MSPR Poster Symposium II - Cardiopulmonary; Cellular Signaling; Bowel / Gut

Thursday, October 8 3:00-4:15 PM CDT

Moderators
Jennifer Bermick – University of Michigan
Steven McElroy – The University of Iowa Hospitals and Clinics

CDT	Abstract	Title	Presenting Author
3:00 PM		Introduction & General Information	
3:03 PM	3475547	Single vessel pulmonary vein stenosis among premature infants	Eli Zettler
3:08 PM	3476474	Contactin-2: A Potential Molecular Marker for Diagnosis of Neonatal Hypoxic Ischemic Encephalopathy	Daniela Villacis Calderon
3:13 PM	3476288	Stent Interventions for Pulmonary Artery Stenosis Improve Ventricular Flow Dynamics in a Swine Model	Ryan Pewowaruk
3:18 PM	3475687	NO increases PDE3A protein expression and activates AMPK in human pulmonary microvascular endothelial cells	Amy Brown
3:23 PM	3476605	Bifidobacterium longum subspecies infantis EVC001 decreases injury in a murine NEC model	Shiloh Lueschow
3:28 PM	3476387	Cholesterol and sterol intermediates lower energetic barriers for membrane bending and fission necessary for efficient clathrin mediated endocytosis	Ruthellen Anderson
3:33 PM	3475705	MPS IVA: Exploration of Novel Biomarkers for Cardiovascular Disease	Brittany Montavon
3:38 PM	3476617	Application of Mucous Fistula Stool Refeeding in Surgical Pediatric Patients following Bowel Resection	Cody West
3:43 PM	3476603	Hypoxia is a modulator of miR-21 expression in oligodendroglial progenitors.	Eli Chapman-Orr
3:48 PM	3476633	Association Between Ventricular Morphology And Protein Losing Enteropathy In Patients With Single Ventricle Physiology	Krishna Kishore Umapathi
3:53 PM	3473038	Teratogenic Effects of Prenatal Alcohol Exposure on Cardiac Innervation	Steven Conlon
3:58 PM	3475590	Risk of Functional Constipation in Children with a History of Infantile Cow's Milk Protein Allergy	Thomas LaRouere
4:03 PM	3475770	Anatomical Concordance of Neonatologist Performed Echocardiography as part of Hemodynamic Consultation and Pediatric Cardiology	Adrianne Bischoff
4:08 PM	3473919	The Altered Gut Resistome in Short Bowel Syndrome	Jocelyn Ou
4:13 PM		Wrap Up	

Note: Schedule subject to change based on presenter availability.

CONTROL ID: 3475547

TITLE: Single vessel pulmonary vein stenosis among premature infants

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 14

ABSTRACT STATUS: Sessioned

PRESENTER: Eli Zettler

AUTHORS/INSTITUTIONS: E. Zettler, B. Rivera, J.L. Slaughter, B. Chen, C. Backes, Center for Perinatal Research, Abigail Wexner Research Institute at Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|C. Stiver, B. Boe, C. Cua, C. Backes, The Heart Center, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|M. Ball, J.L. Slaughter, B. Chen, Division of Neonatology, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|C. Smith, Department of Pediatrics, The Ohio State University College of Medicine, The Ohio State University College of Medicine, Columbus, OH, US, academic/medsch, Columbus, Ohio, UNITED STATES|R. Callahan, Department of Cardiology, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, UNITED STATES|

CURRENT CATEGORY: Clinical Investigation

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Pulmonary vein stenosis (PVS) is a rare, often lethal, cardiac disease obstructing venous return to the left atrium and raising pulmonary venous pressure. In the absence of evidence-based guidance, treatments have been applied broadly, largely irrespective of clinical presentation and disease severity (e.g. number of stenosed veins). Accurate characterization of potential clinical phenotypes may inform prognosis and provide opportunities for more individualized, targeted approaches.

Objective: Primary pulmonary vein stenosis (PPVS) is a rare cardiac disease associated with a dismal prognosis. The present study describes outcomes among infants born <37 weeks' gestation, diagnosed with single-vessel PPVS, and treated initially using conservative management (active surveillance with deferral of treatment until disease progression).

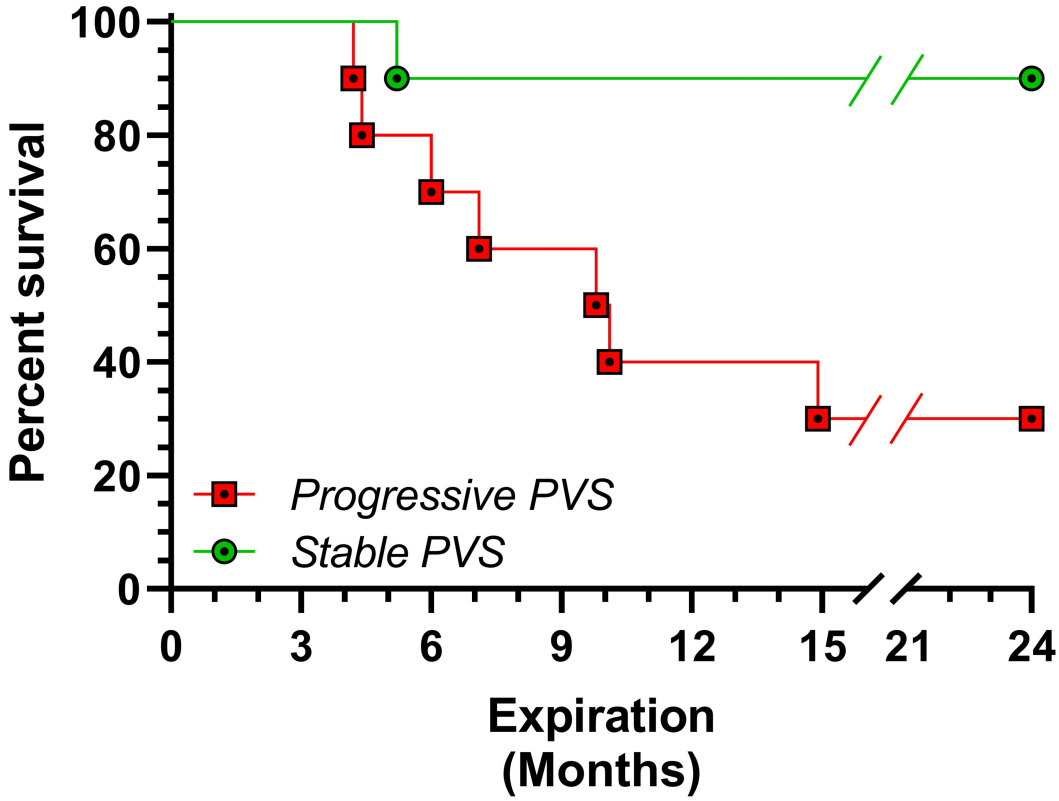
Design/Methods: Retrospective cohort study at a single, tertiary-center (2009-2019) among preterm infants with single-vessel PPVS. Echocardiograms were independently reviewed (n=214). To determine disease severity, veins were assigned a score (PVS Score). Infants were classified into 2 categories: 1) disease progression (stenosis/atresia) in a previously unaffected vein; 2) disease stabilization (≥12 months without disease progression). Cardiopulmonary outcomes (e.g. pulmonary hypertension, PH) were examined for differences across groups. A Kaplan-Meier survival analysis was performed.

Results: Twenty infants with single-vessel PPVS were included. Median echocardiograms prior to a diagnosis of PPVS was 3 (range 1-17). Compared to infants in the stable group (0/10, 0%), all infants (10/10, 100%) in the progressive group had development of at least severe stenosis or atresia (PVS scores ≥3, P<0.01). Infants in the progressive group were more likely to have severe PH (5/10, 50%) than infants in the stable group (0/10, 0%; P=0.03). Survival was lower among infants in the progressive group than the stable group (Log Rank Test, P<0.01).

Conclusion(s): The number of premature infants with single-vessel PPVS exceeds those in multicenter registries. Observed differences between infants with progressive disease versus stable disease suggest that risk stratification may be possible, wherein more targeted, individualized therapies could be applied.

(no table selected)

IMAGE CAPTION: Kaplan-Meier survival plot among infants with PPVS disease progression or disease stabilization. Survival is shown on the y-axis. Follow-up time in months is shown on the X-axis. Difference in survival was determined by log-rank test. P-value <0.01.



Kaplan-Meier survival plot among infants with PPVS disease progression or disease stabilization. Survival is shown on the y-axis. Follow-up time in months is shown on the X-axis. Difference in survival was determined by log-rank test. P-value <0.01.

CONTROL ID: 3476474

TITLE: Contactin-2: A Potential Molecular Marker for Diagnosis of Neonatal Hypoxic Ischemic Encephalopathy

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 15

ABSTRACT STATUS: Sessioned

PRESENTER: Daniela Gloria Villacis Calderon

AUTHORS/INSTITUTIONS: D.G. Villacis Calderon, M.M. Beeson, P.V. Tran, Pediatrics, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Neonatal Hypoxic Ischemic Encephalopathy (HIE) affects 6 in 1000 live-term births per year and is known to impair white matter development. Contactin-2 (CNTN-2), a neural-specific cell surface glycoprotein critical for axonal growth during brain development, is found in exosomes in the peripheral blood. Interestingly, the level of exosomal CNTN-2 in circulation correlates with the risk of abnormal brain development associated with fetal-neonatal iron deficiency. Therefore, neonatal CNTN-2 could provide insight into the state of brain development of infants with HIE. We hypothesize that blood-derived exosomal CNTN-2 is a potential marker to index state of brain injury in a preclinical model of HIE.

Objective: Establish the correlation between peripheral and central CNTN-2 in a mouse model of neonatal HIE.

Design/Methods: Postnatal day (P)10 pups underwent right common carotid artery ligation followed by 45 min hypoxia (9% O_2, 91% N_2) in a BioSpherix animal chamber. Trunk blood and whole brain were collected at 1, 3, 6, 24 hrs, 5 days post-HIE and at baseline. Proteins were isolated from brain hemispheres ipsilateral to the ligation. Exosomes were isolated from plasma by overnight mixing (4°C) in a precipitating solution (10% PEG8000, 0.5M NaCl in DPBS) and were validated by dot and Western blot for CD81 (an exosomal specific cell surface marker) and CNTN-2. Levels of exosomal and brain CNTN-2 were analyzed by ELISA. Two-way ANOVA was used to detect a difference between groups.

Results: Baseline curve for CNTN-2 demonstrated that brain and exosomal CNTN-2 levels peak at P10, with no sex difference (Figure 1, n=6/group/sex). In the HIE model, the mean brain CNTN-2 concentration decreased by 6.8x 1hr post-HIE ($p<0.0001$, n=11/group), corresponding to a decrease in exosomal CNTN-2 at this time point (Figure 2, $p<0.05$, n=11/group).

Conclusion(s): The peak of CNTN-2 level at P10 may represent the peak of axonal maturation in brain development. Our results showed that disruption of brain development by HIE reduced both brain and exosomal CNTN2 levels. The parallel decrease of brain and exosomal CNTN-2 at 1hr post-injury suggests a window for its use as a brain-injury marker. Future experiments will correlate these findings with the extent of brain injury in neonatal HIE and further define this window. The discovery of quantitative molecular markers able to detect subclinical lesions at a stage when routine brain monitoring or imaging is absent would be a major advance in the care of neonates with suspected HIE.

