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T. Blanchard\*/
S Mooney\*
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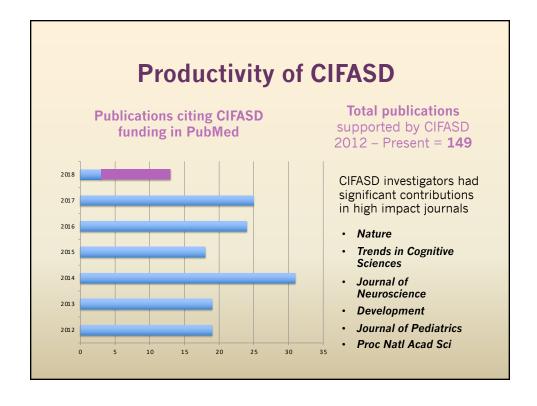
K. L. Jones S. Mattson S. Parnell\*/

S. Parnell\*/
J. Eberhart\*
C. Petrenko\*/

C. Tapparello\*
J. Weinberg
J. Wozniak

Affiliate Scientists: Donald, Miranda, Sakar, Sowell

<sup>\*</sup> Denotes multiple PI project



# Publications since the start of CIFASD4

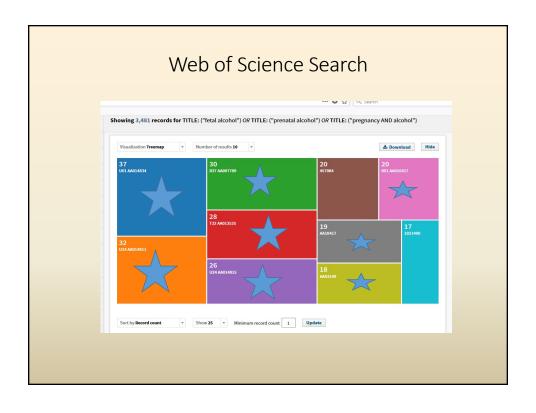
- Fish, E. W., Murdaugh, L. B., Sulik, K. K., Williams, K. P., & Parnell, S. E. (2017). Genetic vulnerabilities to prenatal alcohol exposure: Limb defects in sonic hedgehog and GLI2 heterozygous mice. Birth Defects Research, 109(11), 860-865. doi:10.1002/bdr2.1026
- Fish, E. W., Wieczorek, L. A., Rumple, A., Suttie, M., Moy, S. S., Hammond, P., & Parnell, S. E. (2018). The enduring impact of neurulation stage alcohol exposure: A combined behavioral and structural neuroimaging study in adult male and female C57BL/6J mice. Behavioural Brain Research, 338, 173-184. doi:10.1016/j.bbr.2017.10.020
- Herting, M. M., Kim, R., Uban, K. A., Kan, E., Binley, A., & Sowell, E. R. (2017).
   Longitudinal changes in pubertal maturation and white matter microstructure.
   Psychoneuroendocrinology, 81, 70-79. doi:10.1016/j.psyneuen.2017.03.017
- Infante, M. A., Moore, E. M., Bischoff-Grethe, A., Tapert, S. F., Mattson, S. N., & Riley, E. P. (2017). Altered functional connectivity during spatial working memory in children with heavy prenatal alcohol exposure. *Alcohol, 64*, 11-21. doi:10.1016/j.alcohol.2017.05.002
- Kable, J. A., Coles, C. D., & CIFASD. (2017). Prefrontal cortical responses in children
  with prenatal alcohol-related neurodevelopmental impairment: A functional nearinfrared spectroscopy study. Clinical Neurophysiology, 128(11), 2099-2109.
  doi:10.1016/j.clinph.2017.08.009
- Nation, K., Birge, A., Lunde, E., Cudd, T., Goodlett, C., & Washburn, S. (2017). Video-based data acquisition system for use in eye blink classical conditioning procedures in sheep. Behavior Research Methods, 49(5), 1838-1851. doi:10.3758/s13428-016-0826-

# Publications since the start of CIFASD4

- Suttie, M., Wetherill, L., Jacobson, S. W., Jacobson, J. L., Hoyme, H. E., Sowell, E. R., . . . CIFASD. (2017). Facial Curvature Detects and Explicates Ethnic Differences in Effects of Prenatal Alcohol Exposure. Alcoholism-Clinical and Experimental Research, 41(8), 1471-1483. doi:10.1111/acer.13429
- Taggart, T. C., Simmons, R. W., Thomas, J. D., & Riley, E. P. (2017). Children with Heavy Prenatal Alcohol Exposure Exhibit Atypical Gait Characteristics. Alcoholism-Clinical and Experimental Research, 41(9), 1648-1655. doi:10.1111/acer.13450
- Uban, K. A., Herting, M. M., Wozniak, J. R., Sowell, E. R., & CIFASD. (2017). Sex differences in associations between white matter microstructure and gonadal hormones in children and adolescents with prenatal alcohol exposure. *Psychoneuroendocrinology*, 83, 111-121. doi:10.1016/j.psyneuen.2017.05.019
- Wetherill, L., Foroud, T., & Goodlett, C. (2018). Meta-Analyses of Externalizing Disorders: Genetics or Prenatal Alcohol Exposure? Alcoholism-Clinical and Experimental Research, 42(1), 162-172. doi:10.1111/acer.13535
- Woods, K. J., Jacobson, S. W., Molteno, C. D., Jacobson, J. L., & Meintjes, E. M. (2018). Altered Parietal Activation during Non-symbolic Number Comparison in Children with Prenatal Alcohol Exposure. Frontiers in Human Neuroscience, 11. doi:10.3389/fnhum.2017.00627
- Wozniak, J. R., Mueller, B. A., Mattson, S. N., Coles, C. D., Kable, J. A., Jones, K. L., . . .
  CIFASD. (2017). Functional connectivity abnormalities and associated cognitive deficits
  in fetal alcohol Spectrum disorders (FASD). Brain Imaging and Behavior, 11(5), 14321445. doi:10.1007/s11682-016-9624-4

#### New Publications n=9 Since Last Report in FEB2018

- Huang R, Xie W and Alison Noble J. VP-Nets: Efficient automatic localization of key brain structures in 3D fetal neurosonography. Med Image Anal. 2018 Jul;47:127-139. PMCID:PMC5988265
- Gross LA, Moore EM, Wozniak JR, Coles CD, Kable JA, Sowell ER, Jones KL, Riley EP, Mattson SN and CIFASD. Neural correlates of verbal memory in youth with heavy prenatal alcohol exposure. *Brain Imaging and Behavior*, 2018 Jun;12(3):806-822. PMCID:PMC5745322
- Bodnar TS, Raineki C, Wertelecki W, Yevtushok L, Plotka L, Zymak-Zakutnya N, Honerkamp-Smith G, Wells A, Rolland M, Woodward TS, Coles CD, Kable JA, Chambers CD, Weinberg J and CIFASD.
   Altered maternal immune networks are associated with adverse child neurodevelopment: Impact of alcohol consumption during pregnancy. Brain Behav Immun. 2018 May 5.
- Sowell KD, Uriu-Adams JY, Van de Water J, Chambers CD, Coles CD, Kable JA, Yevtushok L, Zymak-Zakutnya N, Wertelecki W, Keen CL and CIFASD. Implications of altered maternal cytokine concentrations on infant outcomes in children with prenatal alcohol exposure. Alcohol, 2018 May;68:49-58. PMCID:PMC5820219
- Petrelli B, Weinberg J and Hicks GG. Effects of prenatal alcohol exposure (PAE): Insights into FASD using mouse models of PAE. Biochem Cell Biol., 2018 Apr;96(2):131-147. PMCID:PMC5991836
- Hendrickson TJ, Mueller BA, Sowell ER, Mattson SN, Coles CD, Kable JA, Jones KL, Boys CJ, Lee S, Lim KO, Riley EP and Wozniak JR. Two-year cortical trajectories are abnormal in children and adolescents with prenatal alcohol exposure. *Developmental Cognitive Neuroscience*, 2018 Apr;30:123-133. PMCID:PMC5949095
- Chan PH, Xu R and Chambers CD. A Study of R(2) measure under the accelerated failure time models. Commun Stat Simul Comput. 2018;47(2):380-391. PMCID:PMC5881951
- Huang R, Namburete A and Noble A. Learning to segment key clinical anatomical structures in fetal neurosonography informed by a region-based descriptor. J Med Imaging (Bellingham), 2018 Jan;5(1):014007. PMCID:PMC5845099
- Biffen SC, Warton CMR, Lindinger NM, Randall SR, Lewis CE, Molteno CD, Jacobson JL, Jacobson SW and Meintjes EM. Reductions in corpus callosum volume partially mediate effects of prenatal alcohol exposure on IQ. Front Neuroanat., 2018 Jan 12;11:132. PMCID:PMC5771245





### RSA San Diego, CA June 16-20, 2018

#### **SUNDAY, JUNE 17**

10:00am - 11:30am

SYMPOSIUM



HARBOR H

\*\*\*PREDICTING OUTCOMES OF FETAL ALCOHOL EXPOSURE IN THE CIFASD COHORT ORGANIZER/CHAIR: MICHAEL CHARNESS, VA BOSTON HEALTHCARE SYSTEM/HARVARD MEDICAL SCHOOL/BOSTON UNIV. SCHOOL OF MEDICINE, WEST ROXBURY, MA, USA CHAIR: EDWARD RILEY, SAN DIEGO STATE UNIVERSITY, SAN DIEGO, CA, USA

10	0:00 AM	INTRODUCTION
		Michael Charness, VA Boston Healthcare System/Harvard Medical School/Boston University School of Medicine, West Roxbury, MA, USA
10	0:05 AM	PRENATAL ETHANOL EXPOSURE INDUCES A "TRANSIENT CILIOPATHY": A NOVEL MECHANISM FOR ETHANOL'S PATHOGENESIS
		Scott Parnell, University of North Carolina, Chapel Hill, NC, USA
10	D:23 AM	USING 3D FACIAL ANALYSIS TO IDENTIFY MINOR FACIAL ANOMALIES AND ETHNIC DIFFERENCES IN EFFECTS OF PRENATAL ALCOHOL EXPOSURE
		Michael Suttie, University of Oxford, Oxford, United Kingdom
10	0:41 AM	ALCOHOL INTAKE AND IMMUNE FUNCTION: ASSOCIATIONS BETWEEN MATERNAL IMMUNE NETWORKS AND CHILD NEURODEVELOPMENTAL OUTCOME
		Joanne Weinberg, University of British Columbia, Vancouver, BC, Canada
10	D:59 AM	A GROWTH MODELING APPROACH TO PREDICTING FUTURE NEURODEVELOPMENTAL PERFORMANCE IN INFANTS WITH PRENATAL ALCOHOL EXPOSURE
		Christina Chambers, University of California San Diego, La Jolla, CA, USA
1	1:17 AM	DISCUSSANT/QUESTION MODERATOR
		Edward Riley, San Diego State University, San Diego, CA USA

