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Maternal Epidemiology of Brachial Plexus Birth Injuries in California: 1996-2012

Mary Claire Manske[1], Machelle D. Wilson[2], Barton L. Wise[3], Joy Melnikow[4], Herman L. Hedriana[5], Michelle A. James[6,7] and Daniel J. Tancredi[8]

[1]University of California Davis; [2]Principal Biostatistician, Clinical and Translational Science Center, Department of Public Health Sciences, Division of Biostatistics, University of California Davis, Sacramento, California, United States; [3]Professor, Department of Internal Medicine, University of California Davis, Sacramento, California, United States; [4]Professor Emeritus, Department of Family and Community Medicine, University of California Davis, Sacramento, California, United States; [5]Professor and Chief, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine University of California Davis, Sacramento, California, United States; [6]Professor, Department of Orthopaedic Surgery, University of California Davis, Sacramento, California, United States; [7]Department of Orthopaedic Surgery, Shriners Hospitals for Children Northern California, Sacramento, California, United States and [8]Professor in Residence, Department of Pediatrics, University of California Davis, Sacramento, California, United States

OBJECTIVES/GOALS: To evaluate the incidence of brachial plexus birth injury (BPBI) and its associations with maternal demographic factors. Additionally, we sought to determine whether longitudinal changes in BPBI incidence differed by maternal demographics. METHODS/STUDY POPULATION: We conducted a retrospective cohort study of over 8 million maternal-infant pairs using California's Office of Statewide Health Planning and Development Linked Birth Files from 1991-2012. Descriptive statistics were used to determine BPBI incidence and the prevalence of maternal demographic factors (race, ethnicity, age). Multivariable logistic regression was used to determine associations of year, maternal race, ethnicity, and age with BPBI. Excess population level risk associated with these characteristics was determined by calculating population attributable fractions. RESULTS/ANTICIPATED RESULTS: The incidence of BPBI between 1991-2012 was 1.28 per 1000 live births, with peak incidence of 1.84 per 1000 in 1998 and low of 0.9 per 1000 in 2008. Incidence varied by demographic group, with infants of Black (1.78 per 1000) and Hispanic (1.34 per 1000) mothers having the highest incidences. Controlling for relevant covariates, infants of Black (AOR=1.88, 95% CI 1.70, 2.08), Hispanic (AOR=1.25, 95% CI 1.18, 1.32) and advanced-age mothers (AOR=1.16, 95% CI 1.09, 1.25) were at increased risk. Disparities in risk experienced by Black, Hispanic, and advanced-age mothers contributed to a 5%, 10%, and 2% excess risk at the population level, respectively. Longitudinal trends in incidence did not vary among demographic groups. Population-level changes in maternal demographics did not explain changes in incidence over time. DISCUSSION/SIGNIFICANCE: Although BPBI incidence has decreased in California, demographic disparities exist. Infants of Black, Hispanic, and advanced-age mothers are at increased BPBI risk compared to White, Non-Hispanic, and younger mothers.

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Unlocking the Potential of Simalikalactone D as an Anticancer Agent in Ethnically Diverse Breast Cancer Populations

Annelis O. Sanchez-Alvarez[1], Prof. Pablo E. Vivas-Mejia[2] and Prof. Claudia Ospina[3]

[1]Comprehensive Cancer Center-UPR; [2]Medical Science Campus-UPR and [3]Inter American University of Puerto Rico, Bayamon

