OC08 & P59 - **The host microbiota contributes to early protection against lung colonization by *Mycobacterium tuberculosis***

Alexia Dumas, Dan Corral, André Colom, Antonio Peixoto, Denis Hudrisier, Yannick Poquet, Olivier Neyrolles
IPBS, CNRS
alexia.dumas@ipbs.fr

Background: Tuberculosis (TB) is still a disease of major public health importance, with 1.7 million deaths in 2016. TB is caused by the airborne bacillus *Mycobacterium tuberculosis*, an intracellular pathogen residing preferentially inside host macrophages. Indeed, *M. tuberculosis* has evolved mechanisms to escape immune defences and resist degradation within the phagosome. The contribution of microorganisms of the host lung and gut microbiota to TB is poorly understood.
Objective: Here, we hypothesize that the host microbiota might influence *M. tuberculosis* infection through the modulation of the immune system.
Methodology: We used an immune-competent mouse model of microbial dysbiosis based on a combination of wide-spectrum antibiotics (e.g. ampicillin, neomycin sulfate, metronidazole, and vancomycin) to study the role of the microbiota on host susceptibility to *M. tuberculosis* infection and anti-mycobacterial immunity.
Results: We showed that the microbiota depletion increased early colonization of the lungs by *M. tuberculosis*. This phenotype was correlated with an alteration in the TNFα production by alveolar macrophages in microbiota-depleted animals. Moreover, antibiotics-treated mice presented a decrease of the number of mucosal-associated invariant T (MAIT) cells, a population of innate-like lymphocytes whose development is known to depend on the host microbiota. These cells showed a tendency to proliferate less than in control animals, and produced less IL-17A. Notably, dysbiosis correction through the inoculation of a complex microbiota in antibiotics-treated animals reversed these phenotypes.
Conclusions / Implications for practice: Altogether, our results demonstrate that the host microbiota contributes to early protection of lung colonization by *M. tuberculosis*, possibly through sustaining the function(s) of alveolar macrophages and MAIT cells. Our study calls for a better understanding of the impact of the microbiota on host-pathogen interactions in TB.

References

Dumas et al., Front Immunol. 2018 in revision