Exploring the role of SPN-205: an nonsense-mediated decay targeted CD43 isoform

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CD43, encoded by the *SPN* gene*,* is a transmembrane sialomucin primarily studied in leukocytes. It plays an essential role in adhesion, migration, and the activation of immune cells. In cancer, CD43 plays a role in immune evasion, with its expression varying across different types of tumors. .

An important alteration in cancer is the dysregulation of nonsense-mediated decay (NMD), a highly conserved RNA quality control mechanism that degrades transcripts containing premature termination codons, preventing the production of potentially harmful truncated proteins. When NMD is dysregulated, it leads to the stabilization of aberrant isoforms and broad transcriptome remodeling. This remodeling can have dual outcomes: it may restore the expression of stress response factors that control the response to cancer, such as p53. Or on the contrary, promote the accumulation of transcripts that inhibit antitumor mechanisms, thereby promoting cancer development.

In this study, we analyzed publicly available transcriptomic datasets from The Cancer Genome Atlas (TCGA) to evaluate the differential expression of *SPN* and SPN-205, a predicted NMD-marked isoform of the *SPN* gene, in tumor versus normal samples. We found that SPN-205 is overexpressed in several tumor types, including acute myeloid leukemia (LAML), thymoma (THYM), Testicular Germ Cell Tumor (TGCT), diffuse large B-cell lymphoma (DLBC), pancreatic adenocarcinoma (PAAD), and stomach adenocarcinoma (STAD).

Notably, in LAML, the expression of SPN-205 reaches up to 32% of the expression level of canonical *SPN*. This suggests that SPN-205 may not be transcriptional noise, but could have yet unknown functions and interactions, potentially dysregulating the NMD pathway in certain types of cancer. To further explore its potential role, we will incorporate a functional analysis to assess the correlation between the expression of *SPN* and SPN-205 with gene expression signatures associated with cell proliferation, immune evasion, and apoptosis resistance.

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