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Background: The accuracy of a new semiautomatic 3-D monitoring system (PAMP, Duke Center for Emerging Cardiovascular Technologies) for measuring right ventricular volumes (RVV) and stroke volumes (SV) has been tested in vitro. We used RT3D (Volumentrics Imaging System) to image 10 static and 5 dynamic right ventricular latex casts from human hearts in a pulsatile manner. Volume was calculated according to the formula, \( 	ext{RV volume} = \pi \times (r_1^2 - r_2^2) \times h \), where \( r_1 \) and \( r_2 \) are the inner and outer radii, respectively, and \( h \) is the height of one slice of the cast.

Results: There was a strong correlation between the static RVV results of the PAMP system and the true volumetric measurement of RVV in the latex casts (percent difference: 0.31 ± 0.27%, \( r = 0.95 \)); for stroke volume, the correlation was slightly lower (percent difference: 0.81 ± 0.41%, \( r = 0.86 \)). For the dynamic LVV and SV (the latent heart) from the casts, the PAMP system underestimated the true values (percent difference: 4.43 ± 1.39%, \( r = 0.99 \)) compared to the Volumentrics software. The dynamic VAs expressed variance (percent difference: 1.01 ± 0.58%, \( r = 0.95 \)).

Conclusions: The PAMP system is a reliable tool for measuring right ventricular volume and stroke volume in a pulsatile model. However, further studies are needed to validate this system in vivo.

Molecular Cloning and Characterization of a Potential Candidate Gene for Nonsyndromic Atrial Septal Defect on 11p13-1p21

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Background: Atrioventricular septal defects (AVSD) are a common congenital heart defect. The genetic basis of AVSD is largely unknown. We have previously shown that p93 is a cardiac-specific and developmentally-regulated kinase, and it may be a strong candidate gene involved in nonsyndromic AVSD.

Methods and Results: We have identified a cDNA encoding a homolog of p93, the transcription of which is upregulated in the heart, but not in other tissues. RT-PCR analysis showed that p93 is expressed in heart, but undetectable in any other tissues. 2) Right at the ventricular p93 mRNA level was higher than the counter-regulated tissue array analysis (Clontech) showed: 1) p93 was expressed in heart, but undetectable in any other tissues. 2) Right at the ventricular p93 mRNA level was higher than the counter-regulated tissue array analysis (Clontech) showed: 3) p93 was significantly highly expressed in interventricular septum and apex of heart. Immunohistochemistry revealed that p93 was more highly expressed in the nucleus of embryonic cardiac myocytes than in adult. Of note, p93 was substantially decreased in myocardium of subjects with tetralogy of Fallot and with normal heart. In vitro kinase analysis showed p93 could autophosphorylate while its dominant negative form (K490R) couldn't, which indicated that p93 is a functional kinase.

Conclusions: p93 is a cardiac-specific and developmentally-regulated kinase, and it may be a strong candidate gene involved in nonsyndromic AVSD.

Spatio-Temporal Description of the Development of the Mouse Cardiac Conduction System Using a cGATA-6 Gene Enhancer Marker

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Background: A fully developed cardiac conduction system is essential for coordinated cardiac contraction and unidirectional blood flow through the heart. Recently, a cGATA-6/lsic transgenic mouse model has been generated in which the transgene expression is localized to the proximal region of the atrioventricular (AV) conduction system (i.e., AV node) and the right AV ring bundle (Davis et al., Dev. Oct 2001) in the postnatal heart.

Methods: 1) 1.5 × 10^6 cGATA-6/lacZ 2.3 kb mouse embryos were obtained at embryonic day (E) 7.5 to E18. The specimens were stained for lacZ, paraffin embedded, partly sectioned, counterstained with nuclear fast red and examined by light microscopy. Digital images of the sections were then used to generate three dimensional reconstructions using 3D-DOCTOR software (Able Software).

