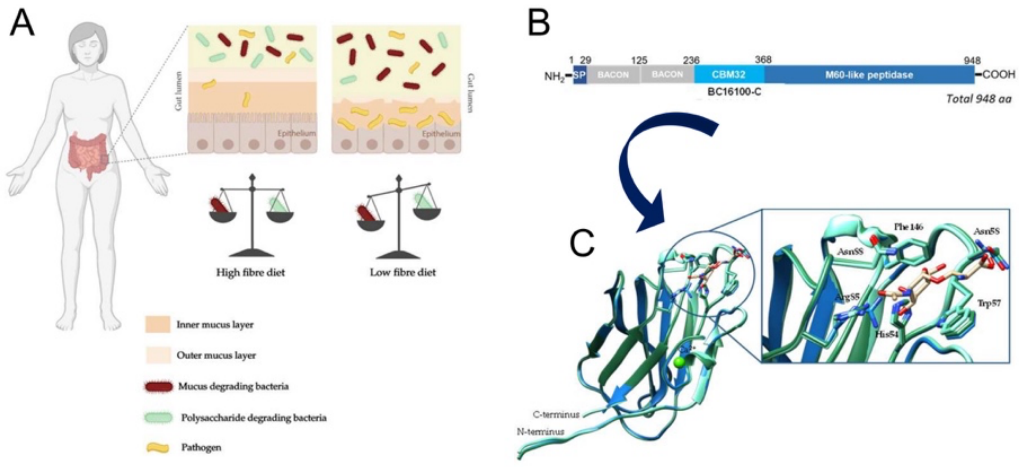
Molecular basis for mucin O-glycan recognition by human gut microbiota

Angelina S. PALMA [1,2,4] Viviana G. CORREIA [1,2], Raquel L. COSTA [1,2], Filipa TROVÃO [1,2], Benedita A. PINHEIRO [1,2], Alicia CANDEIAS [1,2], Sandra BEHREN [3], Antonio DI MAIO [4], Ulrika WESTERLIND [3], Ten FEIZI [4], Wengang CHAI [4], Yan LIU [4], Ana Luísa CARVALHO [1,2]

[1] UCIBIO Applied Molecular Biosciences Unit, Department of Chemistry/Department of Life Sciences, NOVA University Lisbon, Portugal, [2] Associate Laboratory i4HB, Institute for Health and Bioeconomy, School of Science and Technology, NOVA University Lisbon, Portugal, [3] Umeå University, Department of Chemistry, Sweden, [4] Glycosciences Laboratory, Department of Metabolism, Digestion and Reproduction, Imperial College London, UK

angelina.palma@fct.unl.pt

Mucins are extensively *O*-glycosylated proteins, present in the mucus layer of the intestinal epithelial cells [1]. How mucin O-glycans are differentially exploited by intestinal commensal or pathogenic bacteria and influence the crosstalk with the human host largely remains to be elucidated at the molecular level. *Bacteroides thetaiotaomicron* and *B. caccae* are prominent commensal bacteria with increased activity on mucin *O*-glycans in conditions of a low-fiber diet and are implicated in susceptibility to infection [2,3]. In this communication, we will report the characterization of newly identified proteins (glycan-binding proteins and enzymes) from these bacteria, which are encoded by sets of co-regulated genes termed polysaccharide utilization loci systems (PULs) that target a specific glycan structure [2]. We combined i) bioinformatic analysis of bacterial genomes and high-throughput production of putative glycan binding proteins with ii) ligand discovery using microarrays of human mucin-type glycoproteins, glycopeptides and sequence-defined glycans [4-7], and iii) structural characterization of protein-glycan complexes by X-ray crystallography [8]. We will highlight the molecular basis for the unique specificities of proteins targeting mucin *O*-GalNAc-Thr/Ser cores and fucosylated Lewis A structures. Uncovering the molecular determinants for mucin O-glycan recognition by the bacterial proteins can be used to understand the role of commensal bacteria in gut health and to design new therapeutic and diagnostic strategies.



A) Impact of diet on gut microbiota; B) Molecular architecture of B. caccae PUL-53; C) Ribbon representation of BC16100-C in complex with GalNAcα-Ser.

Bibliographic references:

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