#### MONDAY, JUNE 18 9:15am - 10:45am SYMPOSIUM HARBOR G \*IDENTIFYING PRENATAL ALCOHOL-AFFECTED INDIVIDUALS EARLY IN LIFE: THE USE OF NOVEL SCREENING TOOLS AND METHODOLOGIES IN HUMAN POPULATIONS ORGANIZERS/CHAIRS: CHRISTINA CHAMBERS, UNIVERSITY OF CALIFORNIA SAN DIEGO, LA JOLLA, CA, USA AND BILL DUNTY, NIAAA/NIH DIVISION OF METABOLISM AND HEALTH EFFECTS, BETHESDA, MD, USA 9:15 AM Bill Dunty, NIAAA/NIH Division of Metabolism and Health Effects, Bethesda, MD, USA HEMODYNAMIC CHANGES IN THE PREFRONTAL CORTEX AS MEASURED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY AND THEIR RELATIONSHIPS TO NEUROBEHAVIORAL OUTCOMES IN CHILDREN WITH FASD Julie Kable, Emory University School of Medicine, Atlanta, GA, USA EARLY IDENTIFICATION OF EFFECTS OF PRENATAL ALCOHOL EXPOSURE: INFANT CARDIAC ORIENTING RESPONSE AS 9:38 AM A BIOMARKER Claire Coles, Emory University School of Medicine, Atlanta, GA, USA MIRNAS AS BIOMARKERS OF PRENATAL ALCOHOL EXPOSURE AND INFANT OUTCOME Amanda Mahnke, Texas A&M University Health Science Center, Bryan, TX, USA DEVELOPMENT OF AN EPIGENETIC BIOMARKER FOR PREDICTION OF FETAL ALCOHOL SPECTRUM DISORDERS 9:56 AM 10:14 AM Aileen Baldwin, United States Drug Testing Laboratories, Inc., Des Plaines, IL, USA DISCUSSANT/QUESTION MODERATOR Christina Chambers, University of California San Diego, La Jolla, CA, USA 10:32 AM 1:20pm - 2:50pm SYMPOSIUM HARBOR B NON-CODING RNA IN ALCOHOLISM: MECHANISMS, BIOMARKERS AND THERAPEUTIC TARGETS ORGANIZERS/CHAIRS: SUBHASH PANDEY, CTR FOR ALCOHOL RESEARCH IN EPIGENETICS, UNIV OF ILLINOIS & BUYA MEDICAL CENTER, CHICAGO, IL, USA AND ANTONIO NORONHA, NIH/NIAAA/DNB, BETHESDA, MD, USA 1:43 PM ENDOCRINE MIRNAS IN PREGNANT WOMEN, PREDICTIVE OF FASD INFANT OUTCOMES, CONTROL PLACENTAL TROPHOBLAST GROWTH, SURVIVAL, AND MATURATION Alexander Tseng, Texas A&M Health Science Center, College Station, TX, USA 2:37 PM DISCUSSANT/QUESTION MODERATOR Rajesh Miranda, Texas A&M Health Science Center/College of Medicine, Bryan, TX USA



#### FETAL ALCOHOL SPECTRUM DISORDERS STUDY GROUP

June 16, 2018 Manchester Grand Hyatt, San Diego, CA

Sex Differences and Vulnerability

10:25-10:40 **Timothy A. Cudd Award: Nihal Salem, M.S.,** Texas A&M University. Fetal sex is a determinant of maternal plasma microRNA responses to prenatal alcohol exposure: Evidence from an analysis of a Ukraine Cohort

#### Under consideration for the Gordis Student Award: Sunday, June 17 3:10 PM - 4:40 PM

Harbor F

Gordis Paper Session - Students Moderator: Rebecca Gilbertson

098 °S °098 GORDIS AWARD FINALIST: ENDOCRINE MIRNAS IN PREGNANT WOMEN, PREDICTIVE OF FASD INFANT OUTCOMES, CONTROL PLACENTAL TROPHOBLAST GROWTH, SURVIVAL, AND MATURATION A.M. Tseng, S Balaraman, C Chambers, A.M. Allan, R.C. Miranda Texas A&M University Health Science Center, Department of Neuroscience and Experimental Therapeutics, Bryant IX, 77807, USA

ENDOCRINE MIRNAS IN PREGNANT WOMEN, PREDICTIVE OF FASD INFANT OUTCOMES, CONTROL PLACENTAL TROPHOBLAST GROWTH, SURVIVAL, AND MATURATION A.M. Tseng, S. Balaraman, C. Chambers, A.M. Allan, R.C. Miranda

Texas A&M University Health Science center, Department of Neuroscience and Experimental Therapeutics, Bryan TX 77807, USA

#### Poster Session: Sunday, June 17, 2018

TRANSCRIPTOME-WIDE ANALYSIS IN THE NEURAL TUBE FOLLOWING MID-NEURULATION STAGE ETHANOL EXPOSURE IN C57BL/6J MICE

K.E. Boschen, S.E. Pamell

University of North Carolina, Bowles Center for Alcohol Studies, Chapel Hill, NC, 27599, USA

TRANSCRIPTOME-WIDE ANALYSIS OF ETHANOL SENSITIVE AND INSENSITIVE MOUSE STRAINS DURING EARLY EMBRYONIC DEVELOPMENT

K.E. Boschen, J.K. Eberhart, S.E. Parnell

University of North Carolina, Bowles Center for Alcohol Studies, Chapel Hill, NC, 27599, USA

CYTOKINE DISTURBANCES ASSOCIATED WITH PRENATAL ALCOHOL EXPOSURE IN CHILDREN: IMPLICATIONS FOR HEALTH AND DEVELOPMENT

T.S. Bodnar, C. Raineki, W. Wertelecki, L. Yevtushok, L. Plotka, N. Zymak-Zakutnya, A. Wells, G. Honerkamp-Smith, C.D. Coles, J.A. Kable, C.D. Chambers, J. Weinberg, the CIFASD University of British Columbia, Department of Cellular & Physiological Sciences, Vancouver, BC, V6T 1Z3, Canada

EFFECT OF PRENATAL ALCOHOL EXPOSURE AND PARENTAL ALCOHOL DEPENDENCE ON RISK OF EXTERNALIZING DISORDERS IN COGA AND CIFASD SAMPLES

L. Wetherill, S.N. Mattson, T. Foroud, C. Goodlett, CIFASD, COGA

Department of Psychology, School of Science, Indiana University Purdue University at Indianapolis, Indianapolis, IN 46202, USA

Poster Session: Monday, June 18, 2018

VALIDATION OF A DECISION TREE FOR CLINICAL IDENTIFICATION OF CHILDREN AFFECTED BY PRENATAL ALCOHOL EXPOSURE IN A LOW-RISK SAMPLE L.R. Doyle, C.D. Chambers, K.L. Jones, S.N. Mattson, the CIFASD Center for Behavioral Teratology, San Diego State University, San Diego, CA 92120, USA

# ISBRA Congress September 9-13, 2018 in Kyoto, Japan - CIFASD Symposium

### CIFASD and the Genetics of FASD

Organizer: Michael Charness

Presenters:

Michael Charness Johann Eberhart Tatiana Foroud Scott Parnell



### 8th International Conference on Fetal Alcohol Spectrum Disorder in Vancouver, BC, Canada

•CIFASD invited to submit a Plenary Session

# 8th International Conference on Fetal Alcohol Spectrum Disorder

Research, Results and Relevance

Integrating Research, Policy and Promising Practice Around the World

March 6-9, 2019



### Thank you

Jill VanderVelde

Sarah Mattson

Jennifer Thomas

Bill Dunty

Dale Hereld

Publications and Data Sharing Committees

Science Advisory Board

### **PROGRESS**

Ukraine Cohort Study
CIFASD
June 15, 2018

#### **ABSTRACTS 2018**

- Bodnar, T.S., Raineki, C., Wertelecki, W., Yevtushok, L., Plotka, L., Zymak-Zakutnya, N., Wells, A., Honerkamp-Smith, G., Coles, C.D., Kable, J.A., Chambers, C.D., J. Weinberg, & the CIFASD. Cytokine disturbances associated with prenatal alcohol exposure in children: Implications for health and development. Research Society on Alcoholism, San Diego, CA, June 16-20, 2018
- L.R. Doyle, C.D. Chambers, K.L. Jones, S.N. Mattson, & the CIFASD Validation of a decision tree for clinical identification of children affected by prenatal alcohol exposure in a low-risk sample. Research Society on Alcoholism, San Diego, CA, June 16-20, 2018.
- Salem N, Chambers CD, Miranda RC. Fetal sex is a determinant of maternal plasma microRNA responses to prenatal alcohol exposure: Evidence from an analysis of a Ukraine Cohort. Fetal Alcohol Spectrum Disorders Study Group. Research Society on Alcoholism, San Diego, A, June 16-20, 2018.
- Tseng A. Endocrine MicroRNAs In Pregnant Women, Predictive Of FASD Infant Outcomes, Control Placental Trophoblast Growth, Survival, And Maturation. Research Society on Alcoholism, San Diego, CA, June 16-20, 2018.

