice**
Wolfgang Wurst, GSF-IDG, Germany
- 09:35 – 09:50 **Emerging technologies for mutagenesis**
Glauco Tocchini-Valentini, CNR, Italy
- 09:50 - 10:05 **Role and future of archives**
Martin Hrabé de Angelis, GSF-IEG, Germany
- 10:05 - 10:35 **Open Discussion - systematic production and archiving of mouse strains**
- 10:35 – 11:05 ***TEA AND COFFEE***

CHAIR: Johan Auwerx

- 11:05 – 11:35 **Development of phenotyping and European phenotyping centres**
Mary Lyon Centre, Steve Brown, MRC Harwell, UK
German Mouse Clinic, Martin Hrabé de Angelis, GSF-IEG, Germany
Institut Clinique de la Souris, Strasbourg, France
- 11:35 – 11:50 **Australian Phenomics Facility and NHMRC Australian Phenome Bank**
Christopher Goodnow, Director, Australian Phenomics Facility, Australian National University, Canberra
- 11:50 - 12:20 **Bioinformatics – ontologies to databases**
John Hancock, MRC Mammalian Genetics Unit, Harwell, UK
Paul Schofield, University of Cambridge, UK
- 12:20 – 12:40 **Laboratory Animal Science and Welfare**
Rikke Thon, Harlan Scandinavia, Denmark
- 12:40 - 13:00 **Open Discussion - international phenome databases**
- 13:00 – 14:00 ***LUNCH***



CHAIR: Steve Brown

14:00 – 15:15 **Open Forum - presentation of 2 slides from all speakers on priorities for mouse functional genomics**

15:15 - 15:45 *TEA AND COFFEE*

15:45 – 16:30 **Final Open Discussion - Priorities for mouse research in Europe**

17:00 – 18:00 **PRIME SAG by invite only**



EuroMouse **Project Summaries**

EUMORPHIA, FP5 Integrated Project – European Union Mouse Research for Public Health and Industrial Applications

The mouse genome is 95 % identical to the human genome and so mice with genetic diseases are potentially very good models for the equivalent human diseases. These models are essential to develop and test potential new treatments for human diseases. EUMORPHIA (European Union Mouse Research for Public Health and Industrial Applications) is funded by the European Commission under FP5. It brings together a large consortium of 18 research centres in 8 European countries. The project is founded with the intention of advancing research into functional mouse genetics at a height that will significantly enrich both the academic and commercial sectors of our medical research community. Incorporating the expertise and resources of many European mouse genetics centres, the main focus of the project has been on the development of novel approaches in phenotyping, mutagenesis and informatics to improve the characterisation of mouse models for understanding human molecular physiology and pathology through integrated functional genomics.

Coordinator: Steve Brown, s.brown@har.mrc.ac.uk

FunGenES, Integrated Project - Functional genomics in Engineered mouse ES Cells

Self-renewal, commitment and differentiation of murine ES cells will be investigated in this project using a functional genomics approach to discover genes, regulatory pathways and fundamental molecular and cellular mechanisms. This ambitious project is industry-led and has a number of SMEs. The project management will be carried out by a professional project management company to assist the scientific coordinator (at a large pharmaceutical company).

Coordinator: Jürgen Hescheler, j.hescheler@uni-koeln.de

EurExpress, Integrated Project - A European consortium to generate a web-based gene expression atlas by RNA *in situ* hybridisation

The proposal builds on a strong European concentration of skills in gene expression analysis and mouse genomics. The aim is to generate a “transcriptome atlas” of the expression of more than 20 000 genes during mouse development. Image data will be collected using automated scanning microscopes, annotated and entered into a web-linked database for ready access by the scientific community. For a subset of genes, mainly those involved in human diseases, the research will allow a comparison of mouse and human gene expression patterns in adult tissues, with a likely significant impact on the identification of gene expression markers of disease processes.

Coordinator: Andrea Ballabio, ballabio@tigem.it

BIOSAPIENS, Network of Excellence - A European Network for Integrated Genome Annotation

The subject of this network is genome annotation, which is the process of ‘defining the biological role of molecules (DNA, proteins, etc.) in all their complexity’. The field absolutely requires this network to structure and integrate the necessary expertise and European infrastructure to allow distributed and co-ordinated experimental and computational approaches to achieve a unified annotation process. This project is also integrating the mouse Ensembl genome annotation program.



