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Research Foundation India

Professor Sune Bergström Public Lecture

by

Dr. Barry N. Kreiswirth

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A Molecular Epidemiologist's view of *M. tuberculosis* Pathogenesis

At 4.00 p.m. on January 07, 2005

Venue: Ulf Widengren Auditorium, AstraZeneca R&D Bangalore, Bellary Road, Hebbal, Bangalore –560 024

ALL ARE WELCOME

Professor Sune Bergström, (d. August 2004) was a founder member and patron of AstraZeneca Research Foundation India, a distinguished scientist and a Nobel Prize winner in Physiology or Medicine (1982). Whose discoveries on Prostaglandin revolutionized medical sciences particularly in the treatment of post partum haemorrhage. He was keenly interested in medical problems of the developing world, infectious diseases and maternal health in particular. Professor Bergström received his Doctor of Medical Sciences degree from Karolinska Institute in 1944 and carried out his monumental research work at Karolinska Institute. He received many honours from Science Academies in almost all countries of the world including India. Of special interest to us in India, Professor Sune Bergström was honoured by the Indian National Academy of Science with the prestigious Jawaharlal Nehru Centenary Medal in 1990.

THE SPEAKER

Dr. Barry N. Kreiswirth is Director of Public Health Research Institute TB Center, USA

The Kreiswirth laboratory is involved in the molecular typing of bacterial pathogens and the initial focus was on the molecular epidemiology of methicillin resistant *Staphylococcus aureus* (MRSA). In 1992, in response to the New York City tuberculosis outbreaks, the PHRI TB Center was established under Dr. Kreiswirth's direction as a genotyping laboratory to study the molecular epidemiology of tuberculosis. The center characterized the highly multidrug resistant strain W and establishing a large strain and DNA fingerprint library. Since its inception, the Center has worked closely with the Centres for Disease Control and Prevention and the New York City Department of Health's to integrate the tools of molecular biology with tuberculosis control efforts. During the last decade the PHRI TB Center has catalogued and DNA fingerprinted more than 15,000 clinical isolates, extending its local collaborations to include the New Jersey Department of Health and Human Services and the Wadsworth Center in Albany, NY, and global sources, including Russia, South Africa, Czech Republic, India, and Egypt.

The laboratory continues its interest in the molecular typing of MRSA and has recently developed a rapid DNA-sequenced- based genotyping method to differentiate *S. aureus* isolates. This approach has been extended to other nosocomial pathogens and currently the laboratory is running a hospital based program (The Molecular Outbreak Center) to genotype submitted bacterial isolates suspected of being associated with clustered cases in New Jersey hospitals. This program and the construction of a nosocomial surveillance database are both part of a working collaboration with NJ Department of Health and hospitals throughout the state.

A MOLECULAR EPIDEMIOLOGIST'S VIEW OF *M. TUBERCULOSIS* PATHOGENESIS

The genomic revolution has had a major impact on molecular epidemiology and evolution studies on *Mycobacterium tuberculosis*. Comparative DNA sequence analyses based on deletion and single nucleotide polymorphism studies have revealed that the *M. tuberculosis* is highly clonal, a relatively young human pathogen and that it did not directly evolve from *M. bovis*. The genomic data has also identified a rich tool box of genotyping tools for the molecular epidemiologists and over the last 15 years there have been extensive studies on transmission of *M. tuberculosis* and in integrating molecular methods in tuberculosis control efforts. Comparative genomics and molecular epidemiology have together revealed that certain strain families, such as the W-Beijing, have been highly successful as a human pathogen. Laboratory studies in macrophages, in mice and more recently in rabbits support the molecular epidemiological findings as the W-Beijing strains show increased virulence in comparison to CDC1551 and H37Rv. The current hypothesis is that strains of the W-Beijing family express a unique phenoglycollipid that is responsible for evading the Th1 response in the establishment of an infection. The demonstration that *M. tuberculosis* strains are not created equal has a direct impact on a number of major research programs, including drug discovery, proteomic studies and vaccine challenges.

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