



*Fondazione per la Ricerca  
sulla Fibrosi Cistica - ETS*  
italian cystic fibrosis research foundation

**WEBINAR DI  
PRESENTAZIONE**  
**16 GENNAIO 2025**





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**Alessandra Bragonzi**

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**WHAT**

Accelerating innovative treatment strategies for Cystic Fibrosis through pre-clinical research

**WHY**

Provide infrastructure (stably and BSL2/3) and expertise in CF animal models; reduce individual center costs associated with maintaining CF colonies research

**WHO**

Myself and collaborators (Ida De Fino, Davide Gugliandolo & Martina Rossano - Alice Rossi, past) with unique expertise in maintaining CF colonies and modeling respiratory infectious diseases

**WHERE**

Operating in Milan at OSR (Ospedale San Raffaele) with the financial support of FFC colonies

**WHEN**

Ongoing initiative since 2009

# Research Support Services

## Level 1

- Distribution of CF mice ready to be used



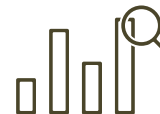
## Level 2

- Scientific and regulatory support to plan preclinical studies
- Pre-clinical models of respiratory infection
- Pharmacological treatments



## Level 3

- Activities described at Level 1
- Processing and analysis of biological samples
- Data analysis including statistical and scientific report



# Cystic Fibrosis Mouse Models



## C57BL/6 *Cftr* <sup>tm1<sup>Unc</sup></sup> TgN(FABPCFTR) (Snouwaert, 1992; Zhou, 1994)

CFTR knock-out gut corrected

C57BL/6J *Cftr* exon 10 replacement (S489X)/ FABPhCFTR insertion

Lung phenotype: abnormal nasal potential difference, inflammatory response, infection clearance; Gut phenotype: normal; Alimentary phenotype: normal; Lethality-postnatal: normal



## C57Bl/6 *Cftr*<sup>Δtm1Kth</sup> (Zheier et al, 1995)

CFTR deltaF508

C57BL/6J *Cftr* delta F508 with 3 bp deletion in exon 11

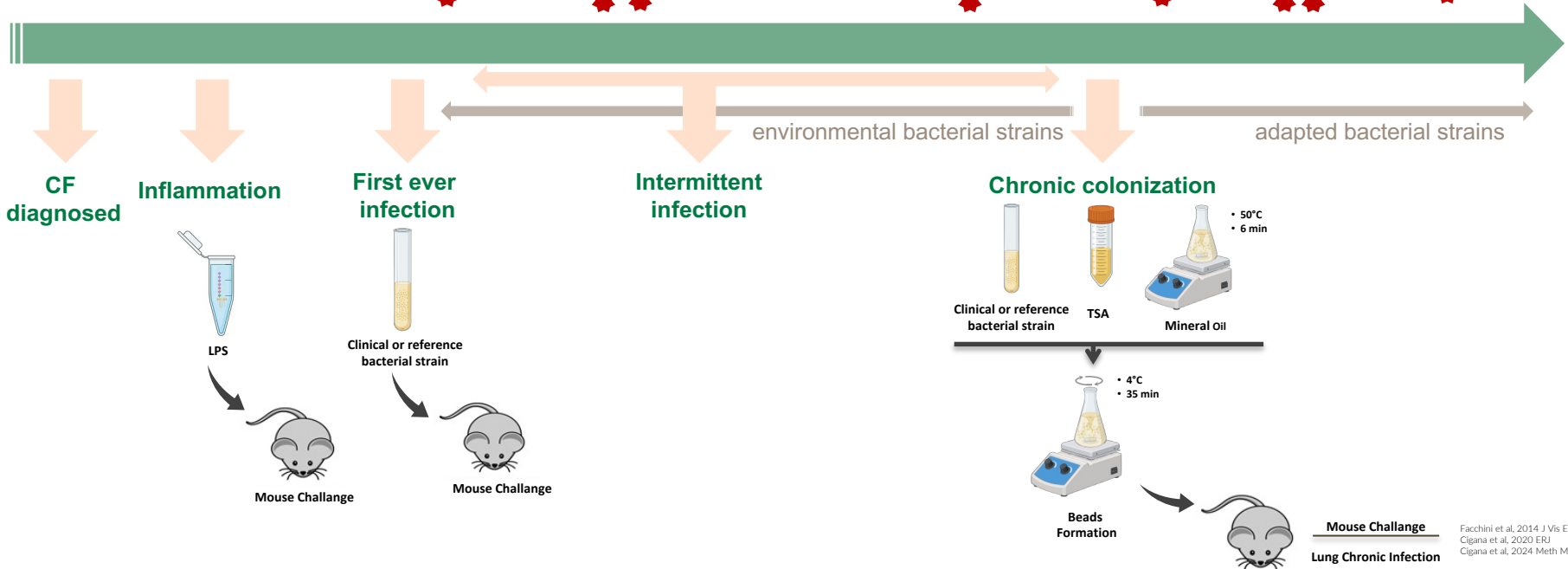
Gut phenotype: obstruction; Lung phenotype: abnormal nasal potential difference, inflammatory response, infection clearance; Alimentary phenotype: normal + laxative; Postnatal lethality: high mortality pre and post-weaning

