ISIDORe Project - Trans-national Access call for CIPHE BSL3 Pipeline

Offered by INFRAFRONTIER Research Infrastructure

Starting June 2022

Call information and application form

Context and aims of the call

INFRAFRONTIER is the European Research Infrastructure for the generation, phenotyping, archiving and distribution of model mammalian genomes. The INFRAFRONTIER Research Infrastructure provides access to first-class tools and data for biomedical research, and thereby contributes to improving the understanding of gene function in human health and disease using the mouse model. The core services of INFRAFRONTIER comprise the systemic phenotyping of mouse mutants in the participating mouse clinics, and the archiving and distribution of mouse mutant lines by the European Mouse Mutant Archive (EMMA).

Main objective of this ISIDORe Trans-national Access (TNA) call is to provide extensive user support to the selected projects for assessing novel potential vaccine and treatment compounds for COVID-19. As starting material for the TNA service, sufficient amounts of the therapeutic candidate and desired mode of administration will be provided by users. It will be incumbent upon users to provide these materials and information. Viral particles, COVID-19 mouse models, cohort production and BSL3 pipeline analysis will be provided by the INFRAFRONTIER service provider. Further functional analysis and advanced readouts like organ histopathological analysis, multiplex assay profiling of cytokines and chemokines in lung and mouse serum etc. can be provided on a collaborative basis outside the scope of this TNA call. A final infection profile report will be provided as a deliverable.

Access will be granted on the basis of scientific excellence and technical feasibility.

The ISIDORe project has received funding from the EU Research and Innovation programme Horizon Europe (Grant Number: 101046133)

Participating INFRAFRONTIER partners

PHENOMIN-CIPHE is dedicated to customized preclinical mouse and cell line model generation, high-content standardized flow, spectral and mass multiparametric immunophenotyping, single cell omics studies and advanced data analysis of the mouse and human immune systems under normal and pathological conditions (inflammation, infection, cancer). It provides academic and industrial partners with a unique integrated technological toolbox to comprehensively characterize the immune system of a wide spectrum of preclinical mouse models and of human samples of interest.

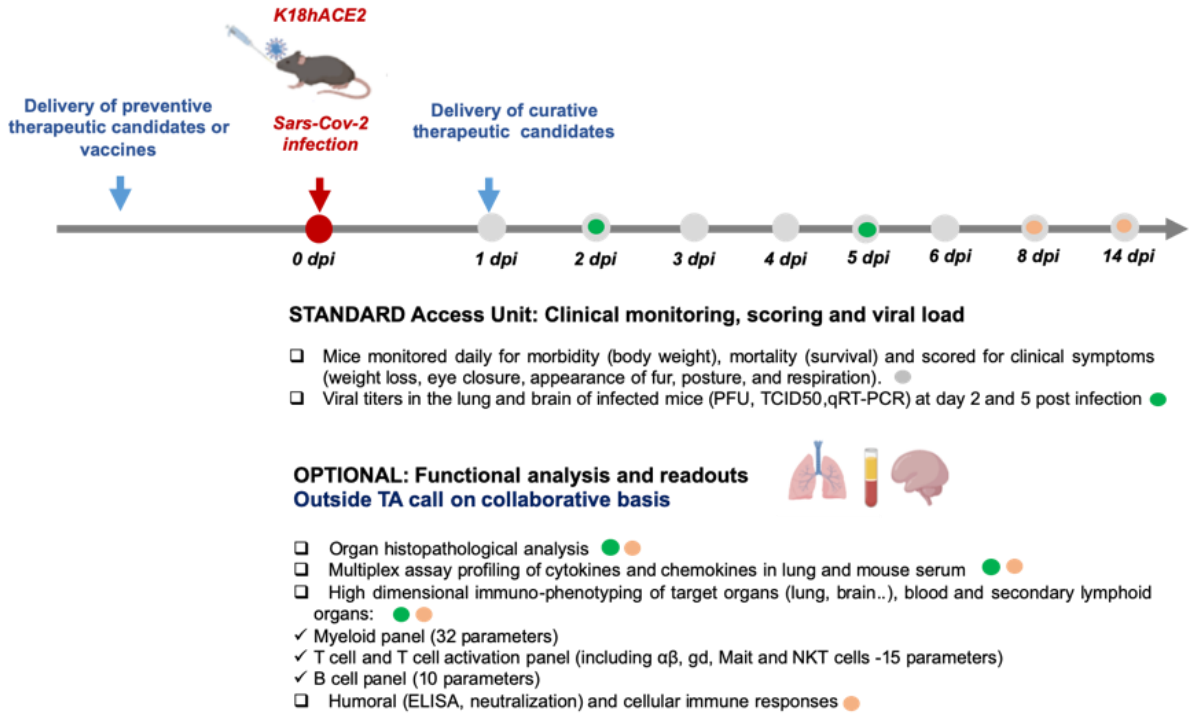
Characterisation of the anti-SARS-CoV2 therapeutics on COVID-19 mouse models in BSL3 facilities

One of the SARS-CoV-2 susceptible mouse strains expresses the human SARS-CoV-2 receptor (angiotensin-converting enzyme [hACE2]) under the cytokeratin 18 promoter (K18). Infection of those mice results in a dose-dependent lethal disease where the virus can be detected in lung airway epithelium and brain. K18-hACE2-transgenic mice are, therefore, highly susceptible to SARS-CoV-2 infection and represent a stringent animal model for the study of viral pathogenesis, and for the development and characterization of vaccines (prophylactic) and antivirals (therapeutic) against COVID-19.

