



# INFRAFRONTIER

mouse disease models

Providing  
**unique scientific resources, services,  
data, and expertise**  
to advance the understanding and  
treatment of  
**human diseases**  
using mammalian models

EPTRI Roundtable – 09 July 2020

**Michael Raess**

**INFRAFRONTIER GmbH**



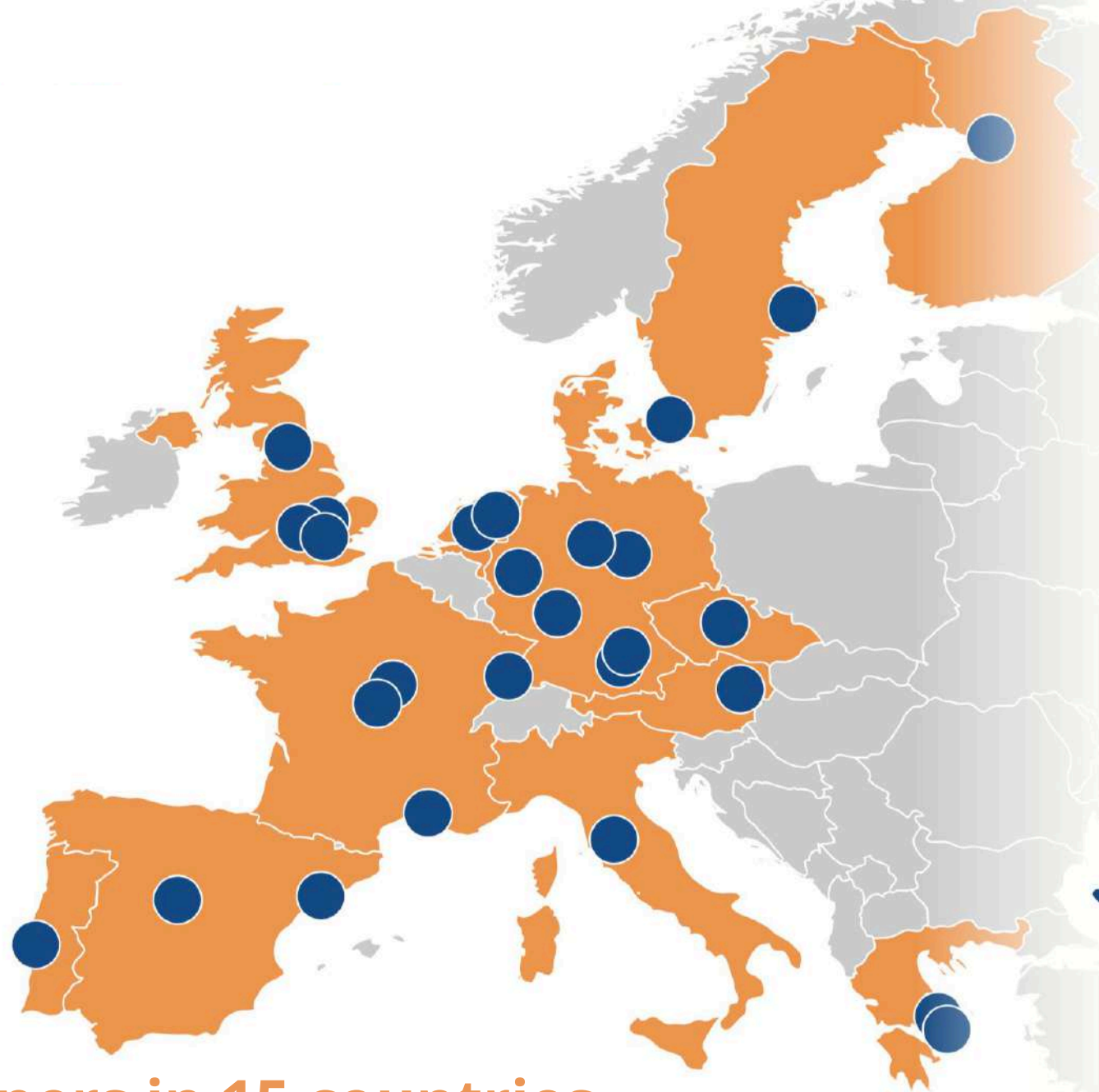
- **48 out of the last 50 Nobel Prizes** in Physiology and Medicine are based on animal experimentation
- **25 out of the last 50 Nobel Prizes** in Physiology and Medicine are based on experiments involving **mice or rats**
- **Mouse experiments** led to breakthrough discoveries in **cancer, metabolic diseases and diabetes, inflammatory diseases** and many more disease areas.





**INFRAFRONTIER**  
mouse disease models

A consortium of leading European research institutions for the **generation, phenotyping, archiving** and **distribution** of mammalian models