Coordinator: Janet Thornton, thornton@ebi.ac.uk

FLPFLEX, STREP – A flexible toolkit for controlling gene expression in mouse

The aim of this proposal is to develop a mouse embryonic stem cell library with incorporated Flt recombinase exchange cassette to facilitate the manipulation of gene expression in derived transgenic mice. This will facilitate the dissection of complex genetic pathways and provide more accurate models of human disease. The panel considered that although there are many existing systems available to develop transgenic models there remains a need for further research to improve reproducibility and reliability of this important technology.

Coordinator: Nadia Rosenthal, rosenthal@embl-monterotondo.it

EUCOMM, Integrated Project - The European Conditional Mouse Mutagenesis Program

EUCOMM integrates European skills, efforts, resources, and infrastructure to produce, in a systematic high throughput way, mutations throughout the mouse genome. A collection of up to 20,000 mutated genes will be generated in mouse embryonic stem (ES) cells using conditional gene trapping and gene targeting approaches. This library will enable mouse mutants to be established worldwide in a standardized and cost-effective manner, making mouse mutants available to a much wider biomedical research community than has been possible previously. For a subset of genes believed to be relevant for human disease, mutant mice will be established, archived and analysed. This will offer an opportunity to decipher molecular disease mechanisms and in some cases provide a foundation for the development of diagnostic, prognostic and therapeutic strategies.

Coordinators: Wolfgang Wurst, wurst@gsf.de and Allan Bradley, abradley@sanger.ac.uk

MUGEN, Network of Excellence – Integrated functional genomics in mutant mouse models as tools to investigate the complexity of human immunological disease

The MUGEN network brings together top European immunologists (including a Nobel Prize winner) with the aims to network and regroup the research effort at the EU level, to share common resources and facilities, and to stimulate training activities. The project is centralised around the integrated functional genomics analysis of more than 200 available mouse mutants that display specific immunological defects reminiscent to human immunological diseases. This top quality NoE project will certainly contribute to increase our knowledge on the immune system thereby having a major and durable impact on EU health issues, society and economy.

Coordinator: George Kollias, g.kollias@fleming.gr

LYMPHANGIOGENOMICS, Integrated Project - Genome-Wide Discovery and Functional Analysis of Novel Genes in Lymphangiogenesis

The aim of this project is to discover novel genes important for lymphatic vascular versus blood vascular development and function. Mouse, xenopus and zebrafish models will be used to identify novel genes involved in lymphangiogenesis processes in a functional genomics approach. Mouse models will be used to characterize the involvement of lymphatic vessels in diseases



Coordinator: Kari Alitalo, kari.alitalo@helsinki.fi

EUROHEAR, Integrated Project - Advances in hearing science: from functional genomics to therapies

This is an outstanding, high impact proposal at the cutting edge of contemporary science and technology and consists of internationally recognized leaders in the auditory sciences. The project aims at the identification of the genes underlying sensorineural hearing impairment and their importance as targets for therapy. Multidisciplinary approaches are being used, including mouse, human and drosophila genetics, 2-hybrid screening, access to patients and high-throughput genotyping. Genetic studies will be complemented by fundamental analyses of critical physiological events in inner ear function. Three SMEs are involved to provide technical expertise in genome-wide screens, and for novel approaches of drug design and delivery. This project is regarded as having a high likelihood of success in all aspects and will bring value to the EU.

Coordinator: Christine Petit, cpetit@pasteur.fr

EuReGene, Integrated Project – European Renal Genome Project

This ambitious integrated project aims to identify new genes that are involved in kidney development and diseases. The consortium, composed of European leaders in the field, will employ a wide variety of functional genomic approaches, including gene expression arrays, proteomics tools, directed and random mutagenic approaches in animal models and genetic analysis in isolated human populations in relation to kidney disease, to identify the genetic determinants of kidney development and diseases. The latter will certainly form the basis for discovering potential targets for new drug treatment. Therefore, this project is likely to contribute to improvement of treatment of serious, widespread and expensive kidney diseases.

