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StopLATENT-TB

#2

NEWSLETTER

WHO WE ARE

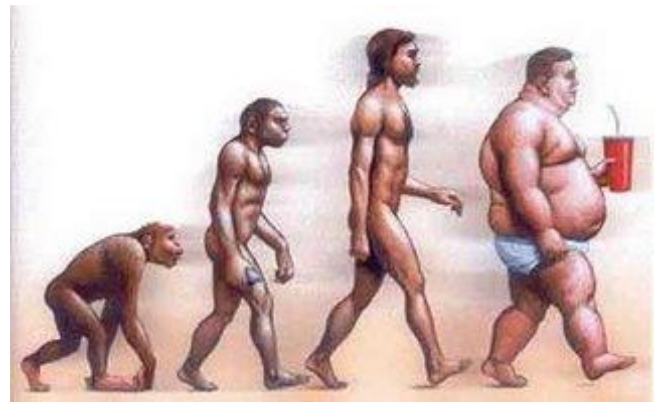
The consortium is composed by seven laboratories. Five laboratories are from four European Countries (France [Beneficiary 8], Italy [Beneficiary 2], Spain [Beneficiaries 1 and 4] and United Kingdom [Beneficiary 5]) and two laboratories are from two Latinamerican countries (Colombia [Beneficiary 6] and Mexico [Beneficiary 7]).

***StopLATENTTB** is a Collaborative Project funded by the European Union under the 7th Framework Programme. The main aim of the project is the analysis of the basic activity of *M. tuberculosis* during dormancy, and the changes in that activity with drug treatment.*

Mycobacterium tuberculosis, lipids and latency: A hot-spot in the recent literature.

The relationship of lipid metabolism with latency and persistence, in the infection of *Mycobacterium tuberculosis*, constitutes a pivotal issue for the StopLatent-TB project (www.latentuberculosis.com). The interest and relevance of that association has been reflected in the recent scientific literature. At least five papers were published recently on that topic: Garton et al, 2008; Erol, 2008; Peyron et al, 2008 (*); Cardona, 2009 (*) and Ehlers, 2009; two of them (*) with participation of members of the StopLatent-TB consortium.

A. Erol (2008) gave evidences to relate the latency of *M.*



M. tuberculosis meets lipids easily when confront to human tissues. Is the bacteria using fat-food during its infection?

This hypothesis is based on the cellular turnover in lungs and the fact that isoniazid treatment, an antibiotic that should not be effective against resting bacteria, has demonstrated to be active to clear "dormant" bacilli during the latent infection. Cardona and his group hypothesized that non-proliferating bacilli are drained out of the granuloma by foamy macrophages but a constant

tuberculosis and the adiposity of the human tissues. Persistent bacilli accumulate fatty-acids (FA) in their cytoplasm, in such a way that any decreasing in the cytoplasmic's FA content of the bacilli could lead to reactivation. When the adiposity of the human body was diminished, as it occurs for example in malnutrition and famine, the risk of Tuberculosis increases. According to the previous, a good model to study latent tuberculosis should be that in which bacilli accumulates FA in their cytoplasm, this was also suggested by N. Garton (2008) when detected intracellular lipophilic inclusions inside the bacilli, in the sputa collected from TB patients. They found correlation between detection of lipid bodies in the bacilli present in sputum with days for positivity of the sputum's cultures. They propose the lipid content bacilli as a suitable biomarker for non-dividing M. tuberculosis.



Fat and dormant: a way of life apparently favourite of the tubercle bacilli

Accumulation of lipid bodies in the bacilli was clearly demonstrated in the electronic micrographs showed by P. Peyron in her paper last year (2008) (P. Peyron is member of the Beneficiary 8 in the StopLatent-TB consortium). This work established beautifully how the bacteria, in a first stage, migrate in the phagosome to the lipid bodies when locates inside foamy macrophages. Later on, the bacilli accumulate lipids in its cytoplasm. These bacilli with lipids inside accomplished the criteria of non-replicating persistent bacilli. P-J Cardona (PI member of the Beneficiary 4 in the StopLatent-TB consortium) assigned a central role for those foamy macrophages in the M. tuberculosis latent infection. He proposed that Tuberculous latent infection could be actually dynamic (Cardona, 2009).

endogenous reinfection could occur, thus maintaining the infection latently.

However, the previous hypothesis is controversial as stated S. Ehlers (2008). Two different viewpoints can be considered even-though they are not mutually exclusive. One consider that, during latency, a dynamic and balanced immunological interplay between M. tuberculosis and the host occurs, reactivation and disease could appear when this equilibrium was broken; other establish that dormant bacilli remains inside adipocytes and other cell-types, reactivation occurs after the appearance of resuscitation promoting factors, giving place to newly dividing bacteria and disease.

Whatever hypothesis was considered it should fit with all the various ways by which M. tuberculosis can infect humans, not just the pulmonary condition that accounts to be its more frequent presentation, but also extra-pulmonary or paediatrics two other also serious presentations of Tuberculosis.

The gambling is not close and more investigations are needed to explain all the factors involved in this successful and intriguing infection: Latent Tuberculosis.

This document was prepared by MJ Garcia (StopLATENT-TB co-ordinator) with the help of MC Menendez and C Vilaplana (members of the StopLATENT-TB consortium).

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