A Multi-Modal Framework for Exercise-Induced Anti-Tumor Immunotherapy

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Despite advances in immunotherapy, up to 60% of melanoma patients do not respond to treatment. Emerging evidence suggests that physical exercise enhances anti-tumor immunity; however, the molecular mechanisms linking exercise-induced immune activation to tumor susceptibility remain unclear. To address this gap, cross-context transcriptomic analyses were performed using publicly available RNA-sequencing datasets from melanoma tumors and exercise-responsive immune cells. Differential expression analysis identified conserved genes with reciprocal regulation, among which decorin (DCN) showed the strongest inverse transcriptional polarity (log2FC -2.47 melanoma; +1.08 exercise; adj. $p < 0.01$) and enrichment in cell-cycle checkpoint pathways. To evaluate functional relevance, in vitro validation in SK-MEL-2 and A375 melanoma cell lines demonstrated that recombinant DCN suppressed proliferation, reducing viability to ~48% at 80 nM ($p < 0.01$), and increased G2/M phase accumulation to ~40%, consistent with CHEK1–WEE1–mediated arrest. A supervised logistic regression model generated an interpretable Immune Readiness Score (IRS) predictive of immunotherapy response (AUROC ˜ 0.82), while a 3D embedding framework captured coordinated immune activation, suppression, and proliferation states, enabling stratification of therapeutic susceptibility. These results were integrated into ImmunoFit, a patient–physician interface enabling real-time interpretation of baseline immune readiness and exercise-induced IRS dynamics to inform personalized treatment strategies. Collectively, this study identifies decorin as a conserved mediator and candidate biomarker of immune susceptibility, and reframes exercise as a dynamic, rapid, low-cost functional probe for stratifying immunotherapy response.

Awards Won:
Second Award of $2,400