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Tuberculosis: Adaptations of man and microbe in order to outcompete and survive

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Tuberculosis (TB) caused by the organism *Mycobacterium* tuberculosis is a deadly bacterial disease infecting approximately one-third of the world's population. The most recent World Health Organization (WHO) report indicates 1.5 million deaths and 9 million newly reported TB cases per annum, 95% of which are in developing countries. Despite the fervent genomic and proteomic based research efforts to date, since its discovery in 1882, TB is still a major global problem and hence new approaches are necessary to better characterize this disease especially the adaptations of the host and microbe/host-microbe interactions as they compete to survive. Using GCxGC-TOFMS metabolomics, we have to date identified 31 new sputum and 12 new urinary metabolite markers never before associated with TB providing new insights into the adaptations of the host and microbe metabolome during active TB. The most significant of these are the TB-induced abnormal metabolites resulting from changes to host fatty acid and amino acid metabolism in particular to that of tryptophan, phenylalanine and tyrosine mediated through INF-γ and possibly also reduced insulin. Additionally, an alternative mechanism by which the host produces hydrogen peroxide via glucose oxidation in order to more efficiently eliminate the bacterial threat is proposed. Through these altered metabolic pathways elevated concentrations of various neurotransmitters and other abnormal toxic metabolites related to some of the symptoms associated with TB were identified, subsequently providing clues to better treatment approaches. Adaptations of the microbe during active TB includes the use of a rather unique citramalic acid cycle in conjunction with an up-regulated glyoxylate cycle accompanied by a greater dependence on fatty acids and glutamate as alternative carbon sources.

Biography

Du Toit Loots currently Heads the "Infectious and Acquired Disease Metabolomics" unit at NWU with a focus on new biomarker discovery for better characterizing and diagnosing diseases, TB in particular. Till date, he has contributed to a total of 68 publications: 60 of which are peer reviewed scientific manuscripts in top international journals, 4 chapters in books and 4 publications in non-peer reviewed popular magazines. He is currently International Editor for *Journal of Cell and Tissue Research* and has additionally registered 1 full patent with application to TB diagnostics and published a new synthesis method for NaFe (III) EDTA, a highly bio-available form of iron for combating anaemia. In recognition of these efforts, he received a number of awards including International Nestle Nutrition Institute for Africa Research Award; Janssen-Cilag Award, International ARP Walker Research Award and International Scripps Centre for Integrative Medicine's Research Award.

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