

Call for collaboration for access to screening facilities for rationally selected compounds against SARS-CoV-2

Background: Exscalate4CoV (acronym E4C) is an EU-funded project that was selected after the emergency Call of expression of interest that the European Commission (DG RTD) issued on 31 January. The project will receive a 3 million EUR of EU funding in the next 18 months. It is consisting of a coalition of three of the most powerful supercomputing centres in the EU (CINECA in Italy, Barcelona supercomputing centre in Spain and Jülich supercomputing centre in Germany) together with a pharmaceutical company and several large Institutes dealing with biology and bio-molecular dynamics. The E4C team use supercomputers in the search of a therapies (small molecule drugs) against SARS-CoV-2 by complementing the classical trial and error clinical approach and possible experimentation in patients, by comparing the signature of the protein of the virus against active molecules that are used in existing databases of compounds. The project is currently processing digital models of the protein of the virus and is matching them against a publicly available database of thousands of known active anti-molecules that are part of existing drugs with the aim to find out which combinations of active molecules could react to the virus.

The E4C project is also establishing a pipeline of phenotypic and target based screens to evaluate the efficacy of repurposed, commercial and de-novo designed compounds.

To supplement the E4C compound pipeline, we invite organisations to submit proposals for screening of their compounds for efficacy profiling on the E4C Biology platforms.

These may include compounds identified from in-silico screening of SARS CoV2 associated targets or rationally selected repurposed compounds and bioactives. Incoming compounds will be tested in phenotypic assays and functional biochemical assays against E4C's priority viral encoded targets, (RNA-directed RNA polymerase; 3C-like proteinase; Papain-like proteinase; Guanine-N7 methyltransferase and 2'-O-methyltransferase). Attractive compounds may then be subject to Mechanism of Action, studies including structural biology assessment by X-ray and Cryo-EM.

The minimum requirements for providing physical compounds are:

- i) rational reason for selection;
- ii) a positive review by E4C medicinal chemists;
- iii) compounds have not already been analysed in E4C or reported assays;
- iv) physical material is available (10mM in 100% DMSO, 20 microliters volume).

Submitters should have access to material for follow up studies or medicinal chemistry resources for synthesis of additional material.

Full criteria and conditions are defined in the "Drug-Box" submission portal on the E4C website - www.exscalate4cov.eu.