Assessing customized multivalent chemokine-binding peptide treatment in a murine model of coxsackievirus B3 myocarditis

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Abstract

Myocarditis, an inflammatory disease of the heart muscle, is often triggered by viral infections. This inflammation, which can lead to severe cardiac dysfunction and adverse outcomes, is mediated by various CC and CXC chemokines that interact with receptors in a "one-to-many" fashion. Ticks have evolved chemokine-binding salivary proteins known as Evasins, which efficiently suppress inflammation. This study explores a tailored Evasin-derived CC chemokine-targeting strategy using a 17-mer synthetic dimeric peptide, BK1.3. This peptide inhibits the inflammatory chemokines CCL2, CCL3, CCL7, and CCL8 in murine Coxsackievirus B3 (CVB3) infection, a viral trigger of myocarditis. Administered at a dose of 5 mg/kg twice daily, BK1.3 effectively maintains virus control without exacerbating CVB3-induced morbidity markers, such as hemodynamic compromise, multiorgan failure with hepatitis and pancreatitis, hypothermia, hypoglycemia, and weight loss. Metabolic profiling combined with proteomics reveals preserved reprogramming of lipid storage and gluconeogenesis capacity in the liver, alongside sustained energy production in the injured heart muscle. In survivors of acute CVB3 infection exhibiting manifestations of the subacute phase, BK1.3 enhances virus control, reduces myeloid cell infiltration in the heart and liver, improves markers of liver injury, and alleviates cardiac dysfunction, as evidenced by echocardiographic global longitudinal strain analysis. These findings affirm the safety profile of BK1.3 peptide therapeutics in a preclinical mouse model of acute CVB3 infection and emphasize its potential for therapeutic advancement in addressing virus-induced inflammation in the heart.