OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Clinical & Cellular Immunology

October 15-17, 2013 Hampton Inn Tropicana, Las Vegas, NV, USA

Fasciola hepatica fatty acid binding protein inhibits TLR-4 pathway activation

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Lipopolysaccharide (LPS) is a major component of the outer membrane of Gram-negative bacteria and a potent activator of the human innate immune system. The immune response to LPS can lead to septic shock syndrome if the inflammatory response is amplified and uncontrolled which can be fatal. Several proteins are important for LPS recognition and pathway activation including lipid binding protein (LBP), CD14, MD12 and Toll-like Receptor 4 (TLR-4). Today, there is a need to develop TLR antagonists that could prevent or circumvent the negative and sometimes fatal effect of inflammatory responses during a variety of human diseases. Here, we demonstrated that the Fasciola hepatica fatty acid binding protein (FhFABP) has antagonist properties through TLR-4 after LPS stimulation. Using a proximity ligation assay (PLA) we showed that FhFABP interact with human CD14 co-receptor of HEK 293 cells to block the activation of NF-kB induced by LPS, functioning as antagonist of TLR4. Furthermore, real-time PCR (qRT-PCR) demonstrated that FhFABP inhibited the production of inflammatory cytokines as TNF-α, IL-1β, IL-12A and nitric oxide production by human monocytes derived macrophage (MDM) in vitro. These findings of TLR4 pathway inhibition open doors to further studies directed to explore the potential of FhFABP as a new class of drug against endotoxemia / septic shock bacterial or others inflammatory diseases in which TLR4 are involved.

Biography

Ivelisse Martin Ortiz has completed her Bachelor degree at the age of 22 from the University of Puerto Rico, Mayaguez Campus and a Medical Laboratory Scientist (MLS) post-bachelor certificate from Inter-American University of Puerto Rico, Metropolitan campus. She is a certified MLS by The Board of Certification of The American Society for Clinical Pathology (ASCP). Currently, she is a Ph.D. student at the University of Puerto Rico, School of Medicine, and conducts investigation with *Fasciola hepatica* proteins and its immunological role.