A novel factor in the immune control of *Mycobacterium tuberculosis*: CD153

New paper co-authored by CIDRI-Africa investigators published today in *Nature Microbiology*.

A study published today in *Nature Microbiology* identifies the molecule CD153 as a potential key to control of *Mycobacterium tuberculosis* (Mtb) infection. The mechanisms of immune protection against Mtb are poorly understood.

In a collaborative effort, researchers from institutions in the United States, South Africa, and the United Kingdom investigated the role of CD153 in two animal TB models (mice and rhesus macaques) and corroborated their discovery in human TB.

Using a knock-out model, they showed that CD153-deficient mice are more susceptible to Mtb infection than wild type animals. The team then investigated the role of CD153 in rhesus macaques, a non-human primate model of TB that more closely mimics human disease. They confirmed the protective role of CD153, showing that the more CD153-expressing CD4+ T cells are present in the lung, the fewer bacteria are found.

To translate these findings to human disease, co-authors Catherine Riou and Elsa du Bruyn of the Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa) assessed CD153 expression in individuals with either active or latent Mtb infection. A lower expression of CD153 was observed in Mtb-specific CD4+ T cells in persons with active disease when compared with healthy individuals.

Overall, these data suggest that CD153 may be a key component in the control of Mtb infection. Moreover, this molecule may be a useful biomarker of protection and could possibly be used to evaluate the efficacy of new TB vaccines.

“These findings are really exciting and may help in the quest for correlates of protection against tuberculosis and the development of much-needed diagnostic tools. Further studies are now needed to investigate the mechanism of action of CD153”, commented Dr Riou.

Dr Pete Gardner, from Wellcome’s Infection and Immunobiology team, said: “We only have a partial understanding of how our bodies fight TB, which is a real barrier to developing new and more effective vaccines. This important study identifies a critical role for a certain type of immune cell, which can bring about a protective response to the disease in the lungs. This information is vital to informing the design of future vaccines that could help to tackle TB which infects over 10m people around the world each year.”

As many as two billion people are infected with Mtb, but most will never go on to develop active TB disease because their immune systems are able to control the infection. They may never experience symptoms and do not transmit the bacterium. However, 10% will progress to active TB, and will experience potentially severe and life-threatening illness. In South Africa more than 100 000 people died due to active TB in 2016.

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Reference: Sallin, MA, Kauffman, KD, Riou, C, Du Bruyn, E, Foreman, TW, Sakai, S, Hoft, SG, Myers, TG, Gardina, PJ, Sher, A, Moore, R, Wilder-Kofie, T, Moore, IN, Sette, A, Lindestam Arlehamn, CS, Wilkinson, RJ and Barber, DL. Host resistance to pulmonary *Mycobacterium tuberculosis* infection requires CD153 expression. Nature Microbiology. (2018) http://dx.doi.org/10.1038/s41564-018-0231-6

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About the Wellcome Centre for Infectious Diseases Research in Africa
The Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa) fosters investigator-led approaches via the overarching scientific objective of combatting infection, especially HIV-1 and tuberculosis, through clinical and laboratory research.

CIDRI-Africa was established at the University of Cape Town to augment acknowledged strengths in the basic and clinical aspects of infectious diseases research in the Faculty of Health Sciences. The prestigious award of centre status from the Wellcome Trust is unique, as CIDRI-Africa is the only Wellcome Centre outside the United Kingdom. Three interlinked platforms support clinical studies in the community (Clinical Research), improve the depth of laboratory investigations for infected materials (Basic Science) and advance cutting-edge integration of high-dimensional, big data (Biomedical Data Integration).

Catherine Riou is a CIDRI-Africa Contributing Investigator and an Associate Member of the Institute of Infectious Disease and Molecular Medicine (IDM) in the Faculty of Health Sciences at the University of Cape Town. Her research focuses on TB immunity and pathogenesis in the context of HIV co-infection.

Catherine completed her PhD at the University of Lyon (France), following which she undertook post-doctoral training in the laboratory of Microbiology and Immunology at the University of Montreal (Canada). There, her work focused on identifying the molecular mechanisms and signalling pathways involved in the persistence of memory CD4+ T cells.

She moved to South Africa in 2007 to conduct collaborative work at the National Institute for Communicable Diseases as a visiting senior scientist. On completion of this one-year collaboration, she decided to stay in South Africa and focus her research on infectious diseases and translational research. She teaches postgraduate immunology courses and supervises Masters, PhD and post-doctoral fellows.

Elsa du Bruyn is a research medical officer at CIDRI-Africa. She is currently overseeing clinical recruitment for the NIH-funded Inflammatory Determinants of Disease Severity and Treatment Outcome in TB patients (IDOTS) study.

Elsa obtained her MBChB degree at the University of Stellenbosch in 2011. She has a long-standing interest in infectious diseases which was cultivated during her internship and community service terms spent in the high HIV and TB burden settings of Kwazulu-Natal and Mpumalanga.

She is currently registered for a PhD in Medicine at the University of Cape Town titled “Acute and chronic influences on death and disability in tuberculosis”.

Robert J Wilkinson is a Wellcome Senior Fellow in Clinical Science held as Professor of Infectious Diseases at Imperial College London, and a senior Group Leader at the Francis

Crick Institute London. He holds an Honorary professorship in Medicine in the IDM and directs CIDRI-Africa. His research interest is understanding TB and HIV-associated TB.

His research is supported by the Francis Crick Institute which receives its core funding from Cancer Research UK, the UK Medical Research Council and Wellcome. He also receives support from Wellcome, NIH, and the South African Medical Research Council.