



INFRAFRONTIER
mouse disease models



The INFRAFRONTIER Research Infrastructure
Michael Hagn – Helmholtz Zentrum München

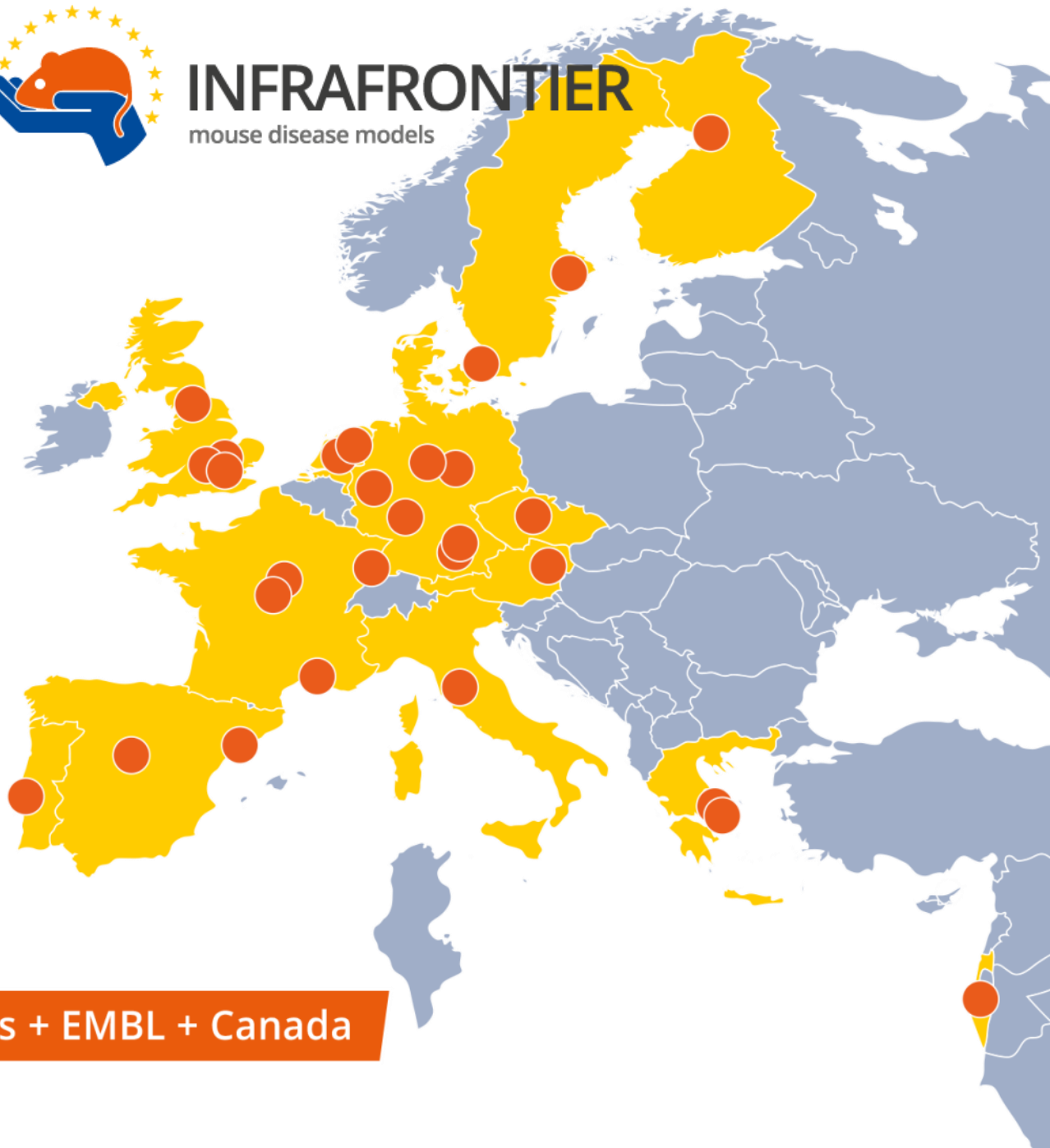
High-quality resources and services for biomedical research



INFRAFRONTIER
mouse disease models



European **Research Infrastructure** for the **generation, systemic phenotyping, archiving** and **distribution** of mammalian models



