[BIOINFO 2025]

Single-nucleus multiome profiling of advanced colorectal polyps suggests putative precancerous epithelial subsets

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Advanced colorectal polyps represent a major class of precancerous lesions in the colon and rectum. They can easily enter the malignant stage, which forms colorectal cancer, one of the leading causes of death worldwide. Characterizing the transcriptional states within advanced polyps is essential for understanding the early steps of tumor initiation and prevention. We performed 10X Genomics single-nucleus multiome sequencing of advanced colorectal polyps from seven Korean donors. We analyzed single-nucleus chromatin accessibility profiles and single-nucleus transcriptomes of 28,448 nuclei across the seven patients. Following quality control and integration, the majority of nuclei were annotated as epithelial, with smaller populations of immune, stromal, and enteric neuronal cells. We focused on epithelial cell heterogeneity, which showed the greatest diversity and may be particularly relevant to early malignant transformation. The stem-like and colonocyte-like epithelial subtypes exhibited typical features of a precancerous state. The stem-like cells displayed stemness-related programs, while the colonocyte-like cells showed elevated expression of genes linked to epithelial barrier function and immune responses. These features suggest that these epithelial subsets may represent the microenvironment transition in adenoma-carcinoma. The identified markers may serve as biomarkers of the precancer-cancer continuum. These findings provide potential implications for early cancer detection and diagnosis.