

## **RESEARCH**

### ***Researchers at the CBTBR and their international colleagues have identified the first genetic resistance factor against tuberculosis infection.***

Why do some people who are exposed to tuberculosis not become infected or develop the disease? The South African PI on this project was Prof Eileen Hoal from the CBTBR at the University of Stellenbosch, together with Dr. Erwin Schurr at the Research Institute from the McGill University Health Centre (RI-MUHC), in collaboration with Dr. Alexandre Alcais, from the Institut national de la santé et de la recherche médicale (INSERM) in Paris. The group shed light on this question for the first time, showing that one or multiple genes might provide certain people with resistance to tuberculosis infection. Prof Eileen Hoal oversaw the finding of suitable families, skin testing and collection of samples, whole blood assays and ELISA analysis. The families came from an area of South Africa with high exposure to Tuberculosis, which was critical for the design of the study. Their findings are published in the Journal of Experimental Medicine.

*Cobat A, Gallant CJ, Simkin L, Black GF, Stanley K, Hughes J, Doherty TM, Hanekom WA, Eley B, Jaïs J-P, Boland-Auge A, van Helden P, Casanova J-L, Abel L, Hoal EG, Schurr E, Alcaïs A. 2009. Two loci control tuberculin skin test reactivity in an area hyperendemic for tuberculosis. J Exp Med 206: 2583-2591.*

Their findings show the existence of a chromosomal site, or a locus, that controls resistance to TB infection. Out of the 128 families studied, after considering non genetic factors such as age, 20 per cent of individuals show natural resistance. They identified SLC6A3, encoding the dopamine transporter DAT1, as a promising gene for further studies.

This is also a major development for people with HIV, for whom tuberculosis is a leading cause of mortality, as it is responsible for about 13% of AIDS-related deaths in the world. The hope is that these genetic resistance factors can be used in the near future to prevent TB infection in the general population by stimulating the mechanism responsible for resistance.

This study was funded by a grant from the Canadian Institutes for Health Research (CIHR), Sequella/AERAS Global Tuberculosis Vaccine Foundation, and the Gates Foundation. Some authors received financial support from Fonds de la recherche en santé du Québec (FRSQ).