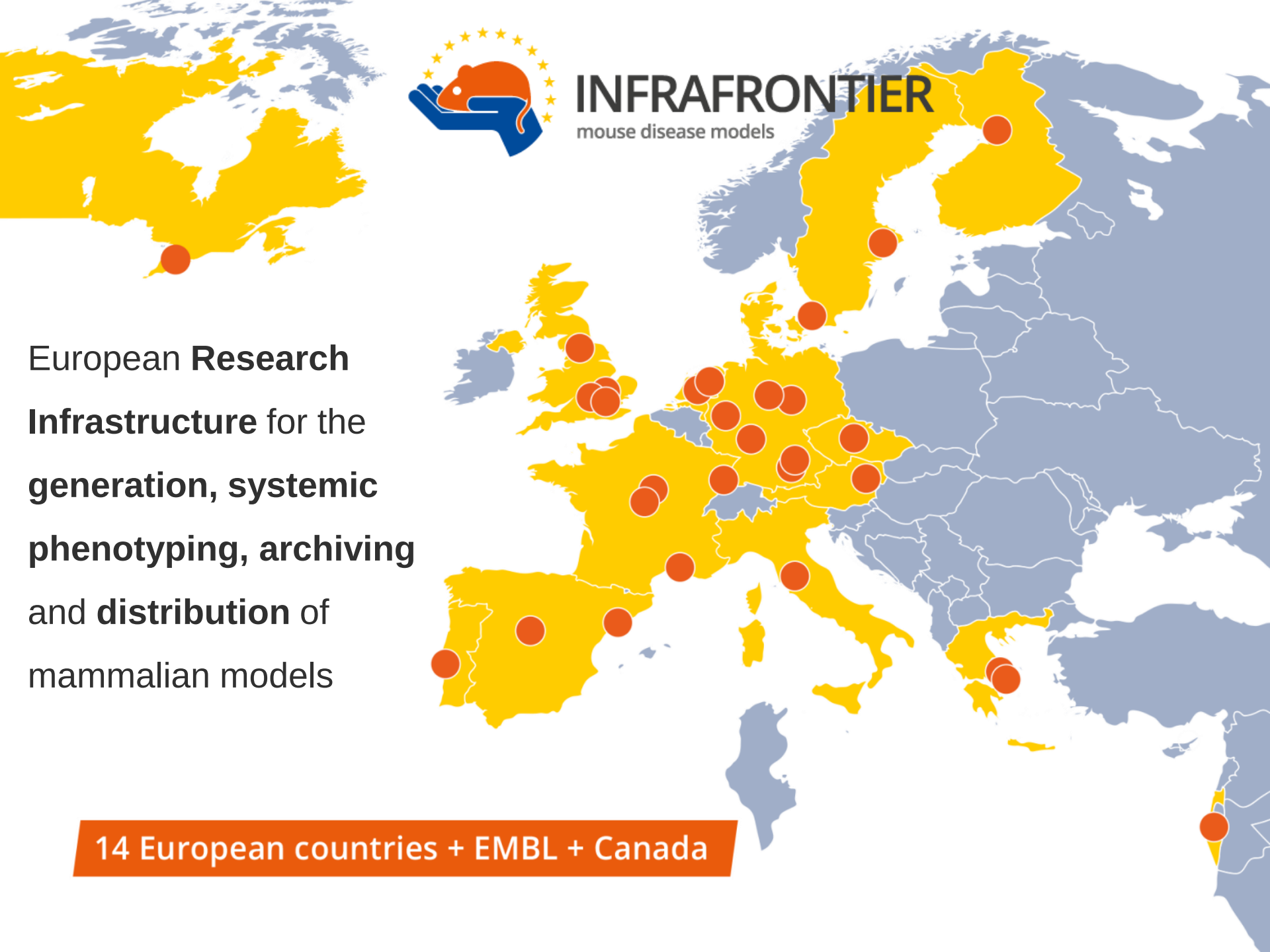
The INFRAFRONTIER Research Infrastructure

