

## IMI2 Project ID 101005077

### CARE - Corona Accelerated R&D in Europe

#### WP3 – WP Hits to leads

# D3.1 A streamlined and efficient drug discovery testing cascade for CoVs

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### Document History

Version	Date	Description
V3.1	22 JUN 2021	A streamlined and efficient drug discovery testing cascade for target based and phenotypic approaches.

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## Abstract

In order to deliver broad-spectrum Coronavirus (CoV) antivirals, efficient and streamlined drug development cascades have been put in place for different approaches: target based and phenotypic approach. Consortium members of WP3-“Hits to leads” have closely collaborated with WP1-“Anti-coronavirus drug discovery in phenotypic virus-cell-based assays” and WP2-“Target-based drug discovery and design” to identify the critical assays necessary to identify and validate CoV antivirals. Using the medicinal chemistry and drug development expertise from the WP3 partners, a detailed cascade for hit to lead and lead optimization has been outlined including ADME/PK, *in vivo* proof of concept and early toxicology studies following the advice of WP6. This report shows two general drug development cascades: one for target based and one for phenotypic approaches.

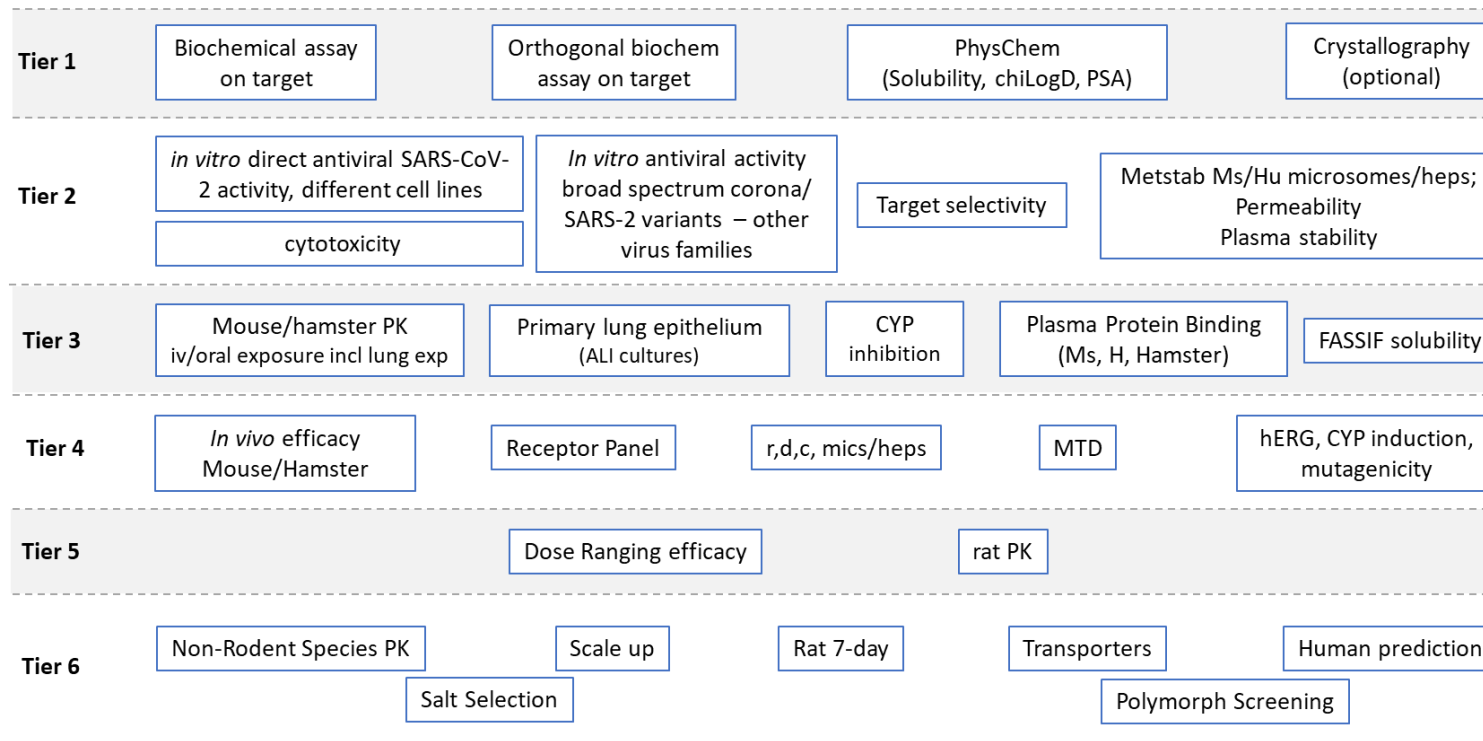
## Results

The drug development cascades depicted in Figures 1 and 2 are general cascades that can be applied to specific targets/phenotypic screens by inserting the target/phenotypic related assays in Tiers 1 and 2. Further steps in hit to lead and lead optimization campaigns follow a similar cascade. The advantage of creating general drug development cascades is that these cascades can be used as a template for newly identified targets and new phenotypic screens. This is convenient as the identification of new starting points to be taken up in the hit to lead campaigns is still ongoing at this stage.

## Conclusion

WP3 has outlined detailed drug development cascades which support the progression of active compounds into hit to lead and lead optimization programs. These flow charts have been established in close collaboration with WP1, WP2 and WP6-“From lead to pre-clinical candidate and proof of concept in animal models.” The general character of these cascades allows them to be applied on a range of interesting targets and phenotypic approaches used to identify broad spectrum CoVs antivirals.

Figure 1: Target based approaches  
A streamlined and efficient drug discovery testing cascade for CoVs – H2L/LO



**Figure 2: Phenotypic approaches**  
**A streamlined and efficient drug discovery testing cascade for CoVs – H2L/LO**