OBJECTIVES/GOALS: This project focuses on investigating the potential of Simalikalactone D (SKD) as an anticancer agent, exploring the mechanisms underlying SKD's induction of cell death, and assessing the impact of SKD on diverse breast cancer cell lines. Also, it Investigates the compound's mechanisms of action beyond caspase 3-dependent pathways. METHODS/STUDY POPULATION: Three breast cancer cell lines were used: SKBR3, MDA-MB-231, and MDA-MB-468. Two triple-negative breast cancer cell lines are included to address cancer disparities across diverse ethnic backgrounds. Viability assays were conducted to determine half-maximal inhibitory concentrations (IC50). Caspase 3 activity assay was performed to evaluate apoptosis as a possible cell death pathway. Wound healing and colony formation assays are used to assess cell migration and clonogenic capacity. Proteomic analysis and phosphoarray analysis are planned for a deeper understanding of SKD's anticancer properties, as well as testing for caspase 3 independent pathways. RESULTS/ANTICIPATED RESULTS: SKD demonstrated substantial cytotoxicity against all three breast cancer cell lines. IC50 values for SKBR3, MDA-MB-231, and MDA-MB-468 were 60.0 nM, 65.0 nM, and 116 nM, respectively. SKD induces cell death via caspase 3-independent pathways. Further experiments are needed to confirm and elucidate the molecular pathways being impacted. SKD inhibited cancer cell migration and clonogenic potential, suggesting it can reduce tumor growth and metastatic tendencies. DISCUSSION/SIGNIFICANCE: The study highlights SKD's cytotoxicity across diverse breast cancer cell lines. It underscores the mechanism of action, a caspase 3 independent pathway. These findings hold promise for the development of innovative anticancer treatments and emphasize the importance of exploring varied cellular responses to mitigate global cancer disparities.

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BUILD EXITO: a successful collaborative training program for STEM undergraduates to improve workforce diversity

De'Sha Wolf[1,2], Thomas Keller[2], Matt Honore[1], Shandee Dixon[1] and Cynthia Morris[1]

[1]OHSU and [2]Portland State University

OBJECTIVES/GOALS: To truly improve health equity and accessibility, we must develop a diverse and inclusive workforce. The BUILD EXITO program developed as a collaboration between a network of undergraduate programs and a CTSA hub and now has become a sustainable resource that will outlive NIH funding. We will disseminate our successful model. METHODS/STUDY POPULATION: The BUILD EXITO program has completed 10 years of NIH funding, a partnership between OCTRI and

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Portland State University (PSU), to create a new model of research training for underrepresented and disadvantaged students. This model provides an opportunity to learn about clinical and translational research academic careers; participate in a research enhancement and professional development curriculum;have a long-term authentic research experience; and receive enhanced mentorship. BUILD EXITO includes PSU, and local and 3 US Pacific territory 2-year colleges. We have developed a sustainable plan that includes these core elements after NIH support for the program ends. We have tracked long-term student outcomes for entry into graduate programs and the research workforce. RESULTS/ANTICIPATED RESULTS: We will describe the experimental model and the network of university and community colleges in BUILD EXITO, including PSU, U of Alaska, and colleges in US territories of Guam, Northern Mariana Islands, and American Samoa. All these universities and colleges have high proportions of underrepresented and disadvantaged students. We will present data on characteristics of the >600 students who have participated in BUILD EXITO to demonstrate the diversity of the cohort. We will also describe 4-year degree completion, engagement in the research workforce, and entry into graduate or professional programs. We will show how this has positively affected faculty inclusion of students in research, institutional policies at the 2-year and 4-year programs, and how this model has become sustainable. DISCUSSION/SIGNIFICANCE: The BUILD EXITO program developed as a collaboration of the CTSA hub at OHSU and a highly diverse undergraduate programs. We have developed a successful model for training a diverse research workforce and will disseminate this sustainable model.

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The Crosstalk between Mitochondrial Dysfunction and Neurodevelopmental Outcomes in Preterm Infants with Pain/Stress in the NICU*

Tingting Zhao[1], Drs. Xiaolin Chang[2], Subrata Biswas[3], Jeremy Balsbaugh[4], Jennifer Liddle[4], Ming-hui Chen[2], Adam Matson[5] and Xiaomei Cong[6]
[1]Yale University School of Nursing; [2]Department of Statistics, University of Connecticut; [3]Department of Molecular and Cell Biology, University of Connecticut; [4]Proteomics and Metabolomics Facility, University of Connecticut; [5]Division of Neonatology, Connecticut Children's Medical Center; Department of Pediatrics, University of Connecticut School of Medicine and [6]Yale School of Nursing

