P-21: Molecular Profiling of Inflammatory Nasal Polyps for Early Recurrence Prediction

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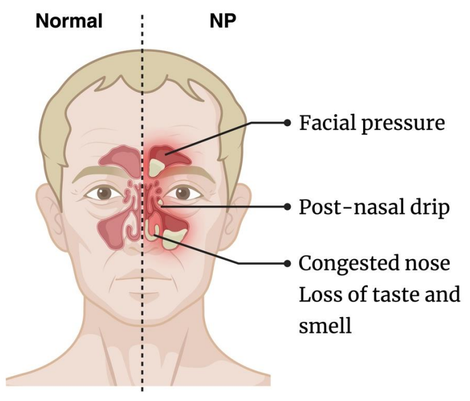
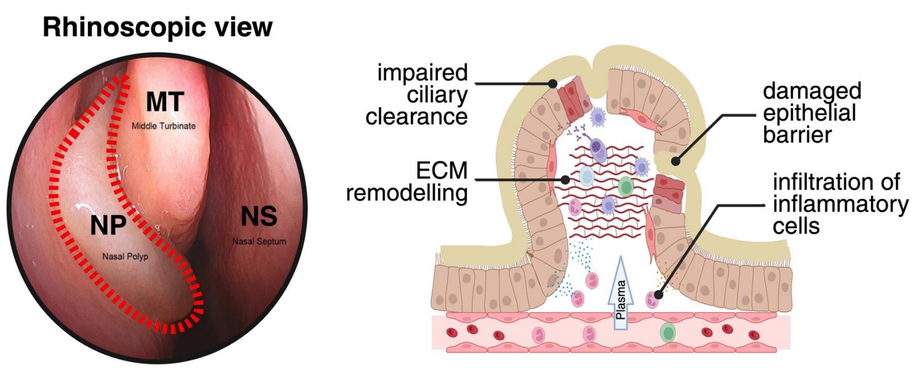
Nasal Polyps (NPs) – A Chronic Disease in Need of Solution

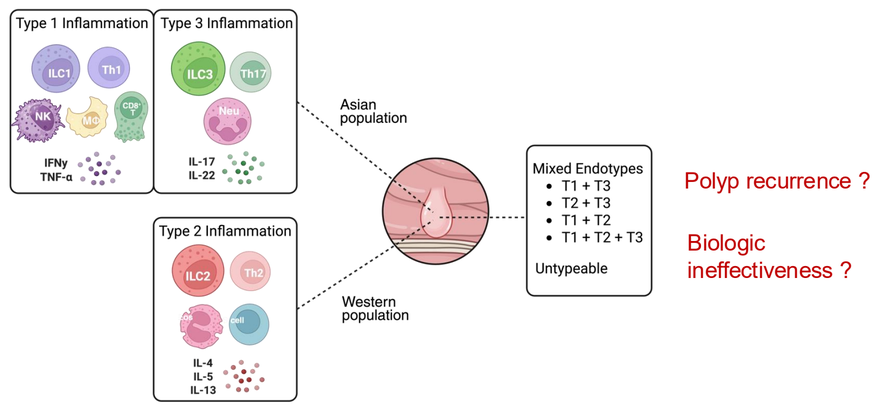
Clinical manifestation of NP



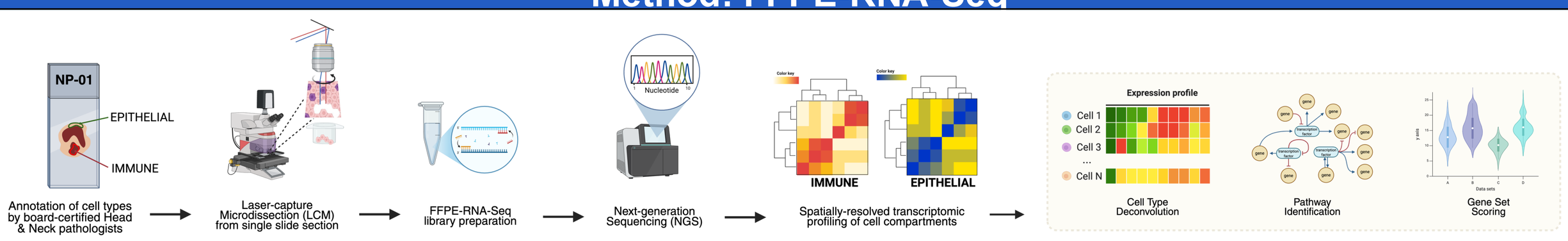
Rhinoscopy view (left) and schematic (right) illustrating **hallmark pathological features of NP**



