Background: There is an ongoing effort to elucidate the molecular pathways that are key to kidney injury in lupus nephritis (LN). One approach is to study the transcriptome utilising kidney tissue obtained during diagnostic renal biopsy [1]. In clinical practice the most common tissue that is surplus to diagnostic requirements is formalin-fixed paraffin-embedded (FFPE) tissue. However, due to RNA degradation, transcriptomic analysis has been sub-optimal and challenging using standard procedures. The NanoString technology platform has the advantage that reliable detection of transcripts can be achieved even with degraded RNA. In this study we explored the utility of NanoString technology in identifying transcripts in RNA isolated from archival FFPE kidney biopsy sections in a cohort of patients with LN.

Objectives: To explore the utility of the NanoString platform in elucidating a renal transcriptomic signature in formalin-fixed paraffin-embedded Lupus Nephritis kidney biopsy tissue.

Methods: We utilised well defined Class III (n=11); Class IV (n=22) and Class V (n=24) LN FFPE kidney biopsies from female patients attending the Imperial College Healthcare NHS Trust. We excluded biopsies with mixed lesions or chronic kidney biopsy tissue. Transcriptomic data passing NanoString nSolver quality control metrics were obtained from all sections. Notably sections included biopsies up to 16 years old (range: 1-16 years). Kidney biopsies from patients with Thin Basement Membrane (TBM; n=14) disease were used as controls. Six 10 micron thick sections were obtained from each biopsy and RNA isolated using the Qiagen RNeasy FFPE Kit. 100 micrograms of RNA was used for the detection of transcripts. We used the NanoString PanCancer immune profiling panel (770 transcript probes) and an additional 30 custom designed probes, enabling us to detect 800 transcripts, including 40 reference genes. Transcript analysis was performed according to manufacturer’s instructions using the NanoString nSolver software. When analysing differential gene expression (DGE) we used Benjamini-Hochberg adjustment to account for multiple testing. The threshold for statistical significance was an adjusted P value of 0.05 (5% false discovery rate).

Results: Statistical significance was an adjusted P value of 0.05 (5% false discovery rate). Benjamini-Hochberg adjustment to account for multiple testing. The threshold for us to detect 800 transcripts, including 40 reference genes. Transcript analysis of OPN (osteopontin) and FN1 (fibronectin-1) in proliferative (Class III and IV) but not Class V LN samples. When we performed DGE analysis using TBM as the baseline we detected significantly increased expression across the classes (Class III = 202; Class IV = 357 and Class V = 237 differentially expressed transcripts).

Conclusion: We have successfully identified transcriptomic signatures in RNA samples derived from a relatively large cohort of FFPE LN samples. Consistent with published reports we could detect a type I IFN signature in the LN kidney tissue [1]. Consistent with a recent study [1], we detected increased expression of OPN (osteopontin) and FN1 (fibronectin-1) in proliferative (Class III and IV) but not Class V LN. We are now performing clinical correlations to determine if the differentially expressed transcripts are clinically informative.

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