Michael Hagn – Helmholtz Zentrum München

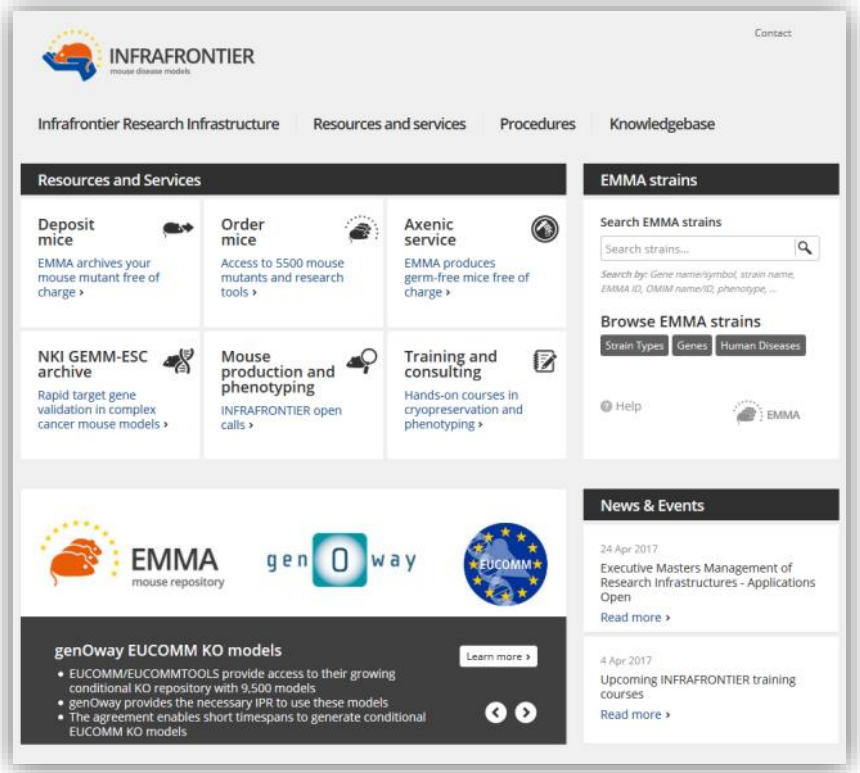
High-quality resources and services for biomedical research


INFRAFRONTIER
mouse disease models
European **Research Infrastructure** for the **generation, systemic phenotyping, archiving** and **distribution** of mammalian models
14 European countries + EMBL + Canada

INFRAFRONTIER-RI and Innovation

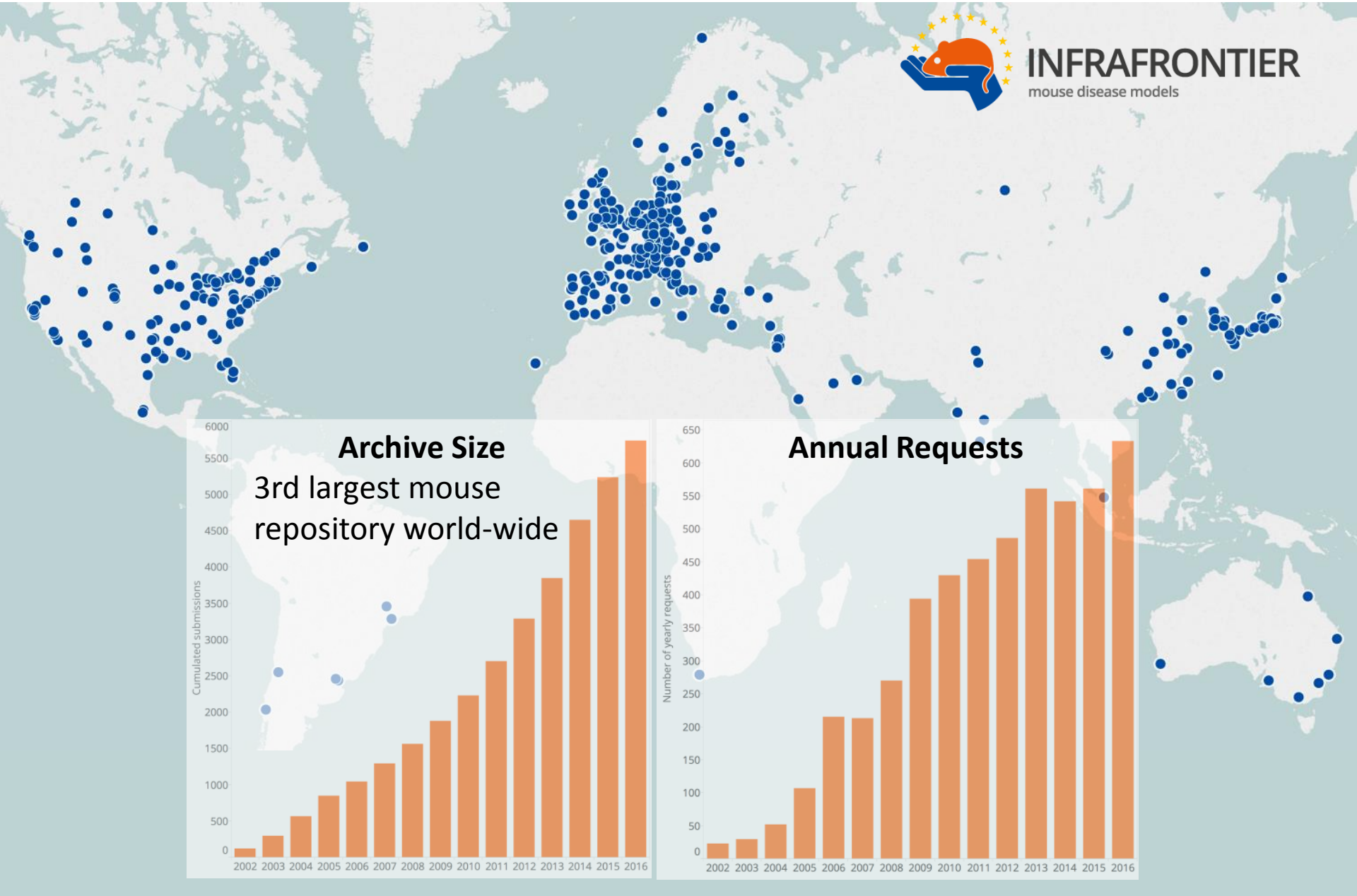
INFRAFRONTIER stimulates innovation by providing open access to:

