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# Neutron crystallographic analysis of protein-ligand hydrogen bonding patterns in galectin-3 guides drug design

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Galectin-3 is an important protein in molecular signalling events involving carbohydrate recognition, and an understanding of the hydrogen-bonding patterns in the carbohydrate binding site of its C-terminal domain (galectin-3C) is important for the development of potent new inhibitors. I will present neutron crystal structures of galectin-3C in three states: apo, in complex with the natural substrate lactose and with glycerol. These structures reveal the exquisite tailoring of the carbohydrate recognition site to recognise the hydrogen bonding patterns presented by galactose and glucose moieties. Comparison of the glycerol and lactose structures reveals the possible importance for molecular recognition of a hydrogen bond from arginine to the cyclic oxygen atom of galactose. The apo structure shows that, though water molecules occupy the positions of the most important oxygen atoms of the ligand [1], not all hydrogen bond directionality is preserved when the oxygen atoms are unconstrained by being "locked"in the ligand.
I will present some of the work required to achieve these structures, e.g. improvement in crystal size for perdeuterated galectin-3C by a crystal growth protocol involving feeding the crystallisation drops [2], which resulted in improved data quality and reduced data collection times. We collected five datasets at three different neutron sources from crystals of similar volume, which gives insights into the crystal volumes and times necessary for the same system at sources with different technologies and data collection strategies.
Finally, I will mention some ongoing work on the orientation of a crucial water molecule and its effect on the affinity of two very similar galectin-3C ligands.

**References**

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