

**ABSTRACT #93 | EGCG inhibits CXCR3+ cell migration, binds proinflammatory chemokines and reduces inflammatory cell recruitment in vivo: potential opportunities for the treatment of HIV/SIV infection?** Shulin Qin, John F. Alcorn<sup>2</sup>, Jodi K. Craig<sup>3</sup>, Charis Tjoeng<sup>1</sup>, Jay K. Kolls<sup>4</sup>, Todd A. Reinhart<sup>11</sup> Department of Infectious Diseases and Microbiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA 15261<sup>2</sup>, Childrens Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, PA 15201, Department of Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261<sup>4</sup>, Department of Genetics, LSUHSC, New Orleans, LA 71002 <sup>3</sup>

Chemokines are small chemoattractant cytokines that likely play multiple roles in HIV/SIV pathogenesis. An important activity of chemokines is recruiting immune cells to inflammatory sites. We have found that proinflammatory cytokines and chemokines - such as IFN- $\gamma$ , CXCL9, CXCL10 and CXCL11 - were up-regulated in the lymphoid tissues of SIV-infected cynomolgus (*Macaca fascicularis*) and rhesus (*Macaca mulatta*) macaques. Correlation analyses revealed that IFN- $\gamma$ , CXCL9, CXCL10 and CXCL11 were positively correlated with each other and with SIV RNA levels. These data indicate that one possible mechanism for the restructuring of the chemokine environment in lymphoid tissues during SIV infection is increased IFN- $\gamma$  production, and a potential consequence of this restructuring is a chemokine-driven Th1 polarizing amplification loop. Chronic states of T cell activation and viral persistence are hallmarks of HIV1 infection, so reduction of inflammatory responses might be beneficial to hosts with HIV/SIV infection. It has been shown that epigallocatechin-3-gallate (EGCG), a green tea catechin, exhibits anti-inflammatory properties, but the mechanism has not been completely defined. We will present new findings that EGCG dramatically inhibits the chemotaxis of rhesus macaque, human and murine cells in response to CXCL9, CXCL10 and CXCL11. Biacore binding experiments revealed that EGCG can bind directly to human and murine CXCL9, CXCL10 and CXCL11. To confirm the anti-inflammatory effects of EGCG in vivo, we used EGCG to treat mice in the context of a Th1 cell adoptive transfer airway inflammation model and found that EGCG decreased murine Th1 and other inflammatory cell recruitment to lung tissues and significantly reduced airway inflammation. These findings suggest that EGCG might have beneficial anti-inflammatory properties if given to SIV-infected macaques. Overall, these results provide biochemical and immunopathological insights into the beneficial properties of EGCG and suggest that EGCG could be a potent and safe anti-inflammatory compound with therapeutic potential for treating the inflammatory aspects of HIV/SIV infection.