S.A.R. of world's smallest carbohydrate-binding protein Odoranolectin using Liquid Glycan Arrays (LiGA)

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Abstract

Glycans are essential carbohydrates that play a role in cell recognition, immune responses, and disease progression. Changes in glycosylation, the process of adding glycans to proteins or lipids, are linked to diseases like cancer. In cancer, altered glycosylation helps tumour cells evade the immune system. Fucosylation is one such modification that supports cancer growth and immune escape, making it a promising target for therapies. Lectins are proteins that bind specific glycans, useful in identifying and separating glycans, especially in cancer biomarkers. However, most lectins have limitations in drug development because of their size, immunogenicity, and potential toxicity. Odorranalectin (Odo), a small, fucose-binding lectin-mimicking peptide (17 amino acid residues) derived from Odorrana grahami, exhibits high affinity toward tumour-associated glycans while maintaining low immunogenicity and potential for nasal drug delivery. Using the Liquid Glycan Array (LiGA) platform (which decodes glycan-binding profiles through DNA-barcoded glycan libraries), we present a structure-activity relationship (SAR) study of Odorranalectin. This approach evaluates Odo modifications, including C- and N-terminal alterations, linker types, and Odo from D-AA (mirror structure), for optimal glycan recognition. Our findings advance the understanding of Odo's glycan binding, offering insight into potential therapeutic applications.

Keywords: glycans; lectins; peptide; SAR; Lectin Glycan Array (LiGA).