

TARGETING THE DIFFERENT BINDING SITES ON SARS-CoV-2 WITH SELF-ASSEMBLING β -CYCLODEXTRINS

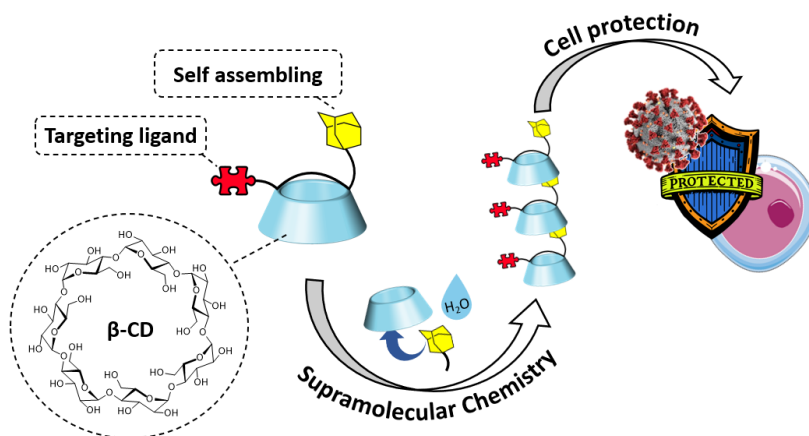
Pedro J. Hernando^a, Laora Boulo^a, Mickaël Ménand^a, Elisa Teyssou^b, Vincent Calvez^b,
Matthieu Sollogoub^a

^a Institute Parisien de Chimie Moléculaire, Laboratoire de Chimie Organique, Sorbonne
Université, Paris, France

pedro.hernando_callejo@sorbonne-universite.fr

^b Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Paris, France

Despite the awareness risen by the global pandemic caused by SARS-CoV-2, there is still a lack of over-the-counter tools to prevent the transmission of this and other respiratory viruses. To fight the infection caused by SARS-CoV-2, the main approach is to target its spike protein, which serves as a point of attachment to the host cells through two binding domains: the glycan- and the receptor-binding domain (GBD and RBD, respectively). Literature has shown examples of both GBD- and RBD-targeting inhibitors to prevent the infection by SARS-CoV-2, taking advantage of their affinity for different carbohydrates [1,2] or peptides [3]. In our laboratory, we have synthesised a system based on β -cyclodextrins decorated with an adamantane unit to promote a thermodynamically favoured self-assembly in water [4]. Now, we have designed and synthesised a library of ligands targeting both the GBD and RBD of SARS-CoV-2, which provides specificity to the scaffold to protect Vero E6 cells against viral infection. This research has provided encouraging results on the development of antiviral therapies against SARS-CoV-2 targeting either or both of its binding domains, informing a toolset of self-assembling cyclodextrins with potential to inhibit the infection not only by SARS-CoV-2, but also by other respiratory viruses.



Acknowledgements: this work was supported by the Marie Skłodowska-Curie Actions (MSCA), as part of the Horizon 2020 programme funded by the EU Commission (Grant Agreement 101149136 – CD-Resvir). The authors thank the Sorbonne University and CNRS for the previous and current support to the project.

References:

1. S. J. L. Petitjean, *et al.*, *Nat. Commun.* **2022**, *13*, 2564.
2. S. E. Guimond, *et al.*, *ACS Cent. Sci.* **2022**, *8*, 527-545.
3. P. Karoyan, *et al.*, *Commun. Biol.* **2021**, *4*, 197.
4. D. N. Tran, *et al.*, *Org. Chem. Front.* **2014**, *1*, 703-706.