Coordinator: Thomas E Willnow, willnow@mdc-berlin.de

MYORES, Network of Excellence – Multi-Organismic approach to study normal and aberrant muscle development, functions and repair.

The MYORES network of excellence combines the best European research groups in muscle research in a highly interactive research programme. This NoE relies on use of integrated genomics approaches in a wide array of model organisms ranging from fly, C.elegans, zebrafish, mouse and human to identify new genes and pathways important for muscle diseases and repair. Because the field of muscle research is not structured in the US, coordination of the European research through this NoE is likely to place Europe at the forefront of muscle research. This project will certainly generate important new knowledge on muscle physiology and diseases and thereby will open new avenues for developing novel therapeutical approaches.

Coordinator: Krzysztof Jagla, Christophe.JAGLA@u-clermont1.fr

MOLECULAR IMAGING, Integrated Project - Integrated technologies for in-vivo molecular imaging

This project brings together a multidisciplinary team (engineers, physicists and biologists) focused on developing and applying high resolution methods of *in vivo* molecular imaging. The



development of these new techniques and probes will enable scientists to solve biological questions on the sub-cellular, cellular and whole small animal (mouse) level.

Coordinator: Eleftherios N. Economou, economou@admin.forth.gr

Pathbase, FP5 project - European Mutant Mouse Pathology Database

Transgenic rodents are a key tool in understanding human and animal disease. Analysis of these systems requires considerable expertise in pathology and it is the aim of this project to integrate this expertise in Europe and to teach and inform scientists using transgenic rodents. Pathbase is a database that stores images of the abnormal histology associated with spontaneous and induced mutations of both embryonic and adult mice including those produced by transgenesis, targeted mutagenesis and chemical mutagenesis. Images of normal mouse histology and strain-dependent background lesions are also available. The database and the images are publicly accessible (<http://www.pathbase.net>) and linked by anatomical site, gene and other identifiers to relevant databases; there are also facilities for public comment and record annotation. The database is structured around a novel ontology of mouse disorders (MPATH) and provides high-resolution downloadable images of normal and diseased tissues that are searchable through orthogonal ontologies for pathology, developmental stage, anatomy and gene attributes (GO terms), together with controlled vocabularies for type of genetic manipulation or mutation, genotype and free text annotation for mouse strain and additional attributes. The database is actively curated and data records assessed by pathologists in the Pathbase Consortium before publication. The database interface is designed to have optimal browser and platform compatibility and to interact directly with other web-based mouse genetic resources.

Coordinator: Paul Schofield, PS@mole.bio.cam.ac.uk

PRIME, Coordination Action - Priorities for mouse functional genomics research across Europe

The key aims of PRIME are:

- to bring together national policy makers, funders and scientists to share information on national policies and funding mechanisms
- to form a durable integration of research capabilities and resource centres across Europe in the field of mouse functional genomics
- to enhance the identification of key goals for future research directions in European mouse genetics

Coordinator: Steve Brown, s.brown@har.mrc.ac.uk

EMMAinf, Integrated Infrastructures Initiative - European Mutant Mouse Archive Infrastructure

The European scientific community is internationally competitive in the production and characterisation of mouse models for inherited diseases. However, it is proving to be impossible, for even the largest and best-funded research institutes, to retain all of their mouse strains, once the purpose for which they were originally made has been achieved. It is essential that all mutants that



have been created be retained and held in a centrally organised, network of repositories from which they can readily be made available to interested investigators. If this is not done, then many valuable mutant animals will be lost because of the constraints of space and finance that affect the individual laboratories and industry. To meet these needs the European Mouse Mutant Archive (EMMA) was established and implemented. Currently, EMMA consists of the following partners: CNR, Monterotondo, Italy (centre); CNRS, Orleans, France; MRC, Harwell, UK; Karolinska Institute, Stockholm, Sweden; Gulbenkian Institute, Oeiras, Portugal, HGF/GSF, Munich, Germany and EBI/EMBL Hinxton, UK. EMMA is running under highest quality standard and was opened to the public in 1999. EMMA will be developed towards a virtual repository appearing as one centre to the outside world. Internally, it consists of one centre facility and several satellites.

Coordinator: Glauco Tocchini-Valentini, g.tocchini@ibc.cnr.it

Project Manager: Martin Hrabé de Angelis, hrabe@gsf.de