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Evaluation of functional drug efflux for ocular drug deliveryPradeep K. Karla and Anne-Marie Ako-Adouno
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Statement of the Problem: Cornea is major barrier for topical drug delivery. Study aims to qualitatively and quantitatively assess the molecular and functional expression profiles of multidrug resistance associated proteins 1-9 (MRPs 1-9), P-glycoprotein (P-gp), and breast cancer resistance protein (BCRP) in the prominent corneal epithelial cell lines, Statens Serum Institut Rabbit Corneal epithelial cells (SIRC) and Transfected Human Corneal Epithelial Cells (HCEC-T).

Methodology & Theoretical Orientation: Two cell lines include SIRC and Simian vacuolating virus 40 (SV-40) (the model for HCEC-T) were employed. Qualitative geneexpression study was performed by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). Gene expression quantification was analyzed using Quantitative Real Time PCR (qPCR). Functional activities of the transporters in both cell lines were tested using various concentrations of MRP substrates (acyclovir: ACV), P-gp and MRP substrate (erythromycin: ERY), and BCRP substrate (mitoxantrone: MTX) in presence and absence of MRP inhibitor (MK-571), P-gp inhibitor (PGP-4008), and BCRP inhibitor (fumitremorgin C).

Findings: RT-PCR gene expression studies indicated the presence of all known MRPs (MRP1-9), P-gp, and BCRP in both SIRC and SV-40 cells. Indeed, qPCR data indicated distinct variations in quantitative transporter expression profiles. The gene expression levels for transporters (MRP3, MRP4, MRP5, MRP6, Si-MRP7, MRP7, MRP8, and MRP9) were found significantly higher in SV40-HCEC compared to SIRC. Interestingly, the expression levels for MRP1, BCRP and P-gp were statically significant higher in SIRC compared to SV-40. Strong correlation was observed between the functional drug uptake profiles of HCEC-T and SIRC.

Conclusion & Significance: Qualitative and quantitative data of cells has confirmed the presence of new major MRPs (Si-MRP7, MRP7, MRP8 and MRP9) in both SIRC and HCEC cells in addition to already established transporters in these cell lines. MRPs are major efflux transporters presence in corneal epithelium cells leading to limit drug absorption.

Biography

Dr. Pradeep Karla currently works as an Associate Professor in the Department of Pharmaceutical Sciences. Dr. Karla completed Bachelors in Pharmacy with distinction from Nagarjuna University, India and interdisciplinary Ph.D. in Pharmaceutical Sciences from University of Missouri in Kansas City. Dr. Karla is the recipient of NIH funded KL2 grant and worked as NIH K Grant research fellow and Principal Investigator. Dr. Karla has been the recipient of AACP New Investigator Grant, Ecobiotix Industrial Grant and Bridge Research Grant. Dr. Karla was the recipient of teaching with technology award at Howard University. Dr. Karla's research on drug efflux transporters was cited as one of the eight promising research findings by American Association of Colleges of Pharmacy.

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