(no table selected)

IMAGE CAPTION: Figure 1. Baseline Brain and Exosomal CNTN-2 Figure 2. Exosomal CNTN-2 baseline vs post-HIE

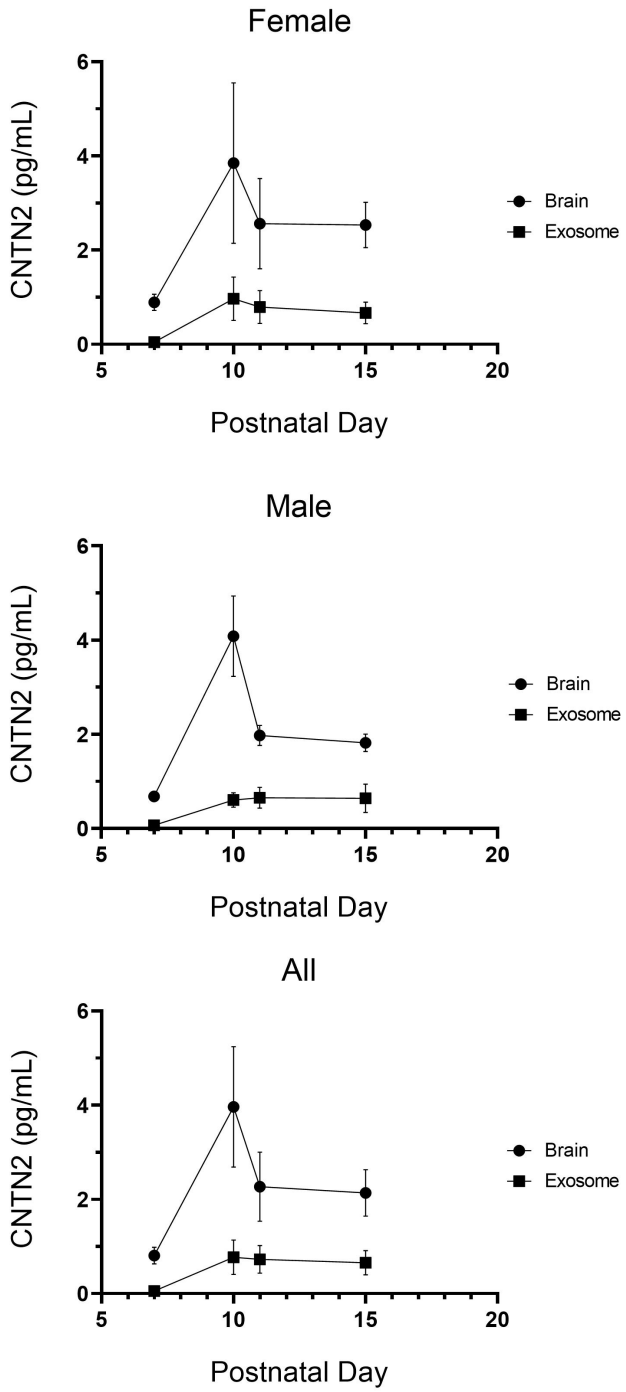


Figure 1. Baseline Brain and Exosomal CNTN-2

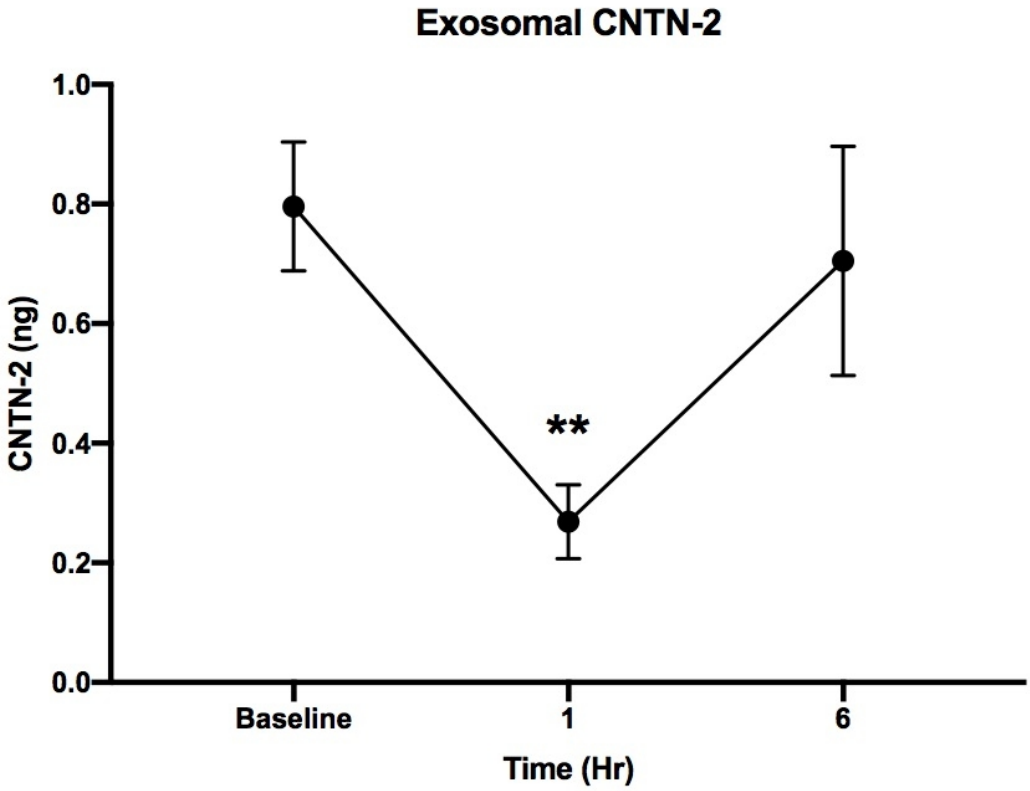


Figure 2. Exosomal CNTN-2 baseline vs post-HIE

CONTROL ID: 3476288

TITLE: Stent Interventions for Pulmonary Artery Stenosis Improve Ventricular Flow Dynamics in a Swine Model

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 16

ABSTRACT STATUS: Sessioned

PRESENTER: Ryan Pewowaruk

AUTHORS/INSTITUTIONS: R. Pewowaruk, A. Roldan-Alzate, Biomedical Engineering, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|L. Lamers, Pediatrics Division of Cardiology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Branch pulmonary artery stenosis (PAS) commonly occurs in patients with complex congenital heart disease (CHD). Catheter interventions are used to treat PAS for many patients. The ventricular response to these interventions is unknown.

Ventricular flow analysis using four dimensional flow magnetic resonance imaging (4D Flow MRI) is an increasingly utilized method to study ventricular function in patients with CHD as changes in ventricular flow represent early signs of cardiac dysfunction.

Objective: Apply 4D Flow MRI in a pig model of PAS and PA stenting and compared the 4D Flow data to conventional anatomic and hemodynamics measures.

Design/Methods: Left PAS (LPAS) was created in 14 piglets and 4 piglets (5kg) had sham surgery. 10 pigs had stent interventions to treat LPAS with 4 untreated LPAS controls. All groups had right heart catheterizations (RHC), computed tomography (CT) angiography and MRI at 20 weeks of age (55kg). MRI included 4D Flow MRI to quantify RV/LV kinetic energy, vorticity, and energy dissipation.

Results: Conventional hemodynamic measurements are summarized in Table 1. LPAS had elevated RA, RV, MPA and RPA pressures and decreased LPA pressure.

Stent interventions increased LPA size vs LPAS group ($p<0.01$). The stented LPA was smaller than the sham proximal LPA ($p=0.03$). Stenting increased LPA flow for intervention (42±2%) vs LPAS (7±2%, $p<0.001$) but was lower than sham (52±5%, $p=0.07$). The intervention group had smaller RV and LV volumes vs LPAS. The intervention group also had elevated ejection fraction (EF) in the RV ($p=0.03$ vs LPAS, $p=0.06$ vs sham).

KE, vorticity and energy dissipation indices are shown in Figure 2. Stent interventions normalized all measures of ventricular mechanics to levels equal to sham controls. In the RV, the LPAS group had increased systolic and diastolic KE ($p=0.04$ and 0.01), vorticity ($p<0.01$) and energy dissipation ($p=0.15$). In the LV the LPAS group had increased systolic and diastolic KE ($p<0.001$ and $p=0.03$), vorticity ($p<0.001$) and energy dissipation ($p<0.01$).

Conclusion(s): In a swine PAS model, stenting normalized RV and LV flow mechanics. Additionally, we identified significantly inefficient RV and LV flow associated with unilateral branch PAS, even in the setting of normal HR, EF and EDVI. These results provide evidence that PAS impacts ventricular function in congenital heart disease in subtle, yet likely important ways. Successful PA stent interventions improve ventricular flow efficiency and may promote long-term health of the ventricle.

(no table selected)

IMAGE CAPTION: Table 1: Hemodynamic measurements Table 2: Standard Cardiac MRI and CT Angiography Figure 1: Maximum intensity projection of RV kinetic energy durign diastolic filling for a sham control. In diastole kinetic energy is highest where blood is filling the RV from the RA and lower in the RV outflow tract. Figure 2: Time curves and bar graphs of flow parameters for both the RV and the LV. Standard error is not shown on the time curve plots. Row 1: kinetic energy, Row 2: vorticity, Row 3: energy dissipation rate. Sys - systolic, Dia - diastolic. An over bar represents $p<0.05$.

Table 1: Hemodynamic measurements

	Sham	LPAS	Intervention
BW (kg)	56±3	57±2	53±3
HR (BPM)	88±4	84±3	94±5
RV/(LV+S) (g/g)	0.42±0.02	0.40±0.02	0.43±0.01
RA Pressure (mmHg)	7±1	10±1	6±1$^{\#}$
RV Systolic Pressure (mmHg)	28±3	38±3*	28±1$^{\#}$
Mean MPA Pressure (mmHg)	19±1	24±1*	17±1$^{\#}$
MPA Pressure (sys / dia, mmHg)	29±1 / 14±1	38±2* / 17±1	26±1$^{\#}$ / 13±1
RPA Pressure (sys / dia, mmHg)	27±2 / 15±1	37±2 / 18±1	25±1$^{\#}$ / 13±1
Distal LPA Pressure (sys / dia, mmHg)	28±1 / 17±1	15*±3 / 13±3	23±1$^{\#}$ / 14±1
Proximal LPA Pressure Gradient (mmHg)	1±1	23*±2	4±1$^{\#}$
PCWP (mmHg)	10±1	11±2	8±0.5$^{\#}$

*p<0.05 versus sham control, $^{\#}$p<0.05 versus LPAS control, sys – systolic, dia – diastolic, PCWP – pulmonary capillary wedge pressure

Table 1: Hemodynamic measurements

Table 2: Standard Cardiac MRI and CT Angiography

	Sham	LPAS	Intervention
Proximal LPA:Ao Diameter (mm/mm)	1.26±0.11	0.12±0.01*	0.94±0.07*#
Distal LPA: Ao Diameter (mm/mm)	0.99±0.05	0.52±0.13*	0.94±0.05#
L Lung Perfusion (%)	52±5	7±2*	42±2#
CI (L/min/m^2)	2.8±0.2	3.2±0.1	3.7±0.4
RV SV/BSA (mL/m^2)	33±3	36±2	36±3
RV ESV/BSA (mL/m^2)	50±7	62±8	35±3#
RV EDV/BSA (mL/m^2)	83±7	98±10	72±5#
RV EF (%)	40±3	37±3	51±2#
LV SV/BSA (mL/m^2)	35±4	41±3	38±3
LV ESV/BSA (mL/m^2)	58±4	62±7	37±4*#
LV EDV/BSA (mL/m^2)	93±4	102±7	75±4#
LV EF (%)	38±3	40±3	50±3

