

## **Eighth Paper**

**Title:** The Ifng antisense RNA 1 (IFNG-AS1) and Growth Arrest-Specific Transcript 5 (GAS5) are Novel Diagnostic and Prognostic Markers Involved in Childhood ITP.

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### **Abstract:**

**Background/aim:** *IFNG-AS1* is a long noncoding RNA that works as an enhancer for the Interferon-gamma (IFN- $\gamma$ ) transcript. *GAS5* (growth arrest-specific 5) is a lncRNA that is associated with glucocorticoid resistance. Aberrant expressions of *IFNG-AS1* & *GAS5* are directly linked to numerous autoimmune disorders but their levels in childhood ITP are still obscure. This study aims to elucidate expressions of target lncRNAs in childhood ITP and their association with pathophysiology and clinical features of the disease as well as their association with types and treatment responses. **Method:** The fold changes of target lncRNAs in blood samples from children with ITP and healthy controls were analyzed using quantitative real-time PCR (qRT-PCR).

**Results:** There were overexpressed lncRNAs *IFNG-AS1* and *GAS5* in serum of childhood ITP patients [(median (IQR) =3.08 (0.2-22.39) and 4.19 (0.9-16.91) respectively, Also, significant higher *IFNG-AS1* and *GAS5* ( $p<0.05$ ) were present in persistent ITP (3-12 months) [ median (IQR)= 4.58 (0.31-22.39) & 3.77 (0.87-12.36) respectively] or chronic ITP ( $> 12$  months) [ median (IQR)= 5.6 (0.25-12.59) & 5.61 (1.15-16.91) respectively] when compared to newly diagnosed  $< 3$  months patients [*IFNG-AS1* median (IQR)=1.21 (0.2-8.95), and *GAS5* median (IQR)=1.07 (0.09-3.55)]. Also, significant higher lncRNAs

*IFNG-ASI* and *GAS5* were present in patients with partial response to treatment [*IFNG-ASI* median (IQR)= 4.15 (0.94-19.25), and *GAS5* (median (IQR)= 4.25 (0.81-16.91)] or non-response [*IFNG-ASI* median (IQR)= 4.19 (1.25-22.39) and *GAS5* median (IQR)= 5.11 (2.34-15.27)] when compared to patients who completely responded to treatment (*IFNG-ASI* median (IQR)= 2.09 (0.2-14.58) and *GAS5* (median (IQR)= 2.51 (0.09-10.33)). In addition, following therapy, the expressions of *IFNG-ASI* and *GAS5* are significantly negatively correlated with platelet count.

**Conclusion:** Findings suggest that lncRNAs *IFNG-ASI* and *GAS5* are novel diagnostic and prognostic genetic markers for childhood ITP that can aid in a precise prediction of the disease's progress at the time of diagnosis and could be a useful tool for treatment planning.

**Keywords:** *IFNG-ASI*, *GAS5*, Childhood ITP, qRT-PCR, Diagnosis, Prognosis, Biomarkers.