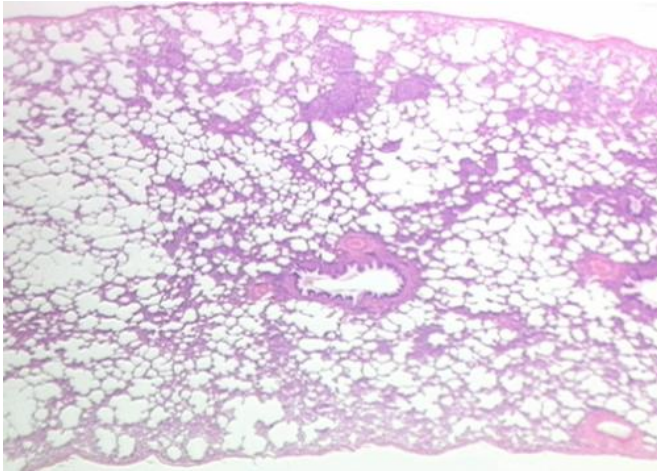# Researchers discover indicator of lung transplant rejection

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Lung tissue. Credit: Rutgers University

Research by scientists at Dignity Health St. Joseph's Hospital and Medical Center's Norton Thoracic Institute was published in the July 12, 2017 issue of *Science Translational Medicine* titled "Zbtb7a induction in alveolar macrophages is implicated in anti-HLA-mediated lung allograft rejection."

This research was conducted at the laboratories of Thalachallour Mohanakumar, PhD and Deepak Nayak's PhD at the Norton Thoracic Institute in Phoenix, Ariz. The labs are dedicated to the understanding of immunologic reactions leading to graft rejection following human lung transplantation.

Lung transplantation, where diseased lungs are surgically replaced by healthy donor lungs, is a viable treatment option for patients with end-stage lung diseases. Unfortunately, long-term success from lung transplantation is limited due to assaults by recipient's immune system that senses the transplanted organ as "foreign" leading to chronic rejection, clinically diagnosed as chronic lung allograft dysfunction (CLAD). Currently, there are no available treatment options for CLAD. Dr. Mohanakumar's research group has been studying the underlying processes of lung transplant rejection more than 20 years and has made several discoveries in the understanding of immunologic mechanisms involved in graft rejection following organ transplantation.

The featured research unveils that monitoring of transcription factor Zinc finger and BTB domain-containing protein 7A (ZBTB7A) can be an early predictor of chronic rejection. This discovery fills the void of a reliable marker and concurrently it opens a new window of opportunities for diagnosis and prevention of CLAD. Its slow onset, lack of early diagnosis and uncontrollable progression have been the most confounding issues for post-transplant caregivers.

"Monitoring for ZBTB7A expression and devising a way to slow it down in lungs may be the way forward to detect and treat CLAD" said Dr. Mohanakumar, the Norton Thoracic Chair for Translational Sciences and Director of Norton Thoracic Institute Research Laboratory.

This research was conducted in collaboration with Washington University School of Medicine in St Louis and Aaron Diamond AIDS Research Center in New York City. Using an animal model of chronic lung transplant rejection, the research identified alveolar macrophages as the sentinel of chronic rejection that was corroborated by analysis of data from human lung transplant recipients.

The purpose of this study was to understand the cellular and molecular alterations in an attempt to identify the early processes and develop interventional strategies for better management of CLAD. Dr. Nayak, the lead author in this paper, devised ways to measure the effect of lung-directed immune responses and identified the alveolar macrophages as the initiator as well as responder

in the post-transplant immune responses. Effect of [lung tissue](link) directed antibodies was measurable in the alveolar macrophages much before the antibodies became detectable in the circulation or diagnosis of CLAD. Dominant role of Zbtb7a was evident when targeted loss of Zbtb7a in the lungs rendered protection from CLAD indicating its pivotal role in the pathogenesis of lung transplant [rejection](link).

The research was funded by National Institutes of Health. Norton Thoracic Institute is one of the busiest lung transplant centers in the nation and conducted the highest number of lung transplantations nationally in 2016. This publication is an attestation of high quality clinical research underway at the Phoenix institute.

Provided by St. Joseph's Hospital and Medical Center