#### **PUBLICATIONS 2018**

Brain, Behavior, and Immunity xxx (xxxx) xxx-xxx



Contents lists available at ScienceDirect

#### Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi



Full-length Article

Altered maternal immune networks are associated with adverse child neurodevelopment: Impact of alcohol consumption during pregnancy

Tamara S. Bodnar<sup>a,\*</sup>, Charlis Raineki<sup>a</sup>, Wladimir Wertelecki<sup>b</sup>, Lyubov Yevtushok<sup>c</sup>, Larisa Plotka<sup>c</sup>, Natalya Zymak-Zakutnya<sup>d</sup>, Gordon Honerkamp-Smith<sup>b</sup>, Alan Wells<sup>b</sup>, Matthieu Rolland<sup>b</sup>, Todd S. Woodward<sup>e,f</sup>, Claire D. Coles<sup>g</sup>, Julie A. Kable<sup>g</sup>, Christina D. Chambers<sup>b,h</sup>, Joanne Weinberg<sup>a</sup>, Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD)

- a Department of Cellular and Physiological Sciences, University of British Columbia, Vancouver, BC, Canada
- b Department of Pediatrics, University of California San Diego, La Jolla, USA

  COMNI-Net for Children International Charitable Fund, Rivne Oblast Medical Diagnostic Center, Rivne, Ukraine
- OMNI-Net for Children International Charitable Fund, Khmelnytsky Perinatal Center, Khmelnytsky, Ukraine
   Department of Psychiatry, University of British Columbia, Vancouver, Canada
   Translational Research Unit, BC Mental Health and Addictions Research Institute, Provincial Health Services Authority, Vancouver, BC, Canada
- 8 Department of Psychiatry and Behavioral Sciences, Department of Pediatrics, Emory University School of Medicine, Atlanta, USA
  h Department of Family Medicine and Public Health, University of California San Diego, La Jolla, CA, USA

#### **PUBLICATIONS 2018**



#### Alcohol

Volume 68, May 2018, Pages 49-58



Implications of altered maternal cytokine concentrations on infant outcomes in children with prenatal alcohol exposure

K.D. Sowell a, J.Y. Uriu-Adams a, J. Van de Water b, C.D. Chambers c, d, C.D. Coles e, f, J.A. Kable e, f, L. Yevtushok <sup>g</sup>, N. Zymak-Zakutnya <sup>h</sup>, W. Wertelecki <sup>c, d</sup>, C.L. Keen <sup>a</sup> <sup>⊗</sup> , Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD)

Feature in September 2018 NIAAA-Spectrum

#### PRESENTATIONS 2018

- Chambers CD, Wells A, Xu R, Wertelecki W, Coles C, Kable J, Zymak-Zakutnya N, Yevtushok L.A growth modeling approach to predicting
  future neurodevelopmental performance in infants with prenatal alcohol exposure. Symposium entitled: Predicting outcomes of fetal
  alcohol exposure in the CIFASD cohort. Organizers/Chairs: Charness, M. and Riley, E. Research Society on Alcoholism, San Diego, CA, June
  16-20,2018.
- Bodnar T, Raineki C., Wertelecki W., Yevtushok L., Zymak-Zakutnya N., Honerkamp-Smith G., Wells A., Woordward T., Coles CD, Kable J, Chambers C, Weinberg J, and the CIFASD. Alcohol intake and immune function: associations between maternal immune networks and child neurodevelopmental outcome. Symposium entitled: Predicting outcomes of fetal alcohol exposure in the CIFASD cohort. Organizers/Chairs: Charness, M. and Riley, E. Research Society on Alcoholism, San Diego, CA, June 16-20,2018.
- Coles CD, Kable JA, Mesa DA, Coleman TP, Jones KL, Yevtushok L, Kulikovsky Y, Wertelecki W, Chambers CD and the CIFASD. Early identification of effects of prenatal alcohol exposure: infant cardiac orienting response as a biomarker. Symposium entitled: Identifying prenatal alcohol-affected individuals early in life: the use of novel screening tools and methodologies in human populations. Organizers/Chairs Dunty, W and Chambers, CD. Research Society on Alcoholism, San Diego, CA., June 16-20, 2018.
- Weinberg J. Developmental origins of health and disease DOHaD: Prenatal alcohol effects on brain and behavior. Department of Cellular and Physiological Sciences Research Retreat, January 20, 2018, Vancouver, BC.
- Raineki C, Bodnar TS, Wertelecki W, Yevtushok L, Plotka L, Zymak-Zakutnya N, Wells A, Honerkamp-Smith G, Coles CD, Kable JA, Chambers CD, Weinberg J, & the CIFASD. Alcohol consumption during pregnancy is associated with altered maternal and child immune function. Gordon Research Conference: Alcohol & the Nervous System, March 4-9, 2018, Galveston, TX
- Miranda RC, Tseng AM, Mahnke A, Wells A, Walter N, Newman N, Grant K, Kroenke C, Allan A, Chambers CD. microRNA biomarkers and mediators of prenatal alcohol effects. ISBRA 2018.
- · Chambers CD. Latin America Consortium on FASD meeting for Chile, Brazil, Colombia, Mexico and US. Monterrey, Mexico, May 2018.
- APHA 2018.

#### SPECIAL ISSUE

 5 manuscripts from CIFASD investigators invited for special issue of Birth Defects Research slated to publish I<sup>st</sup> quarter 2019

#### **TRAINEES**

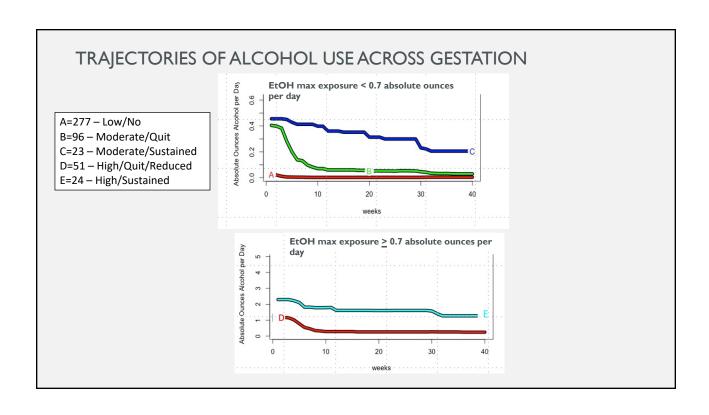
- Nihal Salem at Texas A&M honored with Tim Cudd award 2018
- Annika Montag, PhD, post-doctoral fellow at UCSD previous Tim Cudd honoree – awarded first NIH grant for Native American research on FASD June, 2018
- Alexander Tseng, PhD, Gordis award finalist 2018 and awarded F31 from NIAAA
- Gretchen Bandoli, PhD, post-doctoral fellow at UCSD appointed assistant professor in Dept of Pediatrics June, 2018
- $^{\circ}$  Tammy Bodnar, post-doctoral fellow at UBC moving to Research Associate  $4^{\text{th}}$  quarter 2018

#### AIMS - 2018

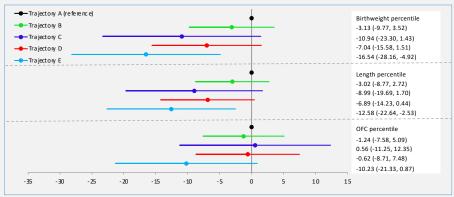
- Aims 2 and 3:
  - New maternal and child samples sent to Rajesh and Joanne
  - New FASD samples to be collected in July (pending NIAAA CofC) (for Kazue and Joanne)
  - Completed analysis of Sarah's decision tree applied to general population sample from CoFASP

#### AIMS - 2018

- Aim I clinical trajectories to characterize risk/resilience:
  - Growth trajectories; manuscript completed and ready for submission
  - Tested inclusion of biomarker assays in model but N too small to tell
  - Preparing to recast model with preschool testing as outcome working with Sarah and Claire to discuss strategies for classifying exposure sample as FASD or not
  - Alcohol exposure trajectories (Bandoli) completed and manuscript in preparation



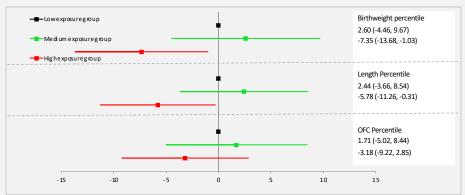
### REGRESSION ANALYSIS OF ALCOHOL EXPOSURE TRAJECTORY AND BIRTH OUTCOMES



Multivariable linear regression models adjusted for vitamin use, SES, pregnancy smoking, maternal age, and gestational age at enrollment

Generally, only the highest use trajectory (E) confers risk of reduced birthweight or length

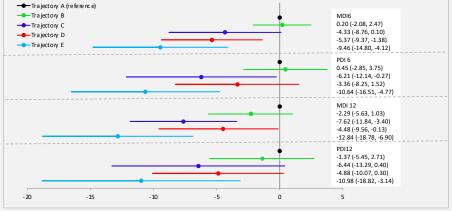
### REGRESSION ANALYSIS OF AVERAGE ALCOHOL EXPOSURE GROUP AND BIRTH OUTCOMES



Multivariable linear regression models adjusted for vitamin use, SES, pregnancy smoking, maternal age, and gestational age at enrollment

In a "traditional" analysis with exposure grouped into terciles, the highest tercile confers risk for reduced birth weight and length, similar to the trajectory analyses

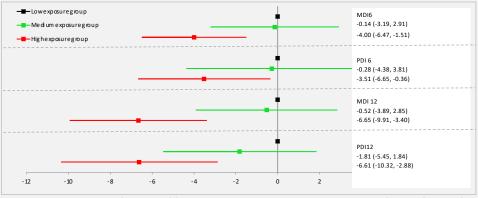
### REGRESSION ANALYSIS OF TRAJECTORY MEMBERSHIP AND NEURODEVELOPMENTAL OUTCOMES



Multivariable linear regression: adjusted for vitamin use, SES, pregnancy smoking, maternal age, and gestational age at enrollment. Stabilized IPCW weights for censoring of BSID at 6 and 12 months

For neurodevelopmental outcomes, lower but sustained use past the first trimester (trajectory C) has a stronger association with deficits than higher but shorter exposure (trajectory D)

### REGRESSION ANALYSIS OF TRAJECTORY MEMBERSHIP AND NEURODEVELOPMENTAL OUTCOMES



Multivariable linear regression: adjusted for vitamin use, SES, pregnancy smoking, maternal age, and gestational age at enrollment. Stabilized IPCW weights for censoring of BSID at 6 and 12 months

From the traditional tercile exposure analysis, only the highest use group is associated with neurodevelopmental deficits.

