KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 2288

"Can epigenetics modulate steroid resistance in Nephrotic Syndrome?"

Rashmika Singh, Harshit Singh, Saurabh Chaturvedi, Kritika Singh
Department of clinical Immunology, sanjay gandhi post graduate institute of medical sciences, India

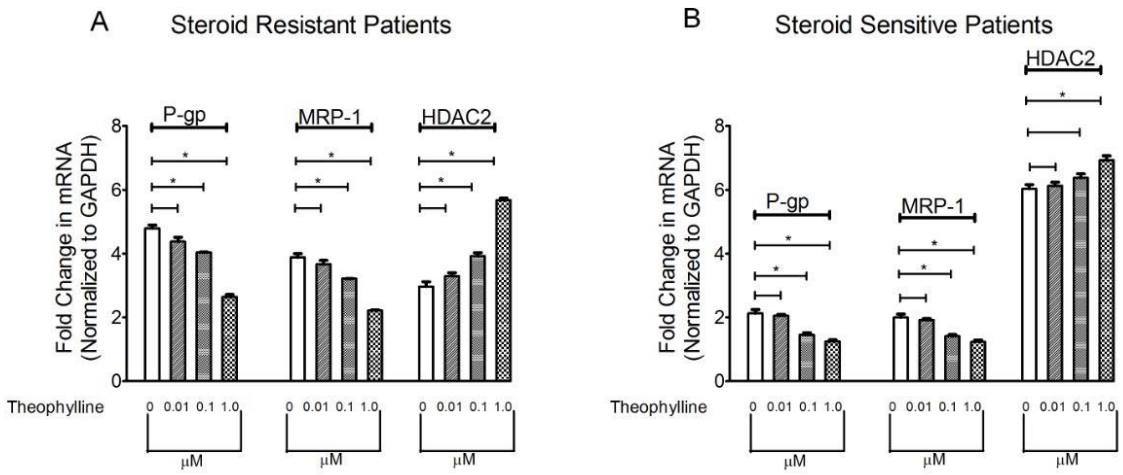
Objectives: Objective : To evaluate the effect HDAC 2 on P-gp and MRP-1 expression.

Methods: 40 subjects enrolled in the study out of which 28 were steroid-sensitive nephrotic syndrome (SSNS), and 12 were steroid-resistant nephrotic syndrome (SRNS) patients. mRNA expression was analyzed on peripheral blood mononuclear cells (PBMCs) in SRNS patients (mean age 9.43±3.8 years), SSNS patients (mean age 8.54±3.5 years). PBMCs were treated with 1μM of Theophylline (HDAC2 stimulator) and 0.8μM of Trichostatin A (HDAC2 inhibitor) for a period of 48 hours. qPCR was performed using SYBR green PCR technology with SYBR premix relative gene expression levels were calculated and normalized to the corresponding levels of housekeeping gene (GAPDH).

Results: Expression of P-gp (5.79±0.70 v/s 3.13±0.52, $p<0.0001$) and MRP-1 (3.99 ±0.98 v/s 1.99 ±0.51, $p<0.0001$) on PBMCs was increased in SRNS compared to that of SSNS. HDAC2 mRNA levels were significantly decreased in SRNS patients compared to SSNS patients (2.97 ± 0.15 v/s 6.02 ± 0.13, $p<0.0001$).
Theophylline culture for 48 hours decreased mRNA levels of P-gp and MRP-1 in PBMCs of SRNS with maximal induction at 1μM (fold change 3.65 and 2.21, *$p<0.0001$) However HDAC2 mRNA expression increased significantly (fold change6.67, *$p<0.0001$). In SSNS patients P-gp and MRP-1 mRNA expression decreased at1μM (fold change 1.90, 1.24, *$p<0.0001$) while the mRNA expression was increased (fold change 6.93, *$p<0.0001$).
TSA culture for 48 hours increased mRNA levels of P-gp and MRP-1 in PBMCs of SRNS with maximal induction at 0.8μM (fold change 7.51, 6.31, *$p<0.0001$) and significantly decreased the level of HDAC2 (fold change1.50, *$p<0.0001$) similarly in SSNS patients P-gp and MRP-1 mRNA expression increased at 0.8μM (fold change 3.49, 3.35, *$p<0.0001$) and HDAC2 decreased (fold change2.53, *$p<0.0001$) at 0.8μM.

Conclusions: We observed HDAC2 regulates P-gp and MRP-1 efflux-pumps, Inducer of HDAC2 may be a probable treatment stratergy for patients of INS

effect of thephylline on P-gp and MRP-1 expression



effect of tricostatin on P-gp and MRP-1 expression