Pharmacovigilance-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference and Exhibition on
Pharmacovigilance & Clinical Trials
November 18-19, 2013 Hilton San Antonio Airport, USA

Improving the bioavailability of the drugs in GI tract by modulating the epithelial targets

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Abstract

The role of gastrointestinal functions mediated by epithelial targets and their further implication on reducing the inflammation by increasing the bioavailability of the drugs in inflammatory bowel diseases (IBD) is poorly understood. Patients with active inflammation have been associated with reduced expression as well as function of drug transporter proteins so its capacity to fight the xenobiotic challenges. More over this problem is potentiated when the patients are administered with the medications and several those medications are the substrates of these drug transporter proteins. Previously we reported that Jak3, a non-receptor tyrosine kinase expressed in the intestinal epithelial cells interact with the actin binding protein villin in a IL2 dependent manner and facilitates the wound repair process in GI tract. Here we determined the post translational modification of the drug transporter protein breast cancer resistant protein (BCRP) by Jak3 that responsible for enhancing its surface expression and to improve its capacity to fight xenobiotic challenges during inflammation. For this we used the Jak3-, BCRP- and β-catenin-expressing Intestinal epithelial cell line HT-29 CL19a and Caco-2 (which duplicate the intestinal model) as well as the wild type and Jak3 knockout mice model. Our results show that drug transporter protein BCRP is phosphorylated by Jak3 and this modulation at post translational level increases its surface expression as well as function restoring the bioavailability of the drugs. Overall, our study will address the major disease-selective mechanisms that could be utilized to develop novel therapeutic strategies to prevent inflammation and improve wound healing in IBD.

Biography

Jayshree Mishra has completed her Ph.D. from Indian Institute of Technology Kharagpur, India in 2005 and postdoctoral studies from University of Tennessee Health Science Center. Since 2008 she is holding a position of Research Scientist at Texas A &M Health Science Center. She has received several national and international awards and published more than 10 papers in reputed journals and one patent to her credit.