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## **Epigenetic regulation of steroid resistant in childhood Nephrotic Syndrome**

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**Objectives:** P-glycoprotein (P-gp) over expression in peripheral blood mononuclear cells (PBMCs) has been reported in patients with steroid resistant nephrotic syndrome (NS). Glucocorticoids suppress NFκB-associated co-activator activity by deacetylation of histones by enzyme histone deacetylase (HDAC)-2. Interaction between HDAC2 activity and P-gp expression in childhood NS patients is not clear.

To evaluate the role of HDAC2 and P-gp expression on PBMCs and steroid responsiveness in patients with childhood NS.

**Methods:** 46 patients were recruited at baseline (n = 46) (before initiating steroid therapy); After six weeks of steroid therapy, 34 patients achieved remission (SSNS n=34 mean age, 7.96±3.90), whereas twelve patients were resistant to steroids (SRNS, n=12, mean age 10.00±3.55). mRNA expression of HDAC2 and P-gp/MRP-1 and functional analysis of P-gp and enzymatic activity of HDAC2 were analyzed at baseline, at 6 weeks of steroid treatment and at the time of relapse, respectively.

**Results:** The expression of P-gp mRNA was significantly lower in subjects (n=34) who achieved remission at 6-weeks of steroid therapy as compared to baseline and those who were resistant (n=12) to steroids (P<0.005). Similarly, expression of HDAC2 mRNA was significantly higher at baseline and at remission following 6-weeks of steroid therapy as compared to their expression in those who were resistant to steroids (P<0.005). The function of P-gp was significantly lower in NS patients who achieved remission after 6-weeks of steroid therapy as compared to baseline (p<0.005) and those who were resistant to steroid therapy (p<0.005). The enzymatic activity of HDAC2 was significantly higher in SSNS patients as compared SRNS patients at 6-weeks of steroid therapy (p<0.005).

**Conclusions:** The expression and function of P-gp and HDAC2 may affect steroid response in NS patients. Combined therapy of steroids with P-gp inhibitor and/or HDAC2 inducers may have rationale in the management of steroid resistant NS patients.

Gene expression of P-gp and HDAC2