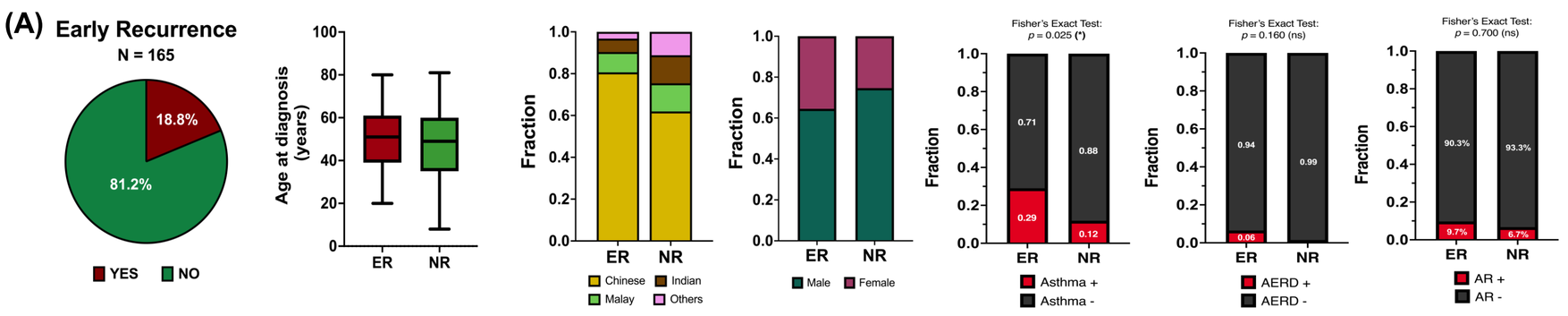
NP immune microenvironment **remains poorly characterized** and may account for **frequent polyp recurrence + poor biologic response**