14 European countries + EMBL + Canada



INFRAFRONTIER stimulates innovation by providing open access to:

- **Mouse disease models and research tools** / European Mouse Mutant Archive (EMMA) repository
 - **Scientific platforms** / Model development / Phenotyping in European Mouse Clinics
 - **Data** / EMMA strain information / Phenotype data
 - **Knowledge** / Cryopreservation and Phenogenomics training courses, dissemination of standards
- Use of the mouse as the foremost mammalian model for studying human disease and human health

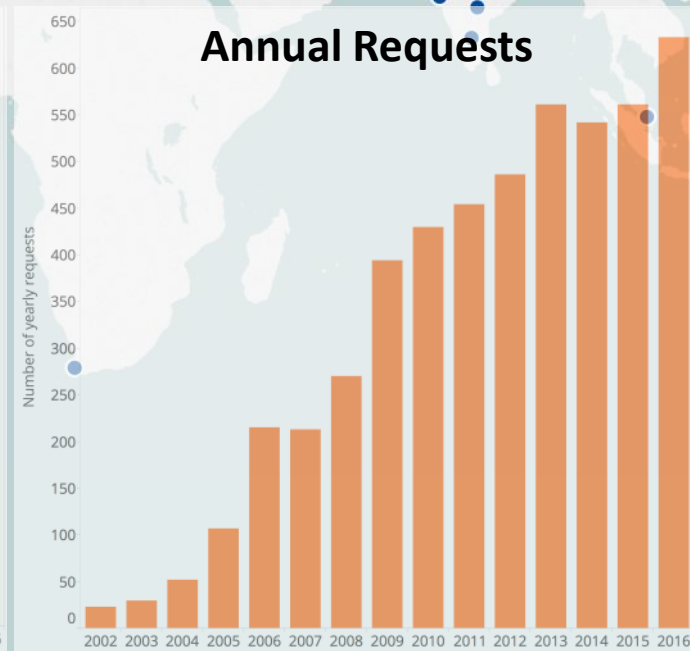
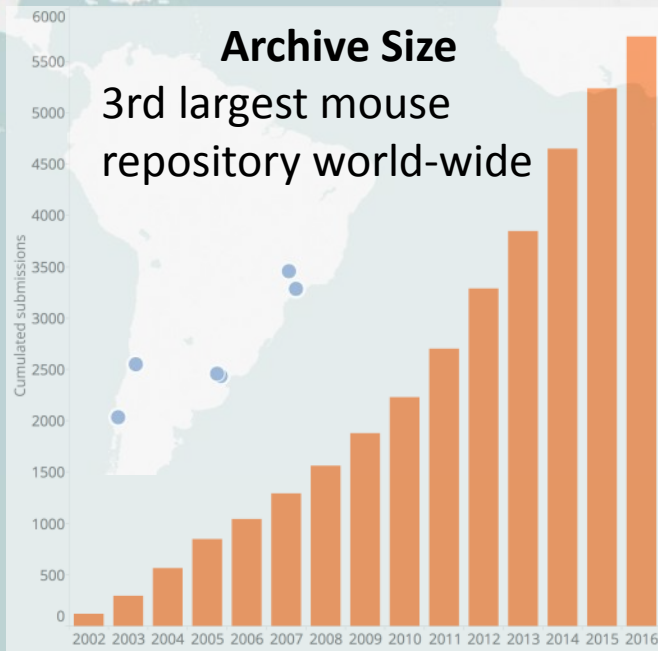
The screenshot displays the Infrafrontier website interface. At the top left is the Infrafrontier logo with the tagline 'mouse disease models'. A navigation bar includes 'Infrafrontier Research Infrastructure', 'Resources and services', 'Procedures', and 'Knowledgebase'. The main content area is divided into several sections:

- Resources and Services:** A grid of six service cards: 'Deposit mice' (EMMA archives mutant mice free of charge), 'Order mice' (Access to 5500 mouse mutants and research tools), 'Axenic service' (EMMA produces germ-free mice free of charge), 'NKI GEMM-ESC archive' (Rapid target gene validation in complex cancer mouse models), 'Mouse production and phenotyping' (INFRAFRONTIER open calls), and 'Training and consulting' (Hands-on courses in cryopreservation and phenotyping).
- EMMA strains:** A search interface for EMMA strains with a search bar and filters for 'Strain Types', 'Genes', and 'Human Diseases'.
- EMMA mouse repository:** A section featuring the EMMA logo and a link to 'genOway EUComm KO models'.
- News & Events:** A list of recent news items, including 'Executive Masters Management of Research Infrastructures - Applications Open' and 'Upcoming INFRAFRONTIER training courses'.