- **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

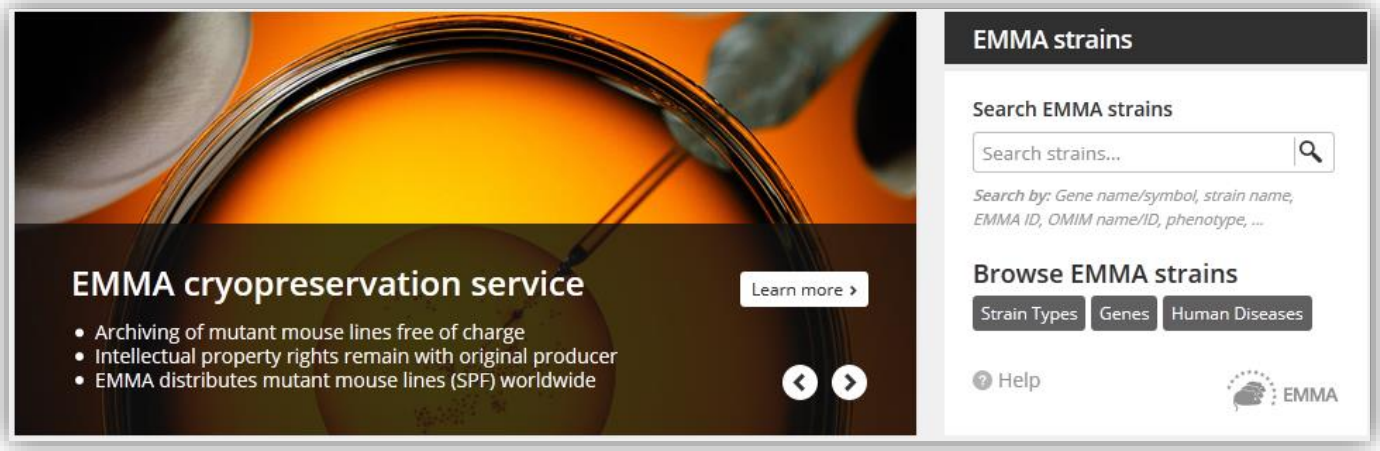


➢ Use of the mouse as the foremost mammalian model for studying human disease and human health