Results: At the paired heart field stage (E7.5), transgene expression is localized to a subpopulation of cells in the lateral portions of the predcardiac mesoderm. At E6.5 the expression is found at the AV junction in the myocardial adjacent to the developing endocardial cushions. From the AV junction two lacZ positive bands extend towards the apex over the anterior and posterior surfaces of the left ventricle. From E6.5 towards the ventricular transgene expression disappears and the lacZ positive region becomes more restricted to the right AV junction involving the region of the developing AV node. As the atrial and ventricular myocardium becomes separated by the fusion of subcutaneous cushion and cushion derived tissues (E12 and beyond), the transgene expression becomes incorporated into the right atrial myocardium along the lateral and posterior rim of the triangular vasa annulans and in the area of the developing AV node. Conclusion: The cGATA-6/lacZ transgenic construct identified a distinct subpopulation of cells in the predcardiac mesoderm at early stages of development. At advanced stages of development the cGATA-6/lacZ expression is found in the proximal portion of the AV conduction system and right AV ring bundle. This cGATA6 construct appears to be the earliest reported marker for the developing conduction system. Further cell fate studies using a cre-lox approach are in progress.

Shortened Outflow Tract Leads to Altered Cardiac Looping After Neural Crest Ablation

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Background: Congenital cardiovascular malformations are associated with the highest mortality risk in utero and after postnatal surgical repair, and frequently involve dextroposed aorta. The pathogenesis of dextroposed aorta is not known but is thought to be due to abnormal looping and/or wedging of the outflow tract during early fetal development. The elongation of the outflow limb of the cardiac tube is a critical step in the normal process of looping in utero as it provides required extra material to lengthen the heart tube. We examined cardiac morphology in an experimental model of dextroposed aorta to determine whether altered lengthening of the outflow limb plays a role in dextroposition of the aorta.

Methods and Results: Hearts were examined in normal chick embryos and compared with those in neural crest-ablated embryos using time-lapse videophotography, scanning electron microscopy and histological sectioning (collected 11 days after neural crest ablation). The elongation of the outflow limb of the cardiac tube is a critical step in the normal process of looping in utero as it provides required extra material to lengthen the heart tube. We examined cardiac morphology in an experimental model of dextroposed aorta to determine whether altered lengthening of the outflow limb plays a role in dextroposition of the aorta.

Results: 1) The data are indicating that aorta. The pathogenesis of dextroposed aorta is not known but is thought to be due to abnormal looping and/or wedging of the outflow tract during early fetal development. The elongation of the outflow limb of the cardiac tube is a critical step in the normal process of looping in utero as it provides required extra material to lengthen the heart tube. We examined cardiac morphology in an experimental model of dextroposed aorta to determine whether altered lengthening of the outflow limb plays a role in dextroposition of the aorta.

Conclusions: 1) The data are indicating that aorta. The pathogenesis of dextroposed aorta is not known but is thought to be due to abnormal looping and/or wedging of the outflow tract during early fetal development. The elongation of the outflow limb of the cardiac tube is a critical step in the normal process of looping in utero as it provides required extra material to lengthen the heart tube. We examined cardiac morphology in an experimental model of dextroposed aorta to determine whether altered lengthening of the outflow limb plays a role in dextroposition of the aorta.

Increased Vascular Endothelial Growth Factor in Patients With Cyanotic Congenital Heart Disease May Not Be Normalized After Fontan Type Operation

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BACKGROUND: There is no data available concerning the change of vascular endothelial growth factor (VEGF) in patients with cyanotic congenital heart disease (C-CHD). Purpose: To determine the change of serum concentration of VEGF in patients with C-CHD. METHODS: Subjects were divided into 2 groups; A (age 1 - 20 years) and B (age > 20 years). Group A was subdivided into 4 groups; A1, 23 patients with uncorrected C-CHD; A2, 13 controls; A3, 8 patients who had C-CHD and were treated with bi-ventricular circulation; A4, 4 patients who had C-CHD and were treated with Fontan type operation. RESULTS: Serum levels of VEGF were significantly higher in patients with C-CHD compared to controls. No significant difference in serum levels of VEGF was observed between groups A1 and A3. CONCLUSIONS: Serum levels of VEGF were significantly higher in patients with C-CHD compared to controls. No significant difference in serum levels of VEGF was observed between groups A1 and A3.