ID der Kurzfassung : **136**

Fragment-based drug discovery against the Influenza virus nucleoprotein

Inhalt

The influenza A virus nucleoprotein (NP) is an essential and highly conserved component of the viral ribonucleoprotein (vRNP) complex, where it mediates viral RNA encapsidation and coordinates multiple steps of the viral replication cycle. Despite its essential role, NP remains unexplored as a therapeutic target.

To identify chemical starting points for structure-based inhibitor design, we performed a crystallographic fragment screen using the XChem platform at Diamond Light Source. A library of 690 fragments was screened against the monomeric NP mutant, and diffraction datasets were analysed using the PanDDA2 pipeline. We identified 53 fragment hits occupying 12 distinct binding sites on NP, demonstrating that the protein contains multiple ligandable pockets. The most prominent site corresponded to the NP oligomerization interface, with 21 fragments binding within the tail-loop pocket that mediates NP-NP interactions during vRNP assembly. Several fragments clustered around residue E339, a residue previously shown to be critical for NP oligomerization, supporting the functional relevance of this site.

Current efforts are directed towards biophysical validation of the identified fragment hits and their optimisation using structure-guided medicinal chemistry. Overall, this ongoing work represents a significant step toward the development of inhibitors that disrupt
viral ribonucleoprotein assembly.

Keywords

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Professional status of the speaker

Postdoc

Junior scientist status

Yes, I am a junior scientist.

Track Klassifizierung: Antivirals and Vaccines

Typ des Beitrags: Oral presentation

Kommentare:

If the abstract is not selected for an oral presentation, I would appreciate consideration for a poster presentation.