*$p<0.05$ versus sham control, #$p<0.05$ versus LPAS control

Table 2: Standard Cardiac MRI and CT Angiography

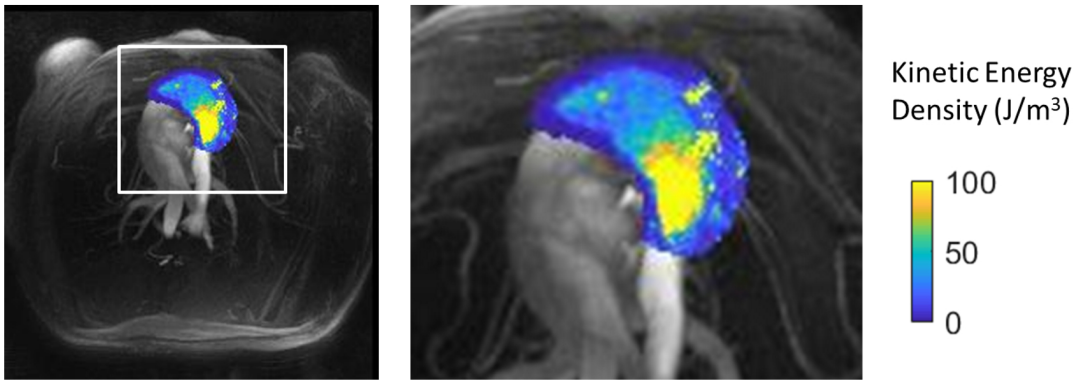


Figure 1: Maximum intensity projection of RV kinetic energy durign diastolic filling for a sham control. In diastole kinetic energy is highest where blood is filling the RV from the RA and lower in the RV outflow tract.

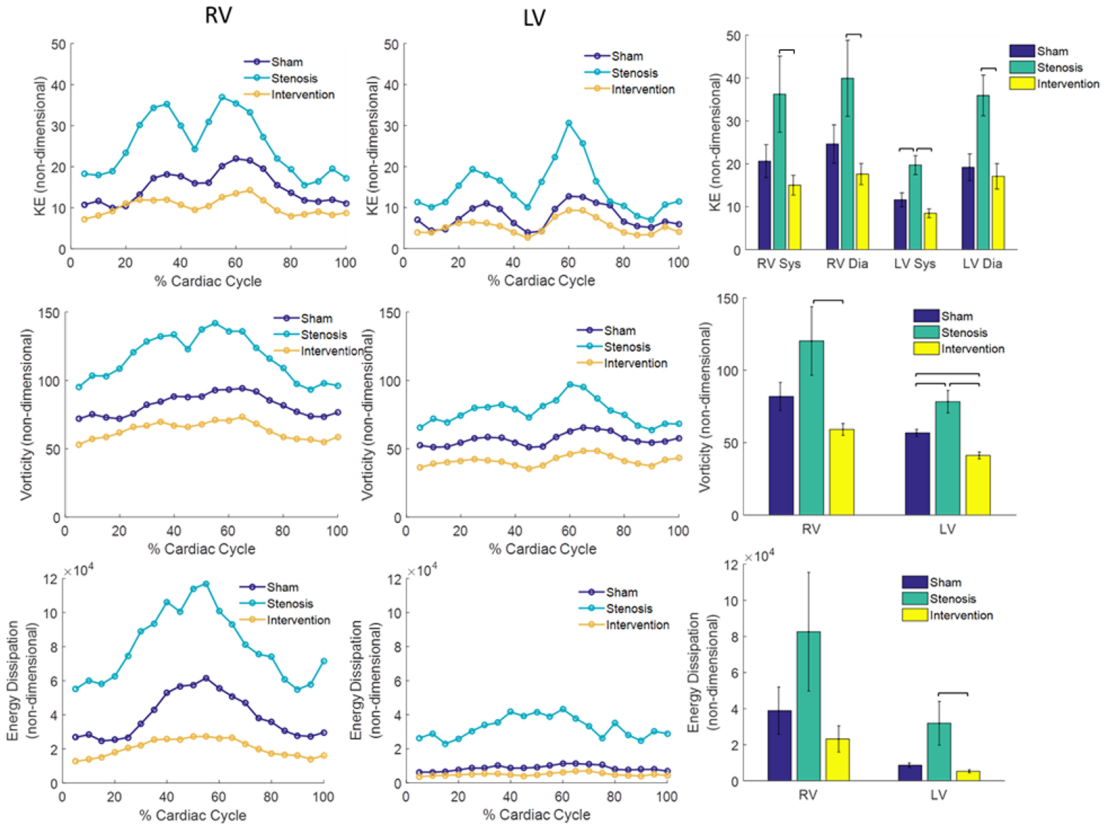


Figure 2: Time curves and bar graphs of flow parameters for both the RV and the LV. Standard error is not shown on the time curve plots. Row 1: kinetic energy, Row 2: vorticity, Row 3: energy dissipation rate. Sys - systolic, Dia - diastolic. An over bar represents $p<0.05$.

CONTROL ID: 3475687

TITLE: NO increases PDE3A protein expression and activates AMPK in human pulmonary microvascular endothelial cells

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 17

ABSTRACT STATUS: Sessioned

PRESENTER: Amy Brown

AUTHORS/INSTITUTIONS: A. Brown, B. Chen, Neonatal-Perinatal Medicine, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|X. Meng, Perinatal Research Institute, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES|J. Dillard, Neonatal-Perinatal, Saint Louis University, Saint Louis, Missouri, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Phosphodiesterase 3 (PDE3), of which there are two isoforms, 3A and 3B, hydrolyzes both cAMP and cGMP to alter vascular tone. In varying cell types, PDE3 inhibition has been shown to increase endothelial nitric oxide synthase (eNOS) expression and activation via AMP-activated protein kinase (AMPK) activation. Additionally, impaired AMPK regulation has been shown to contribute to endothelial dysfunction in models of pulmonary hypertension. Although PDE3 inhibition has been utilized in the treatment of persistent pulmonary hypertension of the newborn (PPHN), the effects of standard of care treatments – inhaled nitric oxide (NO) and supplement oxygen (hyperoxia) – on the PDE3 isoforms have not been elucidated in the pulmonary vasculature. Furthermore, the downstream effects of each PDE3 isoform on AMPK expression are unknown.

Objective: To delineate the effects of NO and hyperoxia on each of the PDE3 isoforms in human pulmonary microvascular endothelial cells (hPMVEC), and evaluate the downstream effects on AMPK and eNOS activation.

Design/Methods: hPMVEC were treated with the NO donor DETA NONOate (250 μM) or vehicle and incubated in 21% O_2 (normoxia) or 85% O_2 (hyperoxia) for 48 h. PDE3A, PDE3B, phosphorylated (p) and total (T)-AMPK and eNOS protein expression were quantified by Western blot analyses (n = 5-10).

Results: In normoxia, PDE3A protein expression was increased in hPMVEC treated with DETA NONOate ($p<0.001$), with no effect on PDE3B. Interestingly, the treatment combination of NO+hyperoxia blunted the NO-induced PDE3A protein expression ($p<0.004$) in hPMVEC, as well as decreased PDE3B protein expression ($p=0.034$) compared to NO+normoxia. Similar to PDE3A protein expression, p/T-AMPK was increased by DETA NONOate in hPMVEC ($p=0.021$) and the combination of NO+hyperoxia prevented the NO-induced AMPK activation ($p=0.014$). T-eNOS was increased in hPMVEC incubated in hyperoxia alone ($p=0.014$), which was blunted with the combination of NO+hyperoxia ($p<0.05$).

Conclusion(s): The combination of NO+hyperoxia resulted in a decrease in PDE3A, PDE3B, and AMPK activation in hPMVEC compared to NO treatment alone. Similarly the combination of NO+hyperoxia blunted the hyperoxia-induced increase in T-eNOS protein expression. We speculate that PDE3 regulates AMPK and that the treatment combination of NO+hyperoxia may have detrimental effects on this pathway in hPMVEC. Isoform-specific PDE3 inhibition may play a role to differentially regulate AMPK activation and eNOS expression in hPMVEC.

(no table selected)

(No Image Selected)

CONTROL ID: 3476605

TITLE: Bifidobacterium longum subspecies infantis EVC001 decreases injury in a murine NEC model

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 18

ABSTRACT STATUS: Sessioned

PRESENTER: Shiloh R Lueschow

AUTHORS/INSTITUTIONS: S.R. Lueschow, S.J. McElroy, Microbiology, University of Iowa, Carver College of Medicine, Iowa City, Iowa, UNITED STATES|S.A. Frese, B.M. Henrick, Food Science and Technology, University of Nebraska, Lincoln, Nebraska, UNITED STATES|S.A. Frese, B.M. Henrick, Evolve Biosystems, Davis, California, UNITED STATES|S.J. McElroy, Pediatrics, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Bifidobacterium longum subspecies infantis (B. infantis) is a vital component of the infant gut microbiome. B. infantis is uniquely able to break down and utilize human milk oligosaccharides (HMOs) completely, giving some strains a competitive advantage in the infant gut. However, HMOs are not in most formulas, thus formula-fed infants do not have as many bifidobacteria in their microbiome. Parallel, Necrotizing Enterocolitis (NEC) is an intestinal disease affecting mainly preterm infants with a 30-50% mortality rate and a higher incidence in formula-fed infants. Treatment strategies for NEC are limited and have not improved in decades, prompting research into prevention. One potential prevention strategy is probiotics, though there is wide strain variation, product quality and potential mechanisms of action. Recent work with B. infantis EVC001 suggests that this organism may result in more appropriate microbiome colonization for preterm infants who are susceptible to inappropriate gut colonization and inflammation, both of which are risk factors for NEC.

Design/Methods: Experimental NEC was induced in P14 C57Bl/6 mice by Paneth cell depletion (IP injection with 75 ug/gbw dithizone) followed seven hours later by induction of bacterial dysbiosis (gavage of Klebsiella pneumoniae $1x10^{11}$ CFU/kgbw). Mice were then gavaged twice with 100 ul B. infantis EVC001 or MCT oil as a vehicle control with or without gavage of the HMO lacto-N-tetraose (LNT) at 250 ul/dose or water as a vehicle control. Sixteen hours after dithizone delivery serum was harvested to look at inflammatory cytokines, then mice were sacrificed and small intestinal tissue was harvested for injury scoring and the cecum for microbiome analysis.

Results: NEC mice given B. infantis alone had significantly lower injury scores compared to NEC animals, while LNT had no impact on injury. Surprisingly, NEC mice given both LNT and B. infantis had significantly decreased injury, but higher average injury than NEC animals receiving B. infantis alone. Evaluation of inflammatory cytokines in NEC mice given B. infantis showed trending decreases compared to NEC animals. In the cecal microbiome, all animals with NEC induction including those given B. infantis had significantly higher Enterobacteriaceae levels compared to shams except NEC animals given LNT alone.

Conclusion(s): These findings support the beneficial properties of B. infantis EVC001 in NEC prevention and drives research into the mechanism of action.

