anomalies, and suggest potential therapeutic approaches to adult heart disease.

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Program/Abstract # 411
Poster: TGF-beta signaling reduces FGF-10 in hypoxic newborn mouse lung during the critical period of lung development
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Introduction: We have recently shown that excessive transforming grow factor (TGF-β) signaling mediates hypoxia-induces inhibition of alveolar development and abnormal pulmonary arterial remodeling in the newborn lung, producing a phenotype that mimics broncho-pulmonary dysplasia (BPD) in preterm infants. The mechanisms by which excessive TGF-β signaling inhibits alveolar septation are not known. Fibroblast growth factor (FGF)-10 is a critical modulator of early lung development and in the saccular stage but its role in alveolar septation has not been defined. It has been shown that the FGF-10 promoter contains a TGF-β response element. *Objective*: We hypothesized that excessive TGF-β signaling in the newborn hypoxia-induced mouse lung inhibits alveolar septation via reduction of FGF-10. *Methods*: In vivo: Wilde type C57BL/6 were exposed to air or hypoxia (12% O2) from birth to two weeks (the critical period of lung development) and evaluated for FGF-10 and TGF-β mRNA and protein. Inhibition of TGF-β signaling was achieved by administration of TGF-β neutralizing antibody (ID11) to WT mice or 20 ug/g ZnSO4 given intraperitoneally daily to DNIIR pups (an inducible dominant-negative mutation of the TGF-β type II receptor) and exposed to hypoxia or air from birth to 14 days of age. In vitro: Newborn Lung Fibroblasts and Pulmonary Microvascular Endothelial Cells (PMVEC) were exposed to air or hypoxia for 24 h. FGF-10 mRNA and protein were evaluated in cell lysates. *Results*: Hypoxia reduces FGF-10 mRNA in both in vivo (Fig. 1) and in vitro studies (Fig. 3). Pups receiving the TGF-β neutralizing antibody (ID11) had increased FGF-10 and better lung development (Fig. 1). FGF-10 staining was not significantly decreased in DNIIR hypoxic mice compared to air control (Fig. 2). *Conclusion*: These results suggest that hypoxia-induced increased TGF-β signaling may reduce FGF-10, which may contribute to impairment of lung development. *Future experiments*: Additional studies are in progress to inhibit FGF-10 signaling in vivo, to determine if FGF-10 is necessary for alveolar septation.

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Program/Abstract # 412
A mouse model for juvenile hydrocephalus
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Juvenile hydrocephalus, the accumulation of cerebrospinal fluid (CSF) in the ventricles of the brain, causes significant morbidity among human children affecting roughly 1 in 500 newborns. The disease manifests due to overproduction, decreased absorption, or restricted flow of CSF. Few genetic causes of this disease are known, and therefore animal models can prove beneficial in identifying candidate genes. The Juvenile hydrocephalus (Jh) mouse line contains a transgenic integration on mouse chromosome 9. Homozygous Jh mice exhibit hydrocephalus by two weeks of age and few survive beyond eight weeks. This phenotype represents a novel cause of the disease since no known hydrocephalus mutations map to the region. Analysis of the integration site showed disruption of an uncharacterized gene, I11. Preliminary data suggests that a transgene carrying a functional copy of I11 can rescue the Jh phenotype. However, the predicted protein product of I11 has no recognizable functional domains and its role in CSF maintenance is unknown. Future research will focus on definitively establishing the role of I11 in hydrocephalus and dissecting its function.

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Program/Abstract # 413
Characterization of zebrafish orthologues of the human B3GALTL gene involved in Peters-Plus syndrome
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Purpose: Peters-Plus Syndrome (PPS) is an autosomal recessive disorder characterized by ocular anterior segment dysgenesis (primarily Peters' anomaly), short stature and brachydactyly along with additional variable features. Mutations in Beta-1,3-glucosyltransferase (B3GALTL) gene were shown to explain 100% of classic PPS cases. No animal models have yet been developed. This study aims to characterize zebrafish orthologues of B3GALTL in terms of sequence, expression pattern and function. *Methods*: Zebrafish orthologues of human B3GALTL were identified using database analysis, RT-PCR and sequencing; expression was analyzed using RT-PCR and in situ hybridization; knockdown was performed via injection of morpholino oligomers targeting zebrafish B3GALTL genes followed by RT-PCR transcript analyses. Gross morphological analysis of morphants was done using alcian blue staining and histology. *Results*: Two orthologues of human B3GALTL gene were identified: B3GALTLA and B3GALTLB. Each is expressed early in development. In situ hybridization showed distinct expression patterns for B3GALTLA in the brain, lens, retina, and other structures. Knockdown of one or both genes produced zebrafish with phenotypes similar to PPS. Alcian blue staining revealed defects in craniofacial cartilage formation. Histology and brightfield examination showed cornea and brain malformations, curved and short trunks, enlarged heart, and fin abnormalities. Semi-quantitative RT-PCR data confirmed morpholino efficiency. *Conclusion*: Zebrafish B3GALTLA and B3GALTLB are essential for normal embryonic development and have conserved function with the human gene. A zebrafish model of PPS is being developed to study mechanisms of this debilitating condition.

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Program/Abstract # 414
The planarian *Schmidtea mediterranea* as a free-living model for understanding and controlling flatworm parasites
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Schistosomiasis is a tropical disease caused by flatworm parasites (*Schistosoma*) that affects hundreds of millions of people in the developing world. Although only a single drug (praziquantel) is available to treat this disease, the complicated life cycle of this parasite, that involves both mollusc and vertebrate hosts, impedes efforts to uncover and validate novel therapeutic targets. Thus, we are