post-infarction remodeling may be difficult. It is not yet clear whether cytokine activation of the patient's bone-marrow cells alone would suffice, or whether concentration of endothelial precursors *ex vivo* will be a necessary intermediate step. Nevertheless, improving the reperfusion of ischemic myocardium with stem cells is a remarkable accomplishment, and future investigation along these lines promises to yield important insights into the ability of the human heart to heal itself.

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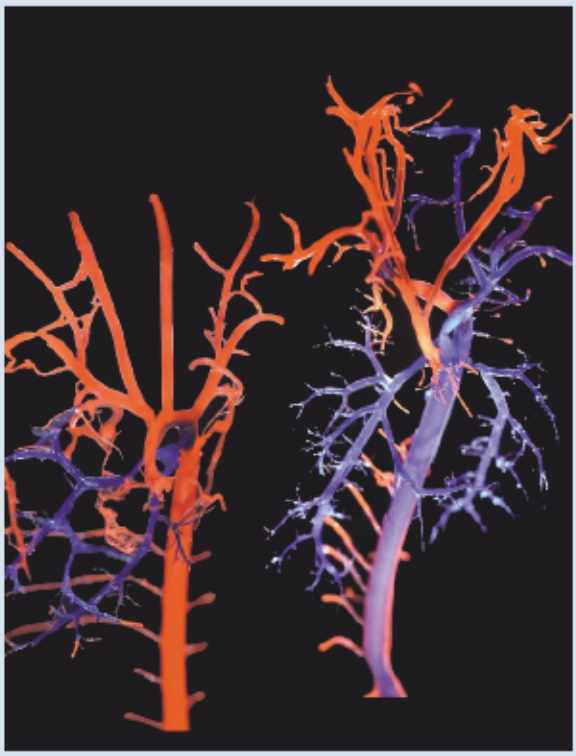
Arch enemy

Although DiGeorge syndrome (DGS) and Velocardiofacial syndrome (VCFS) are complex multigenic diseases, geneticists have made some headway in pinpointing the individual genes responsible for their etiology. The syndromes, which affect 1 in every 4000 infants, are characterized by phenotypic features including aortic arch interruptions, cardiac outflow tract malformation, and a number of facial, thymic, thyroid and parathyroid defects. Most DGS/VCFS patients are hemizygous for a 3 Mb region on human chromosome 22, and haploinsufficiency of one or more genes in this region is believed to underlie these genetic defects. Deletions in this chromosome region are also found in many infants with congenital heart defects unrelated to DGS/VCFS syndrome.

Geneticists have attempted to identify the genes that underlie these defects by creating mice with hemizygous deletions in regions of chromosome 16 that correspond to the human locus. So far, none of the mice have been found to possess all of the cardiac, facial, thymic and parathyroid gland deficiencies associated with DGS/VCFS. In the 23 February issue of *Cell*, Merscher *et al.* report the creation of mice with the largest to-date hemizygous deletion in chromosome 16, eliminating 24 genes. These mice, termed Lgdel/+, exhibited cardiac defects, parathryroid gland aplasia, and significant perinatal lethality, but still developed an intact and normal size thymus as well as thyroid glands.

Most of the Lgdel/+ embryos developed an abnormal pattern of the cardiac great vessels. For example, some developed a right-sided aortic arch with a left sided ductus arteriosus (right panel of picture. The same cardiac vessels of wild-type mice are shown on the left side of the picture). This developmental defect is dangerous, as the aortic arch is posterior to the esophagus and trachea, and can form a vascular ring capable of compressing the trachea. Some embryos possessed other cardiovascular defects, such as complete interruption of the aortic arch, mislocation of the right subclavian artery, and ventricular septal defects.



Merscher *et al.* then used a complementation approach to identify the individual gene(s) responsible for these vascular defects, breeding Ldgel/+ mice with those carrying duplications in the genes from the deleted region. This approach allowed them to narrow the genes down to *Tbx1*, which encodes a transcription factor expressed during early embryogenesis in the pharyngeal arches. *Tbx1* is also a good candidate DGS/VCFS gene because the aortic arches, thymus and parathyroid glands are all derived from neural crest cells that reside in the pharyngeal arches.

The authors created mice carrying a hemizygous *Tbx1* mutation, and found that they developed cardiovascular defects similar to those of the Ldgel/+ mice and DGS/VCFS patients. "Neither the Tbx1 nor the Ldgel/+ mutant mice possess all the phenotypes observed in DGS/VCFS patients, perhaps because of background genetic effects or differences in gene dosage between humans and mice", said Jon Epstein, an author on the study. Alternatively, this syndrome may be a multigenic disorder, forcing the search for additional genes to continue.

Kristine Novak