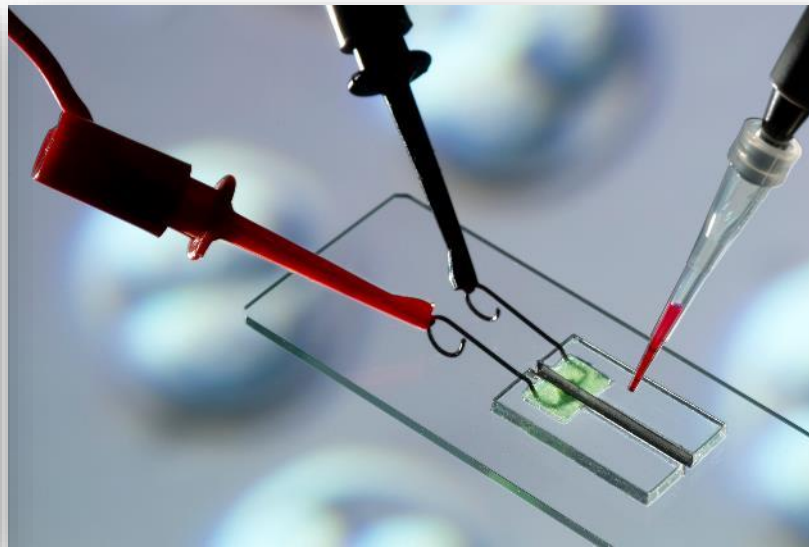
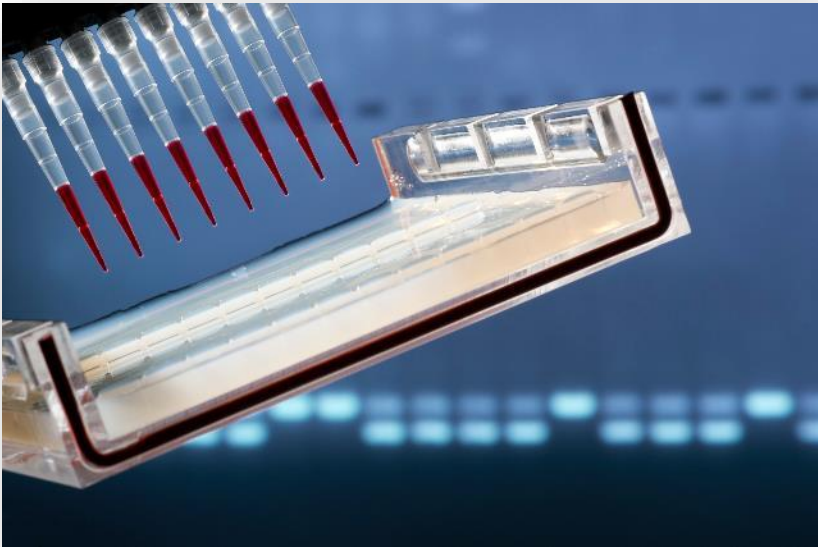




The Infrafrontier RI

Julia Fernández & Lluís Montoliu (CNB-CSIC & CIBERER-ISCI11)



04 July 2023

The INFRAFRONTIER Research Infrastructure

2007



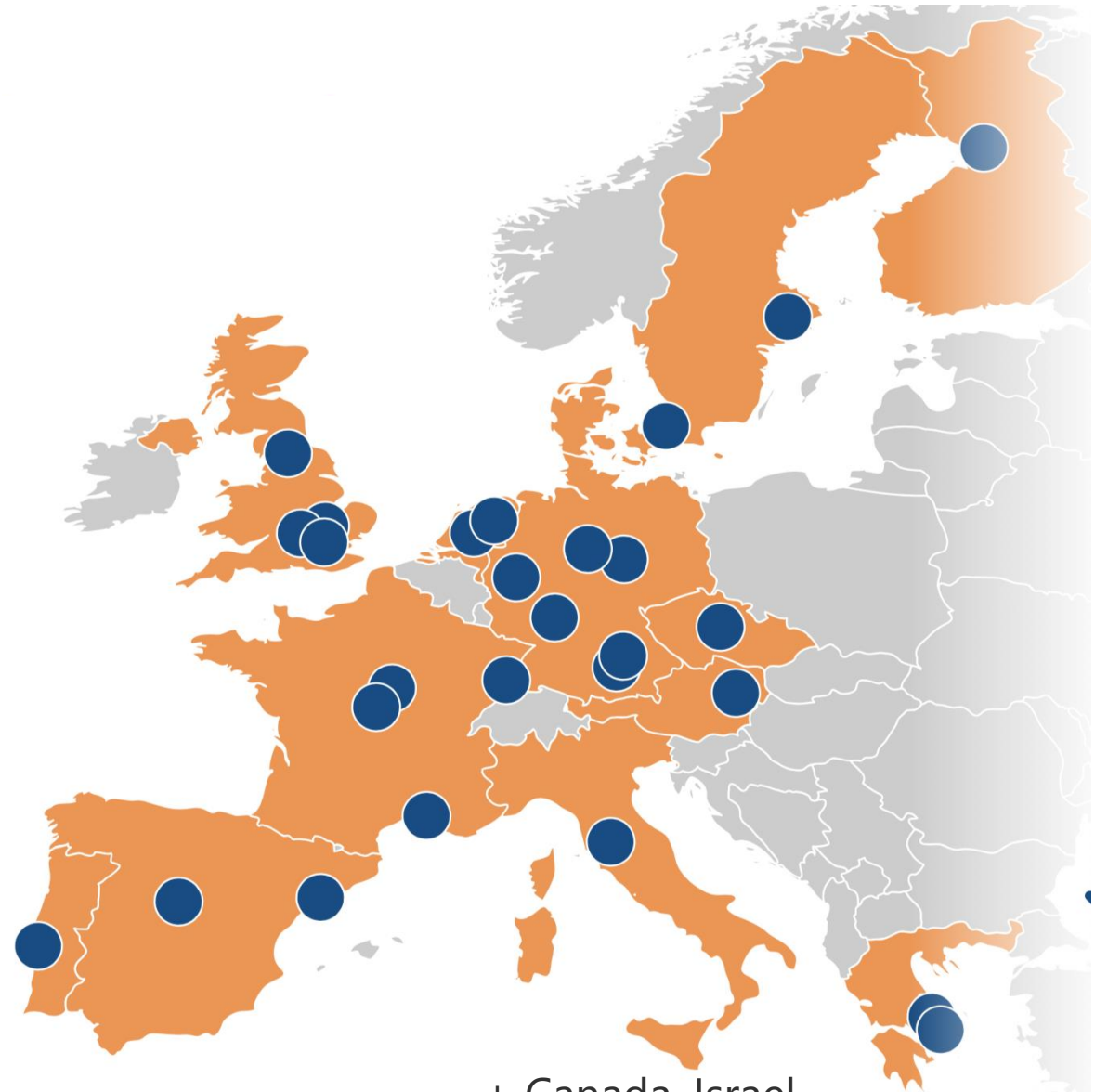
Providing
unique scientific resources, services, and expertise
to advance the understanding and treatment of **human diseases using rodent models**