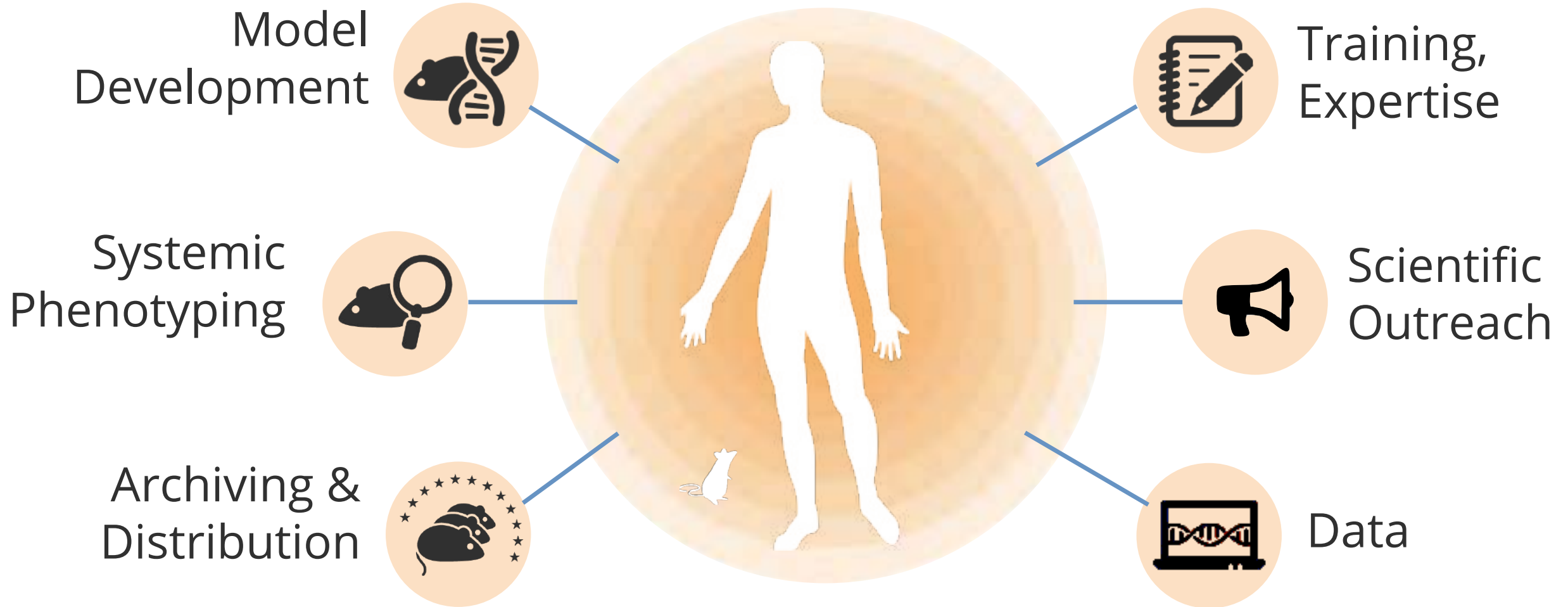


**29 partners in 15 countries**

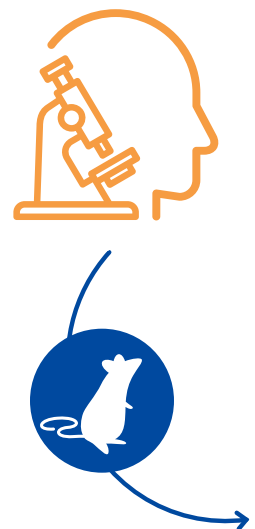
+ Canada, Israel



# Access to physical resources, analytical platforms, knowledge and data



# The European Mouse Mutant Archive (EMMA)



Archiving & Distribution

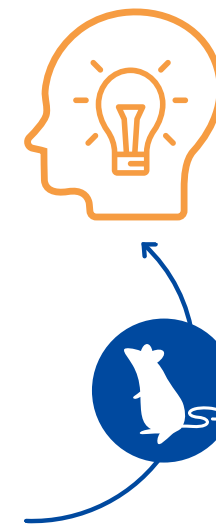


**7300** mouse lines

**16** EMMA centres

**13** European countries

**1** central web portal  
[www.infrafrontier.eu](http://www.infrafrontier.eu)



