**NEW APPROACHES TO IDENTIFY THE GENETIC CAUSES OF CONGENITAL HEART DEFECTS**

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Few specific causes of congenital heart defects (CHDs) are well characterized, and most cases are due to the effects of multiple genetic and environmental factors and their interactions. A genetic predisposition has been suggested, based on familial clusters reported for nearly all cardiac malformations, and the increased recurrence risk after a first affected baby or with an affected parent. Despite multiple genome-wide association studies of large cohorts and numerous candidate gene studies, only a few genes are known for CHD malformations. We perform a step-wise approach to identify novel CHD genes in patients with CHD. The approach involves screening known CHD or related genes, and submitting samples for complete genomic hybridization analysis to identify copy number variants (CNVs). In patients with significant family history we have performed whole exome analysis on DNA samples. In this talk we will present data describing successes and limitations of using candidate gene approaches, identification of novel genes through CNV analysis and the results of exome analysis in families. We will also describe a unique resource, the Utah Population database, which allows distantly related patients to be linked into family clusters. SNP genotyping of patients in these clusters can lead to the identification of shared genomic segments and candidate genes that can be screened.