Rishein Gupta, J Bacteriol Parasitol 2016, 7:2 (Suppl)
http://dx.doi.org/10.4172/2155-9597.C1.016

Host microRNAs contribute to immunity and development of pathology in *Chlamydia trachomatis* infection

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Chlamydia trachomatis (Ct) is the leading cause of human bacterial sexually transmitted infections. In humans, genital Ct infection leads to reproductive sequelae including fibrosis, tissue damage and inflammation. Although molecular events leading to genital tissue exacerbation and tissue remodeling are unclear, early stage host immune responses may lead to collateral damage in the form of upper genital pathological sequelae. Given that immune responses are regulated by non-coding RNA species namely microRNAs (miRs), the objective of this study was to determine signatures miRs and decipher mechanistic contribution of selected miRs in early stage immune responses and subsequent development of pathology. Using the murine model of genital Ct, C57BL/6 wild type (WT) were intravaginally infected with Ct and cellular infiltrates (flow cytometry), miRs and putative targets (real-time PCR and mass spectrometry) and genital pathology was analyzed. *Ex vivo* genital cell cultures manipulated with miR agonists and antagonists were used for gain and loss of function validation. We found Ct infection in C57BL/6 genital tract significantly regulated selected miRs at early stages of infection post challenge. Amongst these, miRs-125b, -182, -214 and 30c were significantly altered and *in vitro* knockdown analyses with specific inhibitors resulted in increase in Ct infectivity corroborating our *in vivo* findings. Additionally, *in vivo* miR-214 was observed to regulate intracellular adhesion molecule (ICAM)-1 and neutrophil infiltration affecting development of upper genital pathology in an IL17A dependent manner. These findings provide evidence for early stage regulation of immune responses via host miRs affecting development of genital pathology.

Biography

Rishein Gupta is currently doing research in the laboratory of Dr. Bernard Arulanandam at the South Texas Center for Emerging Infectious Diseases, University of Texas at San Antonio, SA TX, USA. Prior to joining Dr. Arulanandam's laboratory, he has received his Doctoral degree from the Birla Institute of Technology and Science (BITS), Pilani and National Institute of Pathology, New Delhi, India in 2009. His doctoral studies focused on investigating host immunity in cohorts of *Chlamydia* infected women with reproductive sequelae. His expertize as a clinical immunologist has been further enhanced through his current research on the role of host immune factors and genital chlamydial infections in animal models including mice and guinea pigs. His current focus includes investigating the role of host factors including microRNAs in regulating anti-chlamydial immunity.

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