**Poster**

# Targeting 3Cpro: A Promising Approach for Inhibiting Enterovirus D68

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Enterovirus D68 (EV-D68), a member of the *Picornaviridae* family, has emerged as a significant pathogen associated with severe respiratory illnesses and neurological complications, particularly in children. The virus has been linked to acute flaccid myelitis (AFM), affecting the gray matter of the spinal cord, and leading to polio-like neurological symptoms such as muscle weakness. The viral 3C protease (3Cpro) plays a critical role in the viral life cycle by processing the viral polyprotein into functional units [1, 2], making it an attractive target for antiviral drug development. Both covalent and non-covalent inhibitors have shown potential in preclinical studies. Ongoing research aims to overcome challenges related to resistance, specificity, and drug delivery, with the ultimate goal of developing effective treatments for enterovirus infections [3]. In this study, we present the high-resolution crystal structure of the EV-D68 3Cpro in a complex with a novel inhibitor, RHCDS1a.

The complex was crystallized and the structure was determined using X-ray diffraction to a resolution of 1.81 Å. The inhibitor RHCDS1a covalently binds to the active site of 3Cpro, forming a stable complex that provides insights into the inhibition mechanism. Structural analysis reveals that RHCDS1a interacts with key residues in the catalytic triad and the substrate-binding pocket, leading to the inhibition of protease activity. These interactions highlight potential avenues for the design of more potent and selective 3Cpro inhibitors.

Our findings provide a structural basis for the development of RHCDS1a as a therapeutic candidate against EV-D68. The detailed understanding of the inhibitor binding mode offers valuable information for the rational design of next-generation antivirals targeting 3Cpro. This work underscores the importance of structure-based drug design in combating emerging viral pathogens.

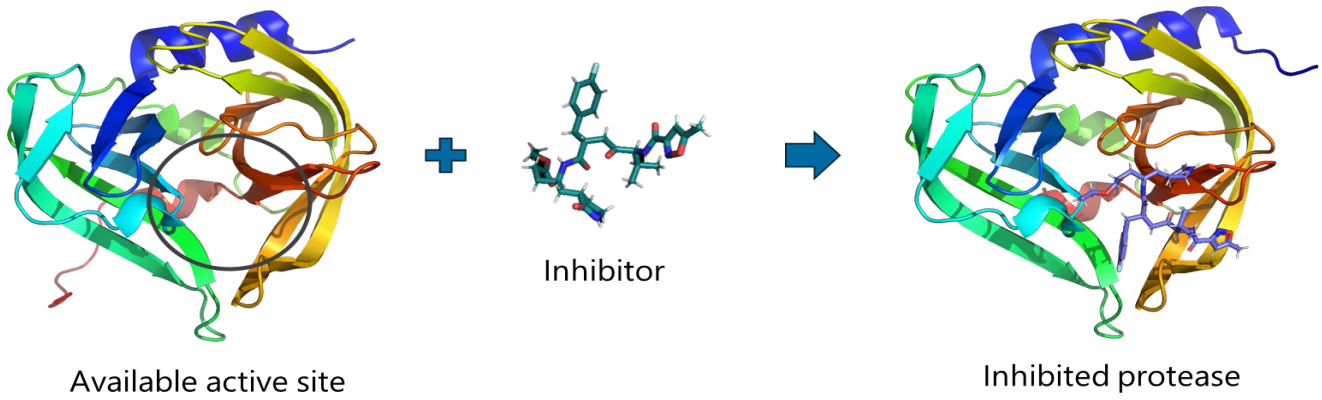


**Figure 1**. Structural visualization of inhibitor binding to the active site of enterovirus D68 3C protease (3Cpro). The image depicts the binding interaction between the enterovirus D68 3C protease (3Cpro) and the inhibitor RHCDS1a.

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