Understanding a global epidemic: Why Africans with HIV are more susceptible to TB

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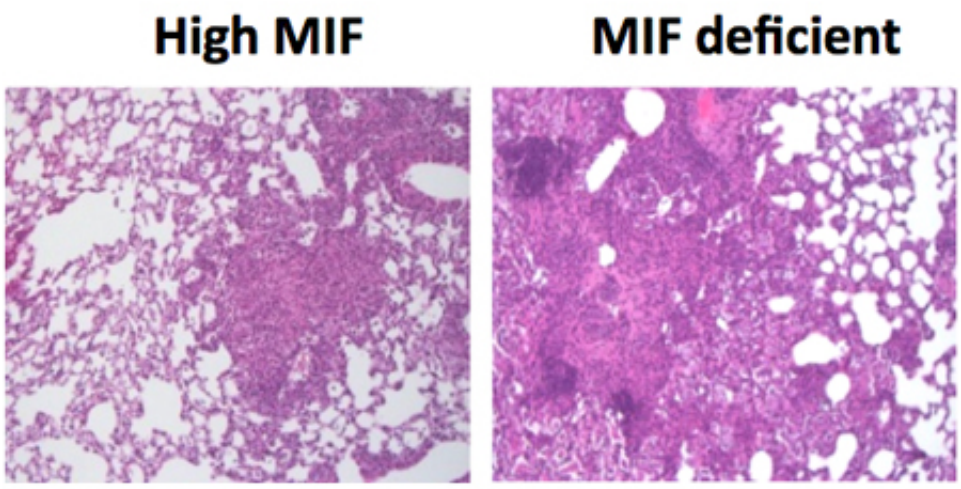

Yale researchers have identified a common genetic variant that makes people infected with HIV much more susceptible to tuberculosis (TB). The study is published in the online Early Edition of the *Proceedings of the National Academy of Sciences*.

Tuberculosis is the leading cause of death by infectious disease, causing 1.5 million deaths around the world each year. Its prevalence is rising

because of drug resistance and an increasing number of patients who are co-infected with HIV. They represent nearly 30 percent of all TB-related deaths. The convergence of these epidemics is particularly prominent on the African continent, which has the highest rates of TB cases and deaths—80 percent of which occur in people living with HIV. Globally, a higher incidence of tuberculosis is known to occur in Africans and African-Americans than in American or European Caucasians, and genetic susceptibility has long been suspected.

The Yale-led team found that a low-expressing version of the immune response gene known as macrophage migration inhibitory factor (MIF)—a cell-signaling molecule secreted by the body's innate immune system—conferred a two-and-a-half two and a half-fold increased risk for severe tuberculosis in a group of patients from Uganda. Low-expressers of MIF are almost twice as common among people of African ancestry as Caucasians.

"This helps to explain the increased incidence of TB in Africa," said senior author Richard Bucala, M.D., professor of rheumatology, pathology, and epidemiology at Yale School of Medicine and Yale School of Public Health.

Furthermore, this variation may be especially important in people co-infected with HIV, who have a compromised immune system. "Therapies to augment MIF action could provide a new tool to combat the global TB epidemic," Bucala said.

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University of Virginia; and John David of Harvard School of Public Health.