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**Molecular mechanisms responsible for antibody-mediated clearance of *F. tularensis***D. W. Metzger<sup>1</sup>, T. Smith Alumni<sup>1</sup><sup>1</sup>Center for Immunology and Microbial Disease, Albany Medical College, Albany, United States

There is a growing appreciation for the role of antibodies in immunity against intracellular bacteria including that of *Francisella tularensis*. We have previously demonstrated that serum antibodies provide protection against pneumonic tularemia and have therapeutic benefits. The antibody-mediated protection was dependent on FcγR-bearing phagocytes such as alveolar macrophages (AMs) and their activation by IFN-γ. Here, we further elucidate the molecular mechanism of synergy between FcγR and IFN-γR signaling that results in the rapid intracellular killing of *F. tularensis*. Activated AMs produced significantly higher levels of nitric oxide (NO) upon infection with antibody-opsonized *F. tularensis*. Chemical inhibition of NO production resulted in the abrogation of intracellular killing of opsonized bacteria by AMs. Increased NO production and rapid clearance of opsonized bacteria by AMs was independent of TLR2 and TNF-α stimulation suggesting a higher order of complexity to the „prime and trigger“ model of macrophage activation. In fact, our preliminary studies suggest that differential trafficking of opsonized bacteria within IFN-γ activated AMs may contribute to the rapid clearance of *F. tularensis*. We are currently establishing the dynamic interaction of the bacteria with the activated phagocytes in order to design effective strategies for sterilizing prophylaxis and therapeutics.