TRANSCRIPTOMIC AND IMMUNE LANDSCAPE OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS REVEALS PHENOTYPE-SPECIFIC PROGRESSION PROFILES

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Transcriptomic and microenvironmental profiling of 135 surgically resected intraductal papillary mucinous neoplasms reveals distinct molecular and immune characteristics across gastric, intestinal, and pancreatobiliary phenotypes.

KEY POINTS

- Among 420 microdissected IPMN regions, intestinal phenotype lesions showed enrichment for cell division and proliferation pathways with significantly higher Ki67 (mean 24% versus 6% in gastric, $p<0.0001$) and an immune-cold profile irrespective of dysplasia grade.
- Gastric phenotype IPMNs demonstrated overexpression of immune response pathways with significantly higher CD4 and CD8 T cell infiltration compared to intestinal samples, independent of dysplasia grade.
- Pancreatobiliary phenotype lesions (all high grade) displayed the highest tumor microenvironment infiltration including active fibroblasts, regulatory T cells, M2 macrophages, and neutrophils, suggesting an immunosuppressive landscape.
- Mixed phenotype IPMNs (19% of resections) tended to cluster independently on transcriptomic analysis, with 8 of 22 cases showing a common clonal origin by DNA sequencing.
- This work may inform development of phenotype-specific biomarkers and surveillance strategies for IPMN lesions with currently unpredictable progression potential.

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