World-wide user community of INFRAFRONTIER / EMMA



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mouse disease models





EMMA cryopreservation service [Learn more >](#)

- Archiving of mutant mouse lines free of charge
- Intellectual property rights remain with original producer
- EMMA distributes mutant mouse lines (SPF) worldwide

EMMA strains

Search EMMA strains

Search by: Gene name/symbol, strain name, EMMA ID, OMIM name/ID, phenotype, ...

Browse EMMA strains

[Strain Types](#) [Genes](#) [Human Diseases](#)

[Help](#)

Major collections

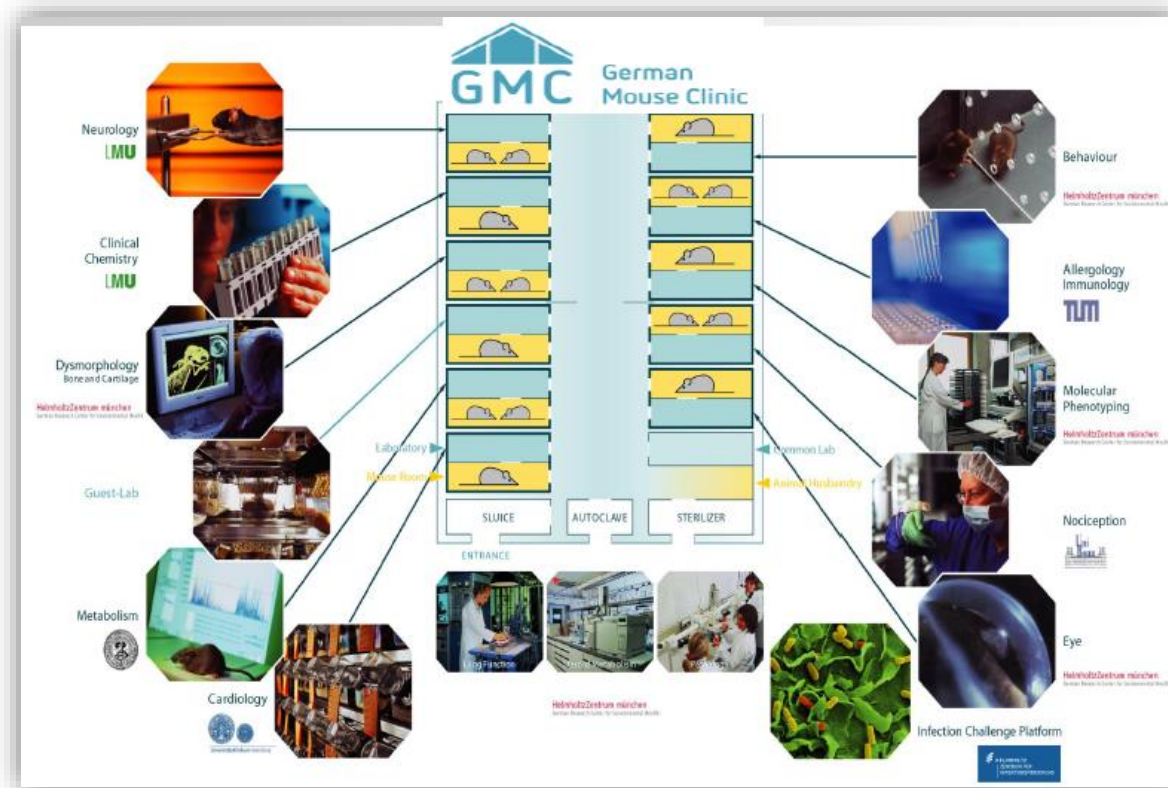
- **2705** mouse strains from IKMC resource
 - **275** Cre expressing strains
 - **62** strains with Tet expression system
- Industry access to IKMC resource via genOway as intermediary (FtO)
- EMMA operating on cost recovery model

