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Structural basis of coronavirus E protein interactions with human PALS1 PDZ domain

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SARS-CoV-2 infection leads to coronavirus disease 2019 (COVID-19), which is associated with severe and life-threatening pneumonia and respiratory failure. However, the molecular basis of these symptoms remains unclear. SARS-CoV-1 E protein interferes with control of cell polarity and cell-cell junction integrity in human epithelial cells by binding to the PALS1 PDZ domain, a key component of the Crumbs polarity complex. We show that C-terminal PDZ binding motifs of SARS-CoV-1 and SARS-CoV-2 E proteins bind the PALS1 PDZ domain with 29.6 and 22.8 μM affinity, whereas the related sequence from MERS-CoV did not bind. We then determined crystal structures of PALS1 PDZ domain bound to both SARS-CoV-1 and SARS-CoV-2 E protein PDZ binding motifs. Our findings establish the structural basis for SARS-CoV-1/2 mediated subversion of Crumbs polarity signalling and serve as a platform for the development of small molecule inhibitors to suppress SARS-CoV-1/2 mediated disruption of polarity signalling in epithelial cells.

Level of Expertise

Student

Presenter Gender

Woman

Pronouns

Which facility did you use for your research

Australian Synchrotron

Students Only - Are you interested in AINSE student funding

Yes

Do you wish to take part in the Student Poster Slam

Yes

Condition of submission

Yes

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