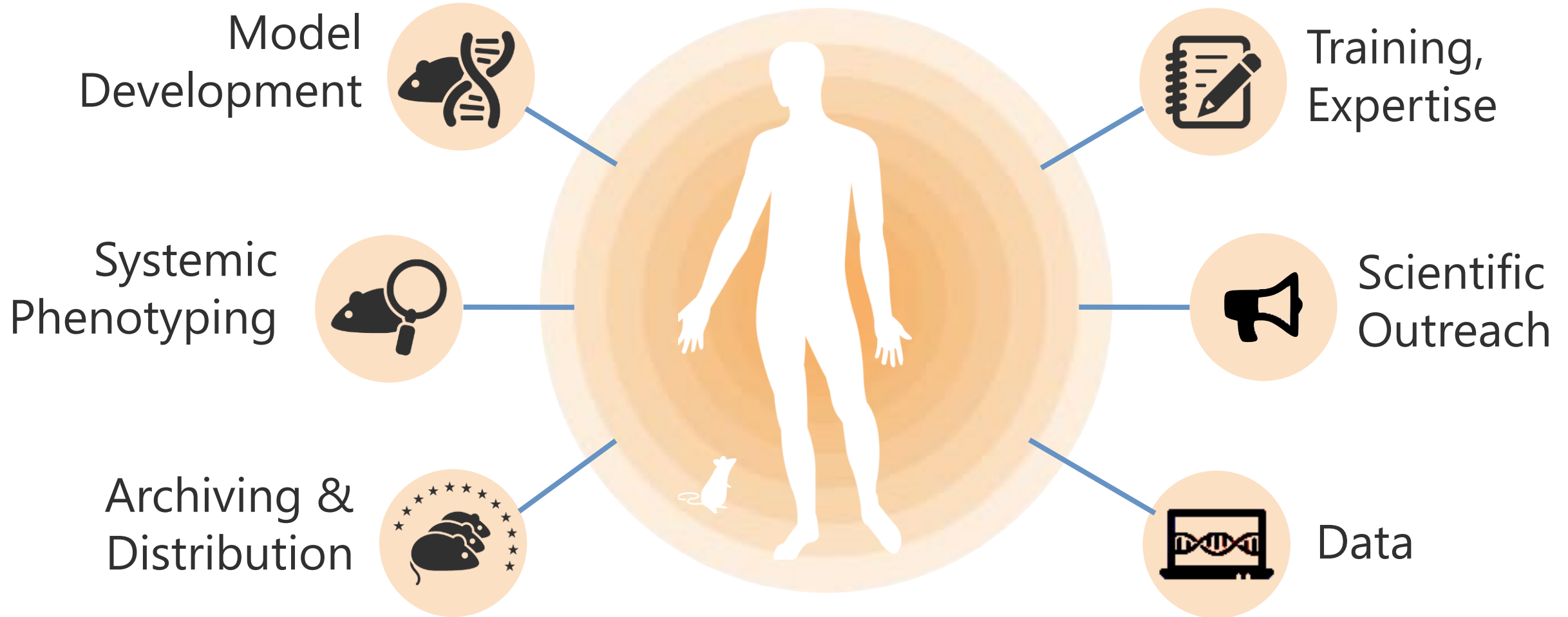
INFRAFRONTIER
mouse disease models

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

A consortium of leading European
research institutions - **29 partners in**
15 countries



Access to physical resources, analytical platforms, knowledge and data



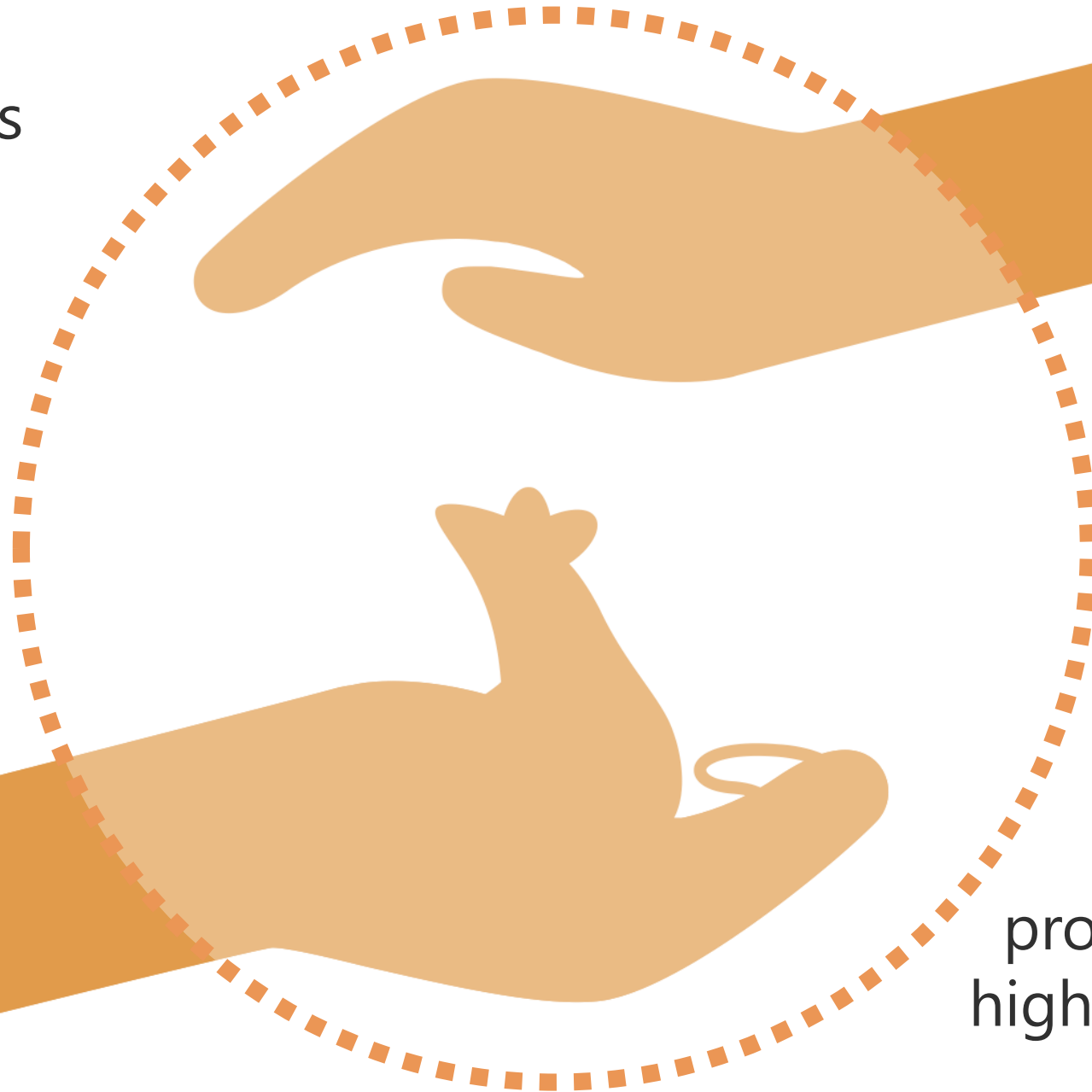
Promoting responsible and reproducible research