Use of mouse models

- Address fundamental scientific questions about in vivo gene function to further our understanding of disease genetics
- BioPharma uses mouse models for the identification and validation of novel drug targets and the analysis of drug action

INFRAFRONTIER phenotyping capacities and expertise

- Systemic phenotyping
- Specialised phenotyping
- Excellence based access (collaboration / TA calls)
- Market based access





- Provision of Trans-national Access to mouse production and systemic phenotyping services
- Delivering 54 new mouse models of human diseases for public access
- 5 TA calls / 206 Proposals

Cell Reports Article

A SLM2 Feedback Pathway Controls Cortical Network Activity and Mouse Behavior

Graphical Abstract

The graphical abstract is divided into four horizontal panels. The top panel shows a circular SLM2 protein with a self-loop arrow, labeled 'SLM2 protein AUTOREGULATES via an RNA processing pathway'. The second panel shows red and black bars representing 'SLM2 protein regulates SPLICING TARGETS encoding synaptic proteins'. The third panel shows a neuron with a blue SLM2 protein binding to a red RNA molecule, labeled 'SLM2 protein controls NEURAL NETWORK ACTIVITY'. The bottom panel shows a mouse with a thought bubble and a brain icon, labeled 'SLM2 controls MOUSE BEHAVIOR dependent on neural networks'.

Authors
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In Brief
SLM2 is an RNA binding protein conserved for ~550 million years. Ehrmann et al. identify a homeostatic feedback pathway that controls SLM2 expression across the brain. Loss of SLM2 protein causes defects in neural network activity and changes mouse behavior.

Accession Numbers
GSE70895

Highlights

- SLM2 splicing targets are spatially controlled within the hippocampus
- RNA-seq reveals SLM2 feedback control and synaptic protein splicing targets
- Loss of SLM2 dampens patterns of hippocampal γ oscillations
- Loss of SLM2 changes mouse behavior that depends on these neural networks

