A Prioritized Screen to Identify Downstream Targets of the Forkhead/Fox Transcription Factor Jumeau that Mediate Cardiac Progenitor Cell Divisions

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While at least eight Forkhead/Fox transcription factors are required for proper cardiac development in mammals and mutations in four Fox genes have been linked to human congenital heart disease, relatively little is known about the molecular mechanisms or the downstream target genes by which these Fox TF-mediated cardiogenic functions are brought about. Previous research has shown that the Drosophila Fox gene jumeau (jumu) mediates three distinct categories of cardiac progenitor cell divisions by regulating the activity of Polo kinase. However, the significant enrichment of Fox TF binding sites in the enhancers of cardiac genes suggested that jumu might also be utilizing additional downstream target genes to regulate these cell division processes. Using RNA-sequencing to compare genome-wide transcriptional expression profiles of flow cytometry-purified mesodermal cells from wild-type and jumu loss-of-function embryos, 1,272 putative jumu targets were detected, i.e. genes exhibiting significant differential expression in jumu mutants compared to wild-type embryos. Ongoing phenotypic analysis of a prioritized subset of these downstream targets with null and hypomorphic mutations shows that jumu does indeed transcriptionally activate at least six additional genes that are necessary for cardiac progenitor cell divisions.

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