Unique “fluorine-codes” for glycan binding proteins in a multi-site fluorinated LewisX library

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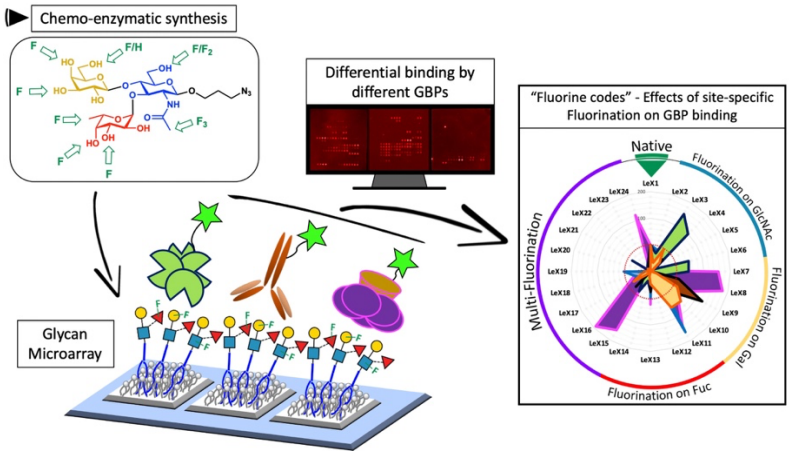
Glycans play many important biological roles, from cellular signalling to pathogen-host interactions. A glycan epitope can be recognized and shared by a diverse range of endogenous and exogenous glycan-binding proteins (GBPs) of humans and microbes. For example, the blood group-related LewisX (LeX) antigen was originally reported as a developmentally regulated embryonic antigen[1], but is also found in epithelia, blood cells and human milk, also on the surface of pathogens such as *Helicobacter pylori* where it is recognised by lectins of immune system and triggers immune responses[2]. Such “promiscuity” in glycan recognition raises the need for GBP-specific molecular probes that can target and intervene in specific glycan binding events.

Glycan fluorination offers great promise for introducing selectivity and distinction between proteins that recognise a particular glycan. With little change to overall glycan conformation, an OH to F replacement can have a range of attractive and repulsive effects on protein recognition[3]. Here we present a diversity-orientated chemo-enzymatic synthesis of a 150-member library of LeX trisaccharides with site-specific fluorination on each monosaccharide residue. A 24-member subset was converted to neoglycolipid probes[4] by a novel click-chemistry method for microarray screening studies with immune lectins, antibodies and bacterial toxins. Unique “fluorine-codes” have emerged for different LeX-binding proteins. The findings could potentially lead to designs of novel F-glycan-based diagnostic and therapeutic agents for bacterial infection.



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