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The Potential Role of ATN-161 as an Integrin α5β1 Inhibitor in Preventing Common Viral Infections

Integrins are transmembrane proteins which mediate many cellular signaling processes such as immunological function, extracellular matrix composition, apoptosis, and cell adhesion. In addition to these features, integrins have been implicated in viral infection. Integrin alpha5beta1, which has an arginine-glycine-aspartic acid (RGD) binding motif, has been shown to play a role in the pathogenesis of many viruses including porcine hemagglutinating encephalomyelitis virus (PHEV), human immunodeficiency virus (HIV-1), and severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2). However, a concise review of the role of integrin alpha5beta1 with regards to viruses and its potential as an antiviral therapeutic, especially with regards to SARS-CoV-2, has not been conducted. Here we review viral pathogensis in regards to ATN-161, a pentapeptide noncompetitive inhibitor of the alpha5beta1 integrin complex, which may represent a novel therapeutic aimed at preventing or ameliorating viral progression. Our results in dicate that integrin alpha5beta1 mediation of cellular entry or attachment is found in a total of seven different viruses, to include SARS-CoV-2. Lastly, we found evidence that alpha5beta1 integrin expression increases upon viral infection and decreases upon treatment with ATN-161 in select models, with treatment of PHEV and SARS-CoV-2 showing decreased viral load and histological improvement. Altogether our review highlights the involvment of alpha5beta1 in viral infection, demonstrates the ability of ATN-161 to mitigate infection, and reviews ATN-161 as a targeted therapeutic against SARS-CoV-2 infection.