# CLASSIFICATION OF FASD BY EXPOSURE GROUP AT PRESCHOOL AGE USING ONE OPTION FOR CRITERIA

FASD Classification	Alcohol Exposed N = 115	Alcohol Low or Unexposed N = 175	
FAS – n (%)	5 (4.3)	0	
pFAS – n (%)	7 (6.0)	3 (1.7)	
ARND - n (%)	47 (40.9)	0	
Total FASD – n (%)	59 (51.2)	3 (1.7)	

Classified by Hoyme et al criteria, 2016, Pediatrics

## Fetal Alcohol Spectrum Disorders in Adults:

Health and Neurobehavior Claire D. Coles, PhD, Therese Grant, PhD, Edward P. Riley, PhD,

IN COLLABORATION WITH JOANNE WEINBERG, PhD

Planning, Organization, Material Development

- Developed, Piloted and Implemented Health Survey/Demographic questionnaire, other forms
- Created Electronic Data Collection instruments and Databases
- Initiated Registry

#### Outreach

Workshop, Mapping the Undiscovered County: Physical and Mental Health in Adults with FASD Presented at:

8th International Research Conference on Adolescents and Adults with FASD,
Vancouver, BC, April 20, 2018

Characteristic	Sample Total (N=52)		
Age	37.71 yrs, (Range 33-59 Yrs)		
Gender	M=36.7%; F=63.3%		
Race	W=44.9%; A-A=40.8%; Native=6.1%		
Education	HS:20.4%; Col/Tech: 42.8 %; Grad:14.3%		
Marital Status	With partner: 40.8%; Single: 59.2%		
M # Children	2.33 (1.33 SD) (Range: 1-6)		
Employment	FT: 54.2%; PT: 27.1%; Not wk: 18.7%		
Income	More than \$4000/mo: 29.2%		

### **U01: Human Genetics**









### U01: Human Genetics - Progress

- DIGS FASD website now at IRB for final edits prior to launch
  - Soft launch after RSA
  - Reach out to other groups to send out information
  - Social media campaign

Web Portal: <a href="https://digfasd.org/">https://digfasd.org/</a>.

#### Assent video:

https://www.youtube.com/watch?v=4VoP44eMAaM&feature=youtu.be.

### U01: Human Genetics - Progress

- Genetic analysis
  - Whole exome sequencing completed targeted genes and also global analysis
  - Working with Peter H, Mike, and Peter C to develop a single facial or profile variable that can be used in sequence analysis (allows deferred subjects to be used)

### U01: Human Genetics - Timeline

	Year 1	Year 2	Year 3	Year 4	Year 5
DIGS FASD protocol	Х				
Recruit DIGS FASD participants		Χ	Χ	Χ	Χ
Implement FONS with Mattson		Χ			
Sequencing and Analysis		Χ	Χ	Χ	Χ
Recruit for Petrenko			Χ	Χ	Χ

### **Central Repository**

- Informed consent
  - Templates for broad sharing language
  - Annual review of ICs for all projects
- Develop requested Central Repository usage for CIFASD4
- Share data with external researchers
  - Ensure CIFASD3 data is compliant for data sharing
  - Genomic data sharing (GDS) to confirm

Nuffield Obstetrics & Gynecology, University of Oxford





#### **Brighton and Sussex University Hospitals NHS Trust**

#### Dr Neil Aiton - Neonatal Facial Analysis

- Continuing to support Brighton in facial image analysis of neonates
- All local ethnics approvals recently (last week) accepted
- Recruitment has begun!

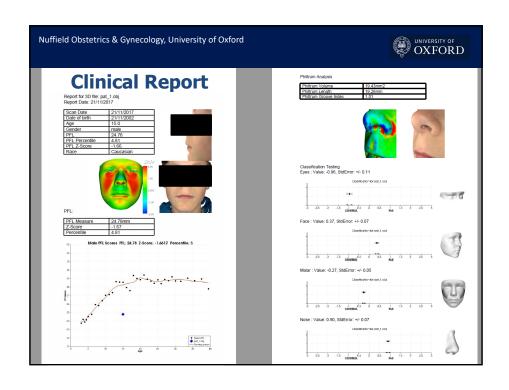
### Surrey and Borders Partnership **NHS**

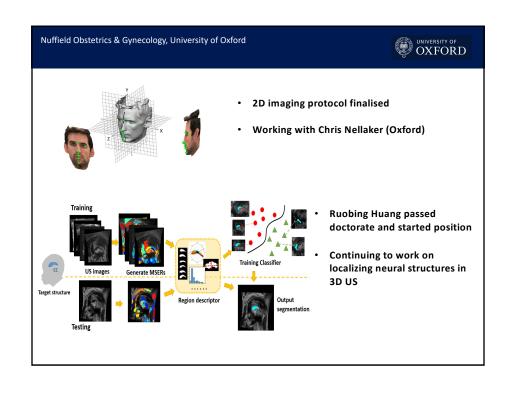


**NHS Foundation Trust** 

Dr Raja Mukherjee

### Nuffield Obstetrics & Gynecology, University of Oxford UNIVERSITY OF OXFORD **Clinical Translation: FaceScreen Concept Proposal** Software very close to beta testing phase Integration with Canfield software -'automated landmarking' PFL %ile ~50 images of PAE suspected children collected from Dr Mukherjee's ~25-30 images agreed with Raja to collect over 6 month period 4-digit as a comparison possible Philtrum: Control → FAS





Nuffield Obstetrics & Gynecology, University of Oxford



### **Deliverables**

#### Concept proposal submitted:

Introducing Objective 3D Facial Analysis into the Fetal Alcohol Spectrum Disorder Clinic Workflow

EUFASD 2018, Berlin, abstract accepted

#### Resubmission to ACER:

 ${\bf Combined\ Face-Brain\ Morphology\ and\ Associated\ Neurocognitive\ Correlates\ In\ Fetal\ Alcohol\ Spectrum\ Disorders$ 

### A Multisite Neurobehavioral Assessment of FASD

Sarah N. Mattson, Ph.D. Center for Behavioral Teratology



### Aim 1a Progress

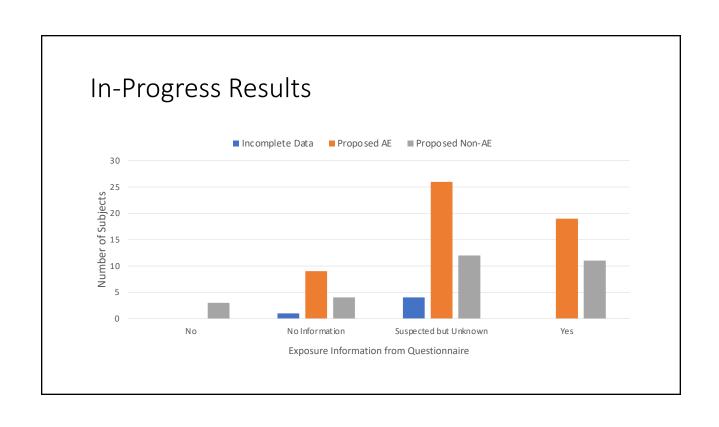
- Obtained and analyzed CoFASP data from San Diego site
- Presenting results at RSA (poster on Monday)
- Current progress: applying revised tree back to C3 data
- Next step: finalize revised tree, obtain CoFASP data (May) and CIFASD Ukraine data (Chambers)

Group	Accuracy
FAS	100%*
pFAS	87.5%
ARND	87%
Controls	90.9%

### Aim 1b Progress

- We have a working version of the app with upload and download capabilities (Thanks Ganz!)
- We have been using it with UCSD and SDSU patients
- We've enrolled 114 people so far
  - >90 have complete tree data

	Patients In Range	Agreed to Participate	E-Consented	eTree Completed	In Progress
Goal (San Diego)	40				
UCSD FASD Clinic	73	72	94	85	9
SDSU CBT	42	42	94	85	9
Goal (MN)	45				



### Aim 1c Progress

- Battery finalized, testers trained, testing in progress
- Database developed

	Y1 Goal	Project Goal	Agreed to Participate	E-Consented	eTree Completed	Testing Completed
SDSU/UCSD	15	120-165	114	94	85	28
UMN	30	90				34

### Aim 2 Progress

• FONS under development

### Collaborations

- Christie helped to recruit focus group members, video actors
- Joanne helping recruit controls
- Tina CoFASP analyses
- Kazue examining steroid use
- Jeff neuropsychological assessment, eTree project, database development
- Ganz eTree project
- Ken eTree project
- Tatiana WebPortal, FONS

### Abstracts and Papers 2018

#### Abstracts

- Doyle, L.R., Chambers, C.D., Jones, S.N., Mattson, S.N., and the CIFASD. (2018). Validation of a decision tree for clinical identification of children affected by prenatal alcohol exposure in a low-risk sample. RSA 2018
- Wetherill, L., Mattson, S.N., Foroud, T., Goodlett, C., and the CIFASD. (2018). Effect of prenatal alcohol exposure and parental alcohol dependence on risk of externalizing disorders in COGA and CIFASD samples. RSA 2018
- Mattson, S.N. A Screening Tool for Identification of Children Affected by Prenatal Alcohol Exposure. To be presented at the American Public Health Association, November 2018

#### · Papers under review

- Doyle, L.R., Glass, L., Wozniak, J.R., Kable, J.A., Riley, E.P., Coles, C.D., Sowell, E.R., Jones, K.L., Mattson, S.N. and the CIFASD. Impact of oppositional and conduct behaviors on executive function among youth with histories of heavy prenatal alcohol exposure.
- Doyle, L.R., Moore, E.M., Coles, C.D., Kable, J.A., Sowell, E.R., Wozniak, J.R., Jones, K.L., Riley, E.P. Mattson, S.N. and the CIFASD. Executive functioning correlates with communication ability in youth with histories of heavy prenatal alcohol exposure.
- Suttie, M., Wozniak, J.R., Parnell, S., Wetherill, L., Mattson, S.N., Sowell, E.R., Riley, E.P., Kan, E., Jones, K.L., Coles, C., Foroud, T., Hammond, P., and the CIFASD. Combined face-brain morphology and associated neurocognitive correlates in fetal alcohol spectrum disorders.