Cryopreservation



Quality Control



Archiving



Quality Control

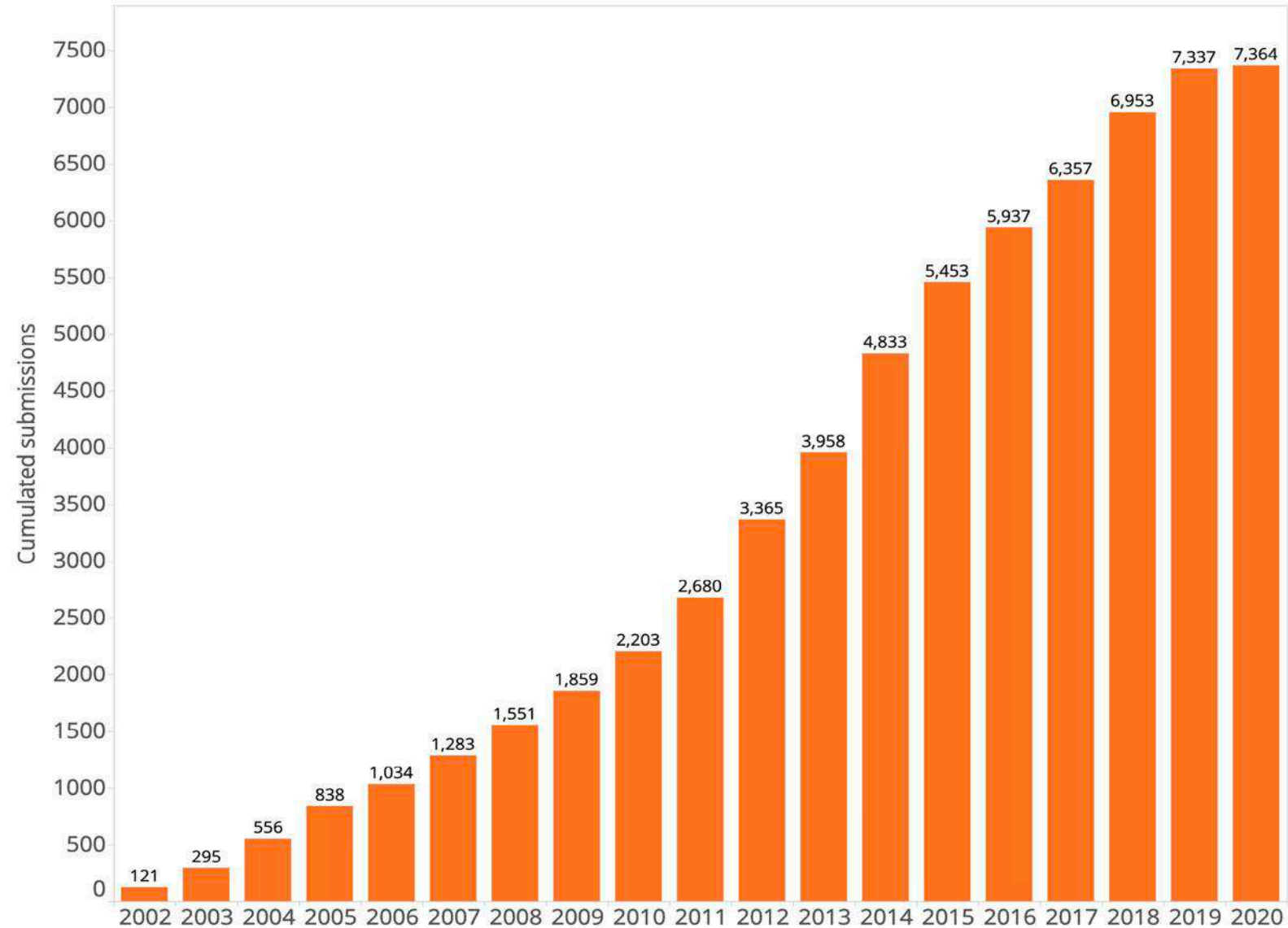


Distribution

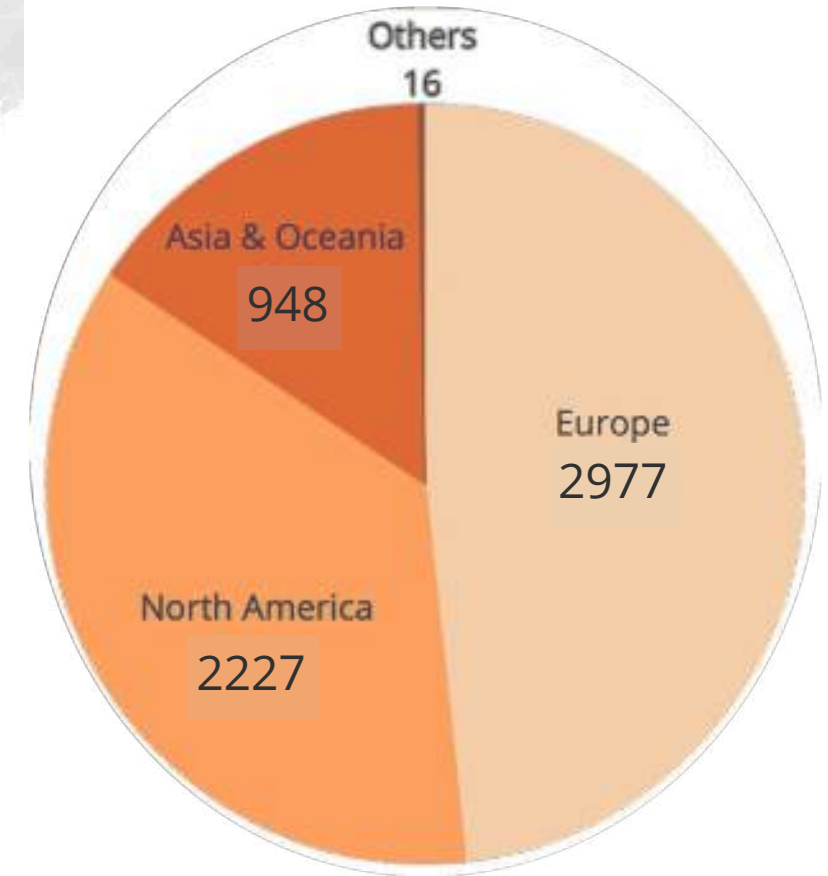
# Archiving of mouse lines in the European Mouse Mutant Archive (EMMA)



- **3rd largest** mouse repository worldwide
- **> 7300** lines archived
- About **half** of these are from large-scale top-down projects like IMPC
- The other **half** are from individual depositors from the scientific community