# Pre-clinical Efficacy Mouse Model

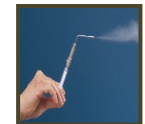
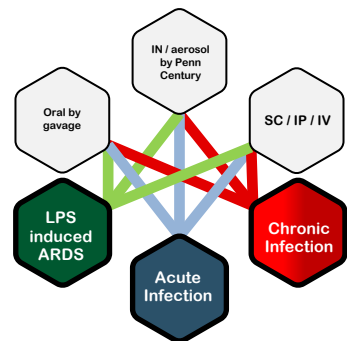
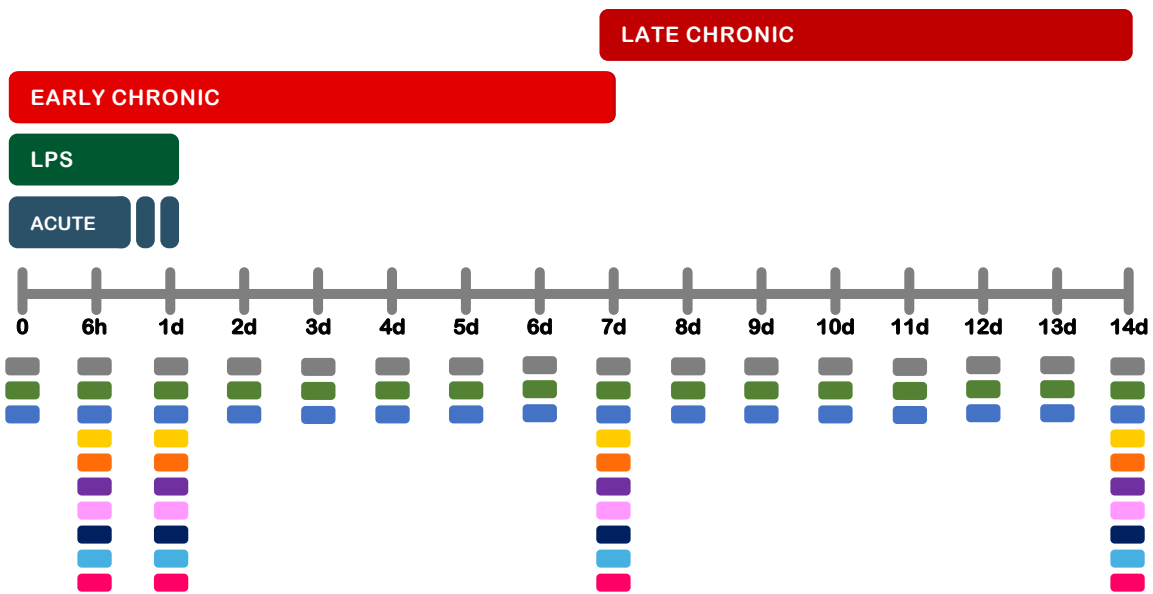
BIRTH

