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INTEGRATIVE BIOINFORMATIC ANALYSIS OF REGULATORY NETWORKS LINKED TO SPRY2 IN PLURIPOTENCY-RELATED CELLULAR STATE TRANSITIONS

Background/Aim. Cellular reprogramming is driven by coordinated transcriptional and signaling changes that promote the acquisition of pluripotency-associated features. SPRY2, a negative-feedback regulator of growth factor-mediated MAPK/ERK signaling, may contribute to the pluripotency-associated cell-state transitions. This study aimed to investigate molecular pathways and regulatory networks associated with SPRY2 using an integrative bioinformatic approach. **Methods.** The GEO dataset GSE90895 was analyzed as a murine reprogramming model comprising mouse embryonic fibroblasts, early OSM-induced stages, pre-induced pluripotent stem cells, and embryonic stem cells. Transcriptomic analysis in R included preprocessing, principal component analysis, differential expression, Gene Ontology and KEGG enrichment, SPRY2-focused correlation analysis, and gene-concept network construction. SPRY2 protein characterization was performed using STRING, AlphaFold, ExPASy ProtParam, and InterPro. **Results.** Transcriptomic profiling revealed sample heterogeneity, while PCA separated samples by distinct cellular states. Expression analysis showed higher levels of pluripotency-associated Sox2 and Myc, whereas Nanog displayed lower expression, suggesting uneven activation of pluripotency-related programs. Differential expression analysis identified 36 significantly altered genes among 33,297 transcripts. Despite this limited number, enrichment analysis indicated functional coherence, with associations involving cell differentiation, ERK1/ERK2 regulation, protein phosphorylation, receptor tyrosine kinase signaling, and epithelial remodeling. Gene-concept and protein-protein interaction analyses positioned SPRY2 within networks related to MAPK/ERK modulation and growth factor receptor signaling. Correlation and structural-functional analyses further supports SPRY2 as a candidate regulatory node linking signaling-dependent regulation with transcriptional programs involved in cellular plasticity and reprogramming. **Conclusions.** Molecular networks associated with SPRY2 were linked to the receptor tyrosine kinase signaling, MAPK/ERK regulation, differentiation, and cellular state remodeling during reprogramming. SPRY2 may represent a candidate negative-feedback node connecting signaling changes with transcriptional programs involved in somatic-to-pluripotent-like transitions. Based on a single public dataset and in silico analysis, these findings remain hypothesis-generating and require independent validation.

Keywords: SPRY2, cellular reprogramming, pluripotency, mouse embryonic fibroblasts, induced pluripotent stem cells, MAPK/ERK signaling, transcriptomics, regulatory networks, bioinformatics.

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