contains polylactosamine repeats representing potential ligands for animal lectins called galectins, implicated in HIV pathogenesis.

Methods CPI-GC was isolated from T. vaginalis LPG by mild acid hydrolysis and C18-SepPak separation. Binding to galectin-1 and −3 (Gal-1 and −3) was determined by Biolayer Interferometry. Inflammation-related proteins and Gal-1 and 3 were measured by a multiplex immunoassay in supernatants from human cervical and vaginal epithelial cells infected with T. vaginalis or exposed to CPI-GC from different clinical isolates.

Results CPI-GC activated NF-κB and upregulated cFos, COX-2, IL-8, MIP-3α, IL-6, IL-1β and VEGF in a MEK1/2 dependent manner. In addition, IL-6, ICAM-1 and VEGF up-regulation was mediated by p38 while IL-8 and MIP-3α were ERK 1/2 mediated. CPI-GC from different clinical isolates varied in their ability to bind Gal-1 and Gal-3, which were constitutively expressed by vaginal and cervical epithelial cells and released at higher levels in the extracellular space during exposure to live trichomonas and CPI-GC. CPI-GC from all isolates invariably reduced levels of the natural microbicide SLPI. Mutant trichomonads that failed to bind Gal-1 and Gal-3 showed higher proinflammatory activity suggesting a role for the CPI-GC–galectin binding in suppressing innate immune responses.

Conclusion Interventions targeting CPI-GC or restoring the balance of natural immune defences represent a promising strategy for preventing adverse outcomes from T. vaginalis infection.

001.4 BLOOD TRANSCRIPTIONAL PROFILING OF WOMEN WITH CHLAMYDIA TRACHOMATIS IDENTIFIES A PELVIC INFLAMMATORY DISEASE (PID) SIGNATURE


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Objective Most women with Chlamydia trachomatis (CT) infection are asymptomatic, while ~3% progress to pelvic inflammatory disease (PID) within two weeks of untreated infection. The identification of biomarkers that predict development of PID would aid in identification of women at risk for complications of infertility and ectopic pregnancy. The specific aim of this study was to identify a whole blood transcription signature for acute PID due to chlamydial infection.

Methods We performed gene expression microarrays using whole blood from 79 women who had a gynecologic exam, and cervical and endometrial microbiologic testing. Samples were divided into five groups: Group 1, women with acute PID who were CT+ at endometrium (PID+, CT+, and E+); Group 2, asymptomatic women who were CT+ at endometrium (PID-, CT+, E+); Group 3, asymptomatic women who were CT+ at cervix (PID-, CT+, E+); Group 4, asymptomatic women who were CT- at cervix and endometrium (PID-, CT-, E-); Group 5, women with symptoms of PID who were negative for CT or other sexually transmitted pathogens (PID+, STI-, E-).

Results We identified a transcript signature that discriminated women with chlamydial PID from all other groups. Pathway analysis revealed that the chlamydial PID signature contained genes from interferon response pathways. Gene transcription in a subset of women with chlamydial endometrial infection clustered with women with chlamydial PID.

Conclusions Our study raises the possibility that transcriptional biomarkers with potential as diagnostic and prognostic tools can be identified to combat chlamydial reproductive tract disease in women.

001.5 EFFICACY OF RG1-VLP VACCINATION AGAINST GENITAL AND CUTANEOUS HUMAN PAPILLOMAVIRUSES IN VITRO AND IN VIVO


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Licensed human papillomavirus (HPV) vaccines, based on virus-like particles (VLP) self-assembled from major capsid protein L1, afford type-restricted protection against types 16/18/6/11 (or 16/18 for the bivalent vaccine), which cause 70% of cervical carcinomas (CxCa) and 90% of genital warts. However, they do not protect against less prevalent high-risk types causing 50% of CxCa, or cutaneous HPV. The minor capsid protein L2 confers low-level immunity to type-common epitopes.

Chimeric RG1-VLP presenting HPV16L2 amino acids 17–36 (RG1 epitope) within the DE-surface loop of HPV16L1 induce cross-neutralisation in vitro. We hypothesised, that RG1-VLP vaccination protects against a large spectrum of mucosal and cutaneous HPV infections in vivo.

L2-specific antibody and CTL responses in RG1-VLP vaccinated rabbits were determined by ELISA and ELISPOT assays. Cross-neutralisation was analysed using native or pseudoviron (PaV) assays. Vaccine efficacy in vivo was determined in a mouse genital challenge model.