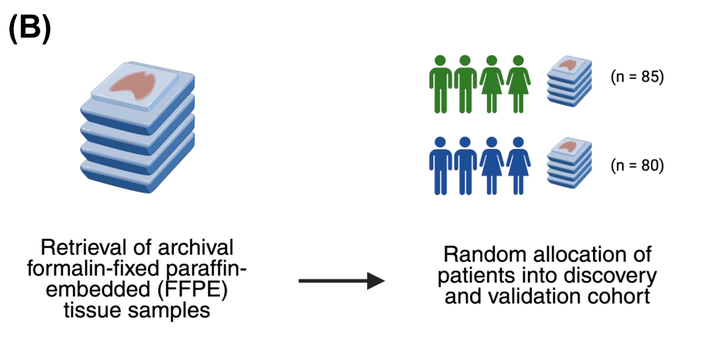


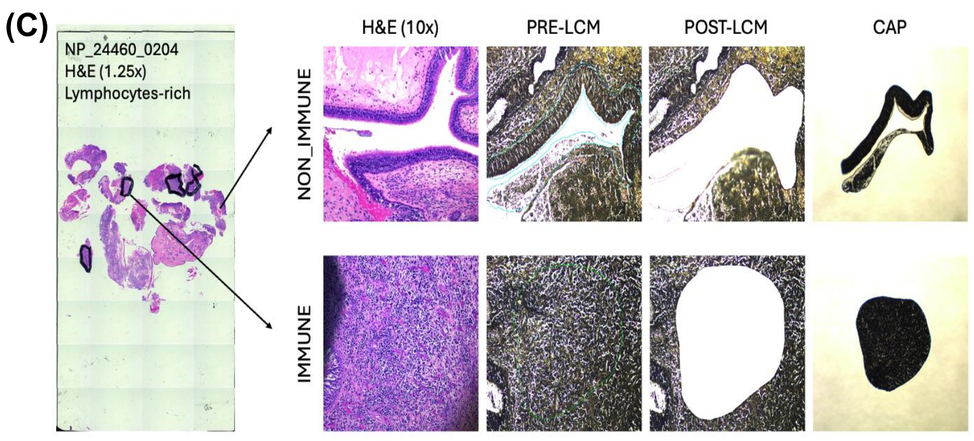
Method: FFPE-RNA-Seq

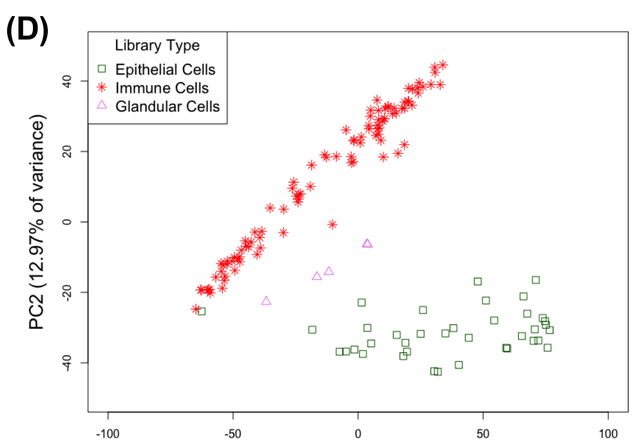


Results









(A) Baseline patient demographics and clinical parameters for this retrospective cohort (n = 165). ER = early recurrence

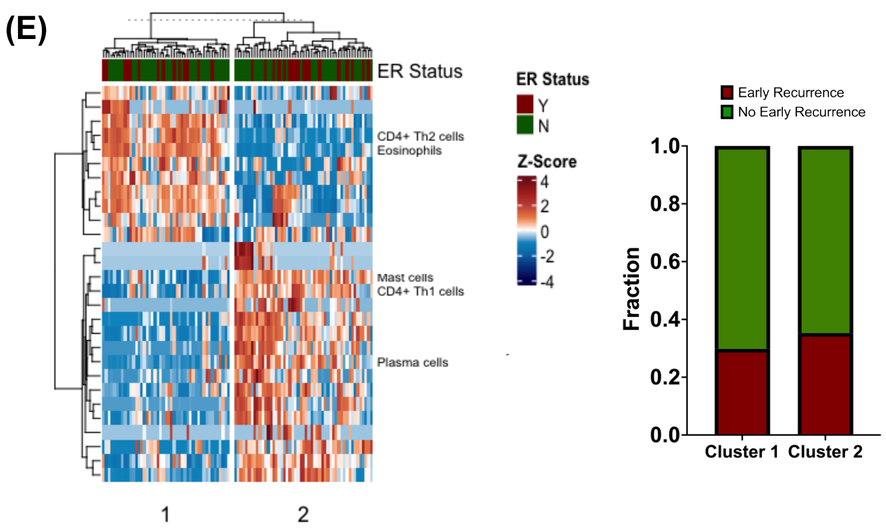
(B) FFPE tissue blocks of patients were retrieved from NUH TR department for tissue sectioning. Patients were randomly allocated into discovery arm (n = 85) and validation arm (n = 80).

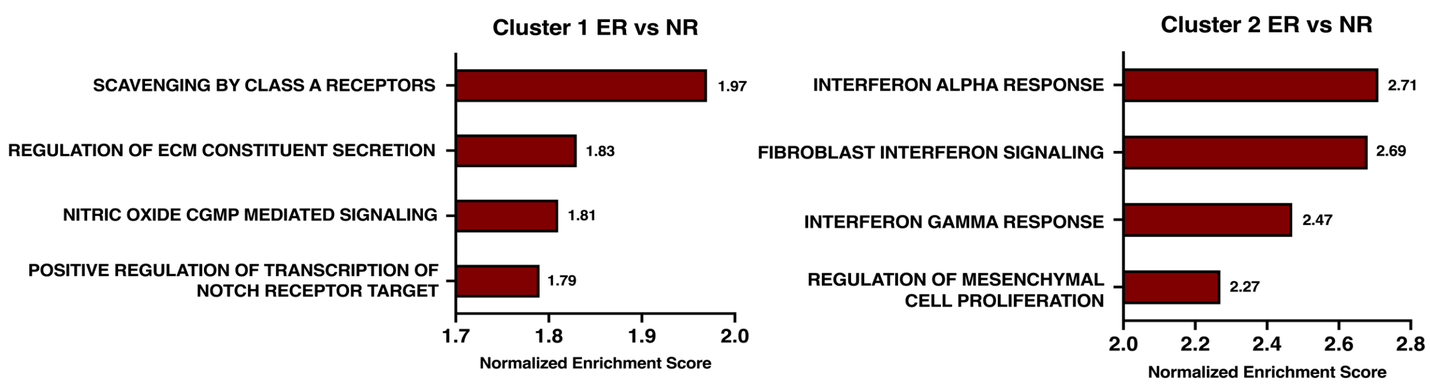
(C) Laser-captured microdissection of different annotated compartments found on each single tissue section for FFPE-RNA-Seq.

