

DBT-CDFD scientists identify a protein that may be helping TB to persist

New Delhi, Feb 05: Mycobacterium tuberculosis is one of the oldest pathogens known to mankind and is responsible for huge numbers of deaths around the year. Tuberculosis pathology is often associated with symptoms like fever, coughing, loss of appetite, body weight and anemia. Pancytopenia (reduced number of cells in peripheral blood) is one of them. Scientists at DBT-Centre for DNA Fingerprinting and Diagnostics (DBT-CDFD), Hyderabad, have identified a mycobacterial protein, PPE2, as being responsible for anemia and the pancytopenia during mycobacterial infection.



Bone marrow niche is a tightly regulated microenvironment where hematopoiesis occurs at a steady rate. Myeloid hematopoiesis is a process of formation of the leukocytes (neutrophils, basophils, eosinophils, monocytes, platelets, RBCs and mast cells) in the bone marrow to maintain the constant supply of these cells in peripheral blood. These are the sentinel cells required for the innate arm of immune response. Often, infections are associated with increased hematopoiesis to increase turnover of these immune cells to fight-off the invading pathogen and provide immunity to the human body. Pancytopenia during TB can be one of the strategies by which bacteria suppress the immune cells for its own better survival.

The study by the scientists has identified one of the proteins of *M. tuberculosis*, PPE2, which suppresses myeloid hematopoiesis in the mouse model of infection. PPE2 is a secretory protein belonging to the PPE family of mycobacterium and is known to come outside the bacterial cell both in culture and infection conditions. In the presence of PPE2, the number of myeloid cells were reduced in the peripheral blood. Also, presence of PPE2 lowers in situ hematopoietic potential of the bone marrow derived myeloid-progenitor cells.

Along with an overall reduction in bone marrow population, PPE2 also brings changes in the bone marrow cytology by reducing the differentiation of myeloid progenitor cells leading to their accumulation in the bone marrow. Moreover, the bacterium expressing PPE2 was present in the bone marrow of the infected mice. They also observed that the PPE2 affects the bone marrow microenvironment by increasing the interferon- γ production which might be the reason for the aberrant myeloid hematopoiesis.

Human immune system requires the myeloid cells for building the innate immunity to avoid the initial infection, and any reduction in the population of these cells would promote the establishment of the pathogen and the disease. Therefore, PPE2-mediated suppression in myeloid hematopoiesis might be one of the mechanisms which eventually helps in the better persistence of the bacterium in the host.

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