Op dinsdag 24 oktober 2006 om 17u00 in auditorium R. Vanden Driessche van de Faculteit Geneeskunde & Farmacie, Laarbeeklaan 103, 1090 Brussel

**Situering van het proefschrift**

This work reviewed molecular techniques for detection and identification of *Mycobacterium tuberculosis* complex bacteria, detection of drug resistance in clinical specimens, and described a new PCR-based method for typing *M. tuberculosis* isolates. The main focus of this work, however, was to determine the frequency and role of heterogeneity and initial mixed *M. tuberculosis* infection in pulmonary tuberculosis (TB) patients. We investigated this by employing two systematic approaches. In one study, we screened individual colonies (clones) from a single *M. tuberculosis* isolate (primary isolate) of 97 TB patients using spoligotyping, standard IS6110-based restriction fragment length polymorphism (RFLP) typing and PCR-based typing targeting multiple loci containing variable number of tandem repeats (VNTRs). We also determined drug resistance profiles (DST) against anti-TB drugs on primary isolates and individual colonies. Infection with different clonal variants of the same strain and with multiple strains (mixed infections) was detected in 8 (8.2%) and 2 (2.1%) patients, respectively. Drug resistance profiles of the predominant colonies for each patient were always concordant with those of the respective primary isolates. In another study, we analysed isolates from multiple sputum specimens before treatment for each of 199 inmates using RFLP, VNTRs and DST. We detected mixed infection in 26 (13.1%) cases, including six cases with different resistance profiles among isolates from different sputa. Our findings have important implications for the correct interpretation of molecular epidemiology data and in treatment evaluation.

**Curriculum Vitae**

Isdore Chola Shamputa was born on 6 May 1970 in Kabwe, Zambia, the town where the skull of the first early human fossil was found in 1921. He studied Biology and Chemistry at the University of Zambia from 1989 to 1993. In 1994, he joined the Department of Pathology and Microbiology of the University Teaching Hospital in Lusaka as a laboratory scientist. One year later, he was appointed Staff Development Fellow in Microbiology at the Tropical Diseases Research Centre (TDRC) in Ndola, Zambia where he engaged in research on diarrhoeal diseases, sexually transmitted infections, upper respiratory tract infections, and later TB. He contributed to obtaining a grant to purchase equipment for molecular biology at TDRC; primarily to use radioisotope technology for diagnosis and detection of drug resistant malaria and TB. From 1998 to 2000, he studied at the Vrije Universiteit Brussel (VUB) for a Master degree in Medical and Pharmaceutical Research. Thereafter, he returned to TDRC to continue work on drug resistant TB. He was granted study leave in 2001 to pursue doctoral studies in medical sciences at VUB under the supervision of Prof. Dr. F. Portaels from the Institute of Tropical Medicine in Antwerp. He has nine publications in peer-reviewed journals to his credit and co-authored a chapter in a book and in an encyclopaedia. He is also a reviewer for three international journals.