

Type: Oral Presentation

Final Abstract Number: 21.011

Session: Oral Presentations: HIV & Tuberculosis

Date: Friday, March 4, 2016

Time: 10:15-12:15

Room: G.05-06

Ps20: A novel correlate of inflammation and infection in TB?

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Background: The soluble factor ps20 encoded by the human WFDC1 gene on Chromosome 16, is an ancient whey acidic protein (WAP) family member, characterized by highly evolutionarily conserved domain comprising eight cysteines that make 4 disulphide bonds. WAPs are soluble innate immune mediators implicated in homeostatic control of inflammation and broad anti-infective activities. Previous studies in our laboratory highlighted a novel function of ps20. We demonstrated ps20 expression in CD4-T cells, which rendered these cells highly susceptible to HIV infection through up-regulation of ICAM-1. Consistent with this observation, we showed that plasma ps20 levels positively correlated to CD4-T cell count. We also demonstrated that ps20 levels at the CD4-T cell level showed a strikingly inverse relationship with IFN γ and silencing of ps20 in CD4-T cell clones led to upregulation of IFN γ . This study was designed to further examine the role of ps20 in IFN γ regulation in a chronic infection, such as TB, where IFN γ levels are known to be impaired.

Methods & Materials: (i) An in-house ps20-specific sandwich ELISA was calibrated and used to confirm ps20 levels in plasma of 30 treatment naïve active TB, 15 TB treated (12 months post treatment), 12 IGRA+ and 10 IGRA- subjects.

(ii) To further test if raised plasma ps20 in active TB correlated with reduced IFN γ expression, we measured the ps20 and IFN γ mRNA and protein levels in PBMC cultured activated with PHA/IL-2 in time-course assays.

(iii) Rapamycin, a known regulator of the mTOR pathway is well established inhibitor of IFN γ expression. We therefore used this regulator to further determine if suppression of IFN γ leads to induction of ps20.

Results: (i) The ELISA data showed active TB subjects had a significantly higher ($p = 0.0356$) plasma ps20 compared to IGRA+ and IGRA- subjects.

(ii) PHA/IL-2 immunomodulation data confirm active TB subjects to have lower IFN γ than IGRA+ and IGRA- subjects with concomitantly higher ps20 expression.

(iii) Rapamycin Inhibition assay confirms IFN γ expression to be significantly reduced in the presence of Rapamycin with a concomitant marginal but consistent induction of ps20.



Conclusion: These studies highlight ps20 may be a novel regulator of IFN γ and provide novel insights on the possible role of ps20 in TB pathogenesis

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Type: Invited Presentation

Final Abstract Number: 22.001

Session: Plenary IV: Tuberculosis: Challenges and Solutions for the 21st Century

Date: Friday, March 4, 2016

Time: 14:30-15:15

Room: Hall 4 (Plenary Hall)

Tuberculosis: Challenges and Solutions for the 21st Century

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Abstract: (no abstract received from presenter)

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Type: Invited Presentation

Final Abstract Number: 23.001

Session: Intestinal Microbiota in Health and Disease

Date: Friday, March 4, 2016

Time: 15:45-17:45

Room: Hall 1

The healthy human antibiotic resistome: a multi-body habitat analysis

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Abstract: The human body habitats are home to an array of micro-organisms, and within these microbial ecosystems there is an exchange of genetic material, including antibiotic resistance genes. Recent metagenomic studies revealed that the human gut microbiota is a reservoir of antibiotic resistant genes (the gut resistome). However, little is known about the diversity and abundances of antibiotic resistance genes in other body habitats and how that compares to the gut resistome. By leveraging the most comprehensive human microbiome dataset of healthy adults generated by the human microbiome project, we characterize the human microbiome resistome from four body habitats including gut (stool), oral, anterior nares and vagina. The human resistome was profiled using a metagenomic shotgun sequencing alignment-based approach. By determining the resistome size per individual we found resistance genes distribute distinctly by body sites with certain body habitats being a better reservoirs than others. Furthermore, while resistance classes were incoming among body habitats (e.g. tetracyclin), the specific resistance genes per class were different (e.g. tetM in oral vs tetQ in gut). The profiles of resistance genes (in the body sites with universally present resistance genes) are more similar for the same subjects over time than between subjects at the same time of sampling. Finally, association analysis with sex, age and geography