Desmin promotes Nkx2.5 expression during early cardiomyogenesis via temporal restricted interaction with the minimal cardiac specific enhancer of the Nkx2.5 gene

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Abstract

Desmin, a type three intermediate filament protein is expressed in all types of muscle cells and contributes to homeostasis in the adult heart. Knock out of the desmin gene lacks a clear embryonic phenotype; however, upregulation of desmin expression resulted in an increased number of developing cardiomyocytes and a temporal restricted upregulation of the cardiogenic transcription factor Nkx2.5 in cardiac progenitor cells during a small window in time. Thus we hypothesize that desmin may directly promote cardiogenic commitment and myocardial differentiation. To test whether desmin influences transcriptional regulation of the Nkx2.5 gene during cardiomyogenesis we choose embryoid bodies as a model system to study the short-lived function of desmin in nascent cardiogenic cells. Desmin indeed interacts with regulatory DNA elements of the Nkx2.5 gene, is present in nuclei of cardiac progenitor cells, activates the Nkx2.5 gene via the cardiac specific enhancer element in fibroblasts, myoblasts, and cardiomyocytes, and rescues Nkx2.5 related haplo-insufficiency during cardiomyogenesis. These results attribute a new dimension to the role of desmin in commitment and differentiation of progenitor cells to cardiomyocytes, by demonstration of its participation in the transcriptional regulation of the Nkx2.5 gene.