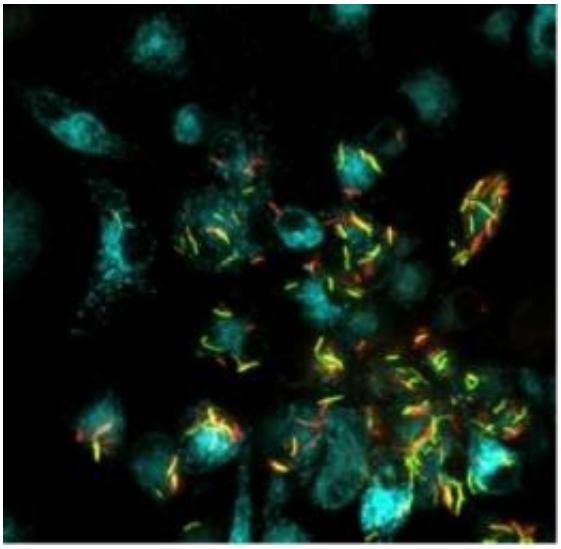
Fat clue to TB awakening

March 28 2010



Macrophages infected with *Mycobacterium tuberculosis* that have been transformed to express the red fluorescent protein (constitutively), and the green fluorescent protein in response to stress from low pH. The macrophages are loaded with a lysosomal tracer (cyan) The picture was taken shortly after infection when the bacteria are stressed and trying to establish the infection. These bacterial strains allow one to probe bacterial fitness during in vivo infections and to evaluate the efficacy of drug treatments and immune therapy. Credit: Robert Abramovitch and David G. Russell

The factors instrumental in triggering latent tuberculosis (TB) infection to progress into active disease have long remained elusive to researchers. New insight into the mystery is provided by Professor David Russell, speaking at the Society for General Microbiology's spring meeting in Edinburgh today. His work could help develop innovative strategies for

treating the disease.

Professor Russell and his group at Cornell University in New York, USA, have demonstrated that TB-causing bacteria are able to hijack fat metabolism in the host to drive the progression of the disease. The team's research shows that *Mycobacterium* tuberculosis (Mtb) is able to stimulate macrophages - the immune cells the bacterium infects - to accumulate fat droplets, turning them into "foamy" cells. This cellular transformation can trigger a reawakening of the TB infection from its latent state.

Following initial infection by Mtb, the infected immune cells in the body can clump together in the lungs in a cellular mass that is surrounded by a fibrous cuff. This containing structure, called a tubercle, physically protects the bacteria from being destroyed by the immune system. This allows them to persist inside the host for years during a latent period in which the host shows no symptoms. The respiratory infection is reactivated only in a small percentage of individuals (often those who are immunosuppressed) in whom it progressively destroys lung tissue. Very little is known about the exact causes of reactivation and the relative roles of the host and the pathogen.

Professor Russell's group discovered that inside the tubercle, surface molecules of Mtb prompted host macrophage cells to take up vast quantities of cholesterol-type lipids from the surrounding blood vessels. "We think that the lipids in the newly-formed foamy cell are then expelled into the cellular environment, which contributes to the collapse of the tubercle," he said.

Once freed from their containing structure, the infectious bacteria are able to leak out into the airways where they can progressively destroy lung tissue. "If our model is correct, it has huge implications for vaccines and chemotherapy programmes. A more detailed knowledge of the

bacterium's life cycle and its host interactions will allow us to spot new targets for drugs - opening up new possibilities for treatment," said Professor Russell.

More information: Professor Russell's talk 'Who put the tubercle in tuberculosis?' will take place on Monday 29 March at 1600 at the Society for General Microbiology's spring meeting at Edinburgh International Conference Centre.

Provided by Society for General Microbiology