# Exploring the Genetics of FASD in Complementary Mouse and Fish Models

Scott E. Parnell & Johann K. Eberhart

### Research Progress

Fish KO: nearly grown

Gene	6N vs 6J Fold Change	Adjusted p-value	Protein
Ccr1	-5.74151091	0.00310	C-C chemokine receptor type 1
Pthlh	-2.293740828	0.0062156	Parathyroid hormone-related protein
Fam65b	1.753490023	0.005015	Rho family-interacting cell polarization regulator 2
Wt1	-1.221098365	0.0481181	Wilms tumor protein homolog
Rhob	-0.619058615	0.0206481	Rho-related GTP-binding protein RhoB
Kit	-0.356554298	0.0481181	Kit Proto-oncogene receptor tyrosine kinase
Nnt	0.238291219	0.0010557	Nicotinamide Nucleotide Transhydrogenase
Dynlt1b	1.452439923	3.98E-25	Dynein light chain Tctex-type 1
Efcab7	2.168248448	1.45E-20	EF-hand calcium-binding domain-containing protein 7
Wdfy1	4.652347744	2.39E-250	WD repeat and FYVE domain-containing protein 1

### Research Progress

- •Fish KO: nearly grown
- Mns1 study completed
- Differential mouse strain response to ethanol currently being sequenced.
- Acquired p53 KO mice

### **RSA Abstracts**

- K.E. Boschen, J.K. Eberhart, S.E. Parnell. TRANSCRIPTOME-WIDE ANALYSIS OF ETHANOL SENSITIVE AND INSENSITIVE MOUSE STRAINS DURING EARLY EMBRYONIC DEVELOPMENT
- K.E. Boschen, S.E. Parnell. TRANSCRIPTOME-WIDE ANALYSIS IN THE NEURAL TUBE FOLLOWING MID-NEURULATION STAGE ETHANOL EXPOSURE IN C57BL/6J MICE
- E.W. Fish, K.E. Boschen, S.E. Parnell. THE PRIMARY CILIA GENE KIF3A MEDIATES VULNERABILITY TO THE EFFECTS OF NEURULATION STAGE ALCOHOL EXPOSURE ON ADOLESCENT EXPLORATORY BEHAVIOR

### Manuscripts

- Accepted:
  - Murdaugh LB, Mendoza-Romero HN, Fish EW, Parnell SE. A novel method for determining sex in late term gestational mice based on the external genitalia. PLoS One. Apr 4;13(4): 2018. PMID: 29617407
- Submitted/In the process of submitting:
  - Fish EW, Murdaugh LB, Zhang C, Boschen KE, Boa-Amponsem O, Mendoza-Romero HN, Tarpley M, Chdid L, Mukhopadhyay S, Cole GJ, Williams KP, Parnell SE. Cannabinoids Exacerbate Alcohol Teratogenesis by a CB1-Hedgehog Interaction. Nature Communications?
  - Boschen KE, Gong H, Murdaugh LB, Parnell SE. Knockdown of Mns1 increases susceptibility to craniofacial defects following gastrulation-stage alcohol exposure in mice. PLOS Genetics
- In prep:
  - Mendoza-Romero HN, Boschen KE, Eberhart JK, Parnell SE. The proapoptotic protein Bax modifies susceptibility to early gestational alcohol exposure.
- Planned:
  - GD 7 RNA-Seq

Aim 1. Use strain-specific differences in ethanol sensitivity to characterize modifiers of FASD

Aim 2. Employ screening approaches to identify and confirm modifiers of gene-ethanol interactions

### Pathway Analyses

- Inflammatory processes
- PI3K/AKT/mTOR pathway
- Rho family GTPase signaling
- G-protein signaling
- PDGF/EGF/VEGF signaling
- cAMP-mediated signaling
- JAK/Stat signaling
- MAPK/ERK pathways

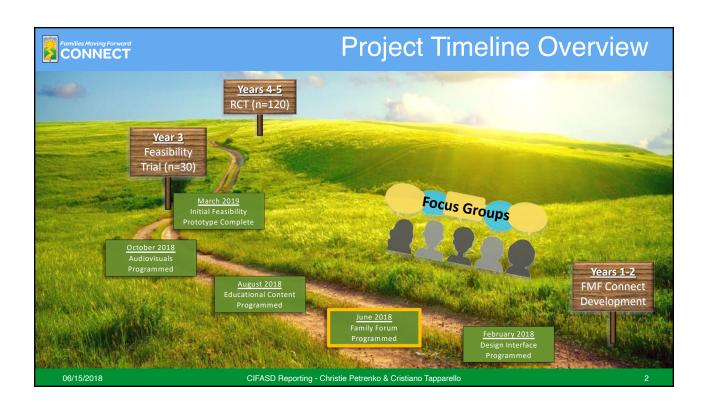
### Genes up-regulated in 6J mice

- Kit: Tyrosine kinase that regulates cell survival and proliferation.
   Activates several pathways; AKT, RAS, RAF1, STAT, ERK1/2
- RhoB: Mediates apoptosis and affects cell adhesion by modulating the AKT signaling
- WT1: Transcription factor important in cell development and survival – mutated in many cancers
  - Top ranked target by NCI
- Fam65b: Small Rho family GTPase important in many inflammatory processes

### Genes down-regulated in 6J mice

- Wdfy1: Regulates TLR3- and TLR4-mediated signaling pathways-activates transcription factors and production of inflammatory cytokines
- Nnt: Integral protein of the inner mitochondrial membrane that converts NADH to NADPH which is important in free radical detoxification
- Dynlt1: Component of the dynein motor complex. Regulates the length of primary cilia
- Efcab7: Component of the EvC complex at the base of the primary cilium. Positively regulates Shh signaling







### **Progress Update**

- Started production of audiovisual content
  - Filmed 6
  - 3 video shoots scheduled for next week in San Diego and Los Angeles, 2 more in Rochester for July
- Conducted 7 focus groups (thanks to other sites for their help!)
  - Rochester, Atlanta, Minneapolis, San Diego, Los Angeles
- Completed development of Family Forum
- Started implementation of learning module content

06/15/2018

CIFASD Reporting - Christie Petrenko & Cristiano Tapparello

3



### **Publication Plan**

- Conference paper on app development process to be submitted during the summer
- Proposing 90-minute symposia at the FASD
   Vancouver conference
- Publication related to data collected from focus groups after the summer

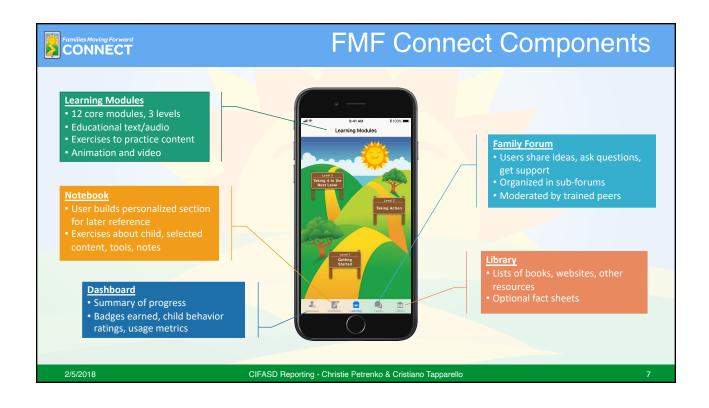
06/15/2018

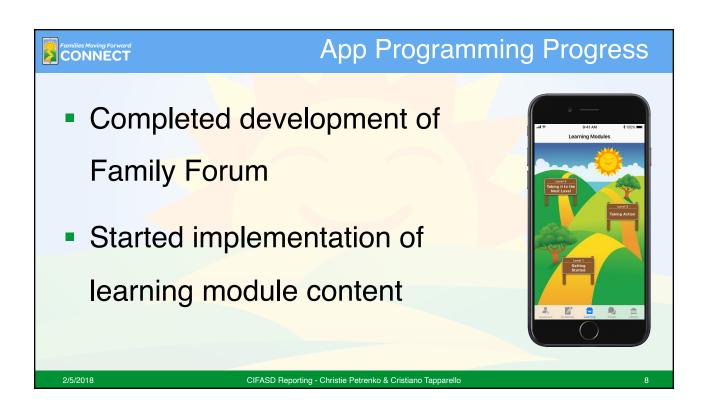
CIFASD Reporting - Christie Petrenko & Cristiano Tapparello

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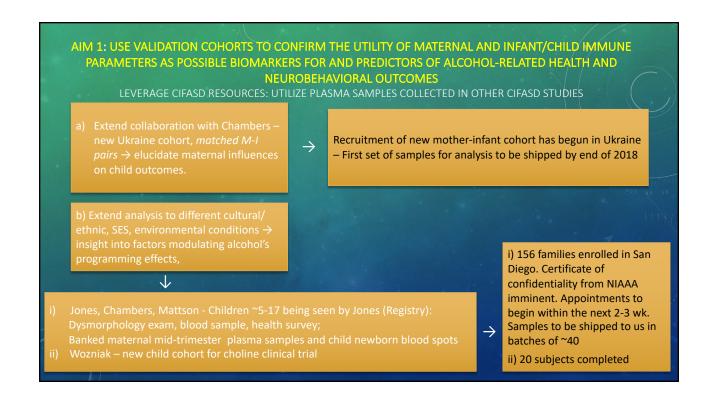












## AIM 2. EXTEND ASSESSMENT OF IMMUNE AND NEUROBEHAVIORAL OUTCOMES INTO ADULTHOOD

- In Atlanta and Seattle Two Tier Assessment :
  - Tier 1 (n=250/site).
     Demographic and Health
     Surveys done remotely;
     Registry developed
  - Tier 2. In subset from Registry (n=120), in-depth assessment of physical characteristics, dysmorphology, immune function (cytokines, health surveys), physical and mental health, behavioral, cognitive and adaptive functioning
- In Vancouver, no broad Registry;
   One Tier Assessment, all measures on/after Study Day (n=120):
  - Demographic and Health Surveys
  - In-depth assessment of physical characteristics, dysmorphology, immune function (cytokines, health surveys), physical and mental health, behavioral, cognitive, and adaptive functioning



