Several studies have shown that cancers actively regulate alternative splicing. Altered splicing mechanisms in cancer lead to cancer-specific transcripts different from the pool of transcripts occurring only in healthy tissue. At the same time, altered presentation of HLA class I epitopes is frequently observed in various types of cancer. Down-regulation of genes related to HLA class I antigen processing has been observed in several cancer types, leading to fewer HLA class I antigens on the cell surface. Here, we use a peptidome wide analysis of predicted alternative splice forms, based on a publicly available database, to show that peptides over-represented in cancer splice variants comprise significantly fewer predicted HLA class I epitopes compared to peptides from normal transcripts. Peptides over-represented in cancer transcripts are in the case of the three most common HLA class I supertype representatives consistently found to contain fewer predicted epitopes compared to normal tissue. We observed a significant difference in amino acid composition between protein sequences associated with normal versus cancer tissue, as transcripts found in cancer are enriched with hydrophilic amino acids. This variation contributes to the observed significant lower likelihood of cancer-specific peptides to be predicted epitopes compared to peptides found in normal tissue.
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