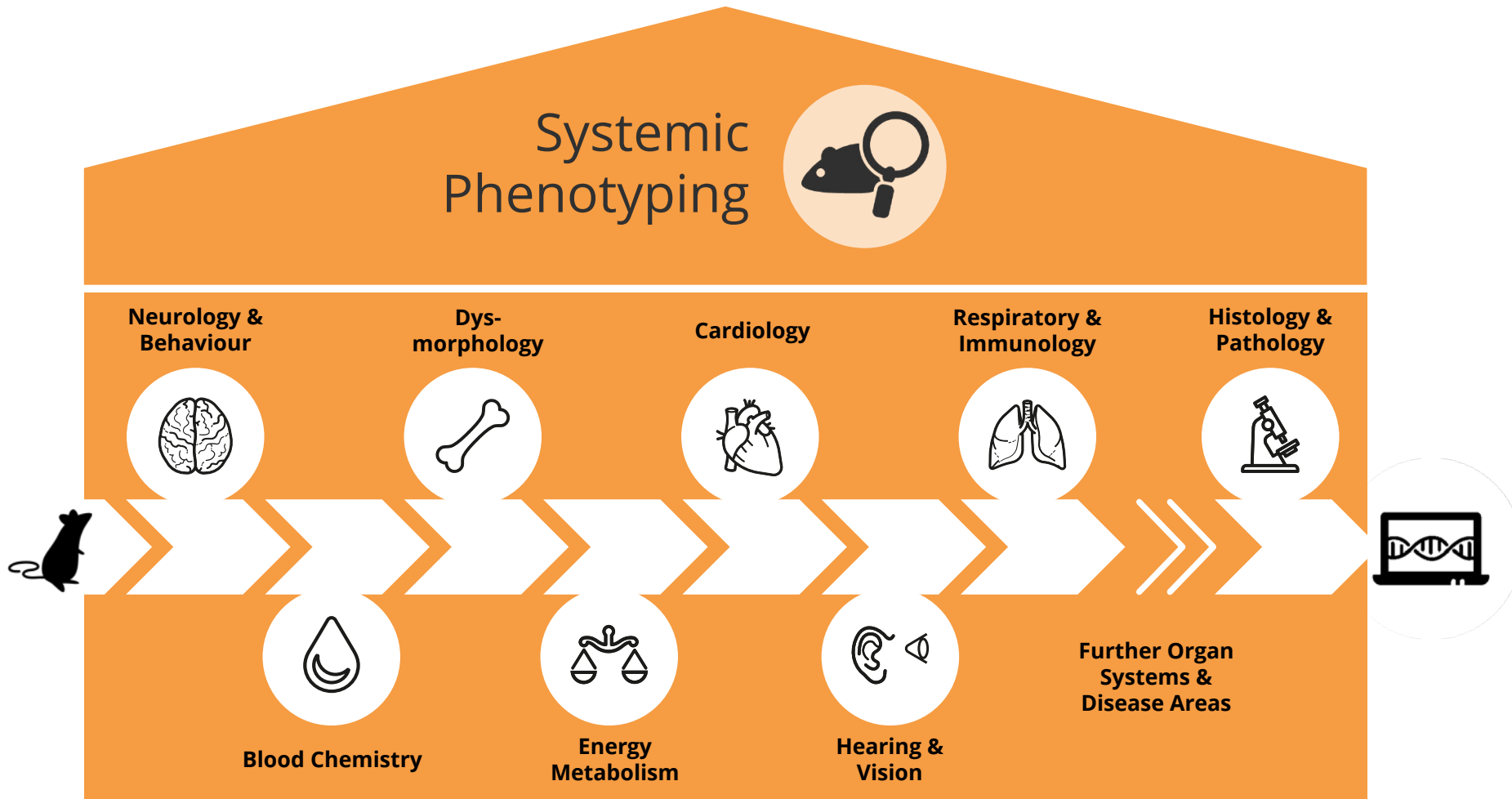


# Distribution of mouse lines in the European Mouse Mutant Archive (EMMA)



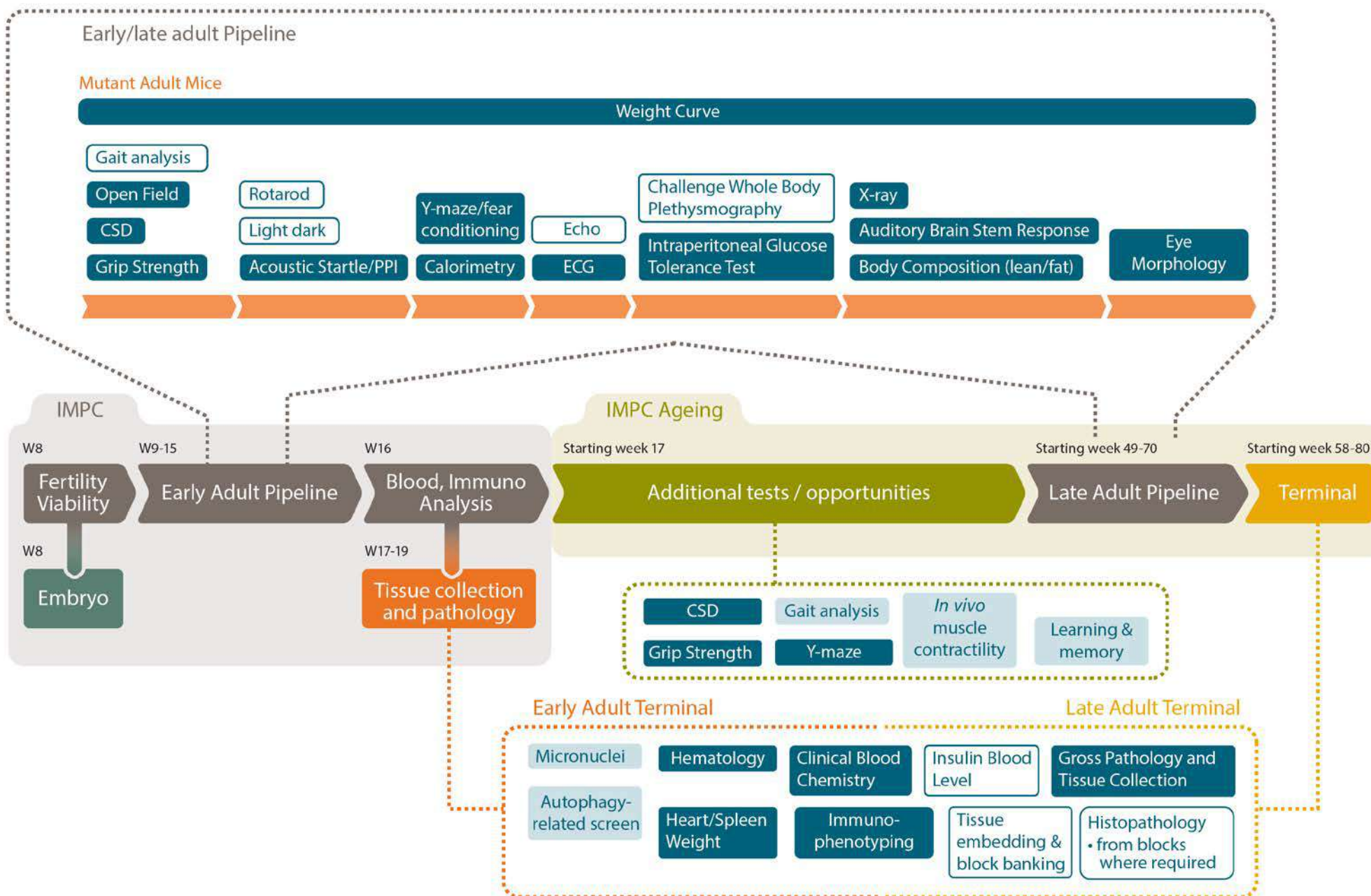
- > **500** distribution requests per year
- > **6100** shipments in total

