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**INFRAFRONTIER Research Infrastructure**

**INFRAFRONTIER2020 Project - Trans-national Access call for COVID-19 Therapeutics Pipeline**

**December 2020**

**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 INFRAFRONTIER2020 Trans-national Access call WP10 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 TA service, only sufficient amounts of the therapeutic candidate and desired mode of administration will be provided by the TA call 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 WP10 partners. 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 TA 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.

H2020 The INFRAFRONTIER2020 project has received funding from the EU Research and Innovation programme Horizon 2020 (H2020-EU.1.4.1.1. Developing new world class research infrastructures)

**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.

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The transgenic and archiving module at **CCP** focuses on generation of mutant rodent models using cutting edge technologies such as zygote electroporation and microinjection of DNA and CRISPR/Cas targeting tools. Other services include microinjection of targeted ES cell lines to produce chimeric mice; mouse archiving; recovery of live mice from cryopreserved embryos and sperm, and also analysis of sperm viability. CCP is also engaged in large scale in-house or international production projects like the IMPC. Services are provided to academic and industry clients from across the world.

**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.

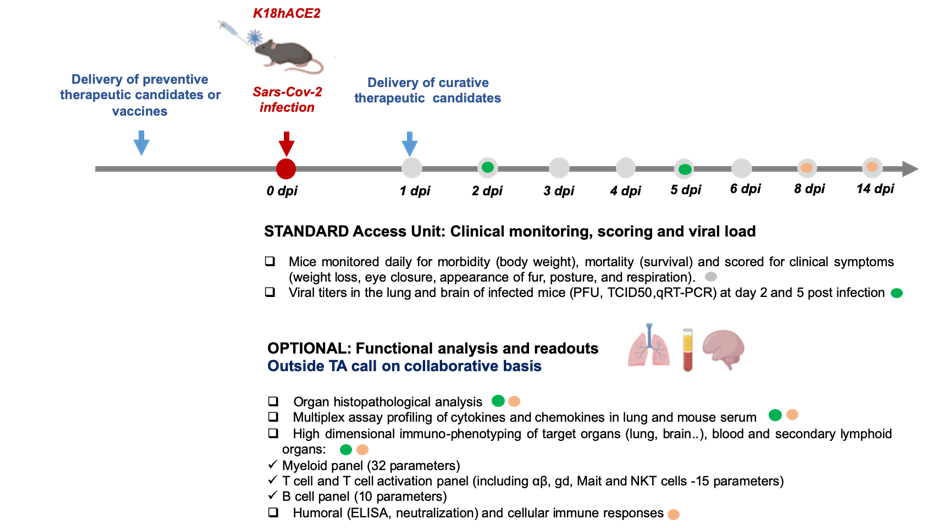
Center for Immunophenomics (CIPHE), a node of the PHENOMIN French National Infrastructure and a member of the INFRAFRONTIER Infrastructure, possesses a BioSafety Level 3 (BSL3) facility which has the capacity to host up to 500 cages of mice infected with respiratory pathogens. Thanks to a collaboration 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.

The other advanced models offered in this call on a case-by-case basis will have hACE2 replacing the mouse ACE2 for a more physiological level of expression and Cre recombinase-mediated conditional over-expression of hACE2 in a tissue-specific manner. These models will add a specialised dimension and will enable the investigation of a larger variety of user projects. These models are in the final stages of production at CCP and will be available in Q1 2021.

To sum up, the aim of this TA call is to enable open-access to CIPHE’s above-mentioned state-of-the-art BSL3 COVID-19 therapeutics pipeline and a selection of COVID-19 models to test user’s COVID-19 drugs, vaccines and treatments.

**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 (TA) activity of the INFRAFRONTIER2020 project**

**Free-of-Charge COVID-19 Therapeutics Pipeline Service**

**Access modalities:**

* The EC Horizon2020 funded INFRAFRONTIER2020 project (2017 – 2020) supports eligible customers with a free-of-charge COVID-19 Therapeutics Pipeline service implemented as a Trans-national Access activity supporting a total of 5 projects in this call.
* 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.
* A collaboration agreement will be established between applicants and CIPHE/CCP.
* 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 TA 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 INFRAFRONTIER2020 COVID-19 therapeutic pipeline service is free-of-charge. However, the shipment of the therapeutic compound to CIPHE must be borne by the applicants.
* **Eligibility:** The INFRAFRONTIER2020 Trans-national Access call is open and proposals can be submitted from non-commercial applicants around the world.
* **Application:** Service requests for the INFRAFRONTIER2020 COVID-19 therapeutic 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 INFRAFRONTIER2020 TA service.
* **Selection procedure:** Proposals from eligible customers for free-of-charge access to the INFRAFRONTIER2020 COVID-19 Therapeutics 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 TA 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 of CIPHE/CCP 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 TA 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 2020 (INFRAFRONTIER2020 - Grant Agreement Number 730879)’. The participating infrastructure, which provided the service, should be specifically mentioned in any publication resulting from the service.

**Application Form - INFRAFRONTIER2020 COVID-19 therapeutic pipeline**

**Deadline: 31. January 2021**

**Contact details of applicant**

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| --- | --- |
| **First name** |  |
| **Family name** |  |
| **Email** |  |
| **Phone** |  |
| **Fax** |  |
| **Institution** |  |
| **Address** |  |
| **Town** |  |
| **Postcode** |  |
| **Country** |  |
| **Link to lab website** |  |
| **Link to publication list** |  |

**The following data is required by the EC for statistical purposes**

**Applications can only be considered if all data are provided**

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

**I have read, understood and agree to the**[**INFRAFRONTIER data privacy policy**](https://www.infrafrontier.eu/procedures/legal-issues/data-privacy-statement)

**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](mailto:proposals@infrafrontier.eu)

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| **Compound to be tested** |  |
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Please, do not extend beyond the provided space (max 2 pages including references)

**Send your proposal to proposals@infrafrontier.eu**