

Cellular safety shelters allow TB agent to survive in infected individuals

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"Foamy" macrophage formation may be the key to persistence of infection by Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis, explains a study published November 14 in the open-access journal *PLoS Pathogens*.

These immunity-related cells are shown to be a safety reservoir where the bacterium can hide for years in infected individuals, before inducing an active disease. According to the research group led by Frederic Altare, the tubercle bacillus circumvents the host immune response by inducing the transformation of aggressive immune cells into a nonaggressive refuge where it is able to survive and have access to large sources of nutrients.

Mtb is responsible for a dramatic global health problem. The World Health Organization has estimated that this pathogen infects one third of the human population and causes three million deaths annually. Most individuals remain asymptomatic for several years before developing an active disease. In such individuals, it is generally admitted that the bacilli are not cleared but rather persist in a dormant state. One of the main goals of TB research is to understand how and where the bacilli survive within infected hosts.

Using a recently developed in vitro assay mimicking the human host immune response, the researchers observed that Mtb uses some of its cell surface constituents to induce the transformation of macrophages (which are supposed to internalize and kill infecting bacteria), into



"foamy" cells. These cells have lost their killing ability and have accumulated large amounts of lipids, the main nutrient for internalized Mtb. They further observed that Mtb remained alive within these cells, and switched into a dormant state.

This observation may direct novel research towards the elucidation of tubercle bacillus survival mechanisms. This study also helps explain the role of a previously uncharacterized cell population participating in the human response to Mtb. "Foamy" macrophages may prove to be a useful tool for the development of new antimicrobial drugs targeted to kill the bug directly within its natural shelter.

Citation: Peyron P, Vaubourgeix J, Poquet Y, Levillain F, Botanch C, et al. (2008) Foamy Macrophages from Tuberculous Patients' Granulomas Constitute a Nutrient-Rich Reservoir for M. tuberculosis Persistence. PLoS Pathog 4(11): e1000204. doi:10.1371/journal.ppat.1000204 dx.plos.org/10.1371/journal.ppat.1000204

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