Cynthia Canan
PhD Candidate

“Impacts of Aging and Inflammation on Mycobacterium tuberculosis Control”

October 17, 2016
BRT 105
9:00am
VITA

01/16/1987 ......................... Born – Taichung, Taiwan

2009 ............................. B.S. Biology,
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COMMITTEE MEMBERS

Dr. Joanne Turner

Dr. Prosper Boyaka

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ABSTRACT

Increasing age is a major risk factor for pulmonary disorders and infectious diseases such as tuberculosis. Systemic basal inflammation that occurs with increasing age is thought to contribute to this susceptibility. However, little is known about the consequences of inflammation on immune function. An interesting phenomenon occurs during *Mycobacterium tuberculosis* (*M.tb*) infection in old mice where bacterial control is transiently increased at early timepoints compared to young mice. This enhanced control is lost at later timepoints when old mice succumb to greater bacterial burden. In this work, we demonstrate that the lungs of naïve old mice had elevated levels of pro-inflammatory cytokines, and pulmonary macrophages isolated from this environment showed altered phenotype and function which may contribute to the early resistance observed in *in vivo* *M.tb* infected old mice. This hypothesis is further supported when early resistance is observed in inflammation-induced young mice infected with *M.tb* *in vivo*. To understand how inflammation may alter immune changes with increasing age, old mice were given the non-steroidal anti-inflammatory drug (NSAID), ibuprofen, prior to any manipulations. Altered responses in pulmonary macrophages from old mice were restored when old mice were given ibuprofen, indicating that inflammation induced changes with advanced age can be restored by decreasing inflammation. To further test the impact of inflammation and ibuprofen *in vivo*, young and old mice on either control or ibuprofen modified diet were infected with *M.tb*. Contrary to our hypothesis, old mice treated with ibuprofen showed a trend for better control during early stages of infection compared to both young and old mice on control diet. Because of the known role IFN in early *M.tb* control between young and old infected mice, we hypothesized that old mice on ibuprofen would have an even greater IFNγ response leading to further enhanced early resistance. However, mRNA expression and intracellular staining suggest that IFNγ production is reduced in old mice on ibuprofen compared to old mice on control diet indicating that
enhanced control in old mice on ibuprofen is IFNγ independent. We were able to confirm this finding by neutralizing IFNγ in *M. tb* infected old mice on control or ibuprofen diet. Current evidence suggests that IL-17, which is increased in old mice on control diet, may drive an adverse response by inducing increased cell death during infection causing increased tissue damage and bacterial burden. In contrast, old mice on ibuprofen demonstrate decreased IL-17 post-*M. tb* infection which is correlated with decreased pulmonary macrophage cell death and may be responsible for early enhanced control. These findings suggest that decreasing inflammation in old age may help to decrease the susceptibility to pulmonary disorders and infectious diseases which may enhance the quality of life in the elderly.
Canan CH, Moliva, JI, Dwivedi V, Turner, J. 2016. Ibuprofen enhances bacterial control in *Mycobacterium tuberculosis* infected old mice. **Poster presentation** at the Center for Microbial Interface Biology Retreat, held in Columbus, OH.

Canan CH, Moliva, JI, Dwivedi V, Turner, J. 2016. Impacts of aging and inflammation on *Mycobacterium tuberculosis* control. **Poster presentation** at the Keystone Symposia on Molecular and Cellular Biology titled “Tuberculosis Co-morbidities and Immunopathogenesis”, held in Keystone, CO.

Canan CH, Gokhale, NS, Carruthers B, Lafuse WP, Schlesinger LS, Torrelles JB, Turner J. 2015. Characterization of lung inflammation and its impact on macrophage function in old age. **Poster presentation** at the 14th Annual Ohio State University Medical Center Research Day, held in Columbus, OH.


AWARDS AND HONORS

2015-2017  NIH/NIAID award # 1-T32-AI-112542, a NRSA training grant administered by the Center for Microbial Interface Biology (CMIB), at The Ohio State University

2015  14th Annual OSUMC Trainee Research Day poster presentation travel award

2014  American Association of Immunologists Careers in Immunology Fellowship

2012-2014  The Ohio State University’s College of Medicine Systems and Integrative Biology Training Program

FUTURE PLANS

I am interested in pursuing a career in community science education in order to bridge the gap between scientific knowledge and community awareness. In order to achieve this goal, I am currently applying for a professional degree in Public Health focused on Health Behavior and Health Promotion.
Biomedical Sciences Graduate Program
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