A173 · Convergent B-cell receptor sequence features point toward shared antigen targets in colorectal cancer

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Colorectal cancer (CRC) is the second leading cause of cancer-related mortality worldwide. Despite recent advances in immune checkpoint blockade (ICB) therapy, its efficacy in CRC remains largely limited to mismatch repair-deficient (MMRd) tumors, highlighting the need for alternative immunotherapies. B-cell receptor (BCR) repertoires and tumor antigens (autoantigens and neoantigens) are key components of anti-tumor humoral immunity, yet their landscape in CRC remains incompletely characterized. We systematically identified BCR clonotypes, autoantibody-reactive self-antigens and somatic mutation-derived neoantigen candidates across CRC to investigate their immunological interplay. Using single-cell RNA-seq data from CRC patients, we reconstructed tumor-infiltrating BCR sequences and quantified BCR diversity and its association with clinical variables. Although exact clonotype sharing across patients was minimal, k-mer-based CDR3 analysis revealed convergent sequence features, suggesting shared antigen-driven B-cell responses across individuals. To investigate potential antigenic drivers, we are integrating MIPSA-based autoantibody profiling, a high-throughput serological assay that measures antibody reactivity against thousands of human proteins, to nominate cancer cell-specific self-antigens, complemented by the identification of recurrent somatic mutations across tumors from different patients as candidate neoantigen sources. CRC patients exhibit convergent BCR sequence features despite largely private clonotypes, potentially reflecting antigen-driven selection by shared tumor-derived neoantigens and autoantigens alike. This integrative framework, combining neoantigen and autoantigen discovery with BCR repertoire analysis, provides a foundation for the rational design of broadly applicable, antibody-informed B-cell-directed therapies in CRC.