A breakthrough in tuberculosis research

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Often causing no symptoms in carriers of the disease, worldwide tuberculosis (TB) infects eight to ten million people every year, kills two million, and it is highly contagious as it is spread through coughing and sneezing.

"It's a global health disaster waiting to happen, even here in Canada, but this new paradigm in TB research may offer an immediate opportunity to improve vaccination and treatment initiatives," explains Dr. Maziar Divangahi of McGill University and of the Research Institute of the McGill University Health Centre.

The ability of TB bacteria to persist in individuals with apparently normal immune systems implies that they have developed strategies to avoid, evade, and even subvert immunity. The bacteria mainly enter the body through inhalation into the respiratory tract. Alveolar macrophages, a type of white blood cell residing in our lungs, initially recognize the bacteria and engulf them. This process is one of our immune system's defense mechanisms. However, TB has evolved into a parasite that can survive and replicate inside the macrophages until they burst out, spreading the infection.

The way infected macrophages die is a determining factor in the development of immunity to TB. Macrophages can induce apoptosis, a type of cell death which keeps their membrane intact, trapping and reducing bacterial viability. However, TB bacteria induce another type of cell death called necrosis. Necrosis causes cell death by disrupting the cell membranes, which enables the bacteria to escape the cell. It may

help to visualize a box with broken walls.

The key to the fate of the macrophages is the balance between two kinds of eicosanoids. Eicosanoids are molecules that contribute to the control of our immune system. The genetic code of TB bacteria enables it to tip this balance in favor of necrosis, and human genetic analysis revealed that modification in eicosanoids production is associated with susceptibility or resistance to TB. Fortunately, drugs that target the production of eicosanoids are already in use for treating other inflammatory diseases, such as rheumatoid arthritis.

"The next steps will be to see exactly how these drugs can be used to treat TB," said Divangahi.

More information: McGill researchers publish an editorial in Expert Reviews of Respiratory Medicine about the increased risk of a TB epidemic following the earthquake in Haiti: www.expert-reviews.com/doi/full/10.1586/ers.10.41

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