Promoting the 3Rs

Replacement

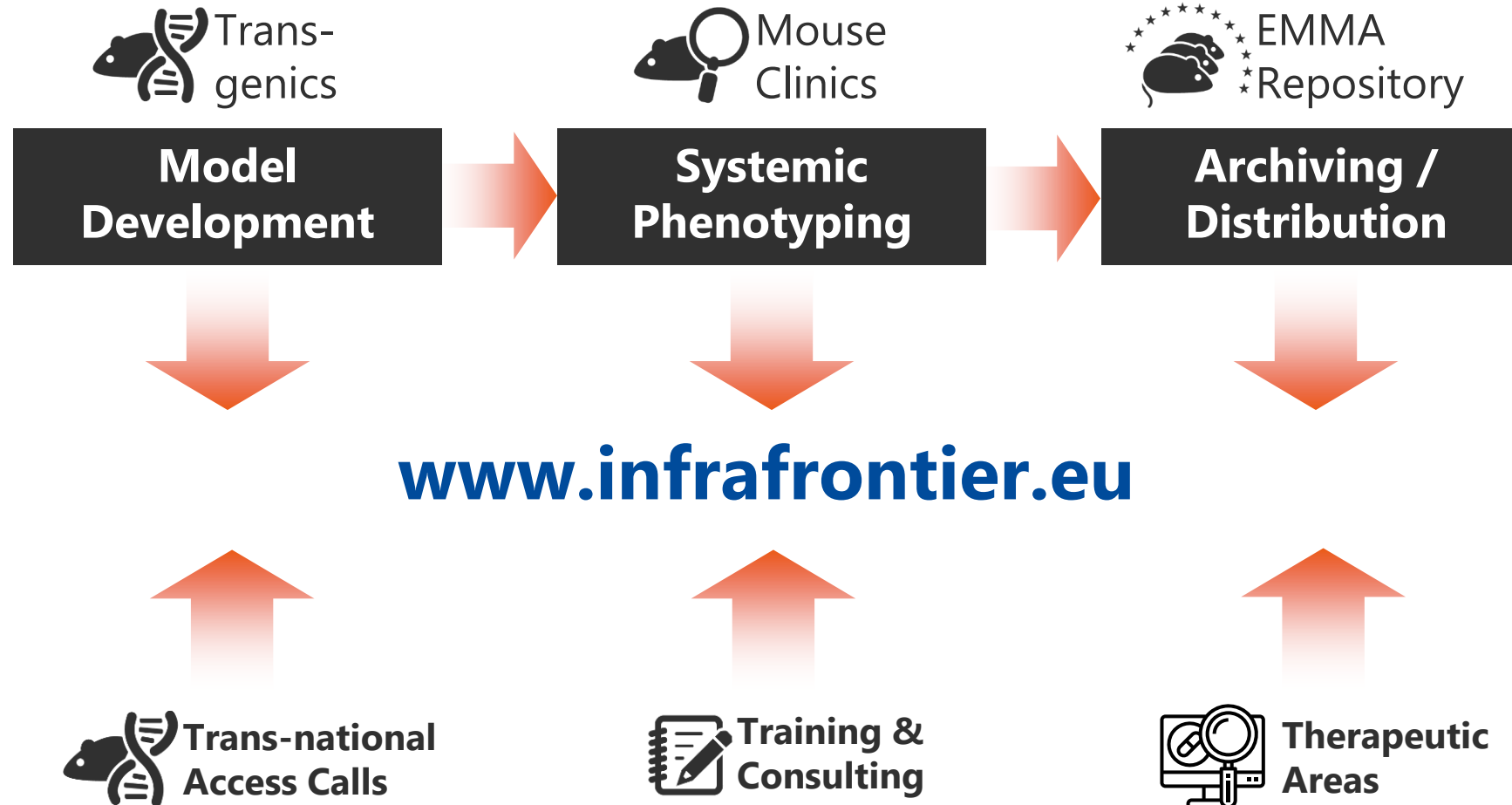
Reduction

Refinement



Minimising
duplication by
providing centralised
high-quality resources

INFRAFRONTIER Resources and Services



Distributed research infrastructure – one face to the customer

Resources and Services

Deposit mice



EMMA archives your mouse mutant free of charge >

Order mice



Access to 7600 mouse mutants and research tools >

Axenic service



INFRAFRONTIER 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 >

Training and consulting



Hands-on courses in cryopreservation and phenotyping >

EMMA strains

Search EMMA strains



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

Browse EMMA strains

Collections

Human Diseases

? Help




Useful information for EMMA users

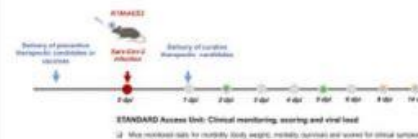
Learn more >

- EMMA repository conditions
- SOPs and FAQs
- Major collections archived at EMMA
- EUCOMM/KOMP-CSD allele conversion service

