Mucin Glycoprotein Microarray towards Glycan Ligand discovery for CBMs of Human Gut Microbiota

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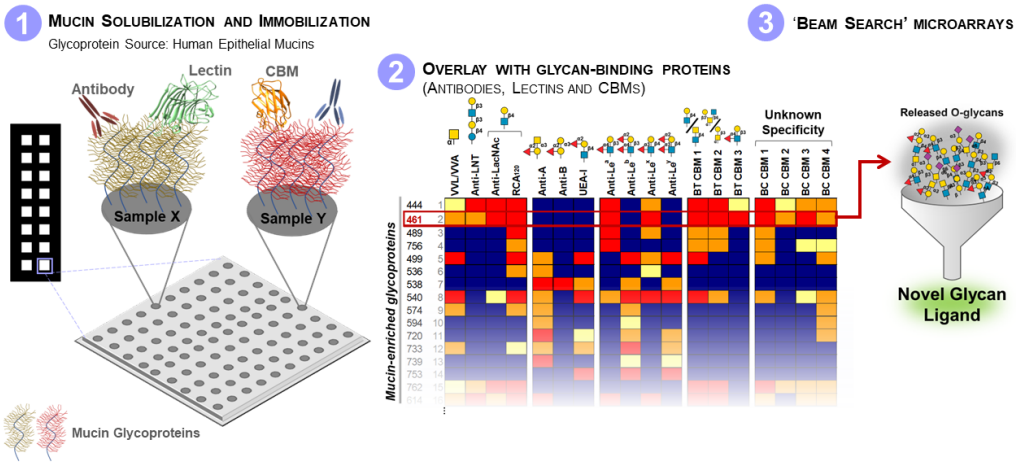
The mucus layer of intestinal epithelium contains extensively *O*-glycosylated proteins, mucins. How mucin O-glycans are differentially exploited by the microbiota and influence the crosstalk with the human host largely remains to be elucidated at the molecular level [1].

The commensal gut microbiota *Bacteroides caccae* is implicated in the digestion of the colonic mucus layer in low fibre diet conditions [2]. During growth on mucin-type glycans, *B. caccae* showed an increased expression of modular enzymes, comprising appended non-catalytic carbohydrate-binding modules (CBMs). The hypothesis is that these CBMs facilitate mucin foraging by the bacteria and thereby render the intestinal epithelium susceptible to pathogen infection, promoting states of dysbiosis [1, 2].

To identify glycan ligands targeted by the bacterial CBMs, we developed microarrays containing mucin-enriched glycoprotein samples that originated from diverse human epithelial cell types as found in the teratomatous tissues of ovarian cystadenomas. They present structurally diverse and complex O-glycans that are representative of the human O-glycome [3].

In initial screening analyses the CBMs showed differential binding to microarrays of various mucin-enriched cystadenoma samples. However, some CBMs did not show binding in our existing sequence-defined glycan microarrays suggesting the recognition of novel O-glycan ligands. Thus, these mucin glycoproteins are an important starting point for the development of mucin O-glycome 'Beam Search' microarrays [4] for discoveries of novel glycan ligands.



Mucin Glycoprotein Microarray Workflow for Glycan Ligand Discovery

Acknowledgements

2022.06104.PTDC, SFRH/BD/143494/2019, UIDP&UIDB/04378/2020, LA/P/0140/2020; HORIZON-WIDERA-2021-10107941 GLYCOTwinning; Wellcome Trust 218304/Z/19/Z.

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