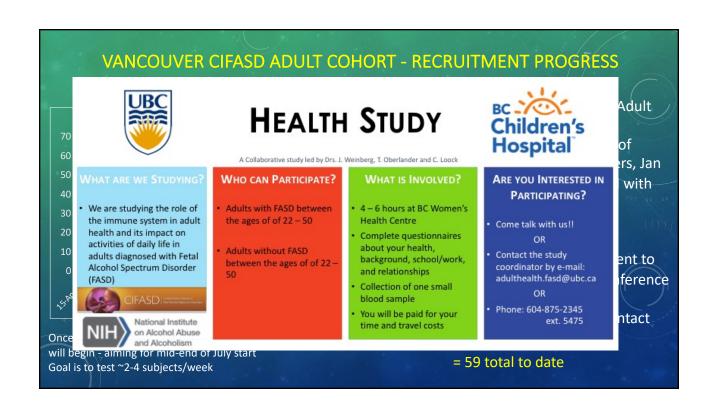


### PROGRESS TO DATE – PREPARATIONS FOR ADULT STUDY SEPTEMBER 2017 – PRESENT:

- CREB (Clinical Research Ethics Board) approvals obtained; final revisions submitted (to be reviewed June 27)
- All UBC investigators have completed UBC and NIH ethics training
- Monthly (now weekly) calls with Claire/Therese teams and with Oberlander team
   planning and logistics
- Research Assistant hired and trained
- Health Questionnaires developed for adults and children (the latter for Ken/Tina San Diego study)
- Instruments/questionnaires identified, ordered, received; iPads and tripod purchased; photo protocol from Peter Hammond test photos to be taken
- Redcap license obtained, questionnaires entered
- Training on new hematology analyzer completed

#### PROGRESS TO DATE (CONT'D)

- Saliva collection protocol from Tatiana/Leah
- Cytokine panels identified [40 + 7 (arthritis/inflammation)]
- Talks on adult study at Douglas College and UBC FASD meeting (the latter with Claire, [Therese])
- Consultation with Jan Lutke, Brenda Knight, Julie Conry to review recruiting materials, support and debriefing of participants, Study Day activities/logistics
- Ken Jones visited Vancouver for training with Chris Loock and Tim Oberlander to standardize dysmorphology exam
- Dysmorphology form for adults developed and finalized reviewed by Ken
- Meeting with Elders and Leaders of Indigenous community
- Posters, banners, cards, etc printed and distributed for recruiting
- Practice for Study Day ongoing
- Practice Study Day with adult(s) with FASD to be completed in early July



# PUBLICATIONS AND PRESENTATIONS JUNE 2017-JUNE 2018:

#### **MANUSCRIPTS:**

- Bodnar, T.S., Raineki, C., Wertelecki, W., Yevtushok, L., Plotka, L, Zymak-Zakutnya, N., Honerkamp-Smith, G., Wells, A., Rolland, M., Woodward, T.W., Kable, J., Coles, C.D., Chambers, C.D., Weinberg, J., & the CIFASD. Altered maternal immune networks are associated with adverse child neurodevelopment: Impact of alcohol consumption during pregnancy. Brain Behav Immun 2018 May 5. [Epub ahead of print]
- Bodnar, T.S., Raineki, C., Wertelecki, W., Yevtushok, L., Plotka, L, Zymak-Zakutnya, N., Honerkamp-Smith, G., Wells, A., Woodward, T.W., Kable, J., Coles, C.D., Chambers, C.D., Weinberg, J., & the CIFASD. Immune disturbances following prenatal alcohol exposure:Implications for neurodevelopment (In preparation)

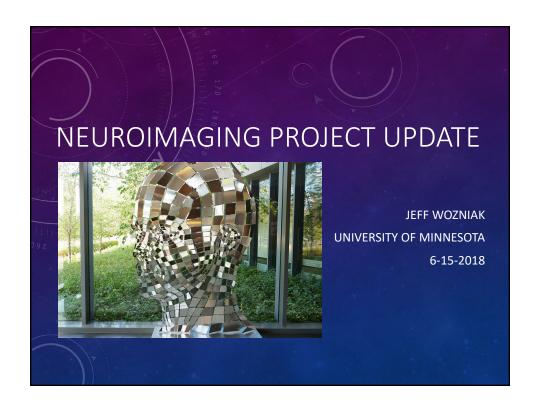
#### **ABSTRACTS:**

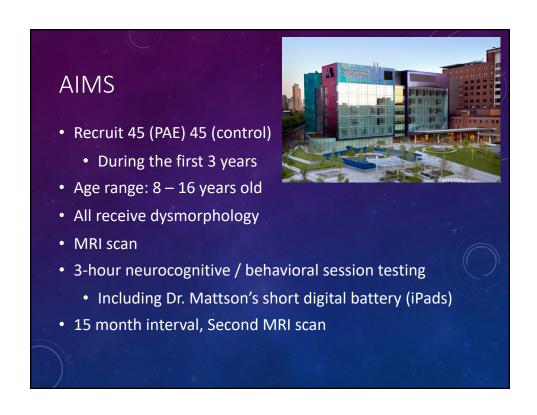
Bodnar, T.S., Raineki, C., Wertelecki, W., Yevtushok, L., Zymak-Zakutnya, N., Chambers., C.D., Weinberg,
 J., & the CIFASD. Identifying an immune signature characteristic of fetal alcohol spectrum disorder.
 Society for Leukocyte Biology 50th Annual Meeting. October 5-7, 2017, Vancouver, BC. Poster 47

## PUBLICATIONS AND PRESENTATIONS JUNE 2017-JUNE 2018:

#### **PRESENTATIONS:**

- Weinberg, J. Effects of prenatal alcohol exposure on health outcomes across the lifespan: From animal models to the clinic. FASD Collaborative Roundtable. Douglas College, New Westminster, BC, November 25, 2017
- Weinberg, J. Developmental origins of health and disease DOHaD: Prenatal alcohol effects on brain and behavior. Department of Cellular and Physiological Sciences Research Retreat, January 20, 2018, Vancouver, BC.
- Raineki, C., Bodnar, T.S., Wertelecki, W., Yevtushok, L., Plotka, L., Zymak-Zakutnya, N., Wells, A., Honerkamp-Smith, G., Coles, C.D., Kable, J.A., Chambers, C.D., J. Weinberg, & the CIFASD. Alcohol consumption during pregnancy is associated with altered maternal and child immune function. Gordon Research Conference: Alcohol & the Nervous System, March 4-9, 2018, Galveston, TX
- Coles, C.D., Grant, T., Weinberg, J., and the Collaborative Initiative on FASD (CIFASD). Mapping the Undiscovered Country. Health and Mental Health in Adults with FASD. 8th International Research Conference on Adolescents and Adults with FASD. Review, Respond and Relate. Integrating Research, Policy and Practice Around the World, April 18-21, 2018, Vancouver, BC
- Bodnar, T., Raineki, C., Wertelecki, W., Yevtushok, L., Zymak-Zakutnya, N., Honerkamp-Smith, G., Wells, A., Woordward, T., Coles, C.D., Kable, J., Chambers, C., Weinberg, J., and the CIFASD. Alcohol intake and immune function: associations between maternal immune networks and child neurodevelopmental outcome. Symposium entitled: Predicting outcomes of fetal alcohol exposure in the CIFASD cohort. Organizers/Chairs: Charness, M. and Riley, E. Research Society on Alcoholism, San Diego, CA, June 16-20,2018.





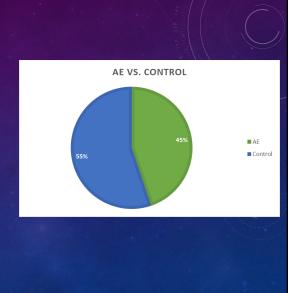
#### PHASE IV PROGRESS

- Coordinators hired and trained
- Imaging protocol developed
- IRB approved / actively enrolling
- Image analysis pipeline development underway
- Parallel HCP Development project underway
  - 1000+ children using matching protocol

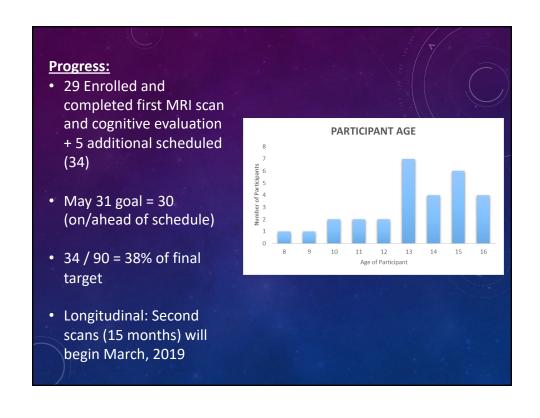


#### **Progress:**

- 29 Enrolled and completed first MRI scan and cognitive evaluation + 5 additional scheduled (34)
- May 31 goal = 30 (on/ahead of schedule)
- 34 / 90 = 38% of final target
- Longitudinal: Second scans (15 months) will begin March, 2019



#### **Progress:** • 29 Enrolled and completed first MRI scan and cognitive evaluation SEX AND AE/CONTROL DISTRIBUTION + 5 additional scheduled 12 (34)• May 31 goal = 30 ■ AF ■ Control (on/ahead of schedule) • 34 / 90 = 38% of final Sex of Subject target Longitudinal: Second scans (15 months) will begin March, 2019



#### **INTERACTIONS**

#### **BLOOD SAMPLES (WEINBERG PROJECT)**

- Collecting blood for choline treatment study (pre and post)
  - Saving plasma for Dr. Weinberg
- N=33 collected thus far (24 unique individuals)

#### FACE (HAMMOND PROJECT)

- Collecting 3D faces (new handheld camera)
  - CIFASD + another study (N=41)

DYSMORPHOLOGY (JONES PROJECT)

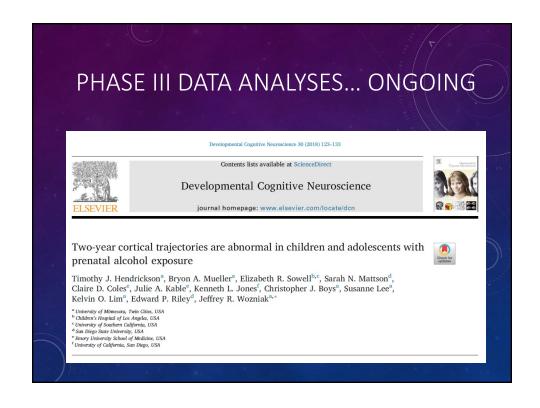
#### **NEUROBEHAVIOR (MATTSON PROJECT)**

- All participants for imaging have "validation" neuropsych battery
- N=34

#### PHASE III DATA ANALYSES... ONGOING

Paper under review with Elizabeth Sowell

Uban, K.A., Kan, E., Wozniak, J.R., Mattson, S.N., Coles, C.D., Sowell, E.R. (revision under review). The relationship between socioeconomic status and brain development is attenuated in children and adolescents with prenatal alcohol exposure.









