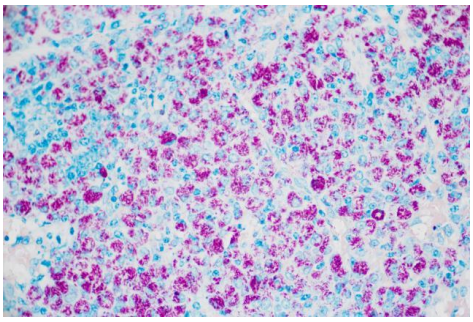
The SMALTIS'tory – episode #10

Mycobacterium leprae, the genetic pirate!



Once upon a time there was a bacillus capable of reprogramming the cells of its host...

Leprosy is a chronic infectious disease whose first descriptions date back to antiquity. It has been and remains today a scourge marked by stigma and exclusion, resulting in numerous nerve and skin lesions. Although it has disappeared in Europe, its incidence remains relatively high in the tropics, with nearly 200,000 new cases each year.

The responsible for this scourge? The bacterium *Mycobacterium leprae*, identified in 1873 in Norway by Gerhard Armauer Hansen.

This particular bacillus, whose main reservoir is man, has lost more than 2,000 genes during its evolution. The loss of entire metabolic pathways, including the catabolism of fatty acids and the synthesis of the envelope and flagellum, explains several traits such as its strictly intracellular character, its very limited cell niche, the necessity of the host for its survival, and its slowest growth in the bacterial world. Indeed, it takes 12 to 20 days for *M. leprae* to duplicate itself in humans!

Its culture is not possible *in vitro* but can be carried out in the plantar pads of mice, which have been the experimental model of choice for his study since 1960. Moreover, it is from this model that in 2013, Anura Rambukkana's team from the University of Edinburgh discovered how the bacterium spreads in the organism.

The team used the fact that *M. leprae* preferentially infects the Schwann cells responsible for myelination of axons as a starting point for infecting and then injecting these cells back into the rodents. What a surprise the researchers were when they discovered that these cells had been transformed into stem cells and had migrated into other tissues! But how is this possible?

After colonizing Schwann's cells, *M. leprae* sets up a fine strategy to infect the entire organism. The bacterium gradually switches off the genes associated with Schwann cell line and activates many genes characteristic of the undifferentiated stage. Such reprogramming, associated with epigenetic modifications, leads to the loss of specialization of the cells, which then return to an immature stage.

These cells, with migratory and immunomodulatory properties, will then allow bacterial dissemination by two distinct mechanisms.
The first leads to the passive transmission of the infection to other tissues, thanks to the migration of the cells in the organism and their spontaneous differentiation into mesenchymal cells. The latter can then fuse with muscle tissue and deliver their cargo to it.
The second relies on the secretion of chemoattractors by infected cells during their transit, attracting macrophages that will phagocytize them. This is followed by the release of macrophages loaded with bacteria, secondary sources of expansion and dissemination of the infection in the body on a large scale.

This fabulous discovery raises the possibility of earlier diagnosis of the pathology through the detection of molecular markers characteristic of stem cells.
Moreover, this unexpected link between cell reprogramming and host-pathogen interaction allows for new therapeutic strategies to fight this infection and is a promising source of prospects in regenerative medicine using cell plasticity.