INDOLEAMINE 2,3-DIOXYGENASE (IDO) ACTIVITY AND REGULATORY T CELLS IN CHILDREN WITH PRIMARY IGA NEPHROPATHY AND HENOCH SCHOENLEIN PURPURA.

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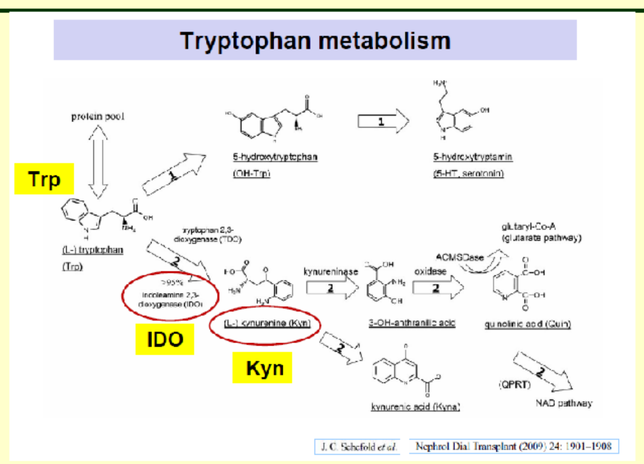
OBJECTIVES

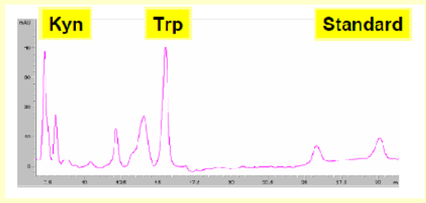
Indoleamine 2,3-dioxygenase (IDO) is an enzyme which catabolizes tryptophan and produces kynurenine (Kyn), a metabolite provided with immunoregulatory activity. IDO-expressing dendritic cells possess potent T cell regulatory properties. Primary IgA Nephropathy (pIgAN) and Henoch Schoenlein Purpura (HSP) are immune-mediated glomerular diseases with similarities but also differences in clinical presentation and outcome in children.



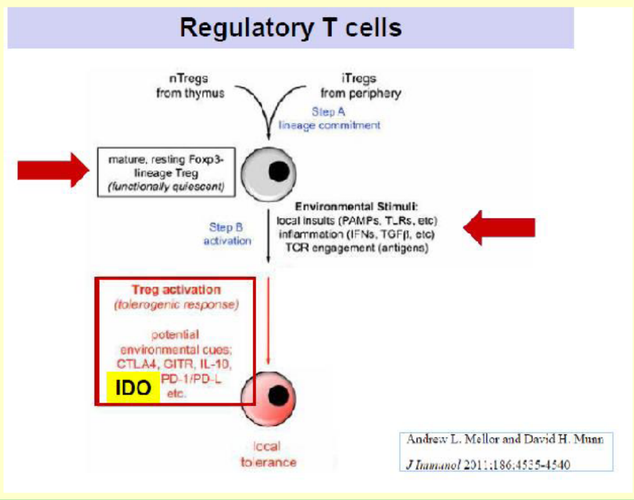
METHODS

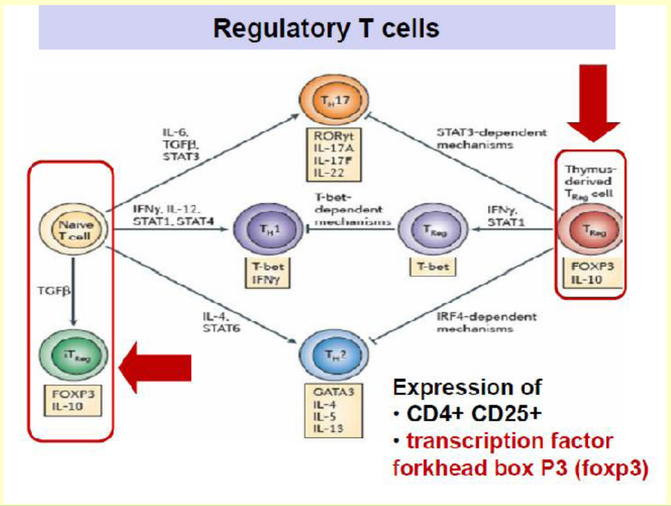
We aimed at investigating IDO metabolites and regulatory T cells (Treg) in 24 children with pIgAN and 23 with HSP (age range 3-14 years) with or without renal involvement; 25 healthy controls (HC) were investigated as well.

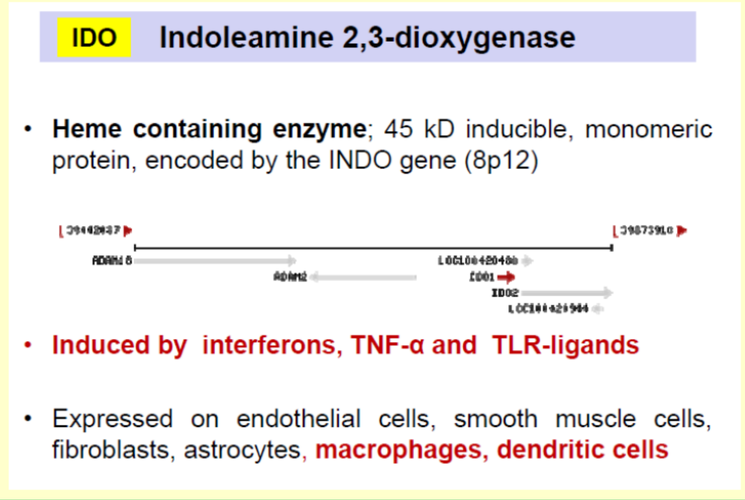
IDO activity was assessed in sera as change in tryptophan (Trp) and its catabolic product kynurenine (Kyn), which were simultaneously determinated using an isocratic RP HPLC method with UV detection. A Kyn/Trp ratio was also calculated.