Potential exacerbations

DEATH

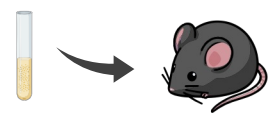


# Schedule of treatment and read-out

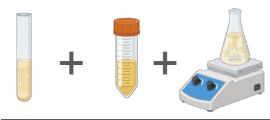


Aerosol delivery by MicroSprayer® Aerosolizer and the Dry Powder Insufflator™

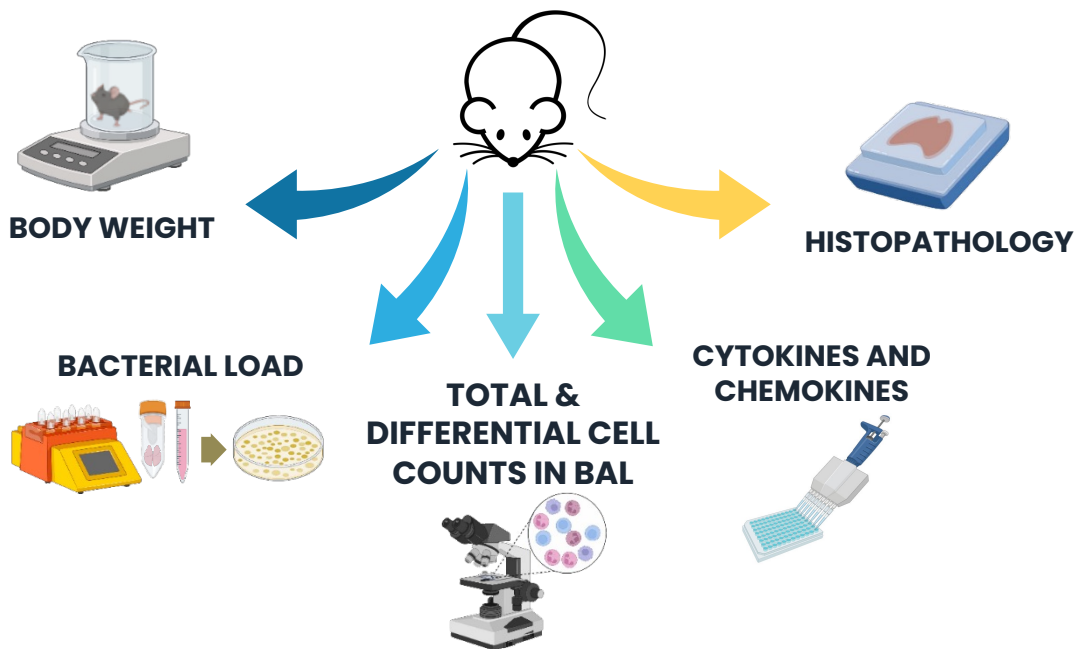
## Acute Infection



## Chronic Infection



# Traditional and extended read-out



## FLEXIVENT LUNG FUNCTION MEASUREMENT



PARAMETER	DESCRIPTION	PHYSIOLOGICAL RELEVANCE
FEV <sub>x</sub>	Forced Expiration Volume data	Amount of air forcefully exhaled (drawn) at different time points
FVC	Forced Vital Capacity	Amount of air the animal can physically exhale
R <sub>rs</sub>	Resistance of the respiratory system	Airway constriction
E <sub>rs</sub>	Elastance of the respiratory system	Stiffness
C <sub>rs</sub>	Compliance of the respiratory system	Ability to stretch





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# Additional Support Services

## Francesca Sanvito

Pathological Anatomy Unit  
Ospedale San Raffaele

### TOXICITY STUDIES

Toxicology; Necropsy and tissues collection managed by computerized system (Ascentos)

### PATHOLOGICAL STUDIES

Histological preparation; Special staining; Immuno histochemistry; Histopathological evaluation;  
Reporting managed by computerized system (Ascentos)



## Micol Ravà

Animal Biochemistry  
Ospedale San Raffaele

### HEMATOLOGY

Complete Blood count (WBC, WBC count, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, and reticulocytes by Idexx Procyte analyzers)

### CLINICAL BIOCHEMISTRY

21 parameters of serum biochemical tests for liver, kidney, heart, pancreas and other





## Critical Success Factors for Effective Drug Evaluation

**ROUTE OF ADMINISTRATION**

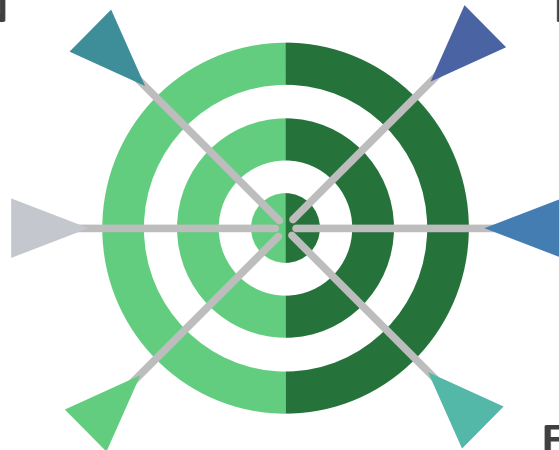
**PRE-CLINICAL MODEL**

**SCHEDULE OF TREATMENT**

**TYPE OF DRUG VS BENCHMARK**

**TYPE OF READOUT**

**ESTABLISHED EXPERTISE &  
COMMITMENT**



# How to Access the Service



## GRANT APPLICATION

- Scientific support to design and write pre-clinical studies
- Statistical analysis to determine the optimal number of animals for the study
- Budget plan



## NEGOTIATIONS

- Revision of experimental plan and budget based on referee feedback
- Request for ethical approval



## EXECUTION

- Drug testing using established protocols and endpoints to ensure predictive values and pre-clinical relevance



## Costs and Payment

### CF mice

Wild type: 100% project charge (20 €)  
CF KO mice : 50% project charge (103 €) and  
50% funded by CFaCore (103 €)

Payment  
to FFC

### Charles River mice

C57Bl/6: 100% project charge (20  
€) Animal delivery: 100% project  
charge

Payment  
to Charles  
River

### Services

BSL2 stabulary: 100% project charge  
Consumable: 100% project charge  
Personnel: 0% project charge, funded by CFaCore

Payment  
after OSR  
invoice



## People and Expertise



**Alessandra Bragonzi**

26 years of experience in CF.  
Since 2009, founder and  
head of CFaCore



**Ida De Fino**

20 years of experience in CF.  
Since 2010, responsible for  
the management of  
transgenic CF mice



**Davide Gugliandolo**

5 years of experience in animal  
models and 3 years in CF.  
Responsible for animal care  
since 2021 and for pre-clinical  
studies since 2024



**Martina Rossano**

NEW!

**Our achievements:** 55 projects for efficacy testing studies  
46 projects for CF mice; 79 publications on mouse models of CF



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