Target-based drug discovery and design



Leads



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Key Objectives of Work Package 2

To support critical protein and enzyme needs of the consortium by performing

- Gene expression and protein purification
- Target-based in silico virtual screening
 - Support of WP1 results and hit-ID optimisation results
 - Structural studies of Spike proteins and replication enzymes
- Create a protein/enzyme toolbox with enzyme assays in HTS screenable format (made available inside and outside the consortium

CONNECTIONS

with other work packages

Work package 1

Functional testing of emerging compounds from phenotypic screening of WP1

Work package 3

Supporting many WP3 partners with MOA determination in many targets plus targetbased screening for HIT-ID and HIT explosion

Collaborative development of Mpro and nsp14 inhibitors

Supporting synthesis of nucleoside analogues for the preparation of triphosphate derivatives tested within WP2



45

analysed

Mpro mutants 100+ antiviral Crystal structures peptides tested determined

Expression plasmids made available to CARE partners covering almost all the high priority drug targets

200-

45

Novel nsp14 inhibitors tested in antiviral assays

Partner compounds analysed for inhibitory activity inhibitory activity against SARS-CoV-2 PLpro

Partner compounds analysed for against SARS-CoV-2 Mpro

BREAKTHROUGH moments

2021

Completed virtual screening of CoV enzymes and structural proteins across multiple targets and partners

2021

Structure based drug design of key CoV enzymes for five targets

2022

Comprehensive study of nirmatrelvir and 13b-K resistance mutations in Mpro and resistance mutations induced by nsp14 inhibitors

2024

Development of SARS-CoV-2 Spike targeting cyclic peptide that inhibits all variants

2024

Profiling in antiviral **experiments** of drug combinations that include nsp14-targeting compounds

DELIVERABLES

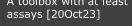


Deliverable D2.2 HTS assay for the RTC under

a 384-well plate format [31May21]



Deliverable 2.4 A toolbox with at least 8





Deliverable D2.3 Crystal or cryo-EM structures of the nsp14 and Spike protein [due 31Mar25]

Deliverable 2.5 A set of emergency/ additional molecules

[12Feb24]

Partner Organisations































