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

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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-SIGNR[2] 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 IC_{50}),[3] suggesting an excellent potential as anti-viral agents.

Reference

1 Bhatia et al. J. Am. Chem. Soc. **2016**, 138, 8654.
2 Guo et al. Nat. Struct. Mol. Biol. **2004**, **11**, 591.
3 Guo et al. Angew. Chem. Int. Ed. **2016**, 55, 4738.