(no table selected)

(No Image Selected)

CONTROL ID: 3476387

TITLE: Cholesterol and sterol intermediates lower energetic barriers for membrane bending and fission necessary for efficient clathrin mediated endocytosis

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 19

ABSTRACT STATUS: Sessioned

PRESENTER: Ruthellen Hope Anderson

AUTHORS/INSTITUTIONS: R.H. Anderson, K. Francis, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota, UNITED STATES|R.H. Anderson, M. Schultz, K. Francis, Cellular Therapies and Stem Cell Biology Group, Sanford Research, Sioux Falls, South Dakota, UNITED STATES|K. Sochacki, J. Taraska, Laboratory of Molecular Biophysics, National Heart Lung and Blood Institute, Bethesda, Maryland, UNITED STATES|H. Vuppula, E. Bailey, J. Kerkvliet, A. Hoppe, Department of Chemistry and Biochemistry, South Dakota State University, Brookings, South Dakota, UNITED STATES|H. Vuppula, E. Bailey, J. Kerkvliet, A. Hoppe, BioSystems Networks and Translational Research Center, Brookings, South Dakota, UNITED STATES|B. Scott, Nanoscience and Nanoengineering, South Dakota School of Mines & Technology, Rapid City, South Dakota, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Human disorders of cholesterol synthesis, characterized by the substitution of cellular cholesterol for sterol intermediates, constitute a group of malformation syndromes that broadly affect tissue development and function. Acute depletion of cholesterol disrupts clathrin-mediated endocytosis (CME), motivating analysis of CME dynamics in the context of disrupted cholesterol synthesis.

Objective: We aim to provide mechanistic insight into the role of sterol homeostasis in the regulation of clathrin-mediated cellular trafficking, explore structure-activity requirements of sterols necessary for supporting CME, and evaluate the functional consequences of altered CME activity within disorders of cholesterol synthesis.

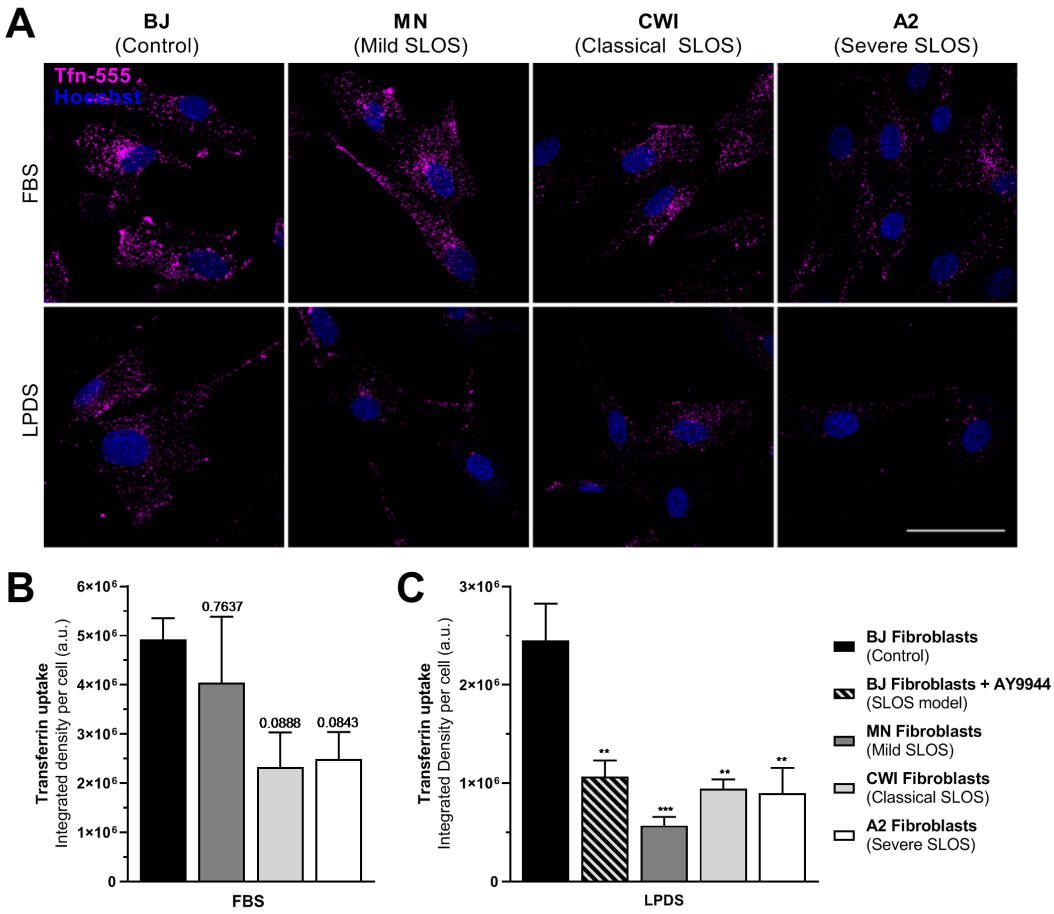
Design/Methods: Altered sterol homeostasis was modeled through small molecule inhibition of the post-squalene cholesterol synthetic pathway as well as fibroblasts, induced pluripotent stem cells (iPSCs), and iPSC-derived neurons derived from subjects with Smith-Lemli-Opitz syndrome. CRISPR/Cas9 gene editing was utilized to fluorescently monitor endogenous CME dynamics in real-time. Vesicular curvature generation in relation to CME assembly was observed through polarized total internal reflection fluorescence (polTIRFM) and platinum replica transmission electron (TEM) microscopy.

Results: We report that disruption of cholesterol synthesis results in striking immobilization of CME and impaired transferrin uptake. Imaging of membrane bending dynamics and CME pit ultrastructure revealed prolonged clathrin pit lifetimes and accumulation of shallow clathrin-coated structures commensurate with total sterol abundance, suggesting progressive impairment of initial curvature generation and formation of the endocytic neck. Furthermore, clathrin trafficking appears robust to sterol identity and total sterol levels correlate with CME productivity. Analysis of Smith-Lemli-Opitz patient fibroblasts and SLOS hiPSC models displayed functional CME deficits.

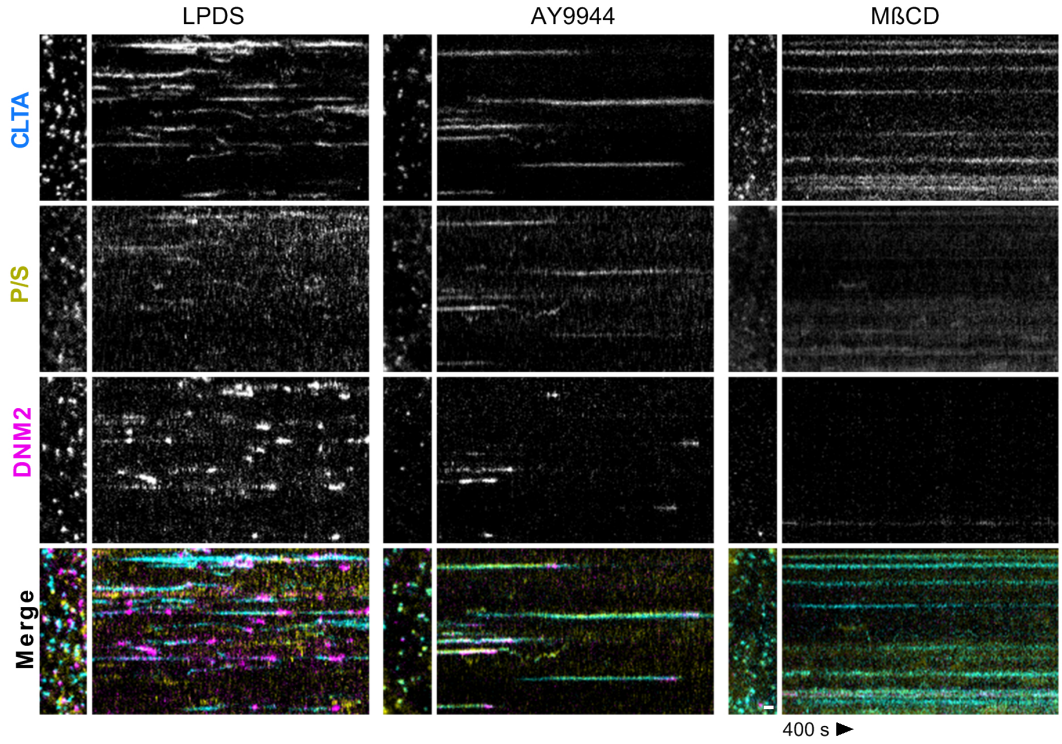
Conclusion(s): We conclude that sterols are a biophysical requirement for efficient endocytic trafficking, acting to lower the energetic costs of membrane bending during pit formation and vesicular scission within CME. These findings also suggest loss of CME activity may contribute to cellular phenotypes observed within SLOS.

(no table selected)

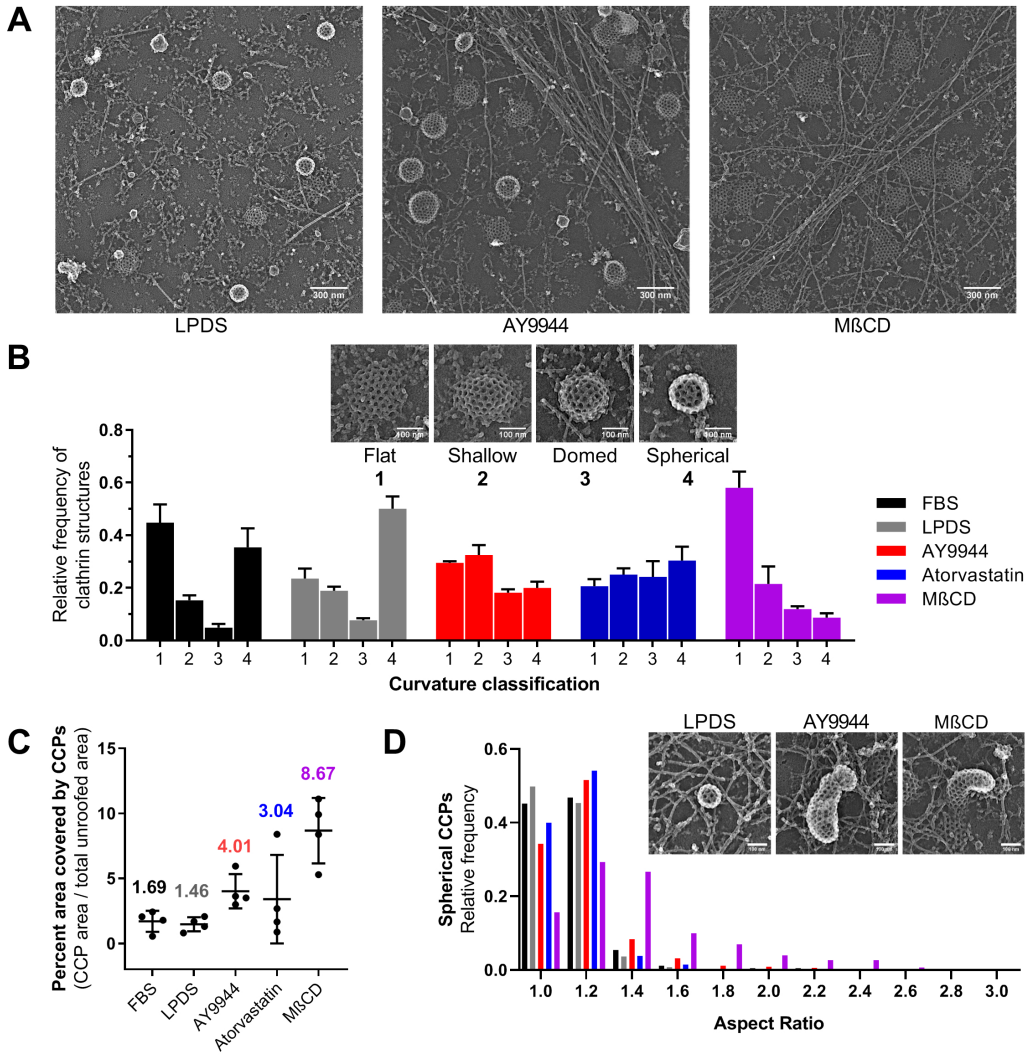
IMAGE CAPTION: CME dynamics are inhibited within Smith-Lemli-Opitz syndrome patient-derived fibroblasts. Loss of cholesterol homeostasis disrupts clathrin-coated pit dynamics. Aberrant clathrin-coated pit ultrastructure under conditions of sterol depletion. Model of cholesterol-mediated stress relaxation during clathrin-mediated endocytosis.