# INFRAFRONTIER mouse clinics



- Whole-system screen covering more than 500 parameters in different disease areas and organ systems
- Provides a maximum of information using a minimum amount of animals







**INFRAFRONTIER**  
mouse disease models

World-wide user community and collaboration



IMPC



EOSC-Life



EJP-RD





**INFRAFRONTIER**  
mouse disease models

World-wide user community and collaboration

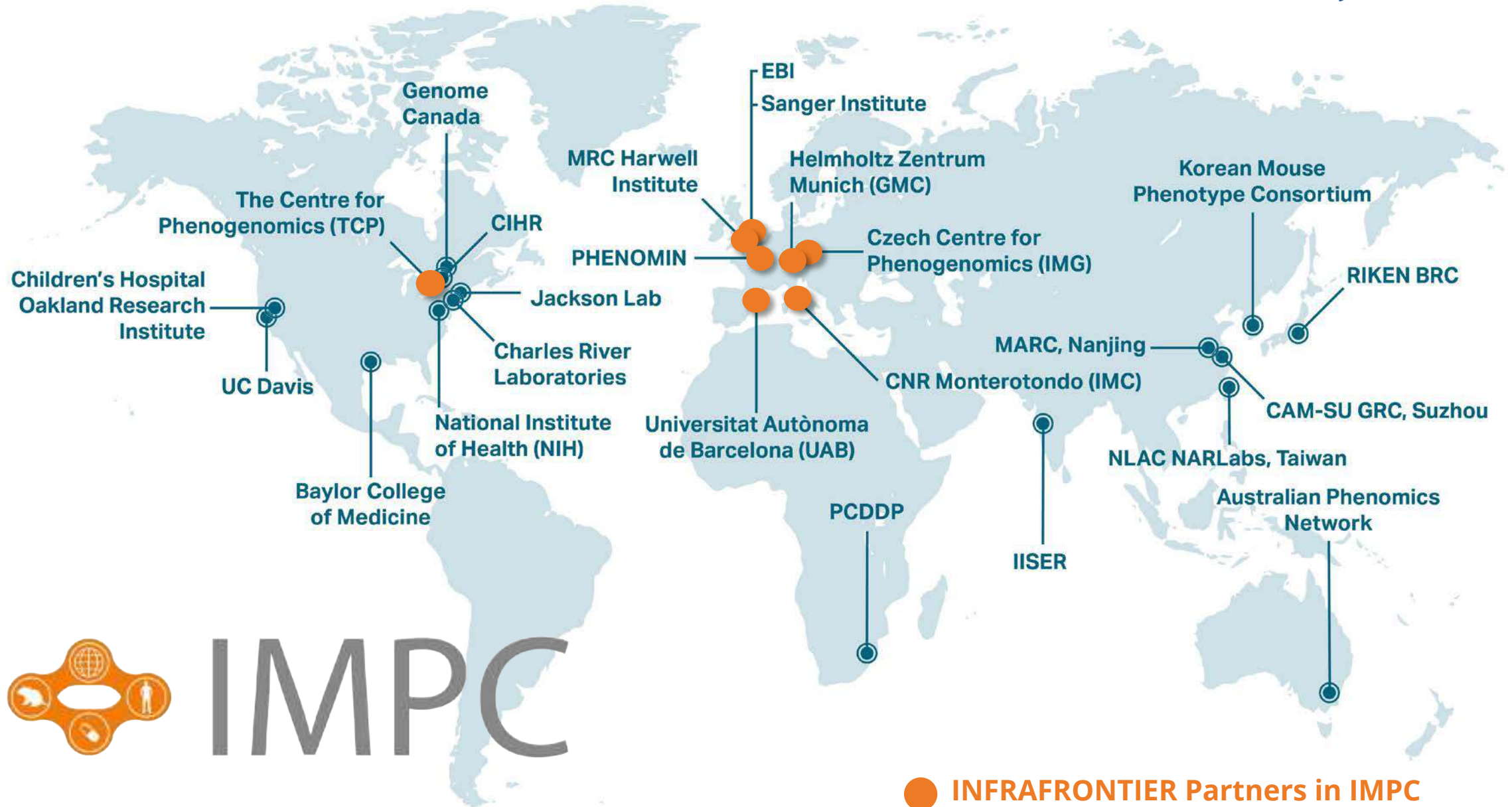


**IMPC**



**EJP-RD**

# International Mouse Phenotyping Consortium



IMPC

# International Mouse Phenotyping Consortium



- Illuminating the dark genome
- Building the first comprehensive functional catalogue of a mammalian genome
- > **6000** mouse lines phenotyped
- **84 million** data points
- > **500** disease-relevant genes discovered and characterised





