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IGF2R Specific Peptide Ligands for Liver Fibrosis

UMKC inventors have identified an IGF2R specific peptide with high binding affinity and specificity that can be used for HSC targeted delivery for liver fibrosis therapy.

Need:

Liver Fibrosis is caused by chronic diseases such as hepatitis, liver cirrhosis caused by alcohol abuse and nonalcoholic steatohepatitis or fatty liver disease. The prevalence of liver fibrosis is ever-increasing and effects approximately 30 million people in the United States alone. Over 11% of people with liver fibrosis will progress to the more severe condition of cirrhosis, in which the liver begins to decompensate and lose overall function. The fibrotic stage is considered a key inflection point where baseline liver function can still be salvaged with adequate treatment. However, no approved treatment exists that ameliorates or reverses the course of fibrosis.

Invention Details:

Liver Fibrosis is characterized by the excessive accumulation of extracellular matrix (ECM) in the liver. Hepatic stellate cells (HSCs) are responsible for the excessive production of ECM in a fibrotic liver. A protein found on the surface of HSCs is insulin-like growth factor 2 receptor (IGFR2), which is upregulated in HSCs during liver fibrogenesis. One of the major functions of IGFR2 is to internalize extracellular ligands; therefore IGFR2 could be used as a delivery system for small molecules into HSCs.

The proposed invention is an IGF2R-binding peptide identified by protein-based and whole-cell-based phage display with high binding affinity and target specificity. The proposed peptide (a.a. sequence - VHWDFRQWWQPS) exhibits high binding affinity and specificity toward IGF2R. The peptide acts via two distinct mechanisms of action, 1) it acts as a carrier to deliver conjugated small molecule agents to HSCs; and 2) it acts as a targeting ligand for nanoparticles encapsulating antifibrotic agents.

Advantages:

Conventional methods for delivering drugs to HSCs have limitations, including inefficient uptake. IGF2R is ubiquitously expressed on HSCs and facilitates entry of extracellular molecules at a relatively rapid rate. Identifying peptide ligands that target IGF2R and bind with high affinity is imperative to the development of a HSC-targeted drug delivery system. The identification of the IGF2R-specific peptide can be used to develop targeted therapeutics or imaging agents for liver fibrosis.

Suggested Uses:

To treat liver fibrosis as well as other diseases in which IGF2R plays an important role.

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