Scientists discover how vitamin A drives the human lung immune system to control TB

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Scientists at Trinity College Dublin and St James's Hospital, Dublin, have discovered how vitamin A drives the lung immune system to deal with tuberculosis (TB). The findings have just been published in a top respiratory journal, the American Journal of Respiratory Cell and Molecular Biology.

TB is the biggest infectious killer in the world, and multiple-drug resistant TB, which does not respond to regular antibiotics, is a major threat to global health. TB killed 1.7 million people in 2016 and is considered the top cause of death related to infection worldwide. With the increased incidence of drug-resistant TB at home and abroad, additional strategies are required to treat the disease. Unlike in the case of antibiotics, TB resistance should not develop against vitamin A.

Vitamin A deficiency is commonly observed in patients with TB and is associated with a 10-fold increase in the risk in developing the disease. It drives the global TB epidemic, yet the mechanism by which vitamin A protects people's lungs against TB infection remains unexplored.

Now a team of scientists at Trinity College Dublin and St James's Hospital, Dublin, have shown for the first time how vitamin A effectively supports lung immunity against TB. Their research explains a crucial mechanism that underpins vitamin A as a therapeutic option for this disease. It shows that vitamin A supports the recycling and waste disposal functions of the human immune system (called autophagy); this in turn allows for better clearance of the bacteria that cause TB. The discovery has the potential of developing more lung targeted treatment of the disease by boosting the patient's immune response, using the nutritional supplement.

The scientists demonstrated how special white cells (called macrophages) in the human lung were more effective at controlling TB bacteria, when supported with vitamin A. In a previous study, they had demonstrated that vitamin A could also drive anti-inflammatory signals in the human lung. Vitamin A therefore not only limits the TB bacteria, but also prevents unwanted inflammation in the lung, which makes it a particularly attractive therapeutic option.

The Trinity scientists also demonstrated that vitamin A supported the immune system in killing other important lung infections such as whooping cough. With the incidence of whooping cough increasing, the research also suggests that vitamin A might be useful to treat that respiratory infection also.

Commenting on the significance of the findings, Dr Sharee Basdeo Trinity postdoctoral fellow at St James's Hospital and co-lead author of the paper said: "TB remains a pressing global issue affecting millions worldwide. The high prevalence of vitamin A deficiency is a major driver in the global TB epidemic. Our next step will be to translate our research from the laboratory bench to the bedside. If this works out, we would plan to add vitamin A to the existing drug therapies to improve the outcome for our patients."

Dr Michelle Coleman was lead author on the paper and Professor in Medicine, Joseph Keane was senior author. The research was funded by the Health Research Board, the Royal City of Dublin Hospital Trust, and the Irish Research Council. It was conducted at the Trinity Translational Medicine Institute at St James's Hospital, Dublin.

More information: Michelle M Coleman et al, All-trans Retinoic Acid Augments Autophagy during Intracellular Bacterial Infection, *American Journal of Respiratory Cell and Molecular Biology* (2018). DOI: 10.1165/rcmb.2017-0382OC

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