In mononuclear cells (PBMC) real time PCR (Taqman) was adopted to measure mRNA levels of FoxP3mRNA and TGF-β1mRNA. Results were normalized to Abl gene and expressed as fold increase.

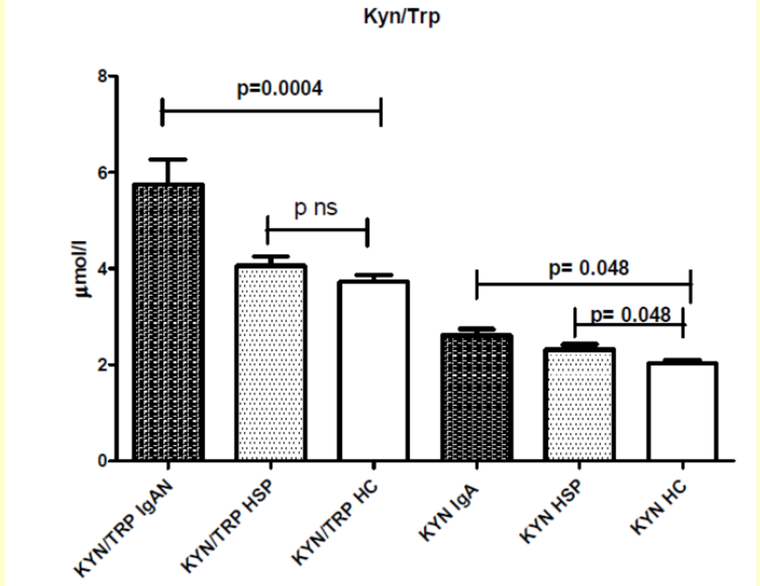


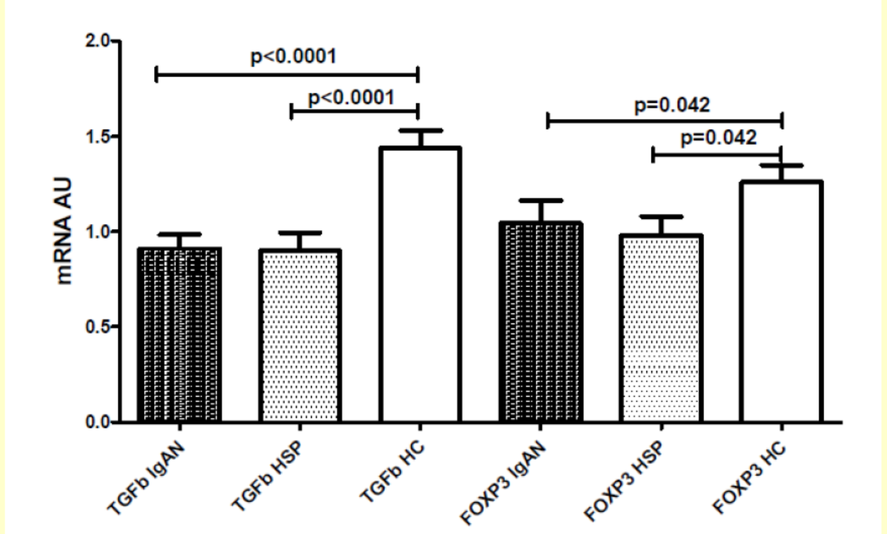




RESULTS

Children with pIgAN and with HSP had significantly increased levels of the Trp metabolite Kyn (pIgAN 2.61 ± 0.72; HSP 2.31 ± 0.54 vs 2.02 ± 0.32 µmol/l; for both diseases P= 0.048 vs HC), while Trp levels were similar to controls. The ratio Kyn/Trp, expression of IDO activity, was significantly increased in pIgAN only (5.74±2.27, p=0.0004). FoxP3 mRNA and TGFβ1 mRNA transcriptional levels were significantly depressed (FoxP3 mRNA: pIgAN 0.94 ± 0.19; HSP 0.85 ± 0.07; HC 1.26 ± 0.09, for both diseases p=0.042 vs HC) (TGFβ1mRNA pIgAN 0.85 ± 0.09; HSP 0.91 ± 0.07; HC 1.44 ±0.09, for both diseases p<0.0001). There was a significant inverse correlation between Kyn levels and TGFβ1mRNA values (P= 0.023).





CONCLUSIONS

Children with pIgAN and HSP present with a similar reduced expression of regulatory T cells transcription factors, while those with pIgAN have also a selective higher activity of IDO enzyme which regulates T cells reprogramming.

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