#### MEDIA: PBS NEWS HOUR

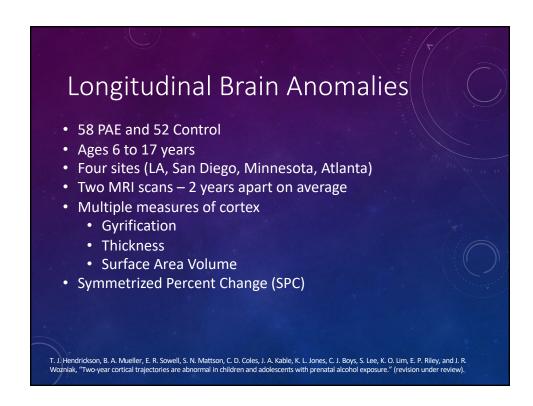
- Interest triggered by Chambers, May, et al JAMA paper on prevalence
- Amna Nawaz filmed segments on brain imaging research, diagnosis (Eckerle), public awareness (MOFAS), and parenting (families raising kids with FASD
- Air date (two segments) possibly early July

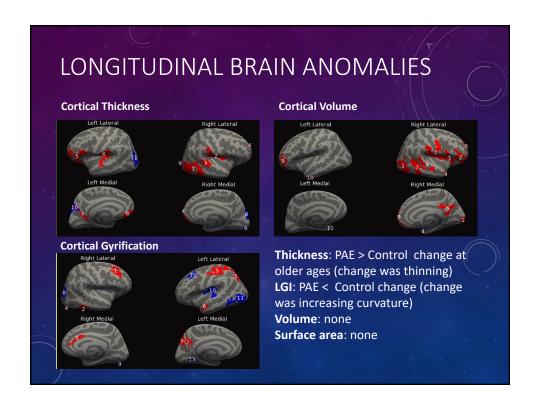


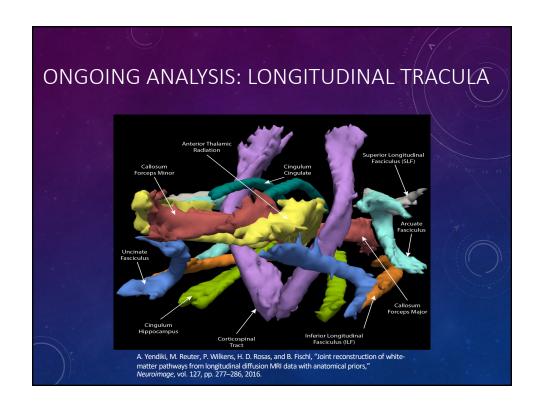


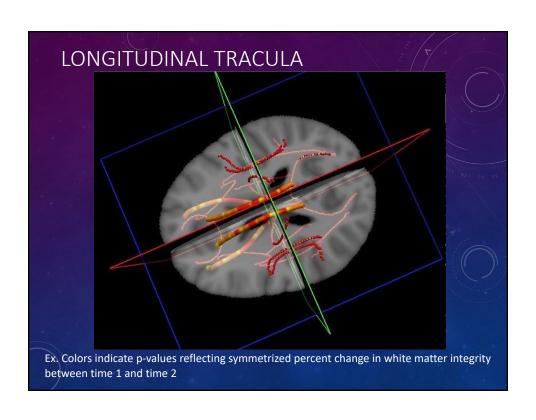
#### **THANKS**

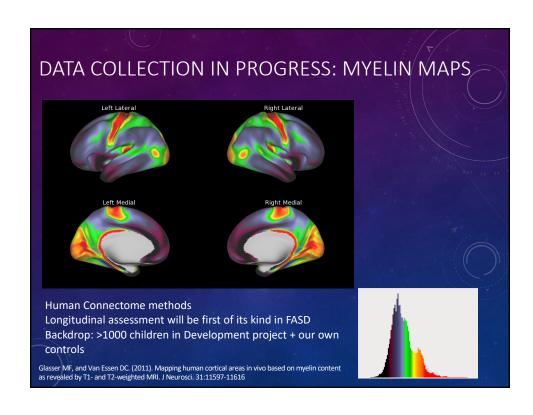
- \* UMN: <u>Timothy Hendrickson</u>, <u>Bryon Mueller</u>, Kelvin Lim, Dan Keefe, Judith K. Eckerle, Birgit A. Fink, Marisa Whitley, Christopher J. Boys, Susanne Lee
- \* CIFASD investigators: Elizabeth Sowell, Sarah Mattson, Claire Coles, Julie Kable, Ken Jones, Kristina Uban, Eric Kan, Helen Yezerets, Bill Barnett
- The Minnesota Organization on Fetal Alcohol Syndrome (MOFAS)
- NIAAA for support and funding











# Peripheral RNA Biomarkers for Intellectual Disability in FASD

First year Progress & Plan:

#### Aim1: Mouse Biomarkers

- 1. 120 RNA sequencing / behavior tests had been processed.
- 2. Compared multiple bioinformatics pipelines to obtain the most accurate data.
- 3. Defined set of biomarkers that show higher correlation of motor learning disability in each PAE animal.
- 4. The genes linked to intellectual disability are enriched. Immune response genes were also screened.
- 5. Will compare these biomarkers with the biomarkers in gestational diabetes model and prenatal opioid exposure model. Then submit a paper.
- 6. RNA seq data will be archived in GEO once the paper is published.
- 7. Related paper is in revision.

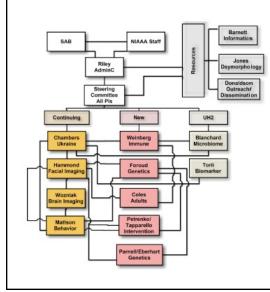
#### **Aim2: Human Biomarkers**

- 1. The analysis pipeline had been established.
- 2. Waiting blood sent from UCSD.
- 3. Will test biomarkers from mouse (supervised approach).
- 4. Will also perform unsupervised screening.



## **CIFASD4** Resource Sharing

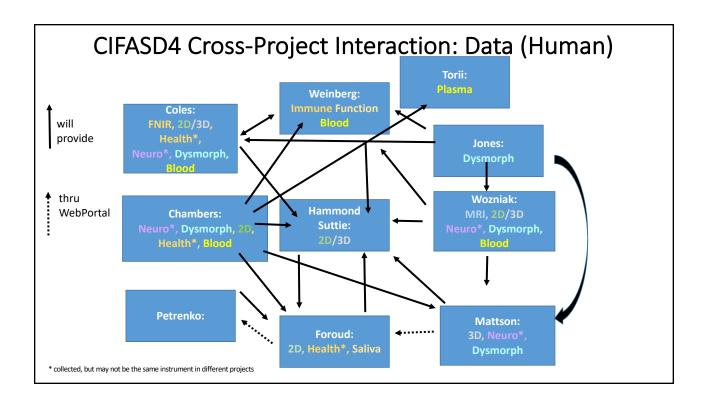
#### **CIFASD4 Interactions**



- How to translate these interactions into action?
  - Provide samples or data to other projects
  - Collect common data to allow for joint (cross-project) analysis
  - Share results between projects to provide replication or new insights
  - Recruit subjects for other projects

#### History of CIFASD Interactions and CIFASD4

- CIFASD4 has a different model from our previous CIFASD interactions
- Previous CIFASD interactions
  - Sites collected a common protocol (MRI, dysmorphology, neurobehavior, 3D facial image, saliva for DNA)
  - · Data loaded into the Central Repository
  - Allowed data to be pooled across sites for joint analysis
- CIFASD4 projects typically are more independent
  - Fewer common protocols
  - Less focus on combining data across projects for analysis
  - Results often shared to inform other projects and guide hypotheses/analyses



#### **Human Data Collection**

Phenotype	Chambers	Coles	Foroud	Hammond	Mattson	Petrenko	Weinberg	Wozniak
MRI								+
FNIR		+						
2D images	+	+	+	+	+	+	+	+
3D images	+			+	+			+
Health/Immune	+	+					+	
Neurobehavioral	+	+	+		+		+	+
Dysmorphology	+	+	+		+		+	+
Ultrasound	+			+				
Samples (blood, saliva, urine)	+	+	+		+	+	+	+

Few common protocols across the sites. Is it important to have this? Do we want to be able to address some questions across projects? Is it important to use common definitions of any key concepts?

#### What might be common elements across projects?

- Basic demographics
  - DOB
  - Sex at birth
  - Race
  - Ethnicity
- Definition of prenatal alcohol exposure
- Dysmorphology

- Environmental information
  - Marital Status (collect same information about partner)
  - · Biological children
  - # people living in household
  - · Level of education
  - Employment status and type of work
  - Monthly household income

#### Definition: Prenatal Alcohol Exposure (PAE)

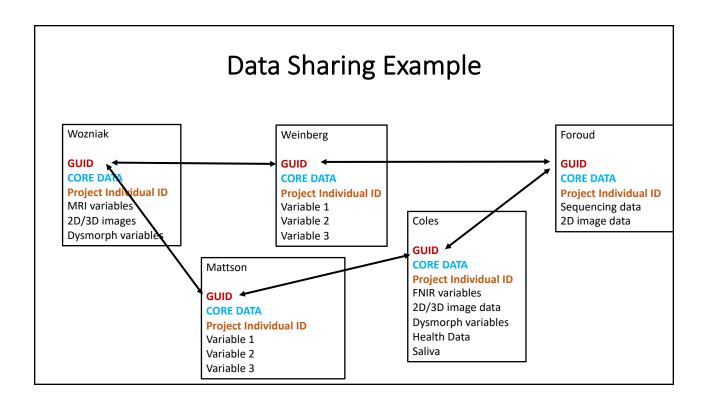
PAE - EXPOSED	Foroud	Coles	Wozniak	Mattson	Torii	Petrenko	Weinberg	Chambers
Heavy (CIFASD3)	+	+	+	+	+			
Dysmorphology Exam/Records	+			+				
FASD dx	+					+	+	

PAE - UNEXPOSED	Foroud	Coles	Wozniak	Mattson	Torii	Petrenko	Weinberg	Chambers
None	NA	+	+	+	+	NA	+	+
Minimal (CIFASD3)	NA	+	+	+	+	NA	+	+

NA = Not Applicable (exposed sample only)

#### GUID: Globally Unique IDentifier

- NDAR (National Database for Autism Research) GUID
  - First name
  - Middle name (full legal name no initials, nicknames)
  - · Last name
  - Sex
  - · Date of birth
  - City/municipality of birth (ONLY city, no state, country, etc)
- May require approval from site university
  - Indiana will provide template instructions
- Allows data sharing with no names; Same GUID generated each time this information is provided
  - If some information missing, can generate a pseudo GUID; would remove ability to identify individuals across projects



# Role of the Central Repository

#### **Central Repository**

- Stores data from CIFASD2, CIFASD3, and now CIFASD4
- Roles
  - Develop tools to submit data
  - Develop data dictionaries
  - Provide query and join (merge) capabilities to combine data across projects to address research questions
  - Provide query/merge to combine historical data with current data?
  - Facilitate sharing of data with external researchers

#### CIFASD4

- All projects in CIFASD are required to have a plan for data sharing.
  - Most projects wrote in their application that they will use the Central Repository
- How can we best use the Central Repository to facilitate interactions among the CIFASD investigators?
  - What needs to be in it?
- How can we best use the Central Repository to facilitate data sharing with external investigators?
  - What needs to be in it?