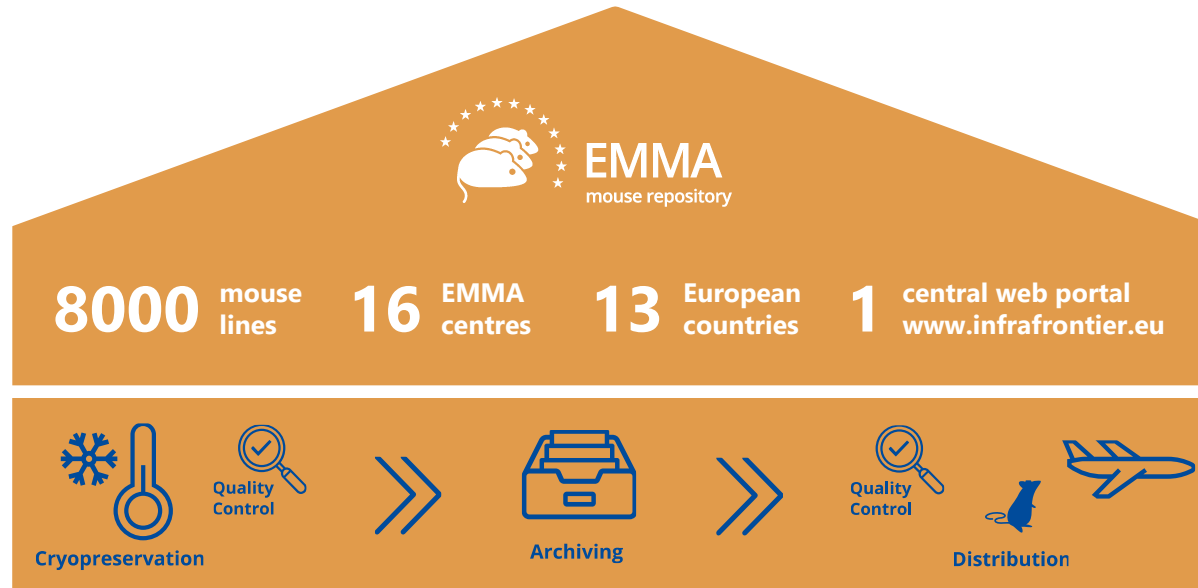
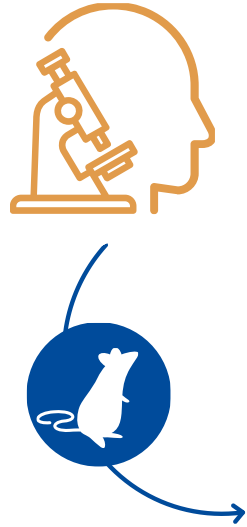
Tweets by @InfrafrontierEU



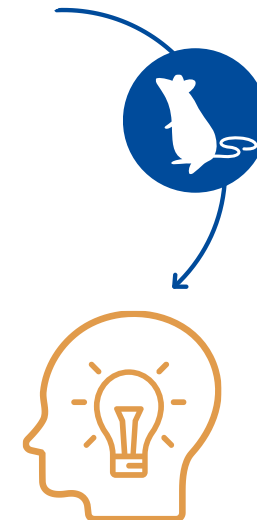
Happy to announce an overwhelming response to our latest #opencall on #COVID19 Therapeutics Pipeline. More than 20 fascinating proposals from 8 countries for 5 slots. Looking