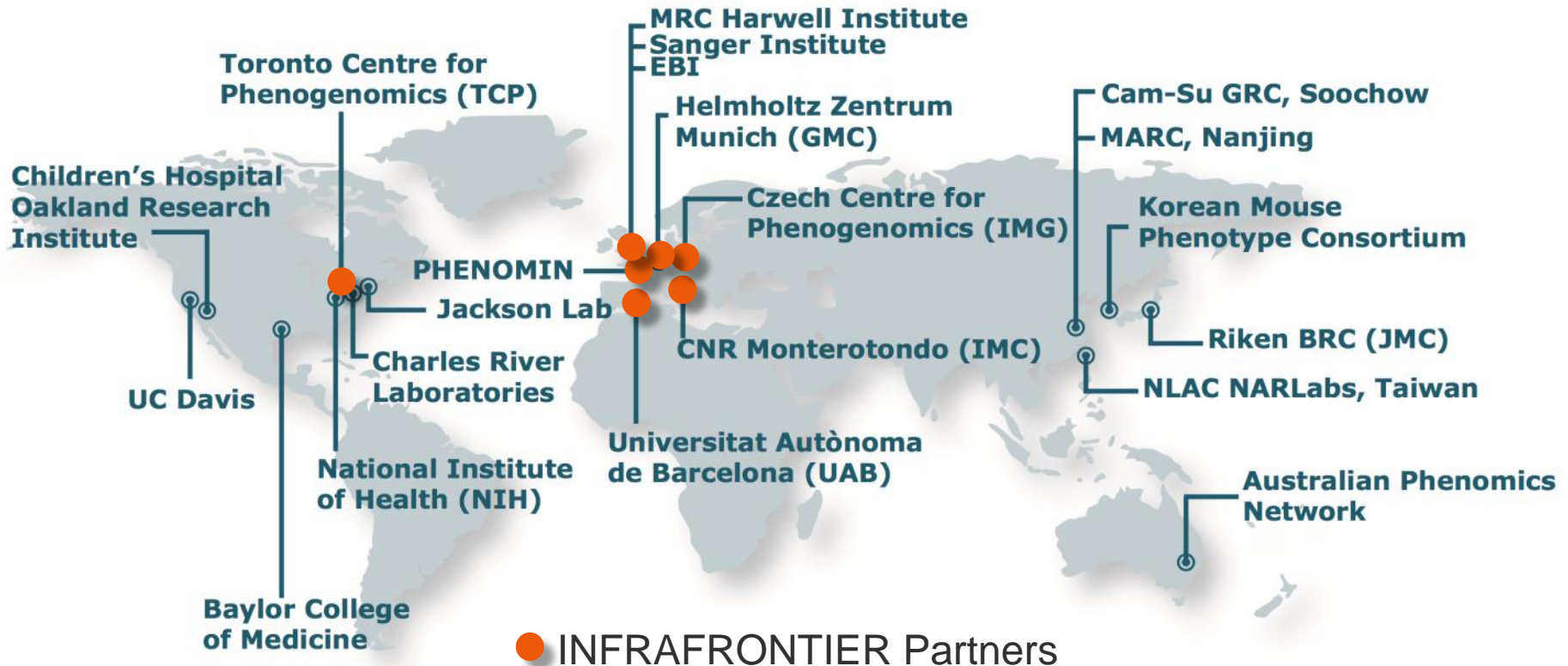


International Mouse Phenotyping Consortium

- First comprehensive catalogue of mammalian gene function
- An engine for discovering the genetic basis for disease
- Open access to data and resources



www.mousephenotype.org





Creation of a catalogue of mammalian gene function

- 5917 mutant lines generated and archived
- 4493 lines with broad phenotyping information
- Rich, multi-dimensional data sets (37.5 M data points)
- Over 750 research papers published using IMPC resources

Transforming the understanding of the mammalian genetic landscape

- NATURE publication on genetic disease to date (1000 genes / doi:10.1038/nature12114)
- 650 new disease associated genes
- Pervasive sexual dimorphism was hitherto unrecognized

IMPC evolves to address new areas of disease

- Strengthen interactions with rare disease consortia and Precision Medicine Initiatives; Use case MLC – Genomics England / deliver mouse alleles for validation of human genetic variation
- 15 % of mutant lines will be aged and re-phenotyped to study late-onset disease



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Biomedcode
Priming drugs for success

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Preclinical drug efficacy evaluation

Biomedcode is a Contract Research Organisation (CRO) providing full preclinical drug evaluation services to the pharmaceutical industry using a unique collection of mouse models of human inflammatory diseases.





More than 250 assays available for various functions

Behavior, cognition & sensory system



- General health, sensory-motor function & pain
- Learning & memory
- Schizophrenia
- Circadian activity & biological rhythm
- Emotional behavior: Depression & Anxiety
- Epilepsy

Nutrition & Metabolism



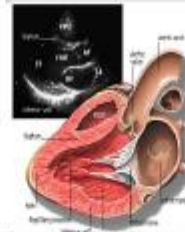
- Energy intake
- Energy expenditure
- Glucose homeostasis
- Bone & Muscle metabolism
- Intestinal and renal function

Clinical chemistry



- Common serum chemistry
- Enzymatic activities
- Lipids & lipoproteins
- Hormones
- Hematology & Coagulation
- Immunology

Cardiovascular system



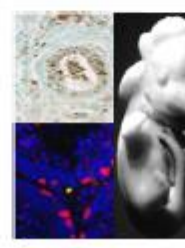
- Blood pressure
- Cardiac electrophysiology
- Cardiac anatomy & function
- Hypertension models
- Hypertrophy models
- Heart failure models

Respiratory system



- Plethysmography
- Bronchoalveolar lavages
- Asthma models
- Airway inflammation models
- Lung fibrosis models

