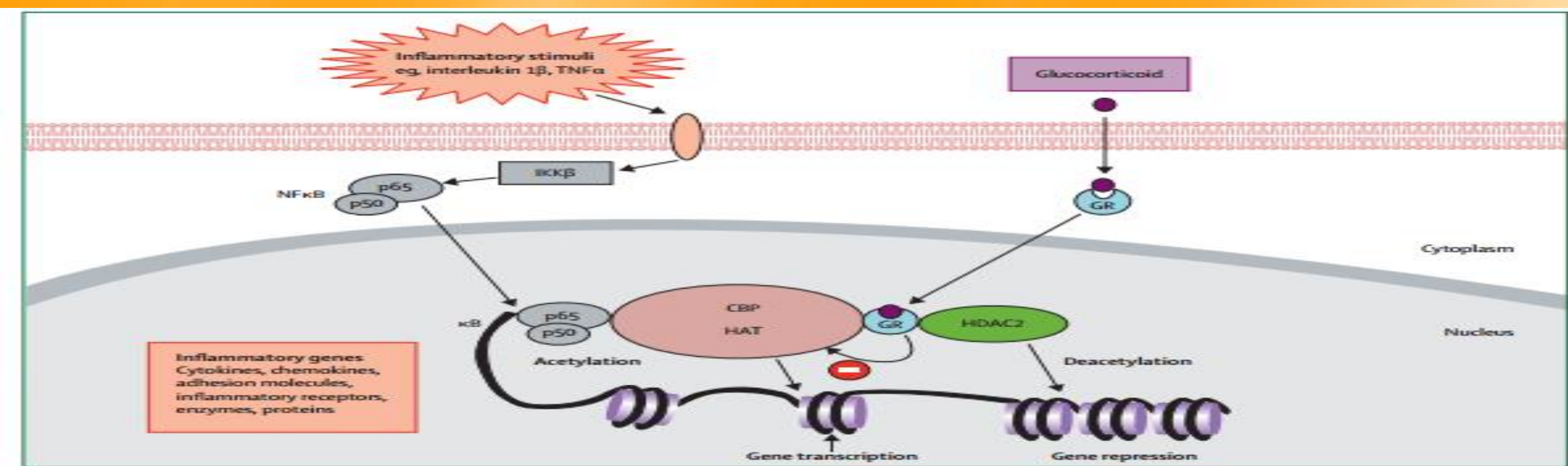


ROLE OF HISTONE DEACETYLASES 2 AND GLUCOCORTICOID RECEPTOR-BETA IN STEROID RESISTANT CHILDHOOD NEPHROTIC SYNDROME

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OBJECTIVES

- Glucocorticoid (GCs) therapy remains important in improving the prognosis of patients with idiopathic childhood nephrotic syndrome (INS)¹
- GCs interact with GCR-alpha, which acts as a ligand dependent transcription factor. GCR-beta, a GCR isoform that does not bind steroids, has been shown to be elevated under SR conditions in various other diseases²



Therefore we hypothesized the following objectives

- To evaluate HDAC-2 expression via immunohistochemistry assay
- Assess the HDAC2, GCR -alpha, GCR-beta mRNA expression in SR INS.

GRAPHS AND FIGURES

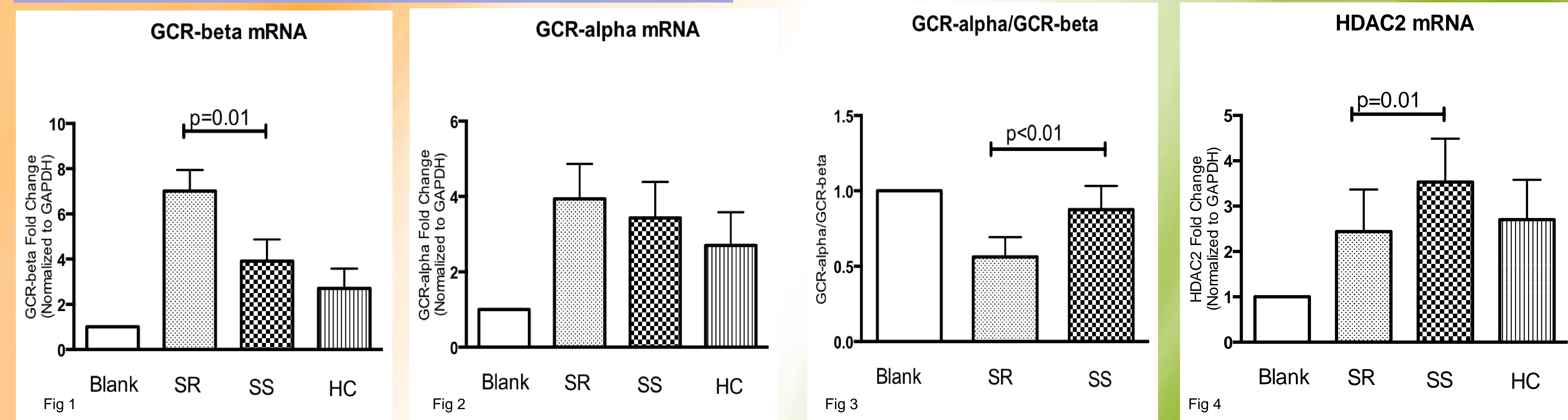


Fig 1: GCR-beta gene expression, Fig 2: GCR-alpha gene expression, Fig 3: Ratio of GCR-alpha/ GCR- beta, Fig 4: HDAC2 gene expression

