expressed. It is then tempting to speculate that this kind of bacterial behaviour might represent a "hiding strategy" that the bacillus adopts to survive in the host. Therefore, the knowledge of the proteins effectively produced by the bacillus in the course of infection would provide useful targets to be addressed by the human immune response. Furthermore, the enlargement of such an analysis to TB patients' clinical isolates would highlight which are the proteins produced by MTB just when it replicates in the human host and in different sites (open and closed lung cavities, for example), and present them as good candidates for post-exposure DNA vaccination.

Bacteria have a "quorum sensing" capacity

Recently, it has been shown that bacteria can communicate with their own species as well as with others, and that they have the capacity to sense and respond to a high population density, which means that they are able to distinguish the environment in which their replication occurs (Strauss, 1999). This «quorum sensing» induces different effects: some bacteria aggregate in biofilms, a common cause of persistent infections (Costerton et al., 1999), while others produce virulence factors (Galan and Collmer, 1999).

In the case of tuberculosis, a low number of studies have focused, so far, on the genes expressed by MTB during infection, either in mouse or human phagocytic cells (Plum and Clark-Curtis, 1994; Lee and Horwitz, 1995; Butcher et al., 1998; Graham and Clark-Curtis, 1999). Another interesting approach to analysing the bacterial behaviour was proposed (Shapio, 1998) by saying that a bacterial population may, in some respects, be considered as a multicellular organism. The thesis is based on the findings that intercellular communication and multicellular coordination are known to be widespread among prokaryotes and to affect multiple phenotypes. Furthermore, many different classes of signalling molecules have been identified in both Gram-negative and Gram-positive species. Therefore, bacteria can benefit from organizing a cellular division of labour, from collectively defending against antagonists, and from differentiating into distinct cell types in order to optimize the population survival. Might it also occur in the *M. tuberculosis* strategy for survival?

Why not, then, an "environment-sensing"?

An ongoing study upon the comparison between human macrophage infection with MTB laboratory strain H37Rv and a peculiar clinical isolate strain (Cappelli et al., in preparation) put in evidence that the longer the period of time the bacillus survived in the host, the better the balance that it found between the host defence and pathogen escape mechanisms. An apparent paradox is that the clinical strain was able to induce more prolonged activation of human macrophages, in which production of IFN-γ and other Th1 type cytokines was detected during a longer period of infection, compared with the laboratory strain H37Rv-infected cells. It might seem that MTB, when taken *ex vivo*, is able to regulate its own metabolism with a fine tuning. In an immunocompetent host it evokes an immune response sufficient not to replicate itself until bacilli dissemination and host death. At the same time, in human macrophages it doesn't transcribe the antigens that would be able to disclose its presence to the immune system, and, most likely, to recruit too powerful antigen-specific T cells.

In a recent study (Russel et al., 1997), it is actually shown that human macrophage response doesn't need to be a degrading experience for mycobacteria; on the contrary, MTB infection has evolved into an extremely stable interaction that, more often than believed, results in cryptic infections with minimal damage to the host.

MTB latency: to become invisible for the host

Differently, in the cases in which the disease takes place, one of the biggest problems related to TB patients treatment (Bloom and McKinney, 1999) is that, even if the isolated clinical strain does not display multidrug resistance, the anti-TB drugs might be very poorly effective *in vivo*. This could be explained by MTB being in that particle physiological state called "latency" that allows it to produce persistent infection, against which conventional drugs are ineffective, since bacteria have exited the cell division cycle and became stationary (McKinney et al., 1998). Again, this would mean that the bacillus "sensed" the hostile environment and escaped in that "stand-by" state of life. In this respect it would be of crucial importance to know whether a "latent" bacillus is somehow able to produce any protein/s, the recognition of which would likely provide the host with a useful target that discloses the MTB presence in his body.

Conclusions

To summarize, let's say that some observations show that *M. tuberculosis* might be able to "sense" the environment in which its replication occurs. In fact, it seems that it is capable to modulate its gene expression in the course of infection, avoiding to transcribe genes encoding the proteins that display immunodominant epitopes.

It is, in many cases, apparently able to find a balance between its own replication and host survival.

It is also found in a latency state, when the host environment is particularly "hostile" for its survival.

Finally, this editorial proposes the idea that studying the behaviour of MTB at the very same moment in which it needs to adapt its metabolism to the host environment will provide us with new information for building up a post-exposure vaccine against tuberculosis.

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