forward to the evaluations and outcomes! bit.ly/3be0Q80



The European Mouse Mutant Archive (EMMA)



- **Open access to more than 8000 mouse lines**
- High-quality health controlled mice with defined and verified genotype
- EMMA ships globally

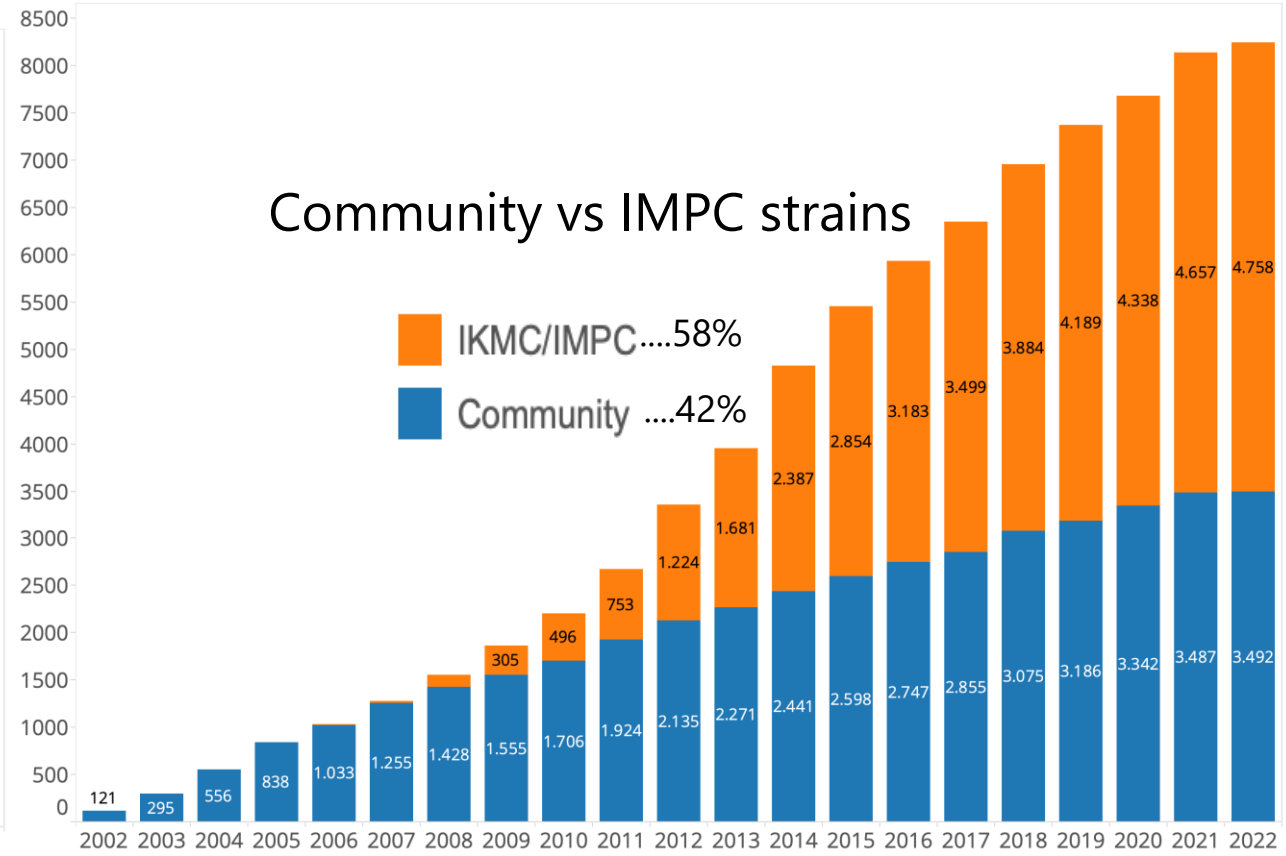
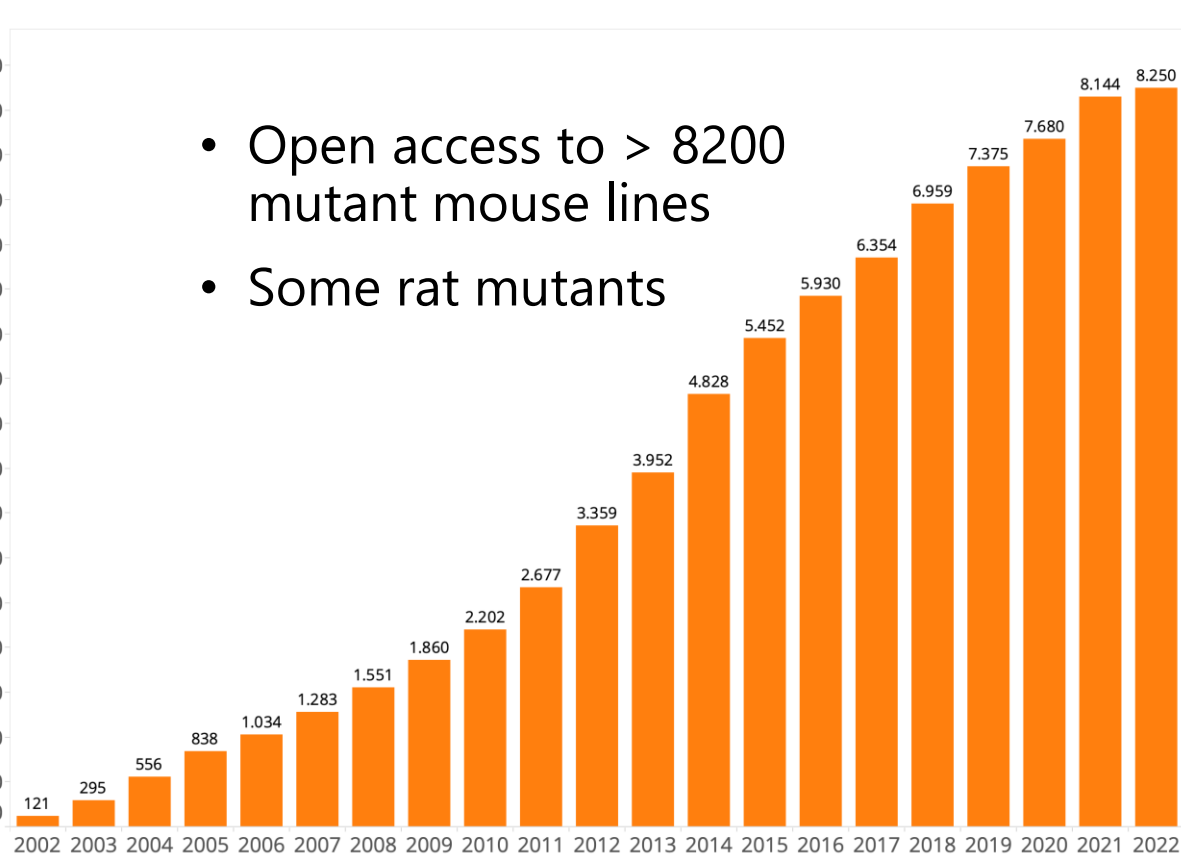


