The Suramin Derivative NF449 Interacts with The 5-Fold Vertex of The Enterovirus 71 Capsid to Prevent Virus Attachment to PSGL-1 and Heparan Sulfate

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Enterovirus 71 (EV71) is epidemic in the Asia-Pacific region, and has been responsible for thousands of cases of fatal neurological diseases in young children. There are no specific therapies available. We previously identified NF449, a sulfated compound derived from the antiparasitic drug suramin, as a compound with anti-EV71 activity, although its mechanism of action was uncertain.

We found that NF449 and related molecules prevent virus attachment both to PSGL-1, a receptor molecule important for virus interaction with white blood cells, and to heparan sulfate, a receptor that may be important for virus interaction with a variety of other cell types. In contrast, NF449 had no effect on virus attachment to another receptor, SCARB2. Mutation of VP1-244 resulted in resistance to NF449, suggesting that this residue is involved in NF449 interaction with the virus capsid. Consistent with this idea, NF449 prevented virus interaction with monoclonal antibody MA28-7, which specifically recognizes an epitope overlapping VP1-244 at the five-fold vertex.

PSGL-1 and heparan sulfate, but not SCARB2, are both sulfated molecules. Based on these observations we propose that NF449 competes with sulfated receptor molecules for a binding site at the five-fold vertex of the EV71 capsid. Our work provides information that may facilitate development of improved antiviral compounds that block the attachment of EV71 to cellular receptors.