
microRNA-138 modulates cardiac patterning during embryonic development.

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Authors: Sarah U Morton, Paul J Scherz, Kimberly R Cordes, Kathryn N Ivey, Didier Y R Stainier, Deepak Srivastava

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Scientific Abstract:

Organ patterning during embryonic development requires precise temporal and spatial regulation of protein activity. microRNAs (miRNAs), small noncoding RNAs that typically inhibit protein expression, are broadly important for proper development, but their individual functions during organogenesis are largely unknown. We report that miR-138 is expressed in specific domains in the zebrafish heart and is required to establish appropriate chamber-specific gene expression patterns. Disruption of miR-138 function led to ventricular expansion of gene expression normally restricted to the atrio-ventricular valve region and, ultimately, to disrupted ventricular cardiomyocyte morphology and cardiac function. Temporal-specific knockdown of miR-138 by antagomiRs showed miR-138 function was required during a discrete developmental window, 24-34 h post-fertilization (hpf). miR-138 functioned partially by repressing the retinoic acid synthesis enzyme, aldehyde dehydrogenase-1a2, in the ventricle. This activity was complemented by miR-138-mediated ventricular repression of the gene encoding versican (cspg2), which was positively regulated by retinoic-acid signaling. Our findings demonstrate that miR-138 helps establish discrete domains of gene expression during cardiac morphogenesis by targeting multiple members of a common pathway, and also establish the use of antagomiRs in fish for temporal knockdown of miRNA function.

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