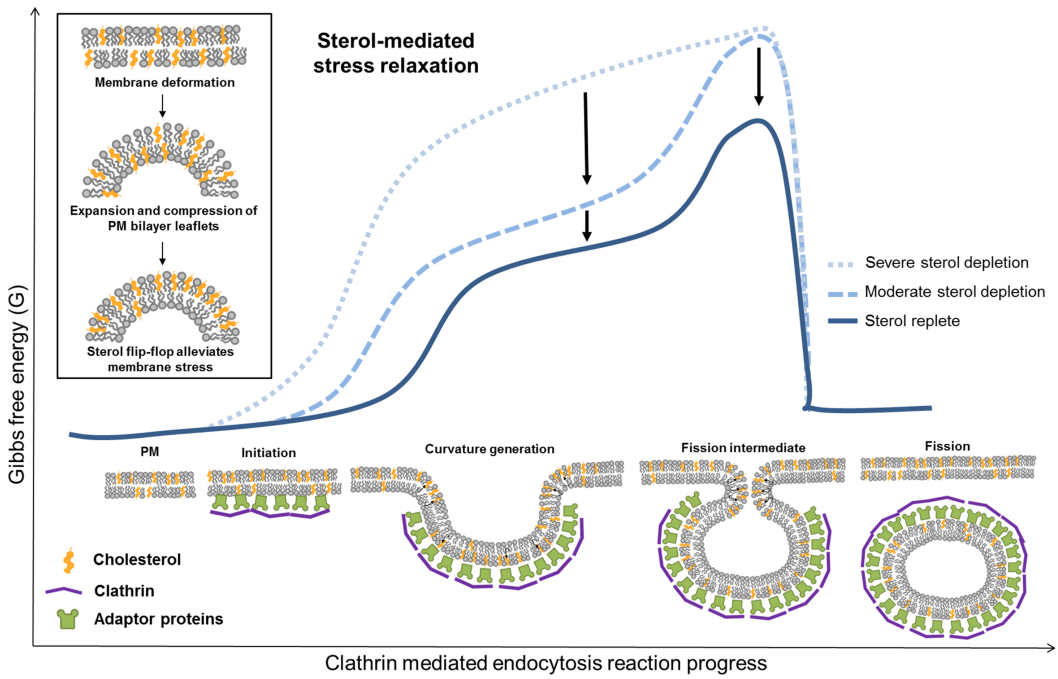
CME dynamics are inhibited within Smith-Lemli-Opitz syndrome patient-derived fibroblasts.



Loss of cholesterol homeostasis disrupts clathrin-coated pit dynamics.



Aberrant clathrin-coated pit ultrastructure under conditions of sterol depletion.



Model of cholesterol-mediated stress relaxation during clathrin-mediated endocytosis.

CONTROL ID: 3475705

TITLE: MPS IVA: Exploration of Novel Biomarkers for Cardiovascular Disease

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 20

ABSTRACT STATUS: Sessioned

PRESENTER: Brittany N Montavon

AUTHORS/INSTITUTIONS: B.N. Montavon, Q. Gan, L. Winter, A.M. Montano, Pediatrics, Saint Louis University School of Medicine, Saint Louis, Missouri, UNITED STATES|A.M. Montano, Department of Biochemistry and Molecular Biology, Saint Louis University, Saint Louis, Missouri, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: MPS IVA (Morquio A Syndrome) is a rare lysosomal storage disease characterized by excessive systemic glycosaminoglycan (GAG) storage, particularly keratan sulfate (KS) and chondroitin-6-sulfate. Cardiovascular disease (CVD) signified by valvular disease and cardiac hypertrophy, the second leading cause of death, remains untouched by current therapies. Determination of accurate biomarkers for CVD could be lifesaving. Cathepsin S (CTSS), a lysosomal cysteine protease, has been linked to cardiac vascular inflammation and calcification. Elastin (ELN), an abundant arterial media protein, is easily attenuated and fragmented by CTSS. Expression of CTSS and ELN in MPS IVA has yet to be explored, and could be potential biomarkers to predict CVD severity and population phenotype.

Objective: To find a novel biomarker that would correlate with the severity of CVD, genotype and phenotype in MPS IVA.

Design/Methods: MPS IVA patients, pediatric, and adult control samples were obtained from de-identified repositories from Saint Louis University and Cardinal Glennon Children's Hospital. Mutation effects were determined by in vitro assays and by using the PolyPhen-2 program. CTSS and ELN levels in plasma were measured via ELISA.

Results: MPS IVA patients were analyzed for CTSS and ELN (n=52-54). Patients were classified by phenotype as mild (35%) or severe (65%) based on pathogenic mutations, GAG and KS levels, and present height on MPS IVA growth chart. 43 different pathogenic mutations were identified, 95% of which caused a mild or severe phenotype. Height correlated with disease severity. Pathogenic mutations correlated with GAG levels. CTSS levels did not correlate with patients' phenotypic severity, but differed significantly among age groups. CTSS levels in MPS IVA children 0-5 years old differed significantly from controls ($p<0.01$). The ROC curve (AUC 0.9889) profile suggests that CTSS levels can be used to discriminate MPS IVA from controls (0-5 y.o.). ELN levels did not correlate with patients' phenotypic severity, but displayed significant difference among MPS IVA vs controls [(>5-10 y.o.; $p<0.05$), (>20-40 y.o. vs > 40 y.o.; $p<0.05$), and (>40 y.o. vs >20-40 y.o.; $p<0.001$)].

Conclusion(s): Identification of life-saving novel biomarkers for CVD remains a major target for treatment of MPS IVA. CTSS shows promising attributes as a biomarker in young MPS IVA children and supports the need for early newborn screening. Further studies are needed to understand how CTSS and ELN levels correlate with MPS IVA severity and treatment outcomes.

(no table selected)

IMAGE CAPTION:

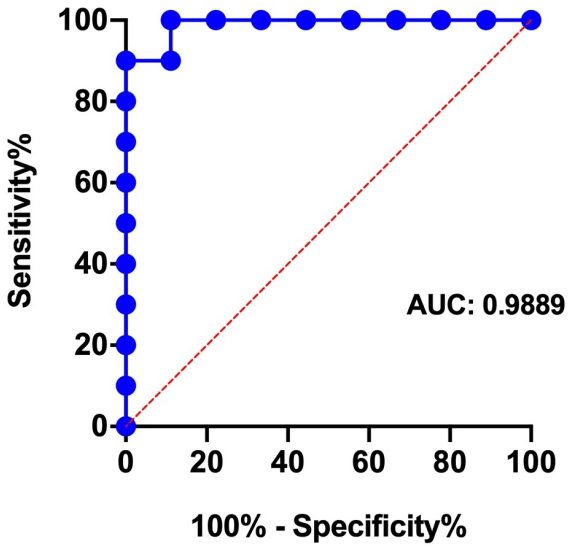


Figure 1. Receiver operating characteristic (ROC) curve of Cathepsin S levels between MPS IVA patients and normal controls 0-5 years old.

CONTROL ID: 3476617
TITLE: Application of Mucous Fistula Stool Refeeding in Surgical Pediatric Patients following Bowel Resection
DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 21
ABSTRACT STATUS: Sessioned
PRESENTER: Cody West
AUTHORS/INSTITUTIONS: R. Rahhal, Pediatrics, Division of Pediatric Gastroenterology, University of Iowa, Iowa City, Iowa, UNITED STATES|C. West, The University of Iowa Roy J and Lucille A Carver College of Medicine, Iowa City, Iowa, UNITED STATES|
CURRENT CATEGORY: Clinical Investigation
CURRENT SUBCATEGORY: None
ABSTRACT BODY:
Background: Pediatric patients, especially neonates, can develop severe abdominal pathology that requires surgical resection with creation of a small bowel ostomy (enterostomy) and mucous fistula (MF). Refeeding of stool output from the small bowel ostomy into the distal MF may help recruit the distal remaining bowel, possibly assisting in improved intestinal absorption with advancement of enteral nutrition, reduced dependence of venous nutrition and reduced liver disease frequency and severity.
Objective: This study evaluated the impact of stool refeeding into the distal MF following bowel resection in children at a tertiary medical center.
Design/Methods: This was a retrospective cohort study of patients who had ostomy creation and takedown at the University of Iowa in those < 5 years of age at the time of initial surgery between January 2010 – February 2020.
Results: In total, 47 patients were identified including 29 patients in the stool refeeding group and 18 in the non-refeeding (control) group. There were no differences in baseline characteristics between groups (gestational age, birthweight, surgery indications, age and weight at ostomy creation, ostomy type) except for more patients in MF feeding group having the entire colon preserved (79% vs 50%, p=0.04).

Median time from stoma creation to start of enteral feeding and number of days of venous nutritional support were similar between groups. The control group had more patients without any enteral nutrition (0 vs 33%, p=0.002) and more deaths (3% vs 33%, p=0.009) during their hospital stay than the MF feeding group. All patients were admitted to an intensive care unit (ICU), neonatal or pediatric. When excluding patients that died, median ICU days and total hospital days were similar between groups. Difference in frequency of cholestasis (defined as direct bilirubin ≥ 1 mg/dL) was not statistically significant (56% in MF refeeding group vs 75% in control group, p=0.2). No complications were encountered that were related to MF refeeding.
Conclusion(s): MF refeeding is safe and shows potential to reduce the incidence of cholestasis and subsequent liver damage.
(no table selected)
IMAGE CAPTION:

Table 1: Cohort Characteristics

Variable	Mucous fistula non-refeeding (control) group	Mucous fistula group	p-value
Number of patients	18	29	
Sex, %female	6/18 (33%)	12/29 (41%)	0.58
Gestational age at birth (weeks), median (IQR)	32.0 (12.0)	33.0 (12.5)	0.88
Birthweight (g), median (IQR)	1565 (2220)	1550 (2165)	0.95
Patients with low birth weight (<2500 g), %	61%	69%	0.58
Age at ostomy creation (days), median (IQR)	20 (40)	10 (28)	0.27
Weight at ostomy creation (kg), median (IQR)	2.3 (2.6)	2.2 (2.0)	0.51
Surgery indications, %			
Necrotizing enterocolitis	8/18 (44%)	6/29 (21%)	0.08
Gastroschisis	0/18 (0)	3/29 (10%)	0.28
Intestinal Atresia	1/18 (6%)	2/29 (7%)	1.00
Spontaneous intestinal perforation	1/18 (6%)	8/29 (28%)	0.12
Volvulus	4/18 (22%)	1/29 (3%)	0.06
Bowel Ischemia	1/18 (6%)	6/29 (21%)	0.23
Mesenteric Avulsion	0/18 (0)	1/29 (3%)	1.00
Inspissated Meconium	3/18 (17%)	3/29 (10%)	0.67
Ostomy type, %			
Jejunostomy	3/18 (17%)	12/29 (41%)	0.08
Ileostomy	14/18 (78%)	17/29 (59%)	0.18
Entire Colon Preserved, %	9/18 (50%)	23/29 (79%)	0.04
Preserved ileocecal valve, %	12/18 (71%)	19/29 (79%)	0.71

Table 2: Patient Outcomes

Variable	Mucous fistula non-refeeding (control) group	Mucous fistula group	p-value
Nutrition			
% remaining NPO	6/18 (33%)	0/29 (0)	0.002
Time from stoma to start enteral feeding (days), median (IQR)	6.5 (5.5)	7.0 (5.0)	0.84
Parenteral nutrition time from ostomy creation to takedown (days), excluding deaths, median (IQR)	35.0 (41.4)	41.0 (31.0)	0.26
Hospital stay and mortality			
Time from stoma to takedown (days), excludes deaths, median (IQR)	59.0 (21.5)	57.0 (21.5)	0.95
Hospital days- Admission to discharge, excluding deaths, median (IQR)	91.5 (123.5)	97.0 (59.5)	0.77
Total ICU days, excluding deaths, median (IQR)	82.5 (119)	91.0 (71.5)	1.00
%Deceased before takedown	6/18 (33%)	1/29 (3%)	0.009
Liver disease			
Peak direct bilirubin level (mg/dL), median (IQR)	2.2 (3.8)	2.3 (3.9)	0.61
%patients with direct bilirubin ≥ 1 mg/dL	12/16 (75%)	15/27 (56%)	0.20

NPO = Nil per os (nothing by mouth)

CONTROL ID: 3476603

TITLE: Hypoxia is a modulator of miR-21 expression in oligodendroglial progenitors.