Center for Immunophenomics (CIPHE), a node of the PHENOMIN French National Infrastructure and a member of the INFRAFRONTIER Infrastructure, possesses a BioSafety Level 3 (BSL3) facility which has the capacity to host up to 500 cages of mice infected with respiratory pathogens. Owing to a collaboration with the Jackson laboratory that kindly has provided K18-hACE2 mice in July 2020, CIPHE has established the K18-hACE2 mouse model of SARS-CoV2 infection and its viro- and immuno-monitoring, permitting to test prophylactic or therapeutic compounds using morbidity (body weight), mortality (survival) and clinical score as end-points. Moreover, combining the K18-hACE2 model of SARS-CoV-2 infection and the CIPHE high-dimensional immunomonitoring capacity permits to define the cellular and molecular basis of lung and brain disease.

COVID-19 Therapeutic Pipeline

The free-of-charge access unit covers the standard COVID-19 therapeutics pipeline from CIPHE that includes clinical monitoring, scoring and viral titration (shown below). Specifically, this access unit will include, (1) suitable delivery of preventive therapeutics or vaccines pre-infection or curative therapeutic candidates after infection, (2) infection of COVID-19 mouse models with appropriate SARS-CoV-2 virus titers, (3) monitoring of mice for mortality, morbidity and clinical symptoms and (4) determination of viral titers in the lung and brain.



Trans-national Access (TNA) activity of the ISIDORe project

Free-of-Charge COVID-19 Therapeutics Pipeline Service

Access modalities:

- The EC Horizon Europe funded ISIDORe project (2022 – 2023) supports eligible users with a free-of-charge CIPHE BSL3 pipeline service implemented as a Trans-national Access activity.

- The access unit offered covers the (1) suitable delivery of preventive therapeutics or vaccines pre-infection or curative therapeutic candidates after infection, (2) infection of COVID-19 mouse models (females) with appropriate SARS-CoV-2 virus titers, (3) monitoring of mice for mortality, morbidity and clinical symptoms and (4) determination of viral titers in the lung and brain.

- Support will be provided by the CIPHE experts to analyse and interpret the data.

- Accepted proposals will start with the provision of the therapeutic candidate that is ready to be injected and end with the delivery of infection data reports to selected applicants.

- Further functional analysis and advanced readouts like organ histopathological analysis, multiplex assay profiling of cytokines and chemokines in lung and mouse serum etc. can be provided on a collaborative basis outside the scope of this TNA call.

- A final infection profile report will be provided as a deliverable. The results may be used for internal reporting purposes for the EC only after approval/consultation from the users.

- **Costs:** The access to the ISIDORe CIPHE BSL3 pipeline service is free-of-charge. However, the shipment of the therapeutic compound to CIPHE must be borne by the applicants.

- **Eligibility:** The ISIDORe Trans-national Access call is open and proposals can be submitted from non-commercial applicants around the world.

- **Application:** Service requests for the ISIDORe CIPHE BSL3 pipeline service can be made via this application form. Applications for the Trans-national Access activity must include a short description of why the therapeutic candidate is a candidate for a COVID-19 vaccine/treatment and future research plans after the ISIDORe TNA service.

- **Selection procedure:** Proposals from eligible users for free-of-charge access to the ISIDORe CIPHE BSL3 pipeline service will be subject to a review procedure. A mixed panel of INFRAFRONTIER members and an external Evaluation Committee will assess service requests supported by the TNA activity. In addition to scientific merit of applicants, relevance and quality of preliminary data, soundness of the proposal and research plans will be assessed. Additionally, experts at CIPHE will assess the technical feasibility of projects. The technical evaluation of projects may require the provision of additional data.

  Applicants will be informed on the outcome of the evaluation within 6 weeks after the end of the call for which the TNA application was submitted. All applications will be handled with strict confidentiality.

- **Acknowledgements:** Please acknowledge any support under this scheme in all resulting publications with 'Part of this work has been funded by the European Union Research and Innovation programme Horizon Europe (ISIDORe - Grant Agreement Number 101046133)'. The participating infrastructure, which provided the service, should be specifically mentioned in any publication resulting from the service.

Application Form - INFRAFRONTIER2020 CIPHE BSL3 pipeline service

Contact details of applicant

ISIDORe TNA project ID*	
First name	
Family name	
Email	
Phone	
Fax	
Institution	
Address	
Town	
Postcode	
Country	
ORCID	
Link to lab website	
Link to publication list	

Applications can only be considered if all data are provided

Please visit https://isidore-project.eu/services/in-vivo-models/ and fill up the form to receive the ISIDORe TNA project ID to your email.

The following data is required by the EC for statistical and project reporting purposes

Gender	
Birth year	
Nationality	
Researcher status (e.g. Prof, Postdoc)	
Scientific background	

☐ **I have read, understood and agree to the INFRAFRONTIER data privacy policy**

Description of proposed project

Please describe briefly the proposed project. This proposal will be the foundation for the evaluation of your project. Informal enquiries prior to proposal submission are welcome via proposals@infrafrontier.eu

Compound to be tested	

Please, do not extend beyond the provided space (max 2 pages including references)

Send your proposal to proposals@infrafrontier.eu