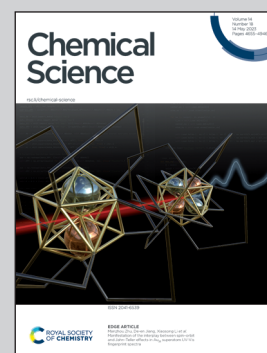


Showcasing research from Professor Yechun Xu's laboratory, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, China.

Unraveling the catalytic mechanism of SARS-CoV-2 papain-like protease with allosteric modulation of C270 mutation using multiscale computational approaches

We present a comprehensive picture of SARS-CoV-2 PL<sup>pro</sup> catalysed proteolysis with a mechanism distinguishable from that of 3CL<sup>pro</sup>, a well-characterized cysteine protease of coronavirus. Additionally, a C270R mutation is revealed to impair the catalytic function of H272 and reduce the PL<sup>pro</sup>-substrate binding by altering the structural dynamics of the BL2 loop, ultimately showing an inhibitory effect on PL<sup>pro</sup>. The present study, therefore, provides clues for understanding the allosteric modulation of C270 modification on the proteolytic activity, which is crucial to the follow-up inhibitor design and development.

As featured in:



See Qiang Shao, Yechun Xu *et al.*, *Chem. Sci.*, 2023, **14**, 4681.