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IMPC



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**EOSC-Life**

# Connecting INFRAFRONTIER to the European Open Science Cloud



- Cluster project of 13 life science research infrastructures
- 46 partners, coordinated by ELIXIR



- *biobanks*



- *curated databases*



- *marine model organisms*



- *systems biology*



- *Plant phenotyping centres*



- *translational research*



- *mouse disease models*



- *screening & medicinal chemistry*



- *microorganisms*



- *clinical trials*



- *structural biology*



- *biological/medical imaging*



- *Highly Pathogenic Agents*

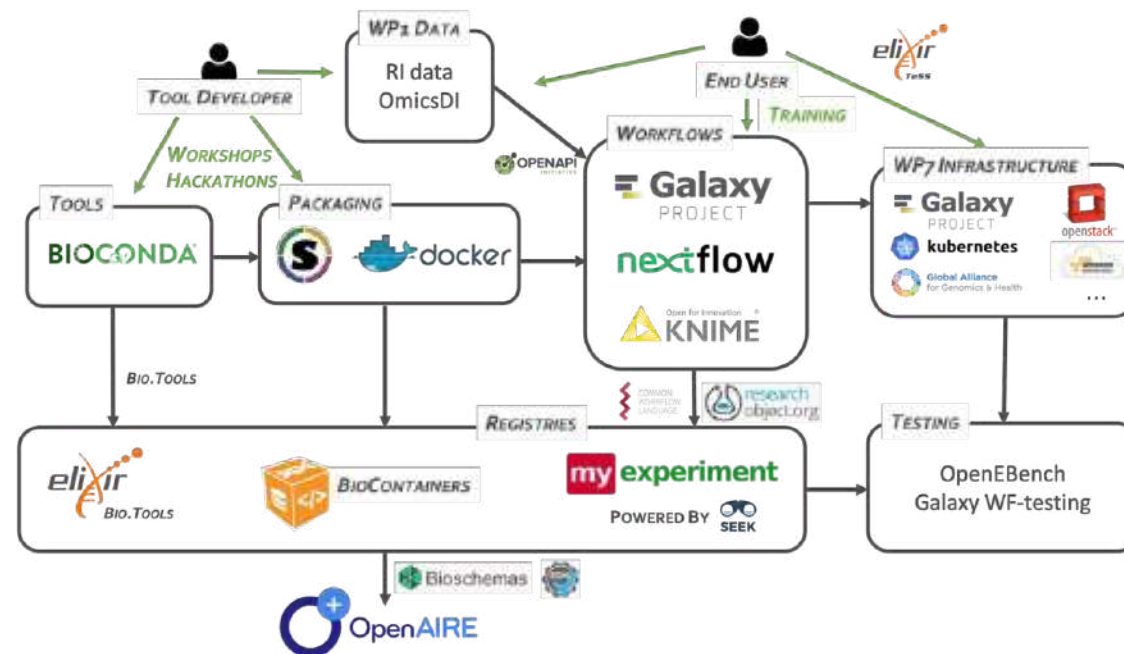
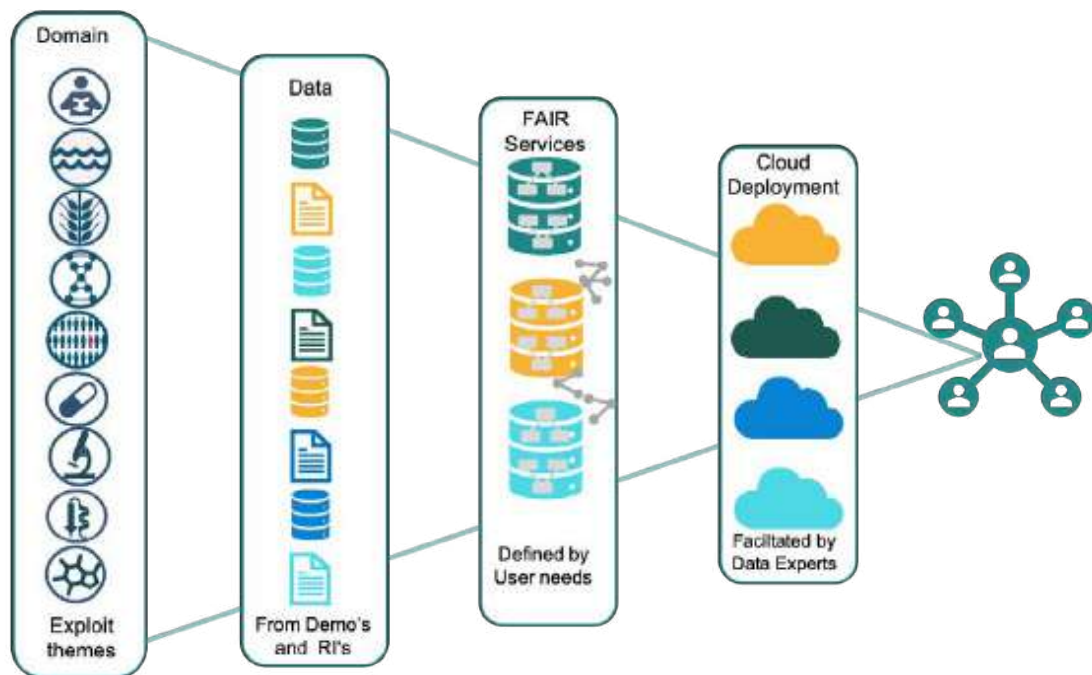


