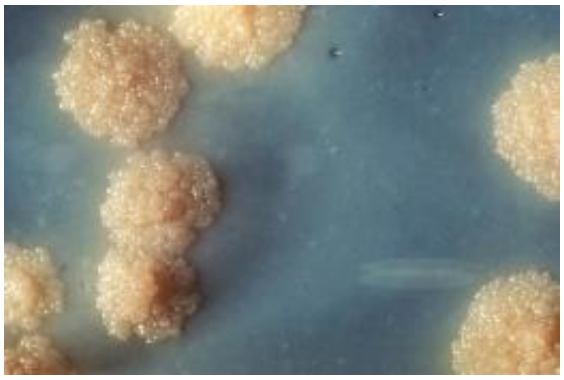
TB bacteria use the body's stem cells to protect themselves

8 December 2010, by Lin Edwards



M. tuberculosis bacterial colonies. Credit: Centers for Disease Control and Prevention.

(PhysOrg.com) -- Tuberculosis kills around 1.7 million people globally each year, and the World Health Organization (WHO) estimates around a third of the human population carries the disease, which becomes active in 10 percent of affected people. The bacteria causing the disease are becoming increasingly resistant to drugs, and new ways of treating the disease need to be found urgently.

Mycobacterium tuberculosis (M.tb), the bacterium causing tuberculosis (TB) is able to produce a persistent presence in its host even if there is a strong immune response, but the mechanism by which it is able to do this is poorly understood. Now, new research by scientists in India has gone some way to solving the mystery.

It was already known that the immune system response to M.tb produces a waxy coating over the bacteria creating clumps called granulomas. The granulomas quarantine the bacteria but do not kill them, and they can remain dormant for many years. If the body's immune system is weakened, the bacteria can go on to produce active tuberculosis.

The researchers, led by Gobardhan Das from New Delhi, infected mice with a low dose of M.tb, and found the infection caused an increase in the number of the host's own mesenchymal stem cells (MSCs) in the mice spleens and lung granulomas, and a suppression of T-lymphocyte cells (T-cells). The stem cells formed a protective coating around the granulomas and produced nitric oxide and other immunosuppressant molecules.

Das said the amount of nitric oxide produced is not enough to kill the M.tb bacteria but it inactivates the T-cells, creating an equilibrium. These actions protected the M.tb bacteria from attack by the body's T-cells and white blood cells, which would otherwise destroy them. The state of equilibrium could further explain why the disease remains latent in 90 percent of those infected and can remain present for the person's lifetime.

Biopsies taken of granulomas in human tuberculosis patients support the findings of the study in mice, and suggest the same mechanism applies in humans.

MSCs originate in the bone marrow and can differentiate to form cells such as muscle, cartilage, bone or blood cells. They also play a role in immunosuppression and can migrate to other areas of the body to help in the repair of inflamed tissue such as that found in tumors and Crohn's disease.

The research findings, which are the first to show a bacterium using the host's own stem cells to help in its own survival, could lead to new methods of attacking the disease. They suggest if drugs could be developed that target the specific MSCs forming the protective layer around the granulomas, this would give the body's own immune responses a chance to destroy the TB bacteria. Das likened the MSCs to creating a "nest" for the TB bacteria and if the nest is destroyed the bacteria would be exposed to attack by the body's immune system.

The paper was published earlier this week in the Proceedings of the National Academy of Sciences (*PNAS*).

More information: Mycobacteriumtuberculosis evades host immunity by recruiting mesenchymal stem cells, Shilpa Raghuvanshi et al., doi:10.1073/pnas.1007967107