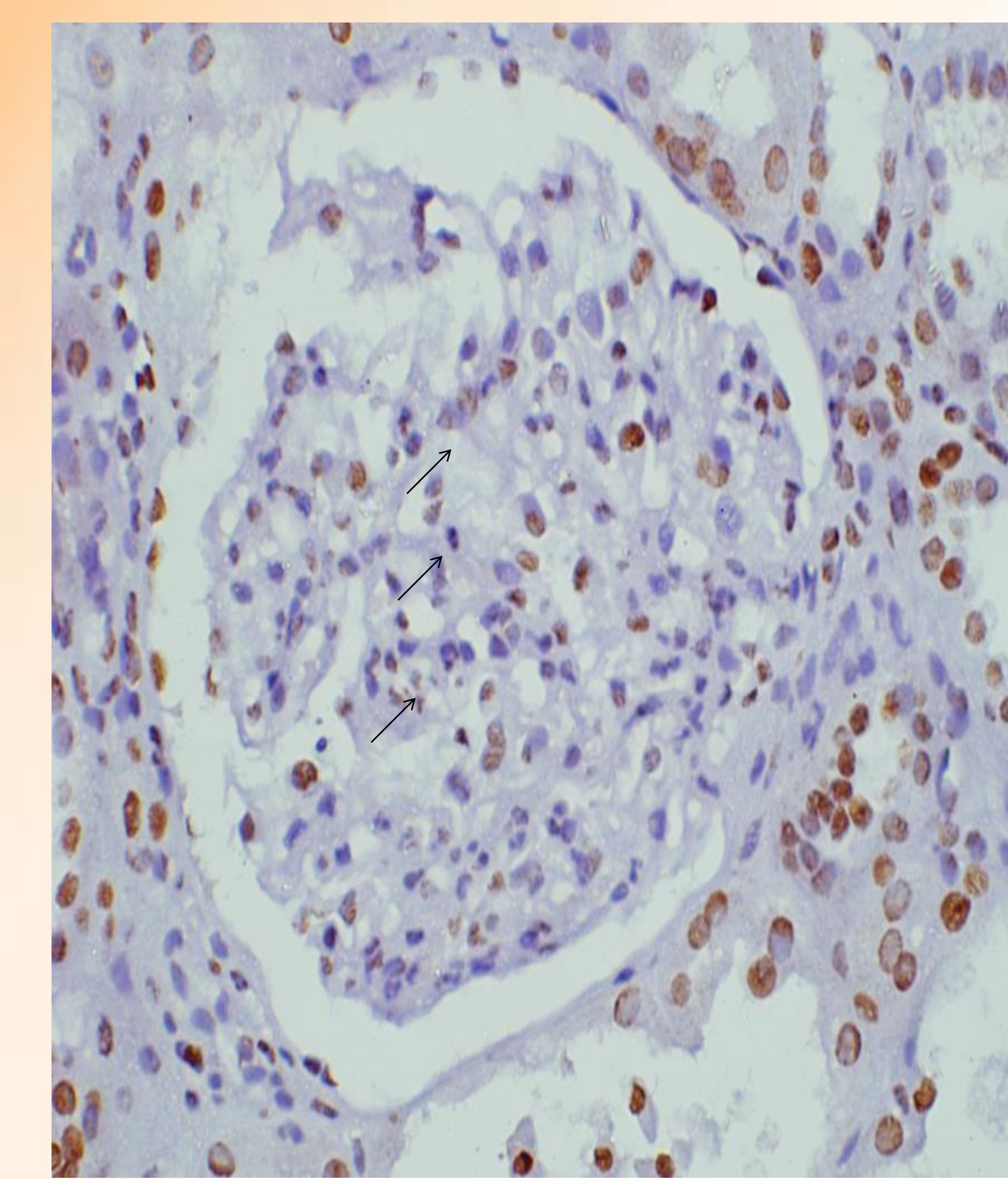


Fig 5: HDAC-2 staining of steroid resistant,

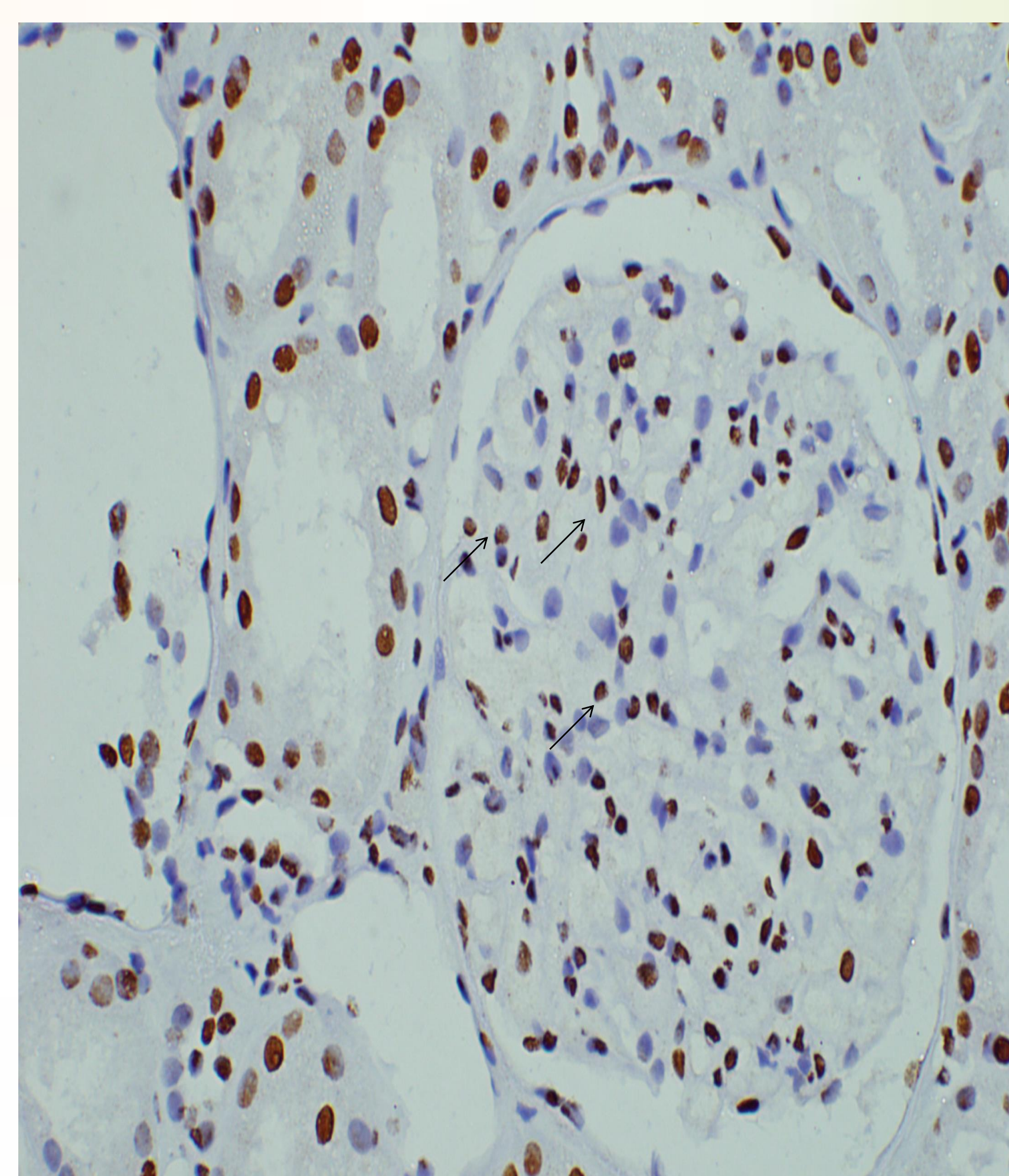


Fig 6: HDAC-2 staining of Healthy Control

RESULTS

- ✓ Demographic significant difference were found in S.Albumin (SSNS=2.87±.98, SRNS=2.27±.79, p=0.012) and proteinuria (SSNS=13.18±3.09, SRNS=284±193.45, p<0.001)
- ✓ HDAC2 nuclear expression in healthy control samples was significantly higher as compared to the nuclear expression of HDAC2 of SR patients (86.67%), (p=0.002).
- ✓ HDAC2 mRNA expression was significantly decreased in PBMCs from SR patients (p=0.01) as compared to that of SR patients. GCR-beta (p=0.01), but not GCR-alpha, mRNA expression was significantly increased in PBMCs from SR patients, resulting in a significantly lower molar ratio of GCR-alpha to GCR-beta (p<0.01).

CONCLUSIONS

- ❖ PBMCs from SR patients have higher baseline GCR-beta mRNA levels, a lower GCR-alpha/GCR-beta mRNA ratio and lower HDAC2 mRNA levels as compared to SS patients
- ❖ Lower nuclear expression of HDAC2 in SR patients suggests use of inducers like theophylline and others, which might lead to restoration of glucocorticoid response and better management of patients.

REFERENCES

1 Narayan Prasad et al. Differential alteration in peripheral T-regulatory and T-effector cells with change in P-glycoprotein expression in Childhood Nephrotic Syndrome: A longitudinal study PMID: 25661194

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