

Session: Host Responses to Infection.

"Evolution of Host-Pathosymbiont Interaction within the *Neisseria* genus"

Alex Rivera-Millot, Laxmi Sharma, Garima Ayachit, Francisco Pulido, Frédéric J. Veyrier

INRS-Centre Armand-Frappier Santé Biotechnologie, Bacterial Symbionts Evolution, Laval, QC, H7V 1B7, Canada

Background: The respiratory tract is a hot spot of host-bacteria interactions. Bacteria from the *Neisseria* genus are, for the majority, commensals of the mammalian upper respiratory tract or oral cavity. Despite their close genetic proximity to commensals, two *Neisseria* have acquired significant pathogenic potential. *Neisseria meningitidis* colonizes the nasopharynx but in some cases may trigger invasive infections such as septicemia and meningitis. *Neisseria gonorrhoeae* has adapted to a new environmental niche to infect the genital tract. These bacteria, despite being closely related, show different type of interactions with their human host. The aim of the project is to characterize the differences in host interactions between *N. meningitis*, *N. gonorrhoeae* and other nasopharyngeal commensals and to correlate them with the genomic and transcriptomic peculiarities of the studied bacteria.

Methodology: Dual RNA sequencing was performed on a model of human epithelial cell infection to study the differences in host-cell infection response. We used 5 strains of *N. meningitidis*, 5 strains of *N. gonorrhoeae* and 5 different nasopharyngeal commensal species. We also confirmed some of the results using immune cells that report on inflammatory activity. Bacterial transcriptomes across species were also studied and compared using innovative and specific bioinformatics tools developed in the laboratory.

Results: The results of these studies show a similar response to colonization between commensals and *N. gonorrhoeae* but not *N. meningitidis*. *N. meningitidis* strains appear to induce a very low inflammatory response, unlike the other two groups. These results were reproduced by measuring the inflammatory response of human monocyte cells. On the other side, analysis of transcriptomic differences between the three different groups of bacteria, *in vitro* or in contact with host cells, and genomics differences identified different proteins likely involved in these distinct interactions.

Discussion: Our analyses suggest that the interactions of the three groups of bacteria with their host seem different. This multifactorial analysis approach allows us to go beyond studying the "presence/absence" of virulence factors and identify differences in the expression of common bacterial genes and the impact of these different factors on host cells interactions.