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Dissecting Multivalent DC-SIGN/R-Glycan Interactions Using Polyvalent Glycan-Quantum Dots

Y. Guo, C. Sakonsinsiri, E. Poole, W. B. Turnbull, D. Zhou

School of Chemistry and Astbury Centre, University of Leeds, Leeds LS2 9JT, United Kingdom.

Multivalent protein-glycan interactions play a key role in viral/bacterial infections.¹ They initiate the pathogen-cell contact that ultimately leads to infection. Glycoconjugates can block such binding and the potency critically depends on their spatial match. A challenge here is lack of structural details of key cell surface multimeric lectins. We show quantum dot (QD)-capped with arrays of simple glycans are powerful probes here. First, we develop a highly efficient method to make polyvalent glycan-QDs. Then, we study their multivalent binding with the HIV/Ebola receptors, DC-SIGN/DC-SIGNR² via a FRET readout strategy for the 1st time.³ We find that the polyvalent glycan-QD not only enhances its DC-SIGN binding affinity by 4-6 orders of magnitude, but also affords an unprecedented >60 fold binding selectivity for DC-SIGN over DC-SIGNR,³ despite almost identical tetrameric structure. This is attributed to their different binding-site arrangements. The QDs potently inhibit a pseudo-Ebola virus infection of DC-SIGN expressing cells (low nM IC₅₀),³ suggesting an excellent potential as anti-viral agents.

Reference

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