HEALTH RESEARCH ABSTRACT SUBMISSIONS #17

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Title of Research *	Genetics Variants in TFAP2B in Preterm Infants with Patent Ductus Arteriosus
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Introduction & Purpose *	Patent ductus arteriosus (PDA) is a common complication of prematurity and has a significant inherited component. Our previous candidate gene study found association of PDA with DNA variants in transcription factor AP-2 beta (TFAP2B), the gene mutated in Char syndrome, a syndromic form of PDA seen in term infants. We hypothesized that sequencing the regions in TFAP2B with significant SNP associations would uncover the etiologic common variant causing the association with PDA and might further identify rare high risk variants.
Experimental Design *	DNA samples and clinical information was obtained from the University of Iowa neonatal DNA repository. Cases were defined as preterm infants born ≤ 30 weeks gestational age with PDA, diagnosed by standard echocardiography. Controls were preterm infants ≤ 30 weeks gestational age without PDA. Exons 3, 4, 5, and 6 of TFAP2B, as well as three highly-conserved intronic regions, underwent DNA sequencing in 95 cases and 95 controls.

Results *

We identified 17 total sequence variations in cases, involving 11 different individuals and 7 unique loci. None of these polymorphisms were found in control samples. We also identified 3 sequence variations in controls involving 3 individuals (one polymorphism per individual), all at unique loci and none of these polymorphisms appeared in cases. The frequencies of observed polymorphisms between cases and controls were significantly different (p=0.0014). All of the polymorphisms found in PDA cases were in conserved non-coding regions, with several in close proximity to known transcription factor binding sites, including IK3, HXA5, CUX1 and PBX1.

Conclusions *	Rare variants in conserved regulatory regions of TFAP2B may predispose extremely preterm infants to PDA. Replication studies are currently underway to validate these findings and future studies will focus on the biological function of the identified variants. Understanding genetic risk factors for PDA may lead to improvements in diagnosis and management.

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