Impact of INFRAFRONTIER on ANIMAL WELFARE

- Number of animals “saved” (not bred, not born, not used) because they are cryopreserved
- ~50 animals/year needed to maintain a colony
- ~ 8.000 mouse lines archived in EMMA-INFRAFRONTIER
- **Up to 400.000 mice are saved (= not born) per year**

3rd largest non-profit mouse repository worldwide

- Open access to > 8200 mutant mouse lines
- Some rat mutants

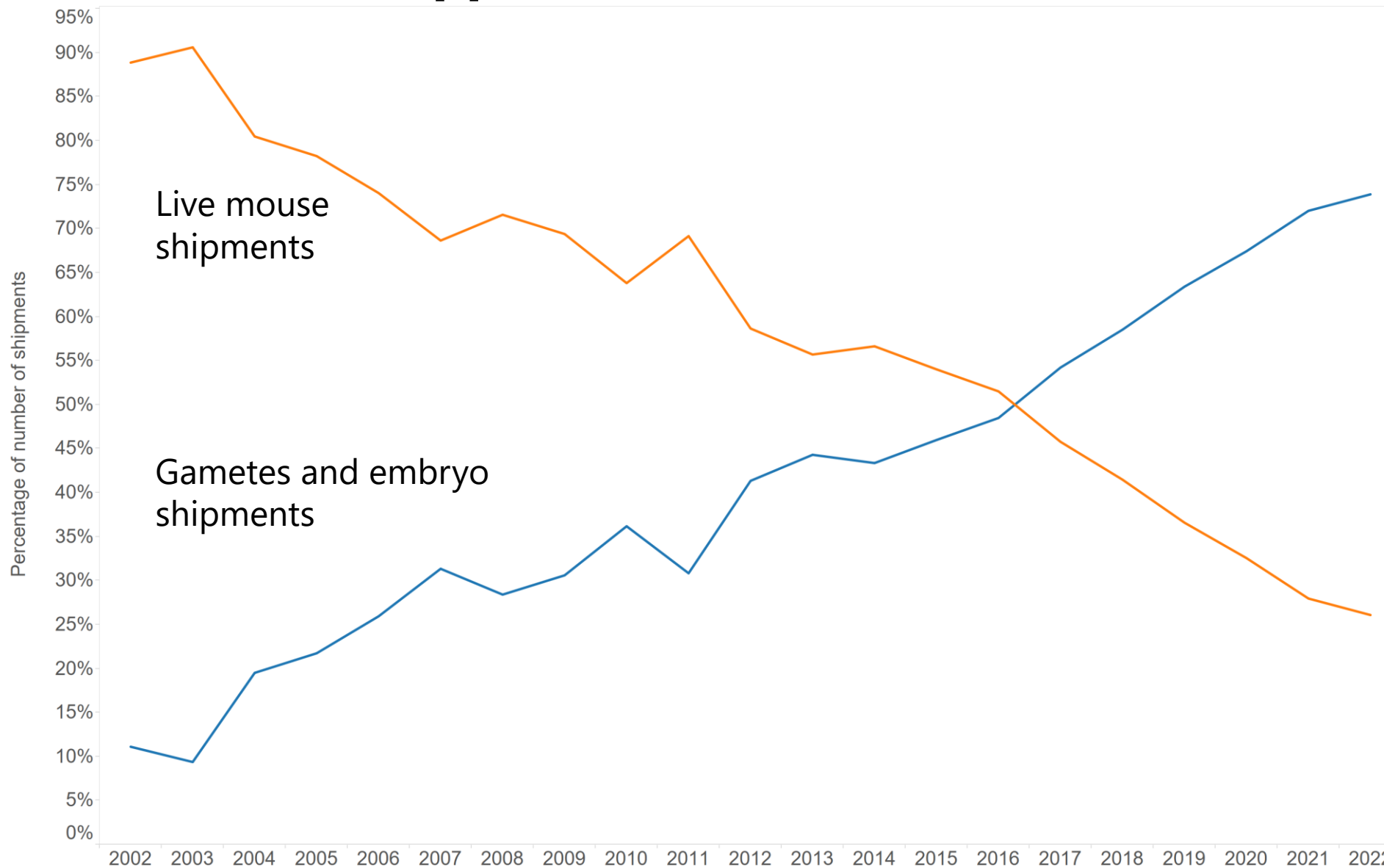


EMMA Shipping Destinations

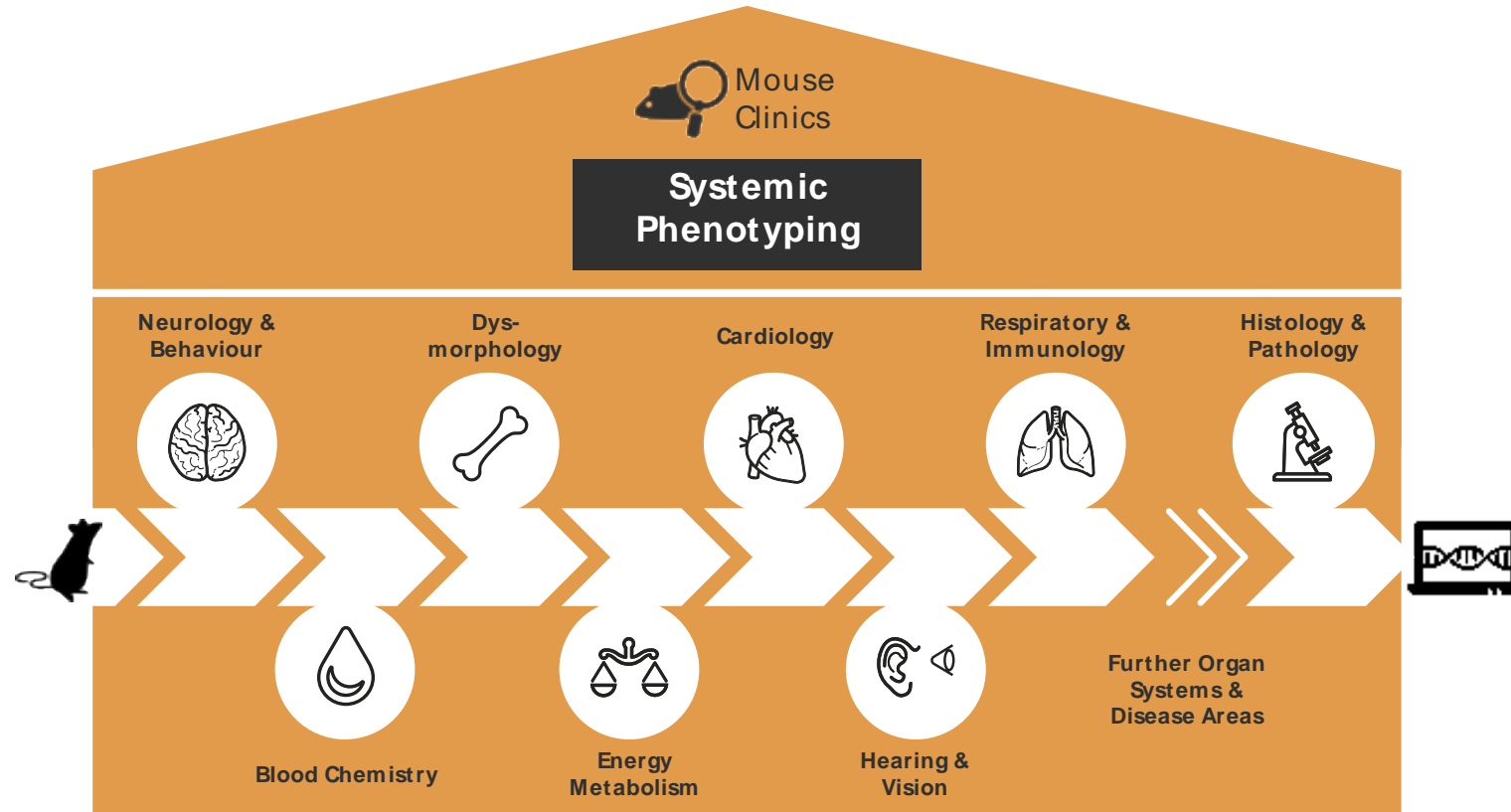


700 unique
destinations (cities)
worldwide

Material shipped from EMMA (frozen/live)



