Unraveling the Cellular Landscape in Lupus Nephritis: A Combined Approach using Hyperion Mass Cytometry and 10X Visium Cytassist Spatial Transcriptomics

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Résumé

Background: Lupus nephritis (LN), a severe systemic lupus erythematosus (SLE) complication, affects almost half of SLE patients, leading to end-stage renal disease in 10.1% and death in 5% of cases within a decade. A crucial role in LN pathogenesis is played by B cells and the B-cell activating factor (BAFF) pathway, as exemplified by the proven therapeutic efficacy of belimumab, a BAFF inhibitor, in LN. Yet, the intricate interplay within the renal, immune, and vascular infiltrate in the kidney of SLE patients is poorly understood. To bridge this gap, we combined the Hyperion mass cytometry system, enabling deep-phenotyping of tissue with more than 40 markers, with the 10X Visium Cytassist spatial transcriptomics, to offer an unprecedented view of the cellular landscape within LN kidney biopsies.

Methods: Kidney biopsies were obtained from 8 patients with class III or IV LN. From each biopsy, we prepared two consecutive slides to enable the superimposition of data from both analytical techniques. We applied the 10X Visium Cytassist procedure for spatial transcriptomics in order to gain insight on the renal tissue organization and heterogeneity in an unbiased approach. In parallel, we utilized Hyperion mass cytometry to perform deep phenotyping of cellular infiltrate in tissues, this time with an emphasis on the B cell and BAFF pathways.

Results: We have successfully performed the 10X Visium Cytassist spatial transcriptomics technique, including quality sample assessments and library preparations. Libraries are currently awaiting sequencing. Additionally, we validated the whole Hyperion panel, encompassing 45 markers. We then plan to overlay data from both technologies: this combined approach is expected to yield deeper insights into both the phenotypic markers and the transcriptomic programs of cells, as well as their interactions within the LN tissue microenvironment.

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Conclusion: The innovative combination of spatial transcriptomics and imaging mass cytometry promises a comprehensive, high-resolution exploration of the immune landscape in class III and IV LN, with a special focus on the B cell and BAFF pathways. This study might significantly enhance our LN pathophysiology understanding and help optimize the use of belimumab and other targeted strategies.

Mots-Clés: Systemic Lupus Erythematosus, spatial transcriptomics, imaging mass cytometry, lupus nephritis