Molecular Embryogenesis of the Heart

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ABSTRACT

Development of the heart is a complex process involving primary and secondary heart fields that are set aside to generate myocardial and endocardial cell lineages. The molecular inductions that occur in the primary heart field appear to be recapitulated in induction and myocardial differentiation of the secondary heart field, which adds the conotruncal segments to the primary heart tube. While much is now known about the initial steps and factors involved in induction of myocardial differentiation, little is known about induction of endocardial development. Many of the genes expressed by nascent myocardial cells, which then become committed to a specific heart segment, have been identified and studied. In addition to the heart fields, several other “extracardiac” cell populations contribute to the fully functional mature heart. Less is known about the genetic programs of extracardiac cells as they enter the heart and take part in cardiogenesis. The molecular/genetic basis of many congenital cardiac defects has been elucidated in recent years as a result of new insights into the molecular control of developmental events.

Key words: heart, myocardium, developmental gene expression regulation, congenital heart defects

CARDIAC MORPHOGENESIS—A BRIEF INTRODUCTION

Heart development in all vertebrates from fish to humans follows the same general pattern: fusion of myocardium and endocardium in the ventral mid-
cretes a thick extracellular matrix called cardiac jelly that forms a layer separating the myocardium and endocardium.

During the next phase of development, the primary heart tube narrows and lengthens by accretion of cells at each end and concurrently loops to the right. Looping allows the caudal, inflow end of the tube to be brought into approximation with the cranial, outflow end of the tube in a process called convergence (Fig. 3). Chambers or segments of the tube become recognizable by constrictions that demarcate the sinus venosus, common atrial chamber, atroventricular canal, ventricular chamber, and conotruncus or definitive outflow tract. The endocardium of the atroventricular canal and outflow tract generates cells that populate the cardiac jelly with mesenchyme in these regions. The bulges formed are called cardiac cushions. At the same time the myocardium of the atrial and ventricular chambers begins to develop trabeculations or ridges of endocardially covered myocardium that extend into the lumen.

With the inflow and outflow ends of the tubular heart now in proximity and the chambers specified and functional, cardiac septation can begin. All of the septa fuse ultimately with the atrioventricular cushions. These cushions divide the atrioventricular canal into a right and left canal. The right atrioventricular canal expands to the right, as does the right ventricle, allowing incoming blood from the sinus venosus to pass directly from the...