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 22

ABSTRACT STATUS: Sessioned

PRESENTER: Eli Chapman-Orr

AUTHORS/INSTITUTIONS: E. Chapman-Orr, R. Dettman, M. Dizon, Pediatrics/Neonatology, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, Illinois, UNITED STATES|R. Dettman, M. Dizon, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Perinatal hypoxia-ischemia (HI) can lead to devastating medical complications in infants including hypoxic-ischemic encephalopathy and seizures, and later cognitive impairment and cerebral palsy. Changes to several signaling pathways have been identified in response to perinatal HI, that may be related to the observation that differentiation of oligodendroglial progenitors is inhibited and white matter decreased. We have observed that the microRNA (miR) miR-21-5p is transcriptionally induced after HI in a mouse model.

Objective: Here we tested if hypoxia alters miR-21-5p expression in oligodendroglial progenitor cells (OPCs).

Design/Methods: Immortalized rat OPCs (CG4 cells) were cultured in a room air (21% O_2, 5% CO_2) or hypoxia (1.5% O_2, 5% CO_2) incubator. Total RNA was purified using a miRNeasy RNA isolation kit. RNA levels were assessed by qRTPCR for mature miR-21-5p transcripts using locked nucleic acid primers. Quantification was calculated using the ΔΔCt method. Next, we conditionally deleted Hif1α in OPCs in vivo using NG2CreERT2;HIF1α F/F mice and tested for miR-21-5p using qRTPCR. NG2CreERT2;HIF1α F/F mice were injected with tamoxifen P7-P10 and tissue was collected at P14. Finally, we identified hypoxic cells using pimonidazole (Hypoxyprobe). Wildtype C57Bl/6 mice were injected P7-P9 then perfused P14, fixed and cryosectioned. Hypoxyprobe was detected using an antibody to pimonidazole.

Results: We observed that hypoxia induced miR-21-5p expression in CG4 OPCs by a 2.33 log2-fold change compared to normoxic controls (miR103a served as internal control). When Hif1α was deleted in OPCs in mouse pups reared in room air, miR-21-5p expression decreased with a 0.027 log2-fold change. Hypoxyprobe analysis in wildtype mice reared in room air, showed that cells in the subventricular zone and corpus callosum incorporated pimonidazole.

Conclusion(s): miR-21-5p is a hypoxia response gene in CG4 OPCs. This is likely regulated by Hif1α, as conditional deletion of Hif1α significantly lowers miR-21-5p expression in the mouse brain. Remarkably, this occurred in mice reared in room air suggesting that Hif1α induces miR-21-5p in OPCs during normal white matter development. This was supported by incorporation of pimonidazole in numerous cells of the subventricular zone and corpus callosum in wildtype mice reared in room air. Thus, miR-21-5p downstream of Hif1α may play a role in normal white matter development. In future experiments, this hypothesis will be tested using a conditional knockout of miR-21-5p in newborn mice.

(no table selected)

(No Image Selected)

CONTROL ID: 3476633

TITLE: Association Between Ventricular Morphology And Protein Losing Enteropathy In Patients With Single Ventricle Physiology

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 23

ABSTRACT STATUS: Sessioned

PRESENTER: Krishna Kishore Umapathi

AUTHORS/INSTITUTIONS: K. Umapathi, B. Muller, S. Awad, Department of Pediatrics, Division of Cardiology, Rush University, Chicago, IL, US, academic, Chicago, Illinois, UNITED STATES|A. Thavamani, UH Rainbow Babies and Children's Hospital Division of Pediatrics, Cleveland, Ohio, UNITED STATES|A. Gupta, Lincoln Medical Center, Bronx, New York, UNITED STATES|

CURRENT CATEGORY: Clinical Investigation

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Congenital heart disease with single ventricle (SV) physiology increases the risk for protein-losing enteropathy (PLE) after Fontan surgery. PLE increases mortality in patients with Fontan circulation but no national-level estimates are available. Hypoplastic left heart syndrome (HLHS) patients depend on the right ventricle for supplying systemic circulation making them prone to high systemic venous pressure and diastolic dysfunction thereby increasing the risk for PLE. We hypothesize that PLE will worsen outcomes in patients with SV physiology and Fontan repair and also that patients with HLHS will have a higher incidence of PLE compared to patients with tricuspid atresia (TA) who have systemic left ventricle.

Objective: Compare the mortality rates and healthcare utilization in PLE vs non-PLE hospitalizations in patients with SV (HLHS and TV) physiology across the United States

Compare the incidence and outcomes of PLE in HLHS vs TA.

Design/Methods: This is a population based retrospective review using KID and NIS data from the Healthcare Cost and Utilization Project (2003-2016). Inclusion criteria: Age 5-20 years with ICD-9 and 10 codes for HLHS (746.7, Q23.4) or TA (746.1, Q22.6). Age, gender, race, length of stay (LOS), hospitalization charges and mortality rates were compared between SV (HLHS and TA) hospitalizations with and without PLE and between HLHS and TA with PLE using independent t-test or Mann-Whitney U test and χ^2 or Fischer Exact as appropriate.

Results: Of 9160 HLHS and 3682 TA hospitalizations, 1590 (17.4%) and 292 (7.9%) had PLE (Table 1). Hospitalizations with PLE occurred later in HLHS/TA compared to those without PLE. Although LOS is longer in patients with PLE, no difference in mortality was noted. PLE onset occurred at a younger age for HLHS (11 years) than TA (13 years), $p < 0.001$ (Table 2). Although PLE mortality more than doubled in HLHS vs TA (3.8% vs 1.7%), statistical significance was not achieved with no difference in healthcare utilization noted in comparison to TA.

Conclusion(s): Incidence of PLE is higher and occurs at a younger age in HLHS compared to TA suggesting a systemic right ventricle in SV physiology is a risk factor for developing PLE.

(no table selected)

IMAGE CAPTION: **Table 1:** Comparison between hospitalizations for hypoplastic left heart syndrome (HLHS) with and without protein-losing enteropathy (PLE) and tricuspid atresia (TA) with and without PLE.

Table 2: Comparisons between hospitalizations for HLHS and TA with PLE.

Table 1: Comparison between hospitalizations for hypoplastic left heart syndrome (HLHS) with and without protein-losing enteropathy (PLE) and tricuspid atresia (TA) with and without PLE.

HLHS (n=9160)	**PLE (n=1590)**	**No PLE (7570)**	**p value**
Age, years (Mean±S.D.)	11.5±4.3	9.9±4.4	<0.001
Female, n (%)	586 (36.9%)	2775 (36.7%)	0.89
African American, n (%)	302 (20.6%)	859 (13%)	<0.001
LOS, days (Mean±S.D)	10.7±20.3	8.8±19.7	<0.001
Hospital charges, $ (Mean±S.D.)	130,148±274519	126,970±344,785	0.73
Mortality, n (%)	61 (3.8%)	231 (3.1%)	0.12
TA (n=3682)	**PLE (n=292)**	**No PLE (3683)**	**p value**
Age, years (Mean±S.D.)	13.3±3.9	11.6±4.9	<0.001
Female, n (%)	158 (53.9%)	1604 (43.6%)	<0.001
African American, n (%)	30 (12.6%)	514 (16.2%)	<0.001
LOS, days (Mean±S.D.)	9.6±15.7	7.2±14.9	0.01
Hospital charges, $ (Mean±S.D.)	122,813±300,138	86,763±160,308	0.04
Mortality, n (%)	* (1.7%)	49 (1.3%)	0.60

***values less than 10 are not reportable per HCUP data user agreement to protect patient confidentiality**

Table 2: Comparisons between hospitalizations for HLHS and TA with PLE.

	HLHS with PLE (n=1590)	**TA with PLE (n=292)**	**p value**
Age, years (Mean±S.D.)	11.5±4.3	13.3±3.9	<0.001
Female, n (%)	586 (36.9%)	158 (53.9%)	<0.001
African American, n (%)	302 (20.6%)	30 (12.6%)	0.01
LOS, days (Mean±S.D.)	10.7±20.3	9.6±15.7	0.35
Hospital charges, $ (Mean±S.D.)	130,148±274519	122,813±300,138	0.76
Mortality, n (%)	61 (3.8%)	* (1.7%)	0.08

***values less than 10 are not reportable per HCUP data user agreement to protect patient confidentiality**

Table 1: Comparison between hospitalizations for hypoplastic left heart syndrome (HLHS) with and without protein-losing enteropathy (PLE) and tricuspid atresia (TA) with and without PLE.
Table 2: Comparisons between hospitalizations for HLHS and TA with PLE.

CONTROL ID: 3473038

TITLE: Teratogenic Effects of Prenatal Alcohol Exposure on Cardiac Innervation

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 24

ABSTRACT STATUS: Sessioned

PRESENTER: Steven Conlon

AUTHORS/INSTITUTIONS: S. Conlon, Neonatology, UH Rainbow Babies and Children's Hospital Division of Pediatrics, Cleveland Heights, Ohio, UNITED STATES|S. Conlon, S. Ford, M. Watanabe, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Ford, UH Rainbow Babies and Children's Hospital Division of Pediatrics, Cleveland, Ohio, UNITED STATES|

CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Alcohol exposure during embryonic development can damage neural crest cells, precursors of the autonomic nervous system. Abnormalities of cardiac innervation are known to result in heart disease, arrhythmias, and are implicated in sudden infant death syndrome (SIDS), the sudden and unexplained death of an infant usually during sleep. Children exposed to alcohol in utero have abnormal heart rate responses to tilt table testing, suggesting dysfunction in the autonomic control of the heart and increased rates of SIDS. We tested our hypothesis that prenatal alcohol exposure would result in changes in heart innervation that could explain this autonomic dysfunction.

Objective: To identify changes in cardiac neuroanatomy after prenatal exposure to ethanol.

