# THE VIRAL CODE: INVESTIGATING CROHN'S DISEASE THROUGH THE LENS OF MOLECULAR MIMICRY, CLONAL EXPANSION AND NEAR-SEQUENCE SIMILARITY

Nazir Sirajudeen

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**Computational analysis of T-cell receptor repertoires in Crohn's disease patients shows significantly decreased near-sequence similarity to viral antigens compared to healthy controls ($p < 0.001$), suggesting oligoclonal expansion consistent with molecular mimicry.**

## KEY POINTS

- Near-sequence similarity between CDR3 sequences of T-cell receptors from Crohn's disease patients and viral antigens was significantly lower than in healthy controls across all tested viral antigens ($p < 0.001$), with relative T-cell expansion patterns preserved between groups.
- The findings suggest oligoclonal expansion to unknown antigens in Crohn's disease patients rather than polyclonal expansion, a pattern consistent with antigen-driven clonal expansion and the molecular mimicry hypothesis proposed in the literature.
- The study used pcDelta, a near-coincidence statistic, to quantify amino acid-level similarity between disease-associated T-cell receptors and viral antigen-specific receptors from the Immune Epitope Database.
- The source antigen driving the oligoclonal expansion in Crohn's disease remains unidentified; the authors propose isolating T-cells from individuals exposed to Caudovirales and analyzing their TCR repertoire as a next step.
- Future investigations could employ structural modeling or functional assays to elucidate the role of molecular mimicry in Crohn's disease pathogenesis.

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