**EOSC-Life**

# Connecting INFRAFRONTIER to the European Open Science Cloud

Providing FAIR life-science data and data workflows for the EOSC

Provide and connect INFRAFRONTIER data to other life science communities







**INFRAFRONTIER**  
mouse disease models



World-wide user community and collaboration



IMPC



EOSC-Life



EJP-RD



# European Joint Programme on Rare Diseases

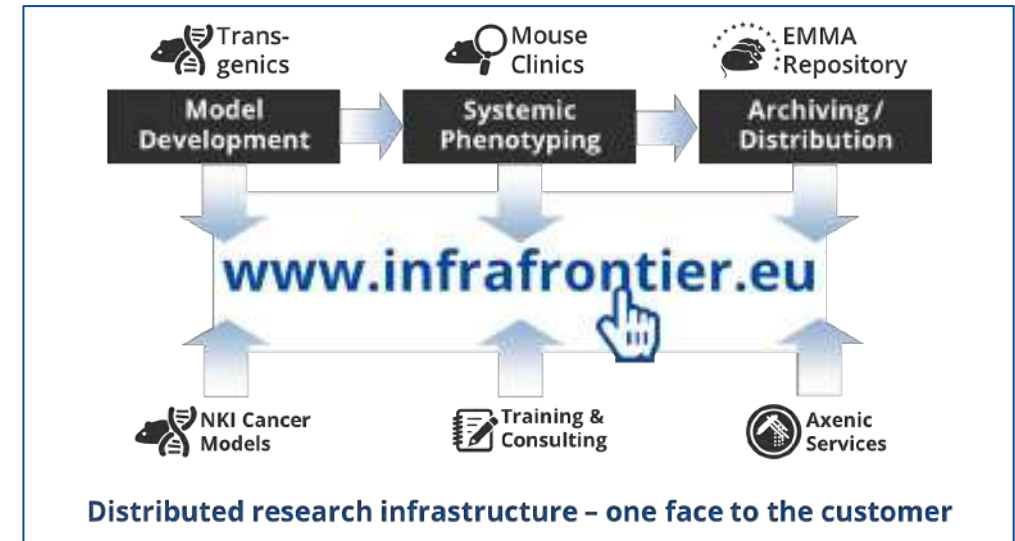
- More than 130 institutions from 35 countries
- 26 EU Member States + 8 Associated Countries + Canada
- Research Infrastructures, Patient Organisations
- Improve the integration, efficacy and impact of Rare Diseases research
- Implement and further develop an efficient model for financial support for RD research (Joint Programming)





## INFRAFRONTIER as resource on EJP-RD's virtual platform

- Make EMMA strains potentially interesting for RD researchers
- Make RD researchers aware of all INFRAFRONTIER services
- Further align data



# INFRAFRONTIER website - Rare diseases



## INFRAFRONTIER & Rare Diseases

### INFRAFRONTIER and Rare Diseases



Mouse Models for Rare Disease Research



According to the [EU](#), a rare disease is defined as a disease afflicting fewer than one in 2000 individuals. It is estimated that 30 million people in Europe suffer from a rare disease. There are currently about 7000 rare diseases known with more being discovered continually ([ref](#)). The field of rare diseases suffers from a deficit of medical and scientific knowledge. They are also referred to "orphan diseases" having been orphaned by the pharmaceutical industry because of small patient populations and consequently a smaller drug market. Scientifically, these diseases reside in the 'unchartered space' of biomedical research with their treatment marred by a dearth of medical and biochemical

#### EMMA Strains and Rare Diseases

Find a list of rare diseases that are related to EMMA mouse strains [here](#) >.

#### EMMA Publications and Rare Diseases

Find all publications about EMMA strains that are related to rare diseases [here](#) >.

#### INFRAFRONTIER and Rare Disease Conferences

- The INFRAFRONTIER Stakeholder Meeting 2018 on rare disease research and gene therapy applications with animal models. Find more information on the conference [here](#) >.
- INFRAFRONTIER members will be present at the [RE\(AC\)T](#) Conference in Toronto.

Search for RD related mouse

strains

Search for strain publications

related to RD

Information on RD

related INFRAFRONTIER

events

[www.infrafrontier.eu/infrafrontier-and-rare-diseases](http://www.infrafrontier.eu/infrafrontier-and-rare-diseases)



INFRAFRONTIER



Supporting COVID-19 Research

<https://www.infracfrontier.eu/knowledgebase/therapeutic-area/covid-19-resources-and-measures>

## COVID-19 Resources and Measures

To combat the rapidly evolving COVID-19 pandemic, INFRAFRONTIER is offering several resources, related strains and emergency archiving services to the global research community with the aim to aid COVID-19 research and minimise the loss of valuable mouse strains during the crisis.

### COVID-19 Resources offered by INFRAFRONTIER Partners

The coronavirus (COVID-19) pandemic is not only a serious threat to global public health, it also deeply affects the social and economic life worldwide. INFRAFRONTIER, the European Research Infrastructure for the generation, phenotyping, archiving and distribution of model mammalian genomes, is fully committed to support researchers around the globe to develop a vaccine against SARS-CoV-2 and to find treatments for COVID-19.

List of INFRAFRONTIER COVID-19 Resources



### COVID-19 related EMMA strains

The following EMMA strains are related to SARS-CoV-2 infection via their human orthologues. The table below contains EMMA strains that could be used for COVID-19 research.