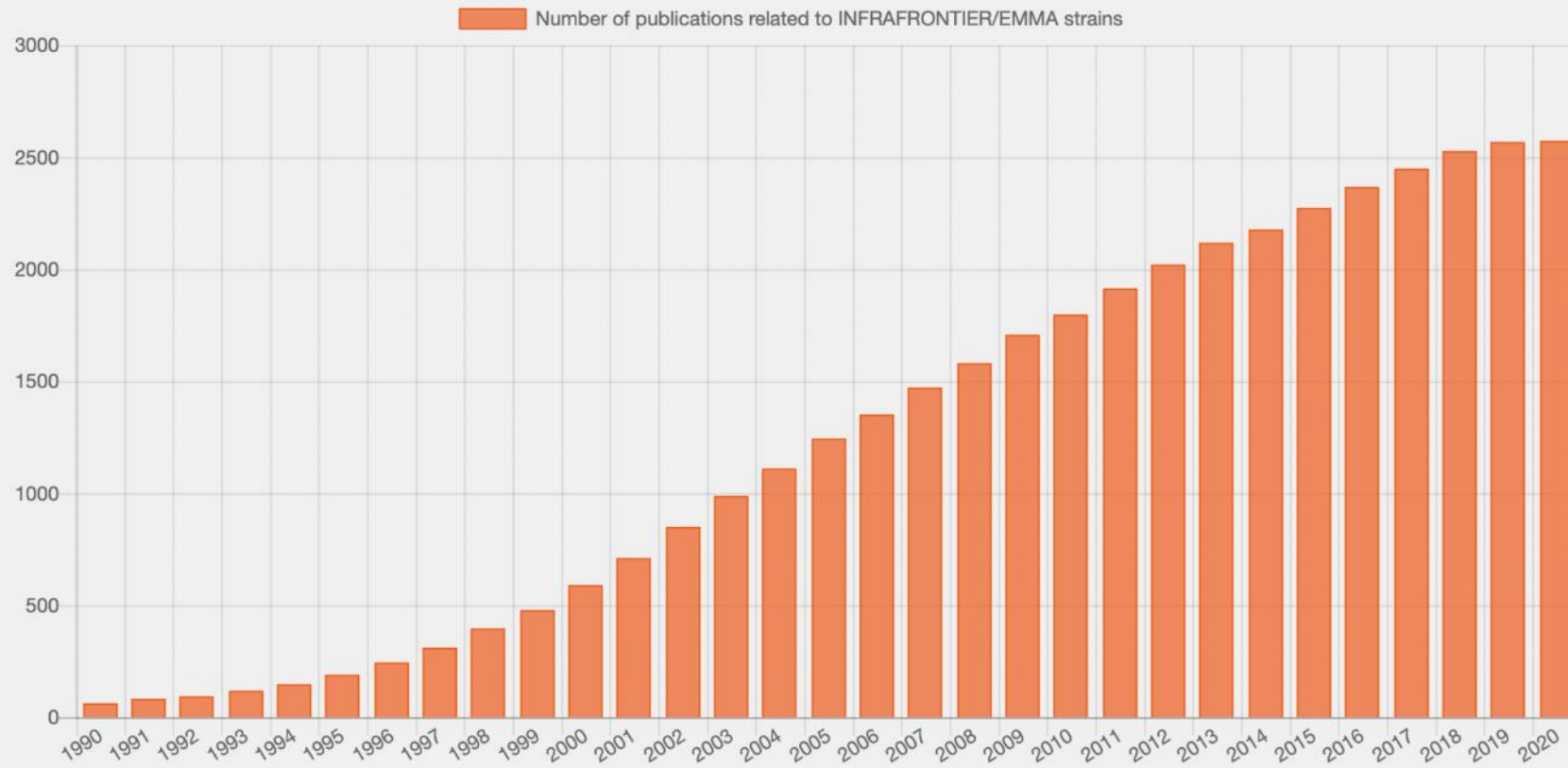
Systemic phenotyping and mouse clinics



- Mouse clinics offer a **whole–system screen** covering more than 500 parameters in different disease areas and organ systems
- Added benefit of obtaining **maximum information** using a **minimum amount of animals**

Publications related to INFRAFRONTIER / EMMA

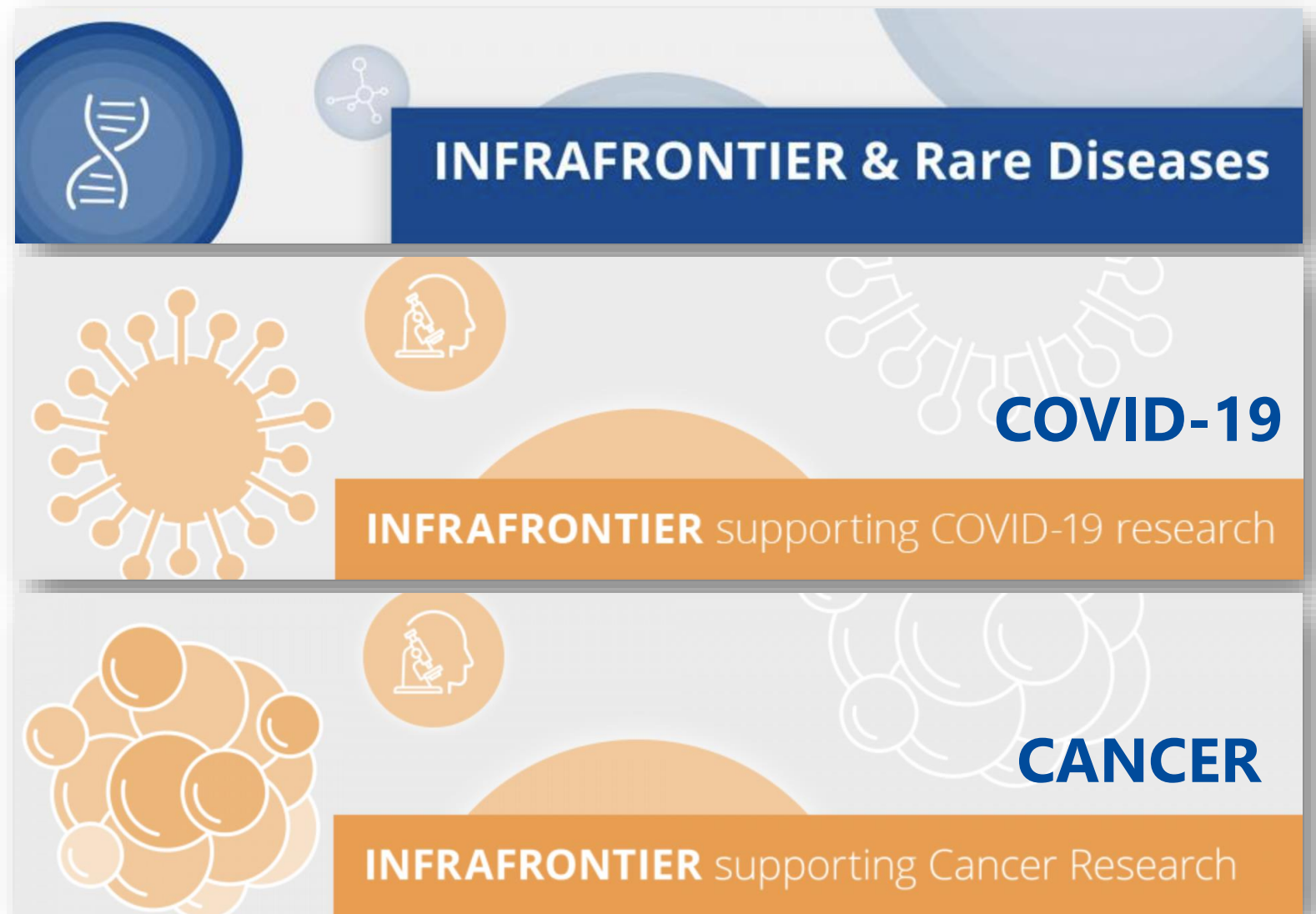
INFRAFRONTIER bibliography



- **2574** publications; both from strain submissions and strain requests
- **49** Cell publications
- **43** Nature Genetics publications
- **82** Nature publications

INFRAFRONTIER Therapeutic Areas

Collection of
INFRAFRONTIER resources
and services related to a
therapeutic area in one
page



The image displays three horizontal banners, each representing a therapeutic area. The top banner is blue and features a DNA double helix icon on the left and a molecular structure icon in the top right. The middle banner is orange and features a virus particle icon on the left and a microscope icon in the top right. The bottom banner is also orange and features a cluster of cells icon on the left and a microscope icon in the top right. Each banner has a dark blue bar at the bottom with white text.

