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Glycan dependent *Helicobacter* spp. and *Streptococcus oralis* binding to mucins in the gastric and oral mucosal niche

Akademisk avhandling

Som för avläggande av medicin doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hörsalen på Geovetarcentrum, Guldhedsgatan 5C, den 16 April, klockan 9:00

av Gurdeep Chahal

Fakultetsopponent:

Professor Karen A Krogfelt, , PhD

Institut for Naturvidenskab og Miljo, Roskilde universitet, Roskilde Danmark

Avhandlingen baseras på följande delarbeten

I. **A complex connection between the diversity of human gastric mucin *O*-glycans *Helicobacter pylori* binding, *Helicobacter* infection and fucosylation.** **Gurdeep Chahal**, Médea Padra, Mattias Erhardsson, Chunsheng Jin, Vignesh Venkatakrishnan, János Tamás Padra, Helen Stenbäck, Anders Thorell, Niclas G Karlsson, Sara K Lindén. Under Review for publication in MCP, 2021.

II. **Effects of *Helicobacter* spp. infection on the pig and human gastric mucin *O*-glycome and mucin-*Helicobacter pylori* interactions.** **Gurdeep Chahal**, Médea Padra, Mattias Erhardsson, A Thorell, NG Karlsson, Sara K Linden. Manuscript.

III. ***Helicobacter suis* infection alters glycosylation and decreases the pathogen growth inhibiting effect and binding avidity of gastric mucins.**
Médea Padra, Barbara Adamczyk, Bram Flahou, Mattias Erhardsson, **Gurdeep Chahal**, Annemieke Smet, Chunsheng Jin, Anders Thorell, Richard Ducatelle, Freddy Haesebrouck, Niclas G. Karlsson, Sara K. Lindén. *Mucosal Immunology* **12**, 784–794 (2019)

IV. **Binding of *Streptococcus oralis* to human salivary mucins is inhibited by Lewis b and sialyl-Lewis x.**
Gurdeep Chahal, John Benktander, Meztlli O. Gaytán, Medea Padra, Samantha J. King, Sara K. Lindén. Manuscript.

SAHLGRENSKA AKADEMIN
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Glycan dependent *Helicobacter* spp. and *Streptococcus oralis* binding to mucins in the gastric and oral mucosal niche

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Abstract

Helicobacter pylori infects the stomach of half of the world's population, while *Helicobacter suis* colonizes pigs and is the most common non-*H. pylori Helicobacter* species that also infects human stomach. Infection with *Helicobacter* spp. is associated with chronic gastritis, peptic ulcer disease, and gastric cancer. *Streptococcus oralis* colonizes human oral cavity and can cause infective endocarditis (IE). First barrier pathogens encounter is the mucus layer constituted by highly glycosylated glycoproteins, the mucins. Mucin glycans provide an extensive surface of interaction for bacteria. Here, we show the interactions of *Helicobacter* spp. and *S. oralis* with glycans in the gastric and oral mucosal niche. In **paper I**, the glycans from *H. pylori* infected and non-infected human stomachs were characterized by mass spectrometry. An enormous diversity of glycosylation exists in the human stomach. Infection with *Helicobacter* spp. is associated with large inter- and intra-individual diversity. The differences in glycosylation between mucins from infected and non-infected individuals are reflected by differences in binding of *H. pylori* to the mucins. In **paper II**, the binding of different *H. pylori* strains J99, P12, 26695 and G27 was analyzed. We show that these strains differ in their binding preferences and that mucins from infected or non-infected human stomachs affect the adhesion of different strains differently. Further, we show that infection, rather than inflammation, determines these effects. In **paper III**, we showed that experimental *H. suis* infection alters the composition of mucins and their glycosylation in a manner that reduces the amount of *H. suis* binding glycan structures, decreases *H. suis* binding ability, and changes mucin phenotype towards more *Helicobacter* spp. growth promoting. Thus, *Helicobacter* spp. infections impair the mucus barrier to create a stable niche in the stomach.

In **paper IV**, the carbohydrate binding of IE isolates of *S. oralis* subspecies was investigated. Mucins were isolated from the saliva from blood group A and B positive individuals. We show that *S. oralis* adhesion occurs to salivary mucins and the binding differs between strains. *S. oralis* binding differs between mucins and individuals. Further, we show that *S. oralis* subsp. *oralis* binding to oral mucins is mediated by a cell wall anchored surface protein(s) and Leb, SLex and LNT like glycans present on the mucins.

We demonstrate that mucin glycans are highly diverse and differ between individuals and with infection status. The glycan repertoire governs the ability of the mucins to bind to pathogens. *Helicobacter* spp. infection increases the diversity of glycosylation in the host and changes the host mucin composition. Understanding the adhesion mechanisms of *H. pylori, H. suis* and *S. oralis* could help develop preventive strategies against these pathogens.

Keywords: *Helicobacter*, diversity, glycosylation, adhesion, *Streptococcus*

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