Design/Methods: Quail eggs were incubated at 38^{O}C in a humidified incubator. Eggs were injected with 40 ml PBS (control) or 40 ml of 50% ethanol at 24 hours, then allowed to incubate until dissection at 8 days. This ethanol administration is equivalent to one bout of binge drinking during early first trimester and results in fetal alcohol spectrum disorder phenotypes.

Using fluorescently labeled TUJ1, an antibody that specifically binds neuronal cytoskeletal components, we immunostained intact hearts and captured images of the thoracic nerve, a cardiac branch of the vagus, which runs the length of the pulmonary artery (Image 1). A binary system was used to evaluate the presence or absence of a split in this nerve branch.

Results: Cohorts included 13 control (PBS) hearts and 20 exposed to ethanol. The Fisher’s exact test demonstrated a statistically significant increase in splitting of the thoracic nerve after alcohol exposure (p= 0.038) (Table 1). Qualitative differences were noted in the pattern and area of the nerve plexus that will require a more complex quantitative analysis.

Conclusion(s): We demonstrated that prenatal alcohol exposure resulted in embryos exhibiting a split of the major nerve that innervates the heart, even in those with structurally normal hearts. Changes in structural innervation can have significant clinical effects including, changes in cardiac function, development of arrhythmias and changes in autonomic response. Inability to increase heart rate and respond to periods of stress has been associated with SIDS, potentially linking these findings to a clinically relevant event. This finding may change the management of those with structurally normal hearts exposed to alcohol in utero, requiring long term follow up, and further investigation of cardiac autonomic function.

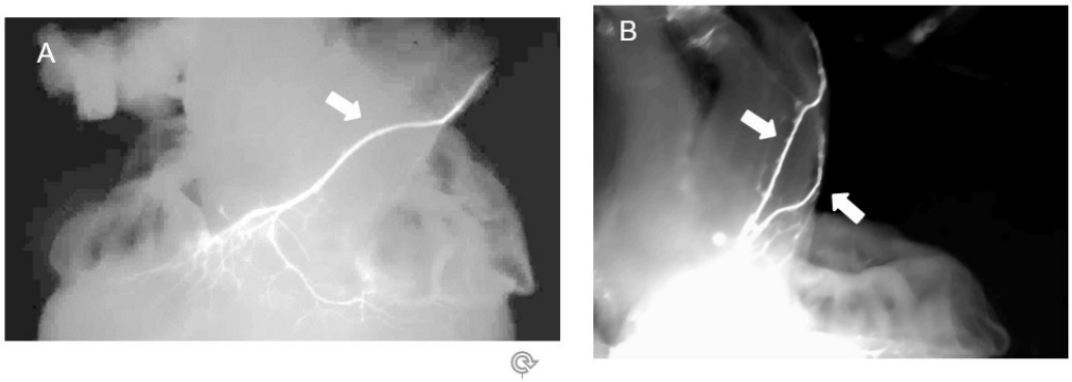
(no table selected)

IMAGE CAPTION: Table 1. The Fisher’s exact test demonstrated a statistically significant increase in splitting of the thoracic nerve after alcohol exposure (p= 0.038) In image A (control) you see a single large thoracic nerve that spreads into the cardiac plexus, image B (Ethanol Exposed) the thoracic nerve is split in two, coming together just before the cardiac plexus

Thoracic Nerve	Split Nerve	Single Nerve
Sham Control	4 (31%)	9
Ethanol Exposed	14 (70%)	6

Table 1: Number of hearts with thoracic nerves that had a split or single nerve. Fisher's Exact test demonstrated a p value of 0.038

Table 1. The Fisher's exact test demonstrated a statistically significant increase in splitting of the thoracic nerve after alcohol exposure (p= 0.038)



In image A (control) you see a single large thoracic nerve that spreads into the cardiac plexus, image B (Ethanol Exposed) the thoracic nerve is split in two, coming together just before the cardiac plexus

CONTROL ID: 3475590
TITLE: Risk of Functional Constipation in Children with a History of Infantile Cow’s Milk Protein Allergy
DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 25
ABSTRACT STATUS: Sessioned
PRESENTER: Thomas LaRouere
AUTHORS/INSTITUTIONS: T. LaRouere, K. Cares, Children's Hospital of Michigan, Detroit, Michigan, UNITED STATES|
CURRENT CATEGORY: Clinical Investigation
CURRENT SUBCATEGORY: None
ABSTRACT BODY:
Background: Cow's milk protein allergy (CMPA) is a common diagnosis seen in infants and usually presents with occult positive bloody diarrhea with fussiness due to underlying colonic inflammation that usually self resolves by 1-2 years of age. Reports suggest that CMPA may increase the risk of functional constipation later in life. Little data exists on how common the association is and its clinical characteristics, specifically the severity of constipation and its management.
Objective: In this study, we aim to define the clinical characteristics, prevalence, duration, and severity of functional constipation in patients with CMPA.
Design/Methods: Using the EMR, we conducted a retrospective chart review to identify patients with a diagnosis of CMPA in infancy that were also diagnosed with functional constipation after 1 year of age from 1/1/2009-12/31/2018. Patient demographics, symptoms, duration, and treatment of CMPA and constipation were analyzed, with patients categorized with severe and non-severe constipation. Those with intractable constipation that required additional therapy besides osmotic laxatives, hospitalization, or additional workup (e.g., labs, rectal biopsy, barium enema) were considered severe. Prevalence and duration of constipation in CMPA were calculated and compared to other studies analyzing similar data.
Results: Over the 10-year period, there were a total of 1261 patients diagnosed with CMPA and 13222 patients diagnosed with constipation. There were 106 patients that met our inclusion criteria. Eight percent of CMPA infants developed constipation. Most common symptoms of CMPA were vomiting, bloody stools, constipation, and diarrhea, with a median duration of 1.3 years followed by successful reintroduction of milk protein into the diet. Thirty-three patients (31%) were categorized as severe constipation. Out of those with a documented duration, 29 of 87 (33%, p=0.016) had improvement in constipation symptoms within 1 year of diagnosis.
Conclusion(s): This study suggests a possible association of CMPA in infants with constipation. Although the prevalence of constipation in CMPA patients was not high, the duration and severity of constipation were significant. A systematic review of pediatric constipation reports that 60.6% of patients improved within 1 year of diagnosis. In comparison, 66% of our patients with a history of CMPA had persistent constipation beyond 1 year. Taking this into consideration, patients with CMPA should be closely monitored and treated for persistent and severe constipation.
(no table selected)
IMAGE CAPTION: Figure 1: Symptoms of CMPA Figure 2: Workup for Constipation

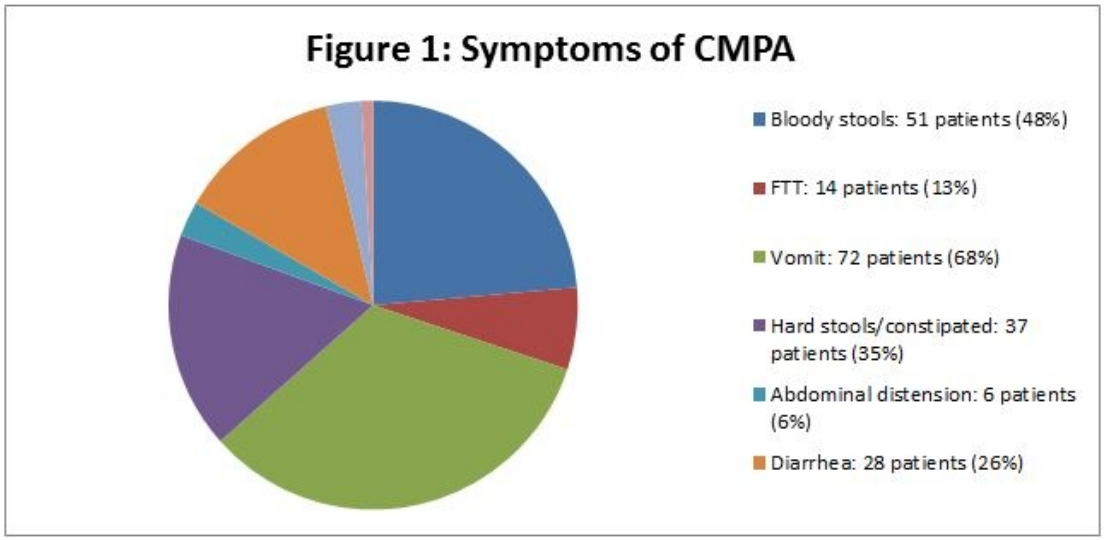


Figure 1: Symptoms of CMPA

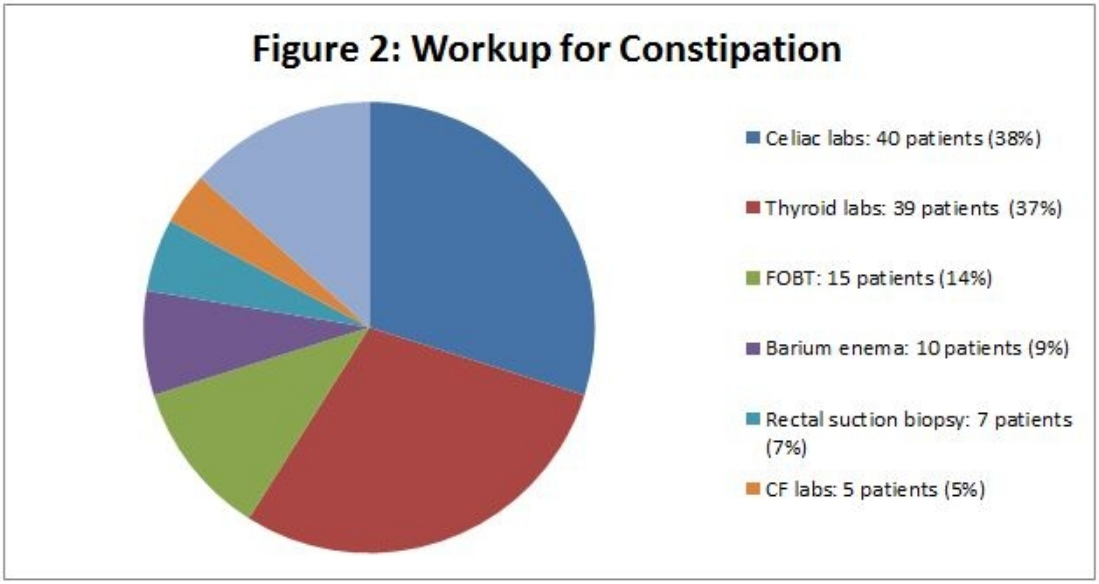


Figure 2: Workup for Constipation

CONTROL ID: 3475770

TITLE: Anatomical Concordance of Neonatologist Performed Echocardiography as part of Hemodynamic Consultation and Pediatric Cardiology

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 26

ABSTRACT STATUS: Sessioned

PRESENTER: Adrianne Rahde Bischoff

AUTHORS/INSTITUTIONS: A.R. Bischoff, R. Giesinger, D.R. Rios, R. Ashwath, P. McNamara, Pediatrics, University of Iowa, Iowa City, Iowa, UNITED STATES|L. Mertens, Pediatrics, The Hospital for Sick Children, Toronto, Ontario, CANADA|

CURRENT CATEGORY: Clinical Investigation

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Targeted neonatal echocardiography (TnECHO) performed by neonatologists as part of a hemodynamics consultation is increasingly being utilized in NICUs around the world. Current guidelines suggest that the first echocardiogram should be reviewed by a pediatric cardiologist to rule out congenital heart disease (CHD). To minimize delays in obtaining physiological data, first echocardiograms, which include imaging sufficient to rule out clinically relevant CHD, may be performed by the neonatal hemodynamics team and reviewed afterwards by a pediatric cardiologist. This practice has not been systematically evaluated.