INFRAFRONTIER & Rare Diseases

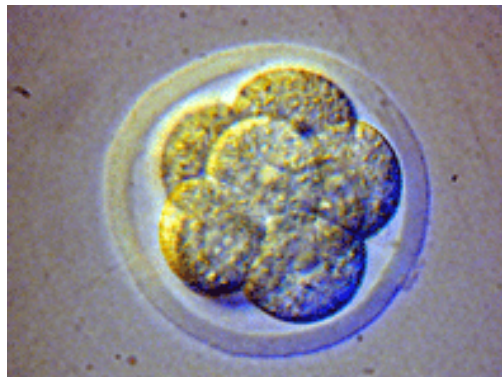
COVID-19
INFRAFRONTIER supporting COVID-19 research

CANCER
INFRAFRONTIER supporting Cancer Research



The EMMA-Infrafrontier Spanish node at CNB

Julia Fernández & Lluís Montoliu

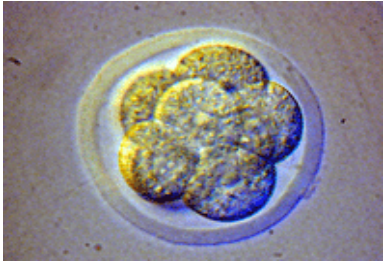


EMMA-Infrafrontier Services provided from CNB



- **Depositing mouse lines into EMMA**
 - Depositing requests evaluated by external committee
 - Approved requests are cryopreserved for **free**
 - Depositor covers shipping costs
 - Cryopreserved mouse lines freely available to everyone
 - Grace period possible (up to 2 years), MTAs accepted
- **Requesting mouse lines from EMMA**
 - Access to EMMA archive requires payment of **repository fee**
 - Frozen sperm/embryos: 1,600 Euros + shipping costs
 - Live mice: 3,200 Euros + shipping costs





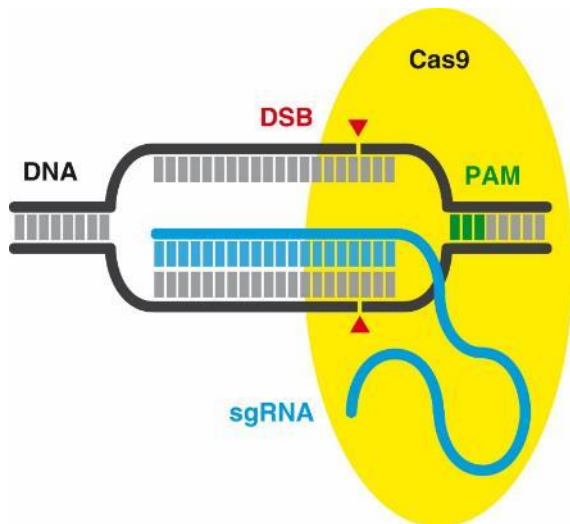
EMMA procedures at CNB- I

- **Cryopreservation of mouse strains**
 - Cryopreservation of mouse embryos, sperm, oocytes
 - Genotyping (single embryos) and quality control
- **Rescue of mouse strains from frozen material**
 - Thawing of mouse embryos, sperm, oocytes
 - In vitro fertilization and embryo transfer
 - Genotyping and quality control
- **Importing/Exporting Mouse Line**
 - Receiving frozen mouse embryos, sperm (LN₂ and dry ice). refrigerated mouse embryos, epididymes (+4/+8°C) Receiving live mice
 - Exporting mouse lines Shipping frozen mouse embryos, sperm (LN₂ and dry ice), Shipping refrigerated mouse embryos , epididymes. Shipping live mice



EMMA procedures at CNB - II

- Rederivation of mouse strains (into SPF zone)
- Generation of knockout mice from ES cell clones (TNAs)
- Generation of genome edited (CRISPR) mice (TNAs)
 - Advice / experimental design / guide RNA selection
 - Gene disruptions
 - Gene deletions/inversions
 - Gene substitutions/mutations (ssDNA oligos)
 - Electroporation of mouse embryos
 - Embryo transfer into pseudopregnant females



INFRAFRONTIER & CRISPR

- Helmholtz Munich licensed the legal distribution of CRISPR mouse lines from **Caribou** and **BROAD**
- CRISPR licenses are paid annually and are distributed among INFRAFRONTIER participating partners
- 10% of INFRAFRONTIER repository fee is added for CRISPR mouse lines to compensate the royalties paid
- CNB-CSIC is offering the generation of CRISPR mouse lines for third parties as long as they are deposited in and obtained from INFRAFRONTIER

Services provided	CNB	CSIC Centres	Public Centres	Private Centres
Cryopreservation and validation of a mouse line as embryos (3xE + 3xA + 1xC)(1 unit = 1 mouse line cryopreserved as embryos)	842,00€	987,70€	1497,07€	1639,65€
Cryopreservation and validation of a mouse line as sperm (B + D)(1 unit = 1 mouse line cryopreserved as sperm)	560,28€	657,22€	844,49€	925,36€
Revitalizing a mouse line from frozen embryos (C + 3xF)(1 unit = 1 mouse line revitalized from embryos)	282,35€	331,21€	481,75€	527,64€
Revitalizing a mouse line from frozen sperm (D + 3xF)(1 unit = 1 mouse line revitalized from sperm)	662,44€	777,06€	1032,22€	1130,54€
Generation of a mouse model genetically edited with CRISPR-Cas9 technology through EMMA-INFRAFRONTIER as frozen embryos or sperm (L + 1600€ service fee + 160€ CRISPR license)(1 unit = 1 mouse line edited with CRISPR-Cas9 and obtained from EMMA-INFRAFRONTIER as frozen embryos or sperm)	3440,62€	3731,37€	4043,80€	4261,30€
Generation of a mouse model genetically edited with CRISPR-Cas9 technology through EMMA-INFRAFRONTIER as live animals (L + 3200€ service fee + 320€ CRISPR license)(1 unit = 1 mouse line edited with CRISPR-Cas9 and obtained from EMMA-INFRAFRONTIER as live animals)	5200,62€	5491,37€	5803,80€	6021,30€



Tarifas Oficiales CSIC - 1 de abril de 2023



**CNB Mouse Embryo
Cryopreservation
Facility
Spanish EMMA node**

Julia Fernández
María Jesús del Hierro
Marta Castrillo
Cristina Bernal
Inés Arroba
Lluís Montoliu



www.user.cnb.csic.es/criocnb/

CNB Mouse Cryopreservation Facility



EMMA
mouse repository



GOBIERNO
DE ESPAÑA

MINISTERIO
DE CIENCIA
E INNOVACIÓN



Centro Nacional
de Biotecnología

ACCESO PRINCIPAL



INFRAFRONTIER
mouse disease models

**Spanish EMMA-Infrafrontier
node at CNB-CSIC in Madrid**

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