RBM15 as a Rheostat of RNA Fate: Context-Dependent m^{6}A Wiring and Immune Evasion in Pancreatic Adenocarcinoma

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Background: RBM15 is traditionally viewed as an m^{6}A methyltransferase scaffold, yet its disease relevance transcends this writer function. How a single subunit pivots between opposing RNA fates—nuclear retention, splicing, cytoplasmic decay, or translational potentiation—across contexts remains unclear. We hypothesized that RBM15 acts as a context-dependent rheostat and sought to decode its mechanism in pancreatic adenocarcinoma (PAAD). Method: We integrated mechanism-oriented synthesis of RBM15 research with pan-cancer profiling. For PAAD, bulk/single-cell transcriptomes and clinicopathological data were analyzed using LASSO-Cox, Random Survival Forest (RSF), and Gradient-Boosted models, validated by 5-fold cross-validation and time-dependent ROC. RBM15-correlated signatures were cross-referenced with eCLIP datasets to nominate direct targets, alongside alternative splicing (AS) and nuclear-cytoplasmic enrichment analyses.' Results: RBM15 emerged as a dose-sensitive rheostat with context-dependent prognostic valence. In PAAD, high RBM15 orchestrated post-transcriptional hijacking: shifting nuclear-cytoplasmic equilibrium toward preferential export of cellcycle/DNA-repair transcripts, while inducing aberrant cassette-exon skipping in immune-checkpoint regulators (PD-L1, CTLA-4), potentially generating decoy isoforms that fuel exhaustion. High RBM15 correlated with broad immune infiltration but anergy markers and >30 checkpoint ligands. RSF achieved a C-index of 0.72 (vs. 0.65 clinically), with RBM15 ranked second by SHAP, boosting 3-year AUC to 0.78. Enrichment confirmed mitotic and TCR-suppressive co-activation, with eCLIP nominating E2F1 and TGFBR2 as putative direct targets. Conclusion: RBM15 is not a mere writer but a dosage-sensitive rheostat that spatially and temporally reroutes RNA metabolism. In PAAD, it synergistically stabilizes proliferative mRNAs while sculpting a pro-tumoral microenvironment via splicing-driven checkpoint remodeling. Its prognostic power is the phenotypic echo of transcriptome-wide rewiring. Our framework establishes RBM15 as a hub where nuclear export and alternative splicing converge, offering a stratified rationale for targeting post-transcriptional checkpoints in pancreatic cancer.