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The cardiac endothelial cell transcriptome in neonatal, adult, and remodeling hearts

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Background: Cardiac microvascular endothelial cells (CMVECs) are the most numerous cells in the myocardium and orchestrate cardiogenesis during development, regulate adult cardiac function, and modulate pathophysiology of heart failure. It has been shown that the transcriptome of CMVECs differs from other endothelial cell types, but transcriptomic changes in cardiac endothelial cells during cardiac maturation and cardiac remodeling have not been studied earlier.
Purpose: To study changes in the transcriptome of CMVECs during cardiac maturation and cardiac remodeling, and to test the hypothesis that the fetal gene program is reactivated during cardiac remodeling in CVMECs.
Methods: CMVECs were isolated from rat hearts based on CD31 expression and were immediately processed for RNA sequencing, without an in vitro propagation step. We compared gene expression levels from primary CMVECs of neonatal hearts, normal adult hearts, and infarcted-hearts (4 weeks post LAD ligation).
Results: Between neonatal and adult CMVECs, 6838 genes were differentially expressed indicating that CMVECs undergo a substantial transformation during postnatal cardiac growth. A large fraction of genes upregulated in neonatal CMVECs are part of mitosis pathways, whereas a large fraction of genes upregulated in adult CMVECs are part of cellular response, secretory, signaling, and cell adhesion pathways. Between CMVECs of normal adult hearts and infarcted hearts, 159 genes were differentially expressed. We found a limited degree of overlap (55 genes) between the differentially expressed genes in neonatal and infarcted-hearts. Of 46 significantly upregulated genes in the infarcted heart, 46% were also upregulated in neonatal hearts relative to sham. Of 113 significantly downregulated genes in the infarcted-hearts, 30% were also downregulated in neonatal hearts relative to sham.
Conclusion: These data demonstrate that CMVECs undergo dramatic changes from neonatal to adult and more subtle changes between normal state and cardiac remodeling. During cardiac remodeling, a small part of the fetal gene program is reactivated in CMVECs.

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