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In vitro spatial and temporal dynamics of Gonococcus interaction with host cells: time resolving dual RNA-seq

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Background

Neisseria gonorrhoeae is an exclusive human pathogen having the human genital tract as the initial site of infection, but it can also colonize the ocular, nasopharyngeal, and anal mucosa. Gonococcus has evolved sophisticated and non-redundant mechanisms to successfully invade the human host, persist within tissues, and evade the immune system.

Aim/Methods

To better understand gonococcal pathogenesis, we examined gonococcal interaction with three cell models representative of the leading anatomical site of infection: urethra, endocervix, and oropharynx. To monitor bacterial adhesion, internalization, proliferation, and persistence, we developed an assay based on a high content screening (HCS) fluorescence microscope platform. Moreover, we monitored the dynamic interplay between infecting bacteria and the human host by dual RNA-seq approach.

Results

The gonococcal interaction/internalization with the different cells models is cell type-dependent: the infection selectively affects only a sub-populatiton of target cells derived from oropharynx and urethra, while it is widespread in cells derived from the endocervix. Upon 15 minutes of infection, the host cells undergo cytoskeletal rearrangements and/or start to mount a pro-inflammatory response which becomes more evident after 2 hours of infection. Several chemokines such us CXCL1, CXCL3, and CXCL20 were upregulated, indicating an active recruitment of neutrophils to the site of infection. Many of the transcriptional changes of the pathogen occur in the first minutes of infection; bacteria upregulate the expression of adhesins and a series of membrane transporters, such as the TonB-dependent transporter TdfJ, to overcome to the nutritional immunity of the host. We also identified several hypothetical proteins co-expressed in the three cell models with unknown functions.

Conclusions

Our work describes specific niches of gonococcal infection, by the use of relevant in vitro models that mimic the different anatomical sites encountered by the pathogen during disease. We highlighted the phenotypical and transcriptional changes during host-pathogen interaction and the differential dynamics in the three cell types. We are now extending the investigation to immune cells to understand how gonococcus exploit them as a protected niche during infection.

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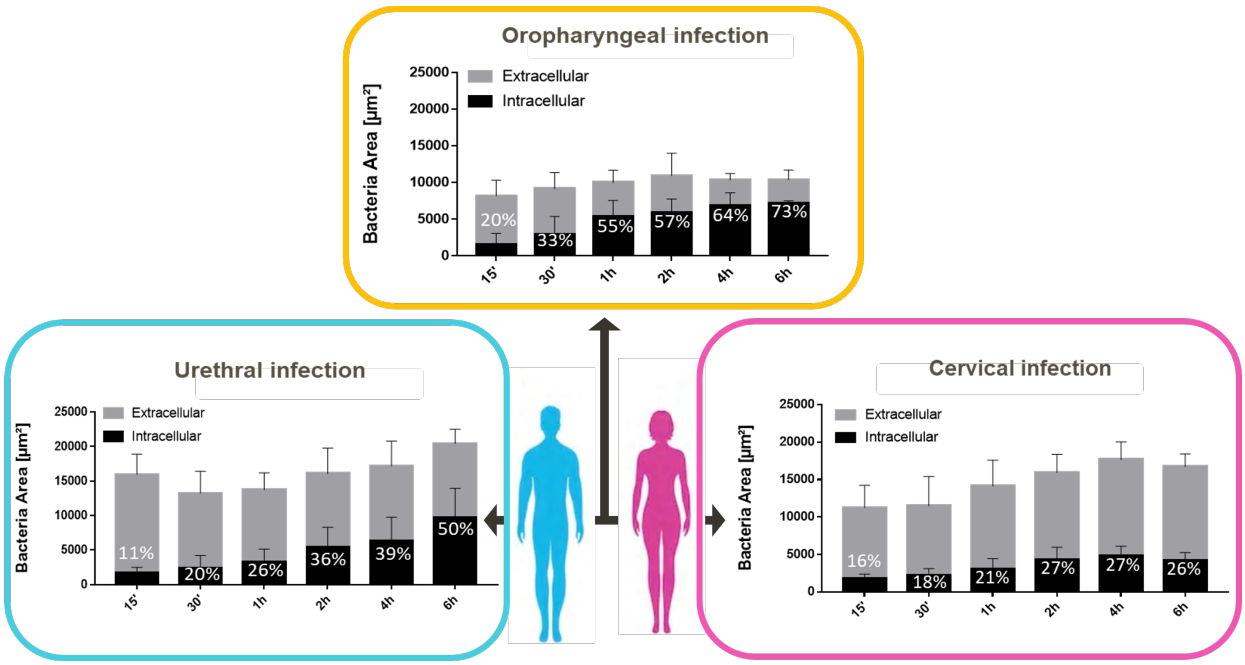
Supplemental Document Upload

Characterization of the kinetics of adhesion of Neisseria Gonorrhoeae on representative cell models



Host transcriptomics overview in the three cell models upon 120 minutes of infection by N. gonorrhoeae.