

Title: Molecular and Phenotypic Characters of Disseminated Gonococcal Isolates from Canada

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Abstract: *Neisseria gonorrhoeae* is notorious for causing STI-gonorrhea, which is a major concern due to its escalating rates of infection worldwide. Occasionally, gonococci enter circulation and cause non-STI disseminated gonococcal infections (DGI) that can present as migrating arthritis, endocarditis, dermatitis and eye infections. Unfortunately, DGI cases rise as gonorrhea cases increase. In addition to reports from Michigan and California, Canadian provinces-Ontario and Manitoba recently had a DGI outbreak (2014-2021), with some incidences being reported from Alberta and Saskatchewan as well. The mechanisms that drive gonococcal infectivity and adaptability remain unclear, so treating gonococcal or preventing the infection is still a challenge. Since the number of isolates have increased remarkably over past decade and there seems to be some divergence, it is imperative to expand our focus at genomic, phenotypic and metabolomic characterization that drive gonococcal infections.

We have initiated detailed comparative molecular and phenotypic analysis of the three prototype strains: MS11, FA19 and FA1090. Similar analyses are being done to include some Ontario isolates and WHO reference strains. Invasive (DGI) strains follow the canonical mechanism of serum resistance by recruiting Factor H or C4Bp. We compared the recruitment of complement factors by flow cytometry. Interestingly, we observed some non-invasive strains that exhibit higher serum resistance and similar levels of Factor H and C4Bp recruitment. Also, most of the recent isolates (2016 and after) tend to aggregate and not all serum sensitive strains develop resistance even after inducing sialylation with CMP-NANA. Hence, it is hard to unravel what are the specific adaptations required during initiation and progression of dissemination. There might also be additional untapped molecular features or metabolic modulations that allow these gonococci to survive in more invasive and unique host environments. This study is initiation of a search beyond! We are directing our efforts towards a more wholistic ‘-omics’ approach to identify conserved and unique gonococcal features that can help us define the invasive vs non-invasive gonococci.