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### Role of cytochrome P450s in mediating the effects of alcohol on HIV pathogenesis

P S Shantanu Rao and Santosh Kumar

University of Tennessee Health Science Center, USA

Compared to general population, drug addiction is highly prevalent amongst HIV positive population. In addition to having an impact on adherence to antiretroviral therapy (ART), several drugs of abuse including alcohol have been shown to exacerbate HIV pathogenesis and decrease ART efficacy. Moderate to heavy alcohol consumption in particular has been identified as a major impediment to optimum HIV care. Cytochrome P450s (CYPs), the major drug-metabolizing enzymes in the body play a critical role in modulating the pharmacokinetic profiles of both ART and commonly abused drugs like alcohol. We hypothesize alcohol mediated changes in expression of CYPs in monocytes/macrophages (major viral target and reservoir), and subsequent increase in oxidative stress, to have a direct impact on HIV replication. Our recent results have demonstrated significant changes in expression of CYPs in U937 monocytic cells following chronic treatment with alcohol and ART. In addition, chronic treatment with alcohol and/or ART resulted in decreased or unchanged expression of major antioxidant enzymes in monocytes. Moreover, chronic exposure to alcohol and/or ART was associated with enhanced production of reactive oxygen species and significant decrease in cell viability. Overall, based on these results, chronic exposure to alcohol (with or without ART) is rationalized to further compromise the immune system and enhance HIV pathogenesis. Further studies are underway to examine the cellular pathways involved in alcohol/ART mediated changes observed in monocytes/macrophages. Results from these studies are expected to yield promising drug targets for therapeutic interventions in HIV positive alcohol users.

#### Biography

P S Shantanu Rao completed his PhD from the Department of Medicinal and Biological Chemistry at the University of Toledo (UT) in Dec 2011 after receiving Bachelor of Pharmacy degree from India. Since then, he had conducted Post-doctoral research/training under the mentorship of Dr. Youssef Sari (UT; 01/12-03/14) and Dr. Santosh Kumar (UTHSC; 03/14-current). His graduate and postdoctoral works have resulted in 7 peer-reviewed research articles (4 first author), 4 review articles, and 1 book chapter. Currently, four other research/review articles (3 first author) are being reviewed for publication by various scientific journals.

[prao3@uthsc.edu](mailto:prao3@uthsc.edu)

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