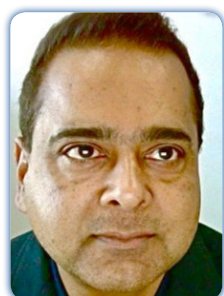


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Pharmacogenomic vigilance of HIV+ patients' pre- and post-highly active retroviral therapy

Pharmacogenomics is a rapidly evolving field and has the potential to reveal the molecular processes that underlie diverse diseases, including HIV/AIDS. In addition, genomic analysis can also unveil pharmacogenomic interactions that guide the success and failure of various treatments, including the highly active antiretroviral therapy in HIV patients. It remains unclear how HIV is able to manipulate and subvert host gene machinery before and after Highly Active Antiretroviral Therapy (HAART) in the same individual. In order to define the underlying pharmacogenomic basis of HIV control during HAART and genomic basis of immune deterioration prior to HAART initiation, we performed a genome-wide expression analysis using primary Peripheral Blood Mononuclear Cells (PBMC) derived from 14 HIV+ subjects pre-Highly Active Antiretroviral Therapy (HAART) (time point-1 or TP1) with detectable plasma viremia and post-HAART (time point-2 or TP2) with effective control of plasma viremia (<40 HIV RNA copies/mL of plasma). Genomic RNA extracted from the PBMCs was used in microarray analysis using HT-12V3 Illumina chips. Illumina®BeadStudio Software was used to obtain Differentially Expressed (DE) genes. Only the genes with p value <0.01 and FDR of <5% were considered for analysis. Pathway analysis was performed in MetaCore™ to derive functional annotations. Functionally significant genes were validated by qRT-PCR. Between TP1 and TP2, 234 genes were differentially expressed. During viremic phase (TP1), there was an orchestrated and coordinated up-regulation of immune, inflammation and antiviral genes, consistent with HIV infection and immune activation, which comprised of genes mainly involved in antiviral action of interferons and their signaling. In contrast, the therapy-mediated control phase (TP2) showed systematic down-regulation of these pathways, suggesting that the reduction in plasma viremia with HAART has a considerable influence on reducing the immune activation, which was able to predict the success of anti-HIV therapy. This is the first study to show the feasibility of pharmacogenomic vigilance in anti-HIV treatment setting. New treatment interventions and possibly personalized treatments can be designed through this vigilance. Further, if the targeted genes are sequenced, rapid pharmacogenomic vigilance tools can be developed in predicting the success and failure of treatments and also in designing new generation of prognostic and diagnostic markers.

Biography

Nitin Saksena is a broadly trained Virologist Neurobiologist, Viral Oncologist, Immunologist and with demonstrated leadership in molecular virology, diagnostics, pathogenesis, viral genetics and translational viral-, pharmaco-, onco-, immuno-, neuro-genomics and proteomics with robust record of achievement in translational genomics, sequencing, proteomics, bioinformatics and gene regulation by miRNA. He has longstanding experience in research teaching, supervising, managing and leading large teams. He was trained at the Pasteur Institute, Paris, France and at SUNY, Syracuse, NY, USA in Molecular Virology and Genetics and Headed the Retroviral Genetics Division at the Millennium Institute, Sydney, Australia for 20 years. He has served the Country Advisor for Infectious Diseases and Genomics with the American Medical Global Exchange, Guest Professor at the Shandong Gallo Institute of Virology, Shandong, China and until recently a Visiting Professor at the Beijing Institute of Genomics in Shenzhen, China. Currently, he is a Chief Scientific Officer at IGO, Sydney, Australia and a Professor and International Advisor to the Beijing Institute of Genomics (BGI), China. He has published more than 200 peer reviewed scientific articles and reviews in health sciences that encompass viral/oncogenetics areas of genomics, gene regulation (miRNA), proteomics and diagnostics in the context of infectious/neurologic diseases and oncology.

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