Anatomopathology

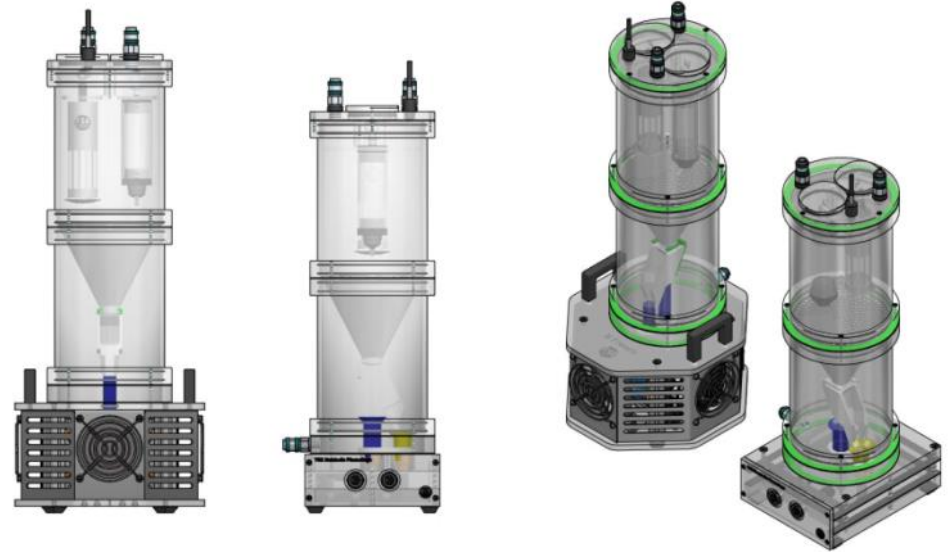


- Necropsy
- Tissue collection
- Histology H&E staining
- Specific stainings
- Immunohistochemistry
- Evaluation of early embryonic death



- To continuously improve resources and services
- To reduce animal use
- To enhance operational efficiencies / cost reduction

TSE Metabolic PhenoCage, 8997 Infrafrontier: features and innovations





INFRAFRONTIER-RI outreach / industry liaison












- 80 participants
- INFRAFRONTIER / IMPC PIs, scientists, advisors
- IMPC Industry Sponsors
- BioPharma
- Research instrumentation developers
- CROs, suppliers and platform companies
- Funders











June 12th - 16th 2017
Château du Liebfrauenberg, Alsace, France

phenomin

EXCELLENCE IN MOUSE PHENOGENOMICS

2nd European Advanced School for Mouse Phenogenomics

The mouse phenog practices regarding the us

- 40 training courses in cryopreservation and phenogenomics
- 400 participants

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Mouse disease models

Infrafrontier Research Infrastructure | Resources and services | Procedures | Knowledgebase

Home / Knowledgebase / Protocols / Cryopreservation protocols

Cryopreservation protocols

All EMMA partners use validated protocols for mouse embryo and spermatozoa freezing techniques, in vitro fertilisation procedures and embryo transfers. However, the EMMA partners use different protocols that are optimized for their individual settings. EMMA distribution centres will provide to customers ordering frozen embryos or spermatozoa the centre specific validated thawing protocols. The protocols provided for download below are practiced in EMMA training courses at the MRC-MGU (Harwell) and are routinely used by the Harwell EMMA node.

Training videos

The Harwell node further provides a number of training videos that enable members of the scientific community to learn the skills and techniques that are used at the MRC. A series of short films that take you step-by-step through the process of freezing mouse embryos and sperm for use in IVF can be viewed at the MRC-Harwell website.

Cryopreservation and IVF protocols

- Introductory presentation on cryopreservation (Feb 2013)
- Mouse sperm cryopreservation and IVF recovery - MBGD+GSH protocol (Feb 2013)
- Mouse IVF recovery using freshly harvested sperm - MBGD+GSH protocol (Feb 2013)
- Rescue IVF protocol for frozen sperm (Feb 2013)
- Mouse sperm cryopreservation from epididymides after transportation at refrigerated temperatures (Jan 2015)



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The INFRAFRONTIER Research Infrastructure

High-quality resources and services for biomedical research



INFRAFRONTIER RI and IMPC deliver quality and reproducibility

- EMMA repository guards health and genetic quality of deposited mice
- EMMA distributes identical reference resources
- IMPReSS (International Mouse Phenotyping Resource of Standardised Screens), contains standardized phenotyping protocols
- Validation of test robustness through reference lines
- Continuous evolution of rigor and standardisation applied to operational procedures and data QC



#Our
Welfare
Works



INFRAFRONTIER stimulates innovation by providing open access to:

- **Mouse disease models and research tools**

EMMA archived 6000 mouse models and shipped 5000 lines

- **Scientific platforms**

EMMA repository (14 nodes) / 7 Mouse Clinics

- **Data**

EMMA strain information / rich multi-dimensional phenotype data

- **Knowledge**

40 Cryopreservation and Phenogenomics training courses

➤ Understanding human diseases