Scientists unlock crucial mechanism driving colliding epidemics of smoking and tuberculosis

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TB is an infectious disease that kills 1.5 million people each year, and smoking is the biggest driver of the global TB epidemic. Medical scientists at Trinity College Dublin and St James's Hospital have unlocked the mechanism underlying the connection between smoking and Tuberculosis (TB). This discovery will considerably strengthen anti-smoking efforts to control TB and uncovers new therapy and vaccine options for TB. Their research has just been published in the top respiratory Journal, the *American Journal of Respiratory and Critical Care Medicine*. The research was funded by the Health Research Board (HRB) and The Royal City of Dublin Hospital Trust.

Tuberculosis spreads from person to person by inhaling infected droplets made when the TB sufferer coughs. The World Health Organization has designated TB a global emergency. Nine million people fall ill with TB each year, and it is the greatest killer worldwide due to a single bacterial infection. There are around 400 cases of TB per year notified in Ireland, where we have recurring outbreaks and multi-drug resistant TB cases.

After infection most people do not become ill with TB, but immunosuppressed patients are susceptible. Smoking increases a person's susceptibility to infection by TB, risk of recurrence, mortality and persistent infectiousness. However, until now the exact reason or mechanism behind this connection between smoking and TB has been unknown.

The research team, led by Dr Seonadh O'Leary, conducted the study with smokers, ex-smokers and non-smokers attending the bronchoscopy suite at St James's Hospital. They found that the white blood cells located in the lungs of smokers and ex-smokers, which are responsible for fighting infections, showed a weakened response to the TB infection. In the smoker's lungs, these cells malfunction, and fail to make the chemical messengers that would normally fight the TB bacteria. In fact, the researchers found that these cells suppress the lungs' immunity after infection, which gives the TB bacteria a chance to take over.

Joseph Keane is Professor of Medicine at Trinity's School of Medicine and St James's Hospital, HRB Clinician Scientist, and the senior author of the study. He said: "TB remains a huge global health problem, affecting millions worldwide. It has been known for some time that smokers are more susceptible to getting TB and nearly 80% of the world's one billion smokers live in countries of high TB prevalence. Therefore, while HIV is a key driver of the disease, numerically, smoking is more prevalent than HIV, making smoking the biggest global driver of the TB epidemic."

"This study provides evidence which explains the link between smoking and TB and should considerably strengthen anti-smoking efforts to control TB. However, the widespread emergence of multi-drug resistance TB means we badly need new therapy and vaccine options for TB. We are already applying the findings of this study to develop new treatment options."

This research was funded by the Health Research Board and The Royal City of Dublin Hospital Trust. Dr Keane is the recipient of the inaugural HRB clinician-scientist award, whose grant funding has been renewed.

Graham Love, Chief Executive at the Health Research Board commented: "Patients worldwide who are affected by TB could benefit

from this Irish research. Professor Keane continues to identify relevant research questions from his clinical work. He determinedly pursues the answers during his protected time for research through his HRB Clinician Scientist Award. This is yielding results which could now lead to new treatment options for TB."

More information: The paper is available online here: www.atsjournals.org/doi/abs/10 … -1385OC#.VGSLi_msWv9

Provided by Trinity College Dublin