

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

## CD8+ T cell exhaustion in human visceral leishmaniasis

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Little is known about the contribution of CD8 cells in control of human VL and it is unclear if these cells serve a protective, pathological and/or suppressive role. CD8 cells are considered to play an important role in experimental visceral leishmaniasis contributing to resistance and parasite control through their ability to produce cytokines and act as CTL. To better understand the role of CD8 T cells in human VL we assessed CD8 cells derived from blood and spleen of VL patients and controls. Gene (mRNA) and surface expression suggest that blood derived CD8 cells, express elevated levels of perforin, granzyme A, PD-1 and CTLA-4 have feature of both CTL and anergic/exhausted cells, whereas splenic CD8 cell only had an anergic phenotype. In active VL, CD8 cells contribute to the background IFN- $\gamma$  secretion that can be detected in whole blood (WB) and splenic aspirate (SA) cultures, but not to the *Leishmania* induced IFN- $\gamma$  release that is revealed in WB cultures. Blockade of PD1 or CTLA-4 had no effect on IFN- $\gamma$  production or parasite survival in SA cultures. CTL activity, measured as LAMP-1 expression on CD3+CD8+ PBMC, in response to stimulation with *Leishmania* antigen was not observed in VL patients or controls, while LAMP-1 release in response to SEB appeared normal. VL "NK" cells express more LAMP than EC "NK" cells with a possibility that these cells are more activated in VL patients compared to EC. *Leishmania* antigen induced IFN- $\gamma$  production by CD8 T cells can be observed following clinical cure in individuals immune to subsequent disease, suggesting that the parasite may benefit from the generation of dysfunctional CD8 T cells in active disease. Thus, we conclude that CD8 T cells in VL subjects show mixed phenotypic expression, but overall they more prominently display features of exhausted/anergic cells.

## Biography

Shalini Gautam has completed her Ph.D. from Banaras Hindu University, Varanasi, India. She is intended to persue her postdoctoral studies from College of Pharmacy, Ohio State University, Ohio. She has published 7 papers in peer reviewed journals and has a keen interest in Immunological aspects of Infectious Diseases.

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