Host-Pathogen Interactions in Tuberculosis

Genetic Aspects

By Olivier Neyrolles
Institute of Pharmacology & Structural Biology CNRS – University of Toulouse - France

Dr. Olivier Neyrolles’ presentation focused on host-cell pathogen interactions in tuberculosis. Firstly, he started with a brief introduction to the TB disease. It was important to remember that merely an estimated 5-10% of individuals exposed or infected with Mycobacterium tuberculosis actually develop TB. In other words, the human population, as a whole, is extremely resistant to the disease. Despite this resistance, approximately 1.5 million people die of tuberculosis each year. Thus, although the activation rates of the disease are rather low, this huge reservoir leads to high numbers of diseased and deaths.

Multiple factors explain why certain individuals are more likely to develop the disease than others, including nutrition and hygiene, HIV co-infection, sex and age, as well as host genetic factors and the genotype of the infecting strain. Here, Dr. Olivier Neyrolles mainly discussed the influence of the host genetics in infectious disease.

1. Host genes in microbial pathogenesis
Infectious disease relies on the immune status of the host. If the individual has genetic immune deficiency (such as IFNγR\textsuperscript{mut}, IL12R\textsuperscript{mut}, STAT1\textsuperscript{mut}), there will be insufficient number of immune effector cells and/or molecules to control the disease. If the host has complex genetic susceptibility, inflammatory mediators will be overproduced and also cause host damage (such as Leprosy, Tuberculosis and TB meningitis). So, the balance is very important.

2. Host genes in treatment outcome
Host genetic factor plays an important role in the treatment outcome and the host genotype-specific therapies can optimize the inflammatory response to mycobacterial infections. For example, the expression of the host ITA4H gene is related to TNF production, and if the individual is T/T genotype, the ITA4H gene will be high expressed and TNF will be highly produced, so using dexamethasone (anti-TNF drug) will be better for treatment. If the individual is C/C genotype, the ITA4H gene will be low expressed and the TNF will be low produced, and using dexamethasone will be worse for treatment.