#### Central Repository and Internal CIFASD

- Current status for Central Repository in CIFASD4
  - Provided assistance to Tina Chambers project
  - Gathering protocol information for each project
- What do people want to get from the Central Repository for CIFASD4?
  - Data from other projects?
  - Results from other projects?
  - Protocol information from other projects?
  - · Other?

#### Central Repository and Data Sharing

- Human Subjects: Informed Consent and Protocol
  - Need to have language in the informed consent that specifically indicates that de-identified data from the project will be shared with
    - · CIFASD investigators
    - external approved researchers
  - For identifiable data (facial image) it is possible for this to be shared as well, but needs to be clearly stated that it is identifiable
  - Template language for data sharing was provided for DNA, facial images, easily modified for other data types
  - Protocol should specify that data/samples will be shared with approved researchers
- Recommend:
  - Central review of all Informed Consent Forms to ensure broad sharing language
    - Wozniak, Mattson, Weinberg, Foroud have uploaded their ICs to Redcap
    - NEED IC from: Chambers, Jones, Coles, Grant, Hammond, Petrenko
  - Draft consent elements available at CIFASD website

#### Central Repository and Data Sharing

- What about non-human data?
  - Should we also store raw data and/or results from animal studies? Assay results?

#### NIAAA Data Archive (NIAAA<sub>DA</sub>)

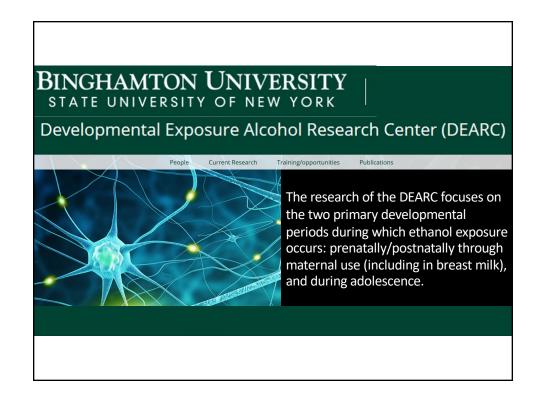
- Not required for CIFASD4, but would be for CIFASD5
  - · Would be wise to prepare for this now
- Human subjects research only
- Submit electronic, de-identified data from human subjects
  - · Obtain informed consent for broad sharing of de-identified data
  - Collect personally identifiable information (PII) to create the NDA Global Unique Identifier (GUID)
    - Get an NDA account for access to the GUID tool
  - Costs to prepare data for submission can be included as a grant expense
  - Data embargo is 2 years after the end of the grant
- CIFASD5 could use the Central Repository to work with the NIAAA<sub>DA</sub>?

NOT-AA-18-010



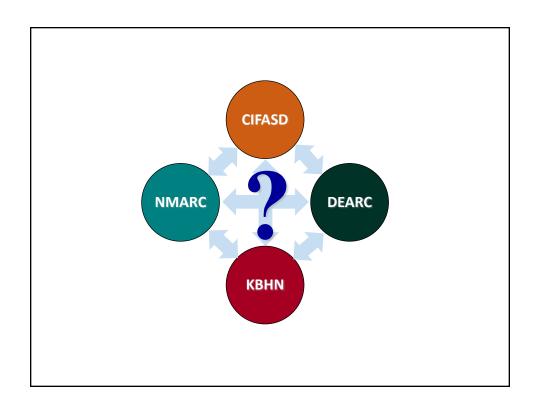
# Opportunities for Cross-Center Interactions

San Diego, June 15, 2018









#### **Overlapping Foci / Expertise**

CIFASD: DEARC: NMARC: KDHN:

Clinical Studies Animals Models (Clinic Affiliates) **Animal Models** 

Animal Models Clinical Study (Clinic Affiliates) Animal Models Clinical Studies Clinical Services

#### **Common Leaders,**

CIFASD: DEARC: NMARC: KDHN:

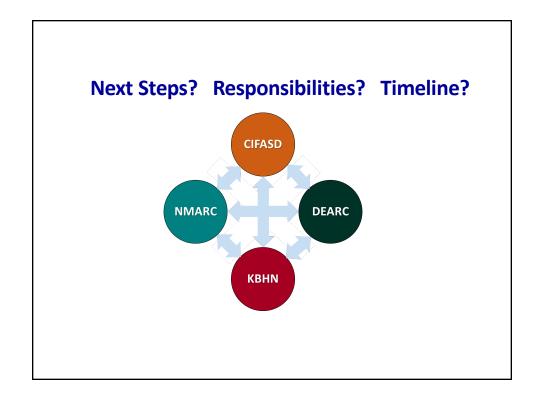
Ed RileyTerry DeakDan SavageJames ReynoldsMichael CharnessLinda SpearFernando Valenzuelaet alia

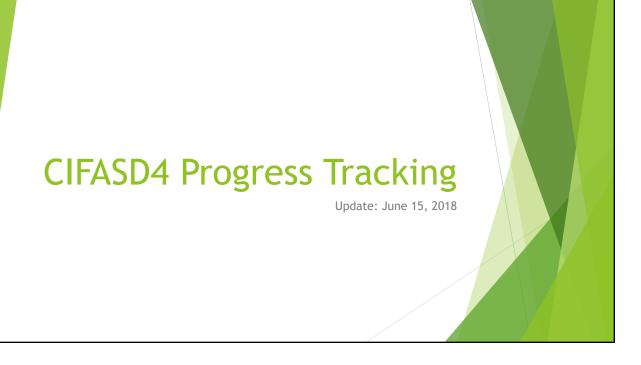


#### **Some Possible Opportunities for Interaction?**

- Joint Thematic Symposia and/or Workshops
- Research Collaboration

   Direct; Shared Specimens; Pooled data
- Review of each other's pilot grant applications
- Cross-Lab Training





# **Goal** = A way to chart progress so we all get to the finish line together <5 years!

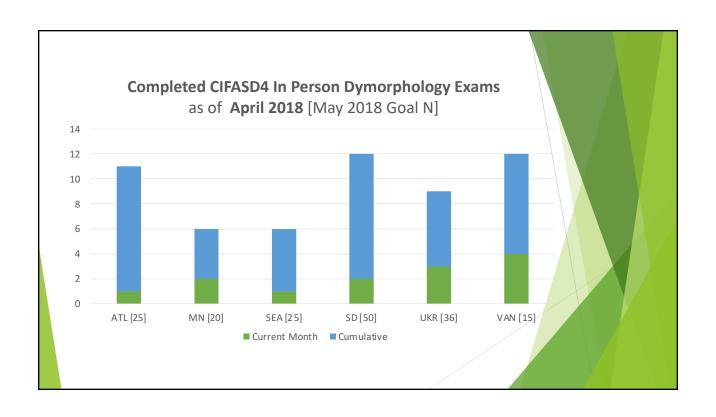
- Focus on DATA and SAMPLES
  - Measurables that will lead to publications
    - Subjects recruited, tested, referred
    - Samples collected, shared, analyzed
- NOT interested in minutia
  - <u>Completed</u>? % or monthly progress
  - NOT a diary of the steps to the goal
  - Goal ≠ micromanagement

#### **Needed Details**

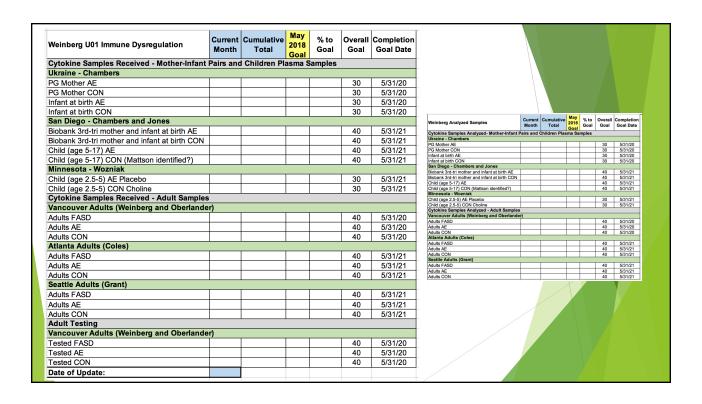
- GOALS
  - Cumulative Goal Ns per year end of each year MAY 2018, 2019, 2020, 2021 and 2022
  - Overall N Goal
  - Goal Completed Date
- Actual Ns or Completion Percentages
  - Current Month = through May 2018 [End of YR1]
- Any information you think might be useful to include on your table (e.g., data being collected in batches once every X months or if your numbers don't match those detailed in your grant proposal - explain why)

Jones U24 Dysmorphology Core	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	
n Person Dysmorphology Exams						
Atlanta	2	20	25	80.0%	120	
Minnesota					90	
Seattle					120	
San Diego					260	
Jkraine					180	
Vancouver Vancouver					80	
Telemedicine Telemedicine						
Minnesota (convergent validity)					48?	
San Diego (convergent validity