List of COVID-19 related EMMA strains



### Emergency Archiving during COVID-19 crisis

Due to the current coronavirus (COVID-19) situation, there is a need to archive various valuable mouse models. Traffic restrictions and other severe measures to slow the spread of the pandemic are in force, but some EMMA nodes are still active and may archive valuable strains.

Please directly contact your closest EMMA node from the list below for archiving possibilities. In contrast to the standard EMMA archiving service, which includes evaluation by an external scientific committee and is free of charge for depositors, the emergency service may come with service charges. Details will be provided by the EMMA nodes.

As the situation in the different countries is changing constantly, we can not give any guarantees. Whether mice can be imported also strongly depends on whether carrier companies are still servicing the respective route from the depositor institute to the EMMA node.

INFRAFRONTIER partners offering Emergency Archiving during COVID-19 crisis





# INFRAFRONTIER Conferences

- ~200 participants per conference
- Connecting mouse genetics to human geneticists and clinicians



# INFRAFRONTIER Conference 2020



INFRAFRONTIER



**INFRAFRONTIER Conference 2020**

Targeting Cancer with Animal Models

**October 7 to 9, 2020 | Brussels**

#InfrafrontierConf | #InfraConfBrussels



# INFRAFRONTIER and pediatrics research

- INFRAFRONTIER/EMMA has provided the mouse model for our studies on a novel early-onset multiorgan syndrome FINCA

Case Reports > *Acta Neuropathol.* 2018 May;135(5):727–742.

doi: 10.1007/s00401-018-1817-z. Epub 2018 Feb 8.

## NHLRC2 Variants Identified in Patients With Fibrosis, Neurodegeneration, and Cerebral Angiomatosis (FINCA): Characterisation of a Novel Cerebropulmonary Disease

Johanna Uusimaa<sup>1 2 3</sup>, Riitta Kaarteenaho<sup>4 5</sup>, Teija Paakkola<sup>6 7</sup>, Hannu Tuominen<sup>8 9</sup>, Minna K Karjalainen<sup>6</sup>, Javad Nadaf<sup>10 11</sup>, Teppo Varilo<sup>12</sup>, Meri Uusi-Mäkelä<sup>13</sup>, Maria Suo-Palosaari<sup>14</sup>, Ilkka Pietilä<sup>6 7</sup>, Anniina E Hiltunen<sup>6 7</sup>, Lloyd Ruddock<sup>7 15</sup>, Heli Alanen<sup>7 15</sup>, Ekaterina Biterova<sup>7 15</sup>, Ilkka Miinalainen<sup>7</sup>, Annamari Salminen<sup>6</sup>, Raija Soininen<sup>7 15</sup>, Aki Manninen<sup>7 15</sup>, Raija Sormunen<sup>7 8</sup>, Mika Kaakinen<sup>7</sup>, Reetta Vuolteenaho<sup>7</sup>, Riitta Herva<sup>8</sup>, Päivi Vieira<sup>6 16</sup>, Teija Dunder<sup>6 16</sup>, Hannaleena Kokkonen<sup>17 18</sup>, Jukka S Moilanen<sup>6 19</sup>, Heikki Rantala<sup>6 16</sup>, Lawrence M Nogee<sup>20</sup>, Jacek Majewski<sup>10</sup>, Mika Rämetsä<sup>6 16 13</sup>, Mikko Hallman<sup>6 16</sup>, Reetta Hinttala<sup>6 7</sup>

> *Hum Mol Genet.* 2018 Dec 15;27(24):4288–4302. doi: 10.1093/hmg/ddy298.

## Biallelic Mutations in Human NHLRC2 Enhance Myofibroblast Differentiation in FINCA Disease

Teija Paakkola<sup>1 2 3 4</sup>, Kari Salokas<sup>5 6</sup>, Ilkka Miinalainen<sup>2</sup>, Siri Lehtonen<sup>3</sup>, Aki Manninen<sup>2 7</sup>, Mika Kaakinen<sup>2</sup>, Lloyd W Ruddock<sup>2 7</sup>, Markku Varjosalo<sup>5 6</sup>, Riitta Kaarteenaho<sup>8 9 4</sup>, Johanna Uusimaa<sup>1 2 3 10 4</sup>, Reetta Hinttala<sup>1 2 3 4</sup>

Affiliations + expand

PMID: 30239752 DOI: 10.1093/hmg/ddy298

# INFRAFRONTIER and pediatrics research


- German Mouse Clinic has phenotyped the mouse model for GRACILE

*Research Article*



EMBO  
Molecular Medicine

## Alternative oxidase-mediated respiration prevents lethal mitochondrial cardiomyopathy

Jayasimman Rajendran<sup>1,2</sup>, Janne Purhonen<sup>1,2</sup>, Saara Tegelberg<sup>1,3,4</sup>, Olli-Pekka Smolander<sup>5</sup>,  
Matthias Mörgelin<sup>6</sup>, Jan Rozman<sup>7,8</sup>, Valerie Gailus-Durner<sup>7</sup>, Helmut Fuchs<sup>7</sup>,  
Martin Hrabe de Angelis<sup>7,8,9</sup>, Petri Auvinen<sup>5</sup>, Eero Mervaala<sup>10</sup>, Howard T Jacobs<sup>5,11</sup>,  
Marten Szibor<sup>5,11</sup>, Vineta Fellman<sup>1,3,12</sup> & Jukka Kallijärvi<sup>1,2,\*</sup> 

# INFRAFRONTIER and pediatrics research

- INFRAFRONTIER offers targeted resources for specific communities, based on their feedback and input
- INFRAFRONTIER is already involved in and provides resources for pediatrics research
- INFRAFRONTIER is open to the input from the pediatrics community on how to improve its resources and services and how to better cooperate!