(D) Principal component analysis (PCA) of gene expression libraries from dissected compartments, showing distinct clustering among libraries of the same tissue type.

Aim 1. Characterize inflammatory microenvironment landscape of NPs

Aim 2. Identify biological processes associated with ER

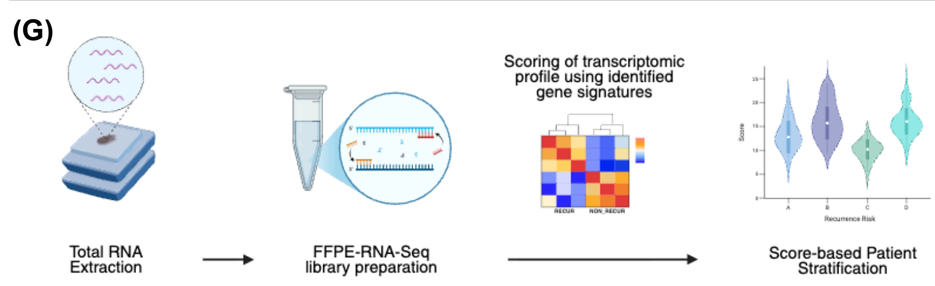


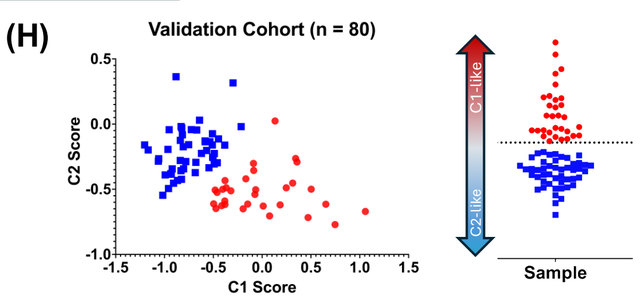


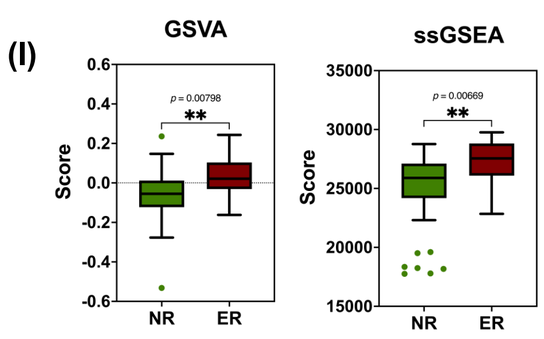
(E) Unsupervised hierarchical clustering of xCell-derived immune scores identified two functionally distinct immunological endotypes in NP tissue from the discovery arm (n = 80). Cluster 1 resembles conventional type 2-skewed inflammatory response, characterized by the enrichment of T_h2 $CD4^+$ T cells and eosinophils, while Cluster 2 represents a hybrid inflammatory phenotype in which elements of both type 1 (T_h1 $CD4^+$ T cells) and type 2 inflammation (mast cells, plasma cells) co-exist. Neither clusters were significantly associated with ER.

(F) Top biological processes (as annotated by Gene Ontology) enriched in immune microenvironment of NP patients in the ER group relative to non-NR (NR) group, for both Cluster 1 and Cluster 2 polyps.

Aim 3. Develop scoring approach to stratify patients by their polyp immune profile + risk of ER







(G) Schematic illustrating bulk RNA profiling of NP from the validation arm (n = 80)

(H) Use of cell-type signature score approach to determine the inflammatory cluster types of NPs from validation arm (n = 80). Higher score represents greater likeliness of cluster characteristics.

(I) Use of preliminary early recurrence gene set (440 genes) to score bulk transcriptomic profile of NPs from patients with ER and no ER in the validation arm using both gene set variation analysis (GSVA) and single-sample gene set enrichment analysis (ssGSEA) algorithm.

Discussion + Future Directions

We provided **extensive characterization of the inflammatory clusters** identified within the largest cohort NPs to-date. We also provided proof-of-concept on the potential utility of gene set scoring approach as a clinical tool to **identify high-risk NP patient based on their recurrence risk** and adopt precision medicine approach that **match patients based on their immune profile to the right treatment.**

Looking ahead, we plan to expand our research **by incorporating additional clinical cohorts across more diverse patient populations** to enhance the robustness of our signature.

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