Objective: To compare concordance between the anatomic findings reported by the hemodynamics NICU team and pediatric cardiology reports.

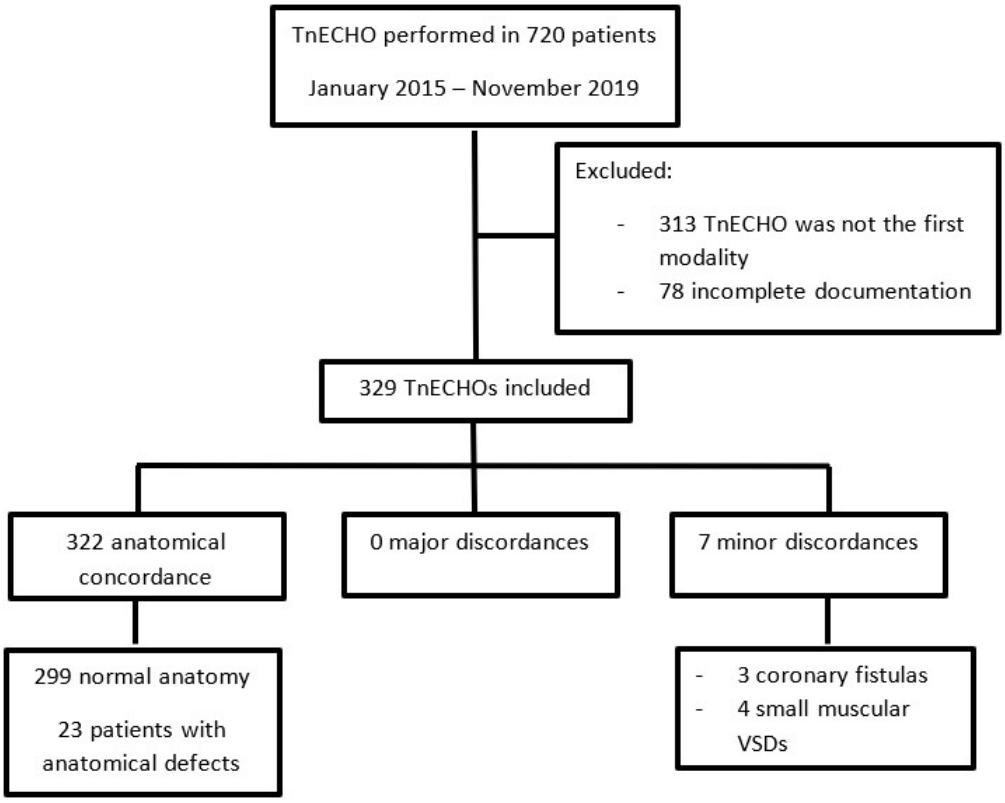
Design/Methods: We performed a retrospective evaluation of infants admitted to two large referral centers with established neonatal hemodynamics programs [Hospital for Sick Children and University of Iowa Stead Family Children's Hospital] who underwent comprehensive TnECHO as their first postnatal echo. The protocol included comprehensive imaging including aortic arch, pulmonary veins, and evaluation for shunts. The hemodynamic consultation note was compared to the cardiology reports to determine anatomical concordance or major/minor discrepancies in all first studies.

Results: TnECHO was performed in 720 patients between Jan-2015 and Nov-2019. A total of 329 infants satisfied eligibility criteria. Anatomical concordance occurred in 96% [K 0.857 (95% CI 0.489-0.697), $p<0.001$]. The index population included 23 infants (7%) with CHD, of whom only one (0.3%) had a ductal-dependent lesion (coarctation of the aorta) which was correctly identified by both teams. Additional imaging was performed by echocardiography sonographers, upon the request of the pediatric cardiologist, for 4 infants (1.2%); however, this did not result in a change in diagnosis and no intervention was required based on additional findings.

Conclusion(s): Although the rate of major CHD in patients considered eligible for hemodynamic consultation was low, there is high diagnostic concordance between trained neo-hemodynamics specialists and pediatric cardiology. First echocardiograms performed by subspecialty neonatologists may provide imaging of sufficient quality to evaluate a critically unwell neonate for CHD. We highlight the importance of formalized and standardized training for neonatologists with hemodynamic expertise who perform timely TnECHO assessments.

(no table selected)

IMAGE CAPTION: Description of the population. TnECHO: targeted neonatal echocardiography Baseline characteristics of infants where Hemodynamic Consultation included echocardiography as first modality



Description of the population. TnECHO: targeted neonatal echocardiography

Table: Baseline characteristics of infants where Hemodynamic Consultation included echocardiography as first modality

Characteristics	**n= 329**
Male	62 (58.5%)
Birth weight (grams)	1210 (420-7081)
Gestational age	22^{+1} – 40^{+4}
Age (days) at the time of first TnECHO	2 (0-186)
Weight at time of the Echo (grams)	1426 (390-7081)
Postmenstrual age at the time of the Echo	22^{+1} – 53^{+1}
Death	40 (12.1%)
ECMO	1 (0.3%)
Indication:	
- Hypoxic respiratory failure	85 (25.8%)
- Hypotension/shock	102 (31%)
- PDA screening/ assessment	103 (31.3%)
- Assessment for chronic pulmonary hypertension	15 (4.5%)
- Others	24 (7.3%)
Invasive mechanical ventilation	262 (79.6%)
High frequency ventilation	115 (34.9%)
Medications for blood pressure support	118 (35.9%)
PDA	243 (73.8%)
PFO/ASD	286 (86.9%)

TnECHO: Targeted Neonatal Echocardiography; ECMO: extracorporeal membrane oxygenation; PDA: patent ductus arteriosus; PFO: patent foramen ovale; ASD: atrial septal defect

Baseline characteristics of infants where Hemodynamic Consultation included echocardiography as first modality

CONTROL ID: 3473919

TITLE: The Altered Gut Resistome in Short Bowel Syndrome

DIGITAL OBJECT IDENTIFIER (DOI): Poster#: 27

ABSTRACT STATUS: Sessioned

PRESENTER: Jocelyn Ou

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CURRENT CATEGORY: Basic Science

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Short bowel syndrome (SBS) occurs in pediatrics as a result of necrotizing enterocolitis, gastroschisis, volvulus, or intestinal atresia. Following intestinal resection, remnant bowel length is inadequate to sustain life and parenteral nutrition (PN) is required. Patients with SBS are frequently exposed to antibiotics for various indications, including line-associated infections and altered gut physiology leading to bacterial translocation or small intestinal bacterial overgrowth. Multiple antibiotic exposures and repeated hospitalizations drive changes in both the microbiota and the genes conferring antibiotic resistance in the gut, known as the resistome. We have previously shown intestinal dysbiosis in patients with SBS through 16S rRNA sequencing. However, the gut resistome has not been studied in this population.

Objective: The purpose of this study was to test the hypothesis that the gut resistome in the SBS patient population is altered.

Design/Methods: Cross-sectional fecal samples and clinical metadata were collected from 19 subjects from the St. Louis Children’s Hospital Pediatric Intestinal Rehabilitation Clinic. Metagenomic shotgun sequencing was performed on stool samples of SGS subjects and healthy, age-matched controls. Shannon diversity index was used to measure the alpha diversity, richness, and abundance of the microbiota and gut antibiotic resistance genes (ARGs).

Results: SBS subjects have distinct taxonomic differences in their microbiota (Fig 1) and significantly decreased alpha diversity compared to healthy controls. Children with SBS also have a significantly greater abundance of ARGs and a trend toward increased ARG diversity and richness, though statistical significance was not reached. There is a distinct ARG pattern in SBS subjects, including enrichment of genes modulating antibiotic resistance, drug efflux pump complexes that confer resistance, and encoding resistance to tetracycline, bacitracin, and polymyxin (Fig 2).

Conclusion(s): To our knowledge, this is the first study describing antibiotic resistance genes in patients with SBS. The perturbed resistome in these patients may make effective treatment of infections more challenging. Further research should clarify the long-term effects of antibiotics on the resistome of SBS patients, as well as identify strategies to prevent resistance development and more effectively treat infections in SBS patients.

(no table selected)

IMAGE CAPTION: Figure 1 Figure 2

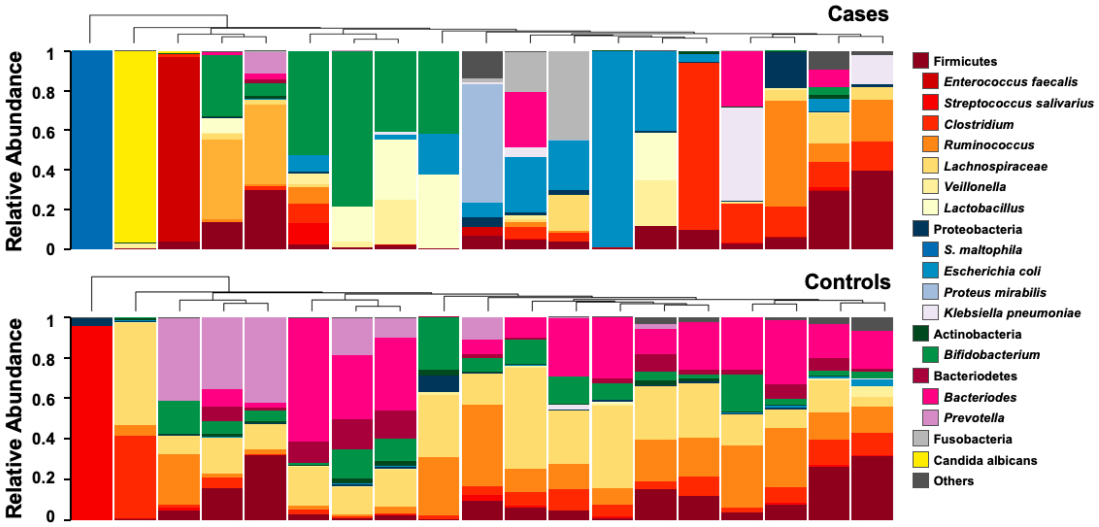
Cases
Controls
Relative Abundance
1
0.8
0.6
0.4
0.2
0
Firmicutes
Enterococcus faecalis
Streptococcus salivarius
Clostridium
Ruminococcus
Lachnospiraceae
Veillonella
Lactobacillus
Proteobacteria
S. maltophila
Escherichia coli
Proteus mirabilis
Klebsiella pneumoniae
Actinobacteria
Bifidobacterium
Bacteriodetes
Bacteriodes
Prevotella
Fusobacteria
Candida albicans
Others

Figure 1


Cases
Controls
Mupirocin Resistance
Gene Altering Cell Wall Charge
Bacitracin Resistance
Sulfonamide Resistance
Polymyxin Resistance
Lincosamide Resistance
ABC-F ATP-binding Cassette Ribosomal Protection Protein
Resistance to Nucleoside Antibiotics
Efflux Pump Complex or Subunit Conferring Antibiotic Resistance
Tetracycline Resistance
Macrolide Resistance
Fosfomycin Resistance
Diaminopyrimidine Resistance
Phenicol Resistance
Glycopeptide Resistance
Gene Modulating Resistance
Rifamycin Resistance
Aminoglycoside Resistance
rRNA Methyltransferase
Fluoroquinolone Resistance
Beta-lactam Resistance
Sqrt(RPKM)
100
75
50
25
0

Figure 2