

Carbohydrate Mimetics for Macrophage Activation

ABSTRACT

Purpose of the Study: To identify peptide mimetics of the sugar that interacts with the macrophage receptor leading to the activation of macrophages.

Project Background: Vitamin D-binding protein is a serum glycoprotein that has macrophage activating activity when its oligosaccharide group is processed. The macrophage-activating domain contains an O-glycosylated threonine composed primarily of galactose (Gal), sialic acid (SA), and N-acetylgalctosamine (GalNAc). The process of immune system activation requires selective removal of Gal and SA by B cell and T cell glycosidases. Consequently, the macrophage activating form contains a single GalNAc and is one of the most potent stimulators of phagocytic activity of macrophages. Unfortunately, viruses and cancers produce glycosidases that cleave the remaining GalNAc, thereby inactivating the protein.

Goals of the Project:

- Obtain sequences from Phage Display libraries that mimic GalNAc and have therapeutic potential through activation of macrophages
- Construct an algorithm to search for consensus in 'unrelated' sequences that are selected during panning of a phage library
- Identify the molecular basis of functional peptide mimicry for rational de-novo design.