Host-Pathogen Interactions in Tuberculosis

Cellular aspects

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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.

When an individual is infected with Mycobacterium tuberculosis, the bacilli enter the lungs through aerosol droplets. In order to become potentially infectious, the bacilli must first enter the alveoli. Inside the alveoli, they interact with cells, mainly macrophages and dendritic cells, through different receptors. He mainly focused on the interactions between the bacillus and the first cells that encounters in the lungs during the infection. In spite of the immune response, one of the major virulence mechanisms in TB is the ability of the bacillus to parasitize the macrophages, that is, to persist and multiply within the cells. One of the fundamental questions of tuberculosis basic research is how the bacillus can persist and multiply within these cells.

Here, he focused on three aspects. The first one is the entry of the bacillus into the cell, and the receptors involved in this phagocytosis process. The second is the cell’s reaction to the infection. Finally, he reviewed the strategies used by the bacilli to persist and survive inside the cell.

1. Cell Entry

Many receptors are involved in the phagocytosis of Mycobacterium tuberculosis, which will be discussed extensively, with a particular focus on DC-SIGN, a receptor on which they have worked in the past years.

2. Host Cell Response To The Infection

He discussed the host cell response to infection and the consequences, in terms of intracellular signalling and cytokine secretion, of the mycobacteria-host cell interactions through the receptors discussed above, notably DC-SIGN and Dectin 1.

3 Intracellular Survival Strategies Of The Bacillus

Mycobacterium tuberculosis can survive inside macrophages and that is not typical in bacteria. He believed that if we manage to understand how the bacillus can parasitize the host cell, and to identify the mycobacterial genes involved in this process, we might be able to design new antibiotics, which are specifically directed against these genes. We might also be able to generate new mutants and attenuated strains of TB, in order to develop new vaccines.

a. Understanding the TB Genome

The publication of the TB genome in 1998 was a major milestone in the history of TB. We can now wonder how to convert this mass of information into a useful understanding. Indeed, the TB genome is extremely frustrating, since over 40% of its genes do not reveal any information.
b. Functional Genomics

Functional genomics can help understand the TB genome, which will be discussed, through mainly the example of Signature tagged Transposon Mutagenesis (STM) used at various levels, from the whole organism to the subcellular level.