Discovery of cancer neoantigens using a proteogenomics approach

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Abstract:

The extent of genomic polymorphisms across human individuals can vary significantly even for monozygotic twins who can develop somatic mutations during development. However, the impact of these polymorphisms on the repertoire of peptides presented by major histocompatibility complex class I (MHC I) remains unknown. This presentation will highlight a novel proteogenomic approach that combines transcriptomic and MS-based proteomic data to profile MHC class I peptides and identify minor antigens (MiHAs) and other variants that harbour non-synonymous nucleotide polymorphisms. Using this approach we detected more than 45,000 MHC I peptides from B lymphocytes of 18 individuals and identified a subset of 39 MiHAs that share optimal features for immunotherapy of hematological cancers. These analyses also revealed that the immunopeptidome is represented by a limited number of source proteins with distinctive features, and that approximately 8% of MHC I peptides are derived from non-canonical reading frames. The notion the only a small fraction of the protein-coding genome is presented to our immune system has profound implications in autoimmunity and cancer immunology.