OBJECTIVES/GOALS: Early life pain/stress impacts infants' neurodevelopmental outcomes. Mitochondrial dysfunction may interface between infants' stress and neurodevelopment. The study aims to investigate the associations between pain/stress, proteins associated with mitochondrial dysfunction, and neurobehavioral responses in preterm infants. METHODS/STUDY POPULATION: A prospective cohort study was conducted with 33 preterm infants enrolled between September 2017 and July 2022 at two affiliated NICUs in Hartford and Farmington, CT. Daily pain/stress experienced during NICU was documented. At 36-38 weeks post-menstrual age (PMA), neurobehavioral outcomes were evaluated using the NICU Network Neurobehavioral Scale (NNNS) and buccal swabs for Mass spectrometry-based proteomics analysis. Lasso statistical methods were conducted to study the association between protein abundance and infants' NNNS summary scores. Multiple linear regression and Gene Ontology (GO) enrichment analyses were performed to examine how clinical characteristics and neurodevelopmental outcomes may be associated with protein levels and underlying molecular pathways. RESULTS/ANTICIPATED RESULTS: During NICU hospitalization, preterm premature rupture of membrane (PPROM) was negatively associated with neurobehavioral outcomes. The protein functions, including leptin receptor binding activity, glutathione disulfide oxidoreductase activity, and response to oxidative stress, lipid metabolism, phosphate, and proton transmembrane transporter activity, were negatively associated with neurobehavioral outcomes. In contrast, cytoskeletal regulation, epithelial barrier, and protection function were found to be positively associated with neurodevelopmental outcomes. In addition, mitochondrial dysfunction-related proteins (SPRR2A, PAIP1, S100A3, MT-CO2, PiC, GLRX, PHB2, and BNIPL-2, ABLIM1, UNC45A, Keratins, MUC1, and CYB5B) were found to be associated with neurobehavioral outcomes. DISCUSSION/SIGNIFICANCE: Mitochondrial dysfunction-related proteins were observed to be associated with early life pain/stress and neurodevelopmental outcomes in infants. Buccal proteins could be used to predict potential neurobehavioral outcomes. In addition, individualized skin integrity protection should be provided to preterm infants during their NICU stay.

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Using LGBTQ+ Community Expertise to Co-Develop Inclusive Sexual Orientation and Gender Identity (SOGI) Screening for Research Studies

Jennifer Poger[1], Jennifer Kraschnewski[1], Raffy Luquis[1], Paula Moodie[1], Gelise Thomas[2], Jess Abrams Schrodel[1], Jennifer M. Poger[1], Paula Moodie[1], Gelise Thomas[1], Raffy Luquis[1] and Jennifer L. Kraschnewski[1]
[1]Penn State University and [2]Case Western Reserve University

OBJECTIVES/GOALS: To promote diverse research engagement and address health disparities by creating an inclusive tool to collect sexual orientation and gender identity (SOGI) data from potential participants #_msoanchor_1 METHODS/STUDY POPULATION: The Penn State Community Health Equity & Engagement in Research (CHEER) team, part of our Clinical and Translational Science Institute (CTSI), developed inclusive screening guidance to collect SOGI data from potential research participants to fill an identified gap in the literature. Guidance was developed through an iterative feedback process, leveraging expertise from local, regional, and national organizations, healthcare systems, and leaders throughout Clinical & Translational Science Award hubs. By eliciting expert feedback, CHEER co-developed a comprehensive SOGI data collection form, filling an important gap of inclusivity in the consenting process. Training of this new tool was delivered to CHEER's far-reaching listserv researchers (internal and external) and community partners. RESULTS/ANTICIPATED RESULTS: Feedback collected from our LGBTQ+ expert partners resulted in a total of five inclusive SOGI screening questions; two 'Gender Identity' questions, one 'Sexual Orientation' question, and two 'Sex' questions, with "prefer not to answer" and "another option not listed" provided. The goal of this effort is to equip research teams with a tool that integrates SOGI characteristics that may be particularly important to determine study eligibility

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