World-wide user community of INFRAFRONTIER / EMMA



INFRAFRONTIER-RI / EMMA repository



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**

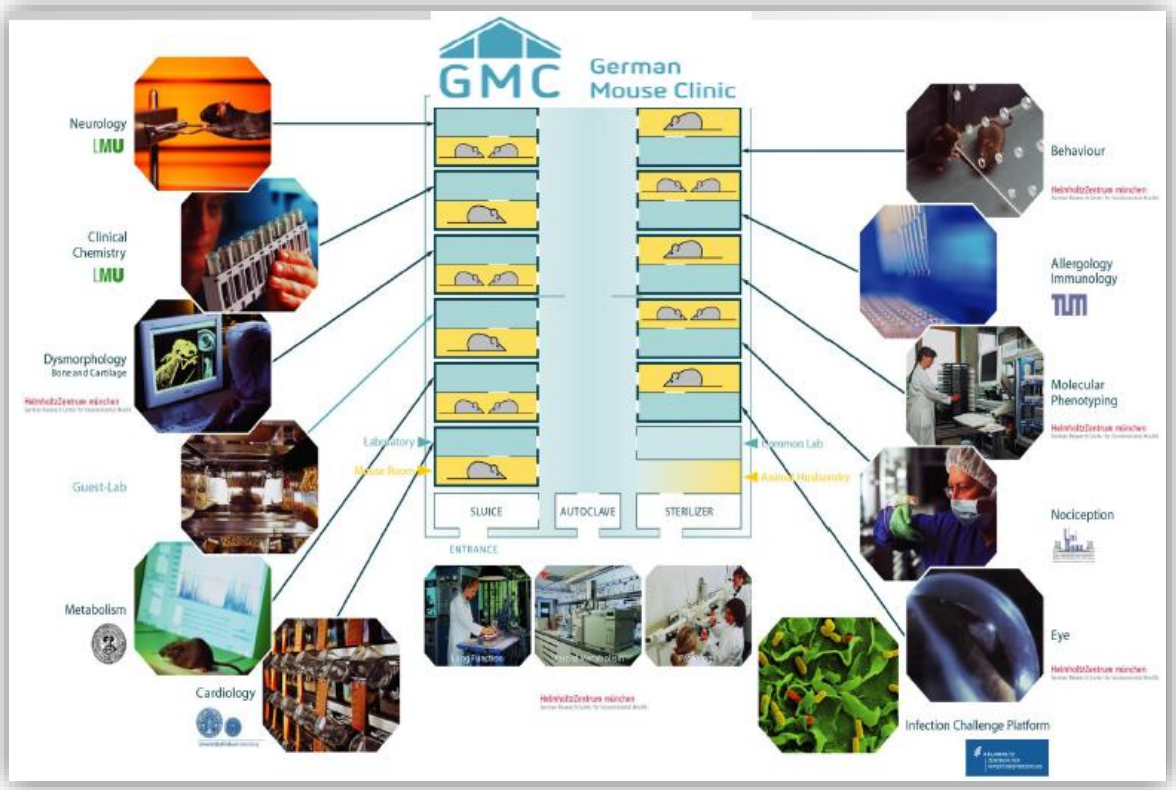
Use of mouse models

➢ **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**

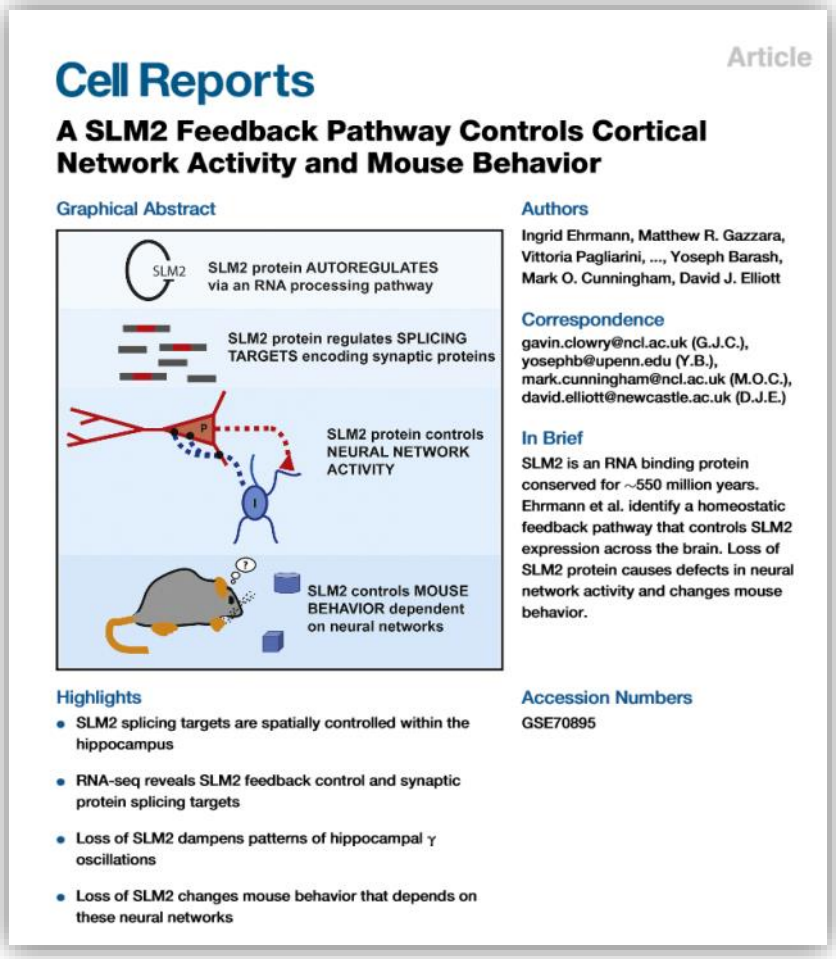
INFRAFRONTIER phenotyping capacities and expertise

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



INFRAFRONTIER-I3 Trans-national 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



Article

Cell Reports

A SLM2 Feedback Pathway Controls Cortical Network Activity and Mouse Behavior

Graphical Abstract

SLM2 protein AUTOREGULATES via an RNA processing pathway

SLM2 protein regulates SPLICING TARGETS encoding synaptic proteins

SLM2 protein controls NEURAL NETWORK ACTIVITY

SLM2 controls MOUSE BEHAVIOR dependent on neural networks

Authors

Ingrid Ehrmann, Matthew R. Gazzara, Vittoria Pagliarini, ..., Yoseph Barash, Mark O. Cunningham, David J. Elliott

Correspondence

gavin.clowry@ncl.ac.uk (G.J.C.), yosephb@upenn.edu (Y.B.), mark.cunningham@ncl.ac.uk (M.O.C.), david.elliott@newcastle.ac.uk (D.J.E.)

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.

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

Accession Numbers

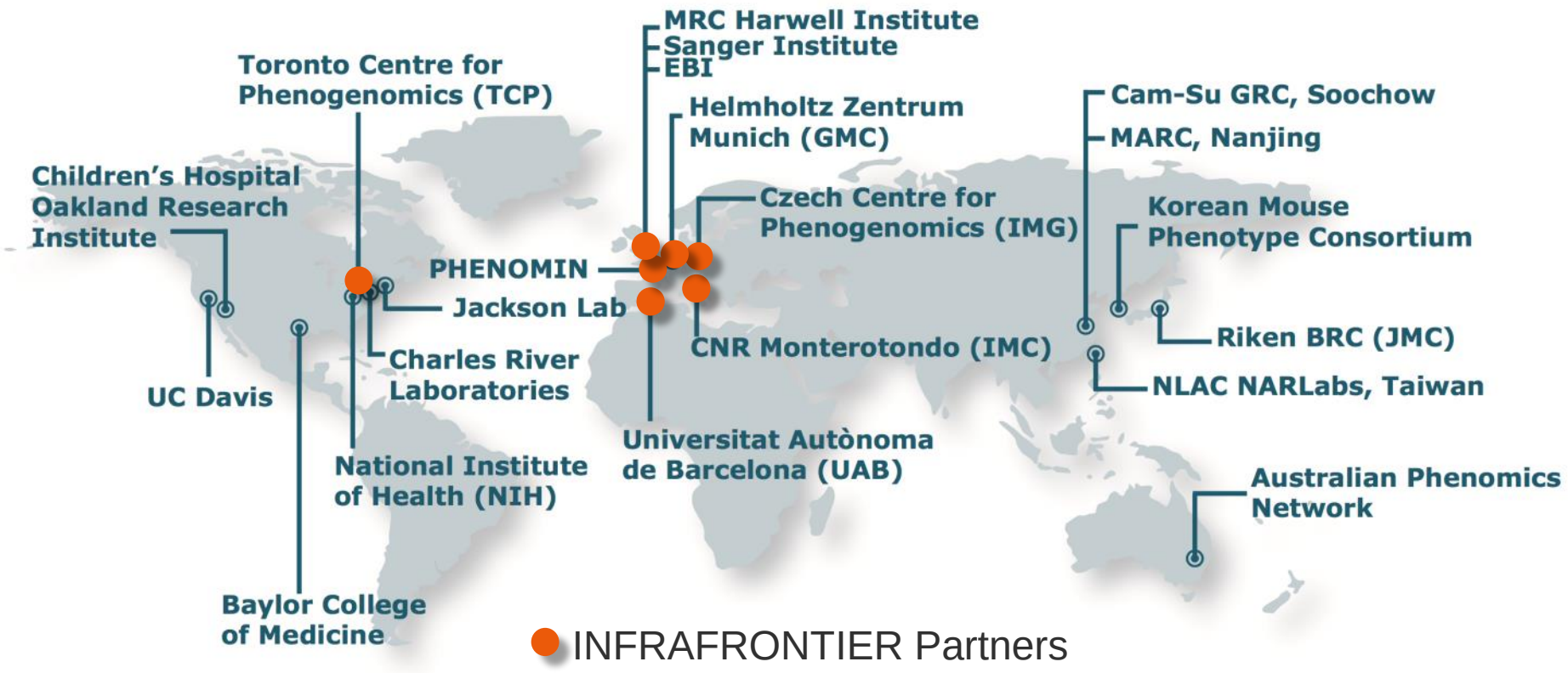
GSE70895

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

IMPC
International Mouse Phenotyping Consortium

www.mousephenotype.org



IMPC Achievements and outlook

Creation of a catalogue of mammalian gene function

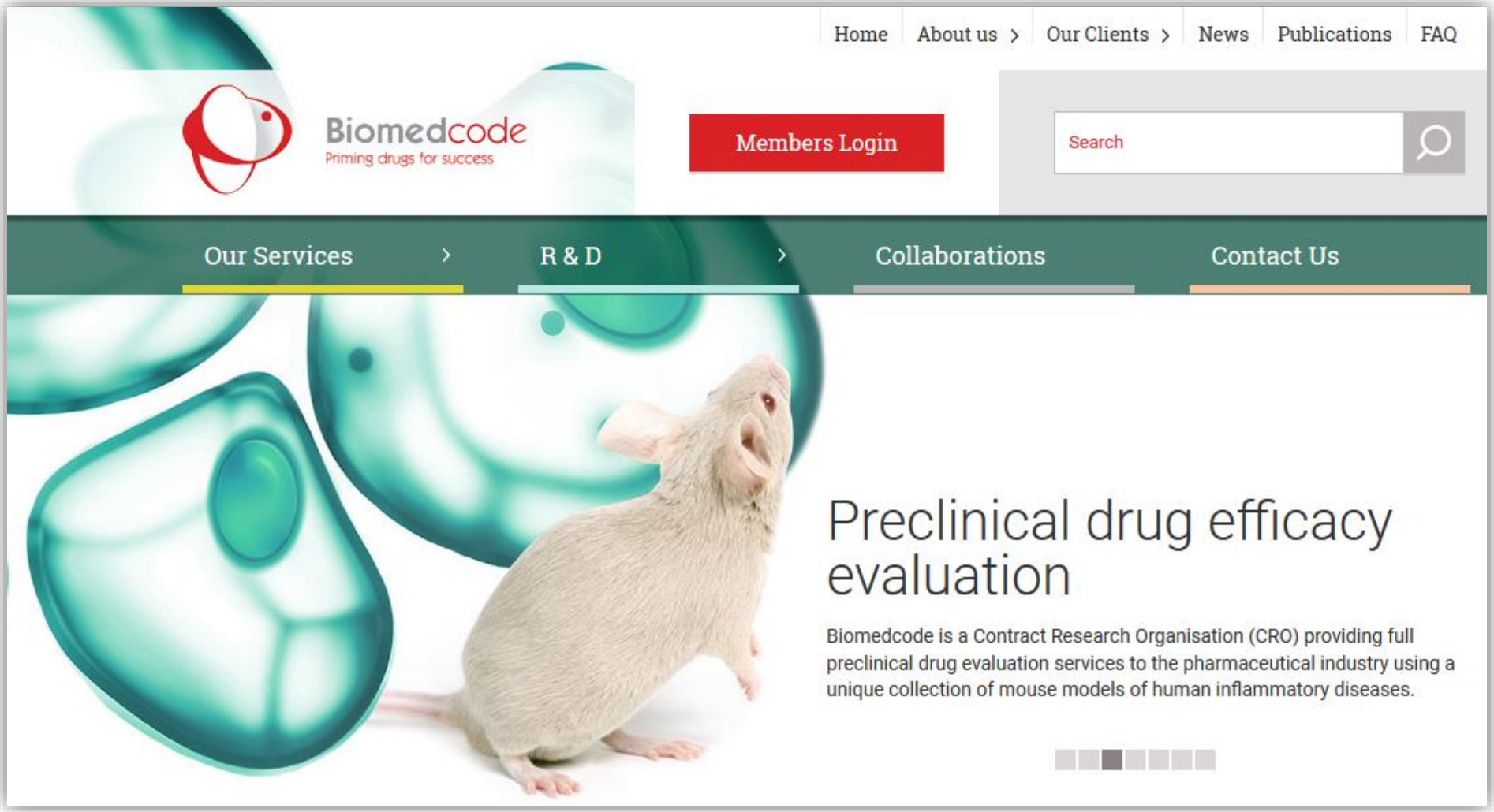
- 5917 mutant lines ge
  archived
- 4493 lines with broad
  phenotyping informat
- Rich, multi-dimensior
  37.5 M data points
- Over 750 research p
  use of IMPC resourc

Transforming the understanding of the mammalian genetic landscape

- NATURE publicati
  genetic disease to
  genes / doi:1038
- 650 new disease n
  disease genes
- Pervasive sexual d
  was hitherto unrec

IMPC evolves to address new areas of disease

- Strenghthen 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 sudy late-onset disease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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.

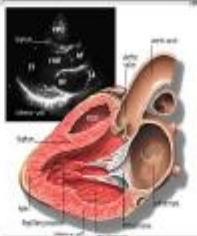
INFRAFRONTIER RI – Specialised phenotyping

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

Cardiovascular system



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

Nutrition & Metabolism

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

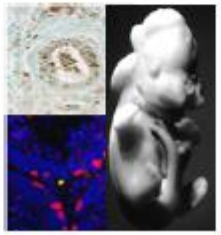
Respiratory system

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

Clinical chemistry

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

Anatomopathology

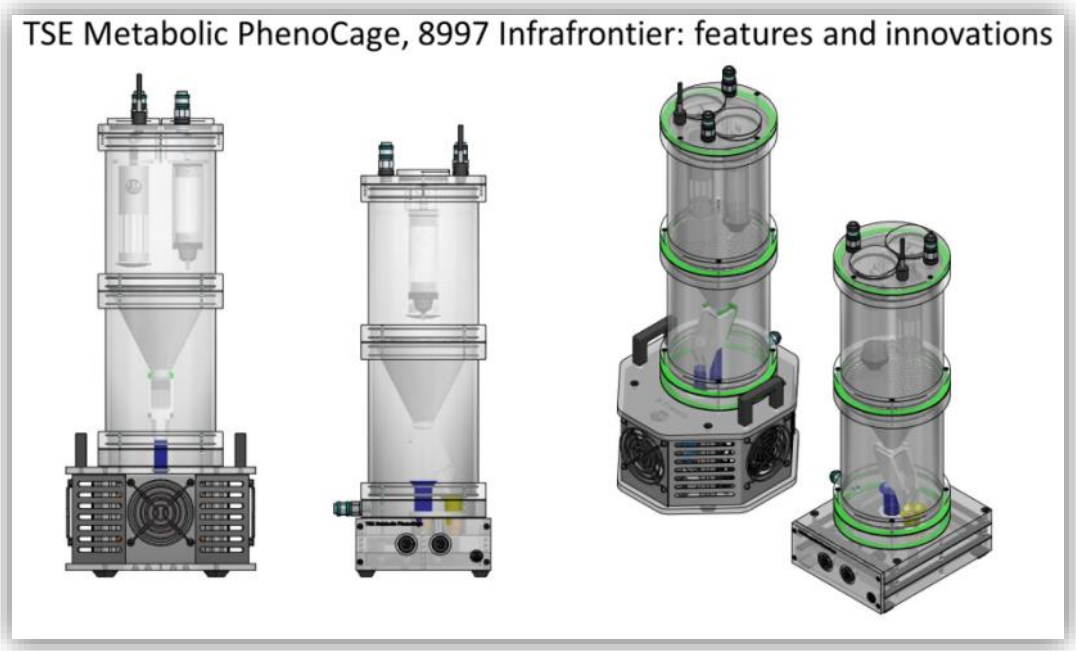


- Necropsy
- Tissue collection
- Histology H&E staining
- Specific stainings
- Immunohistochemistry
- Evaluation of early embryonic death

German Mouse Clinic · ICS · MRC The Mary Lyon Centre · wellcome trust sanger institute · Czech Centre for Phenogenomics

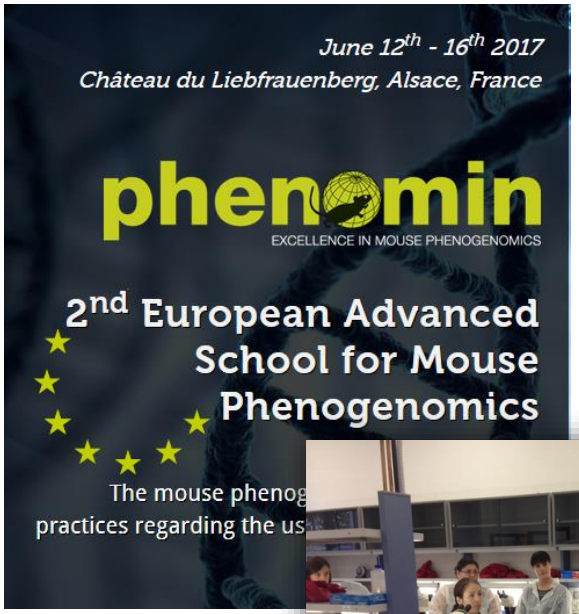
INFRAFRONTIER-RI technology development

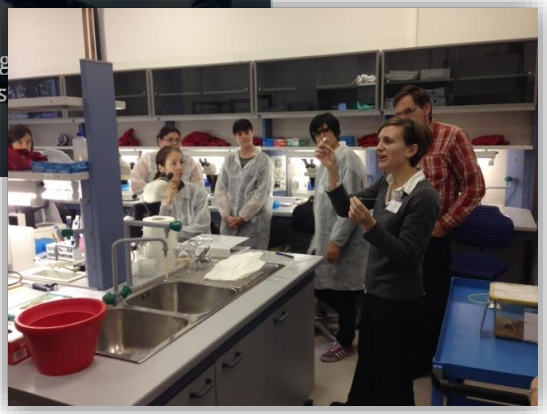
- To continuously improve resources and services
- To reduce animal use
- To enhance operational efficiencies / cost reduction

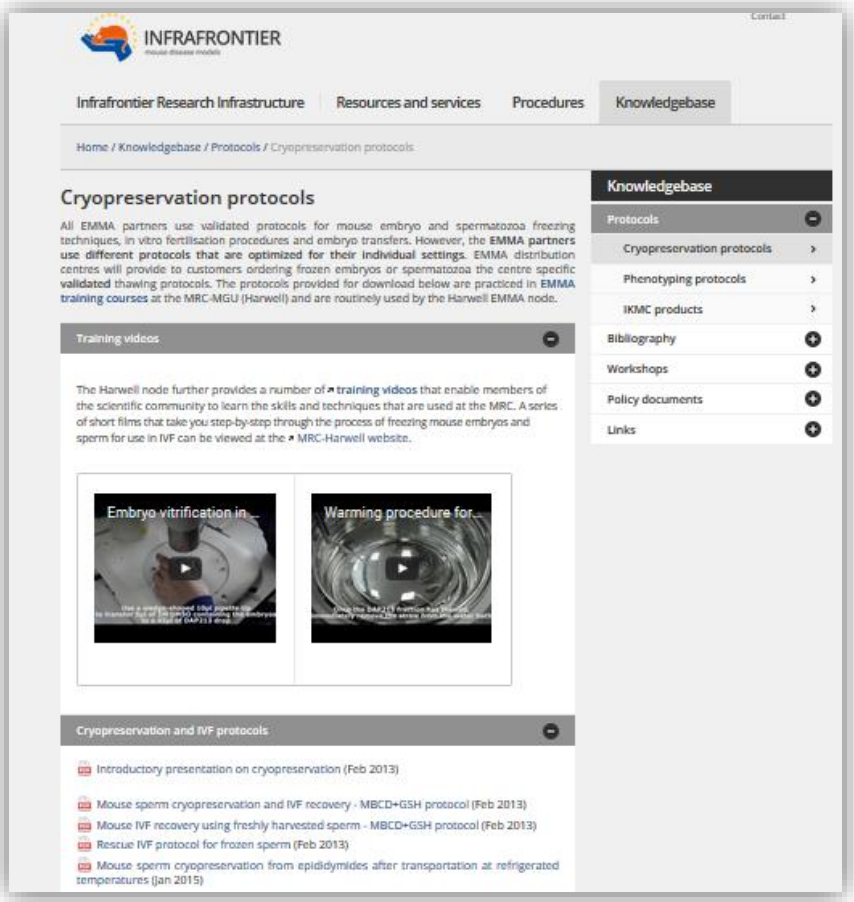


INFRAFRONTIER-RI outreach / industry liaison

INFRAFRONTIER-RI outreach / training







- 40 training courses in cryopreservation and phenogenomics
- 400 participants

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 evolvement of rigor and standardisation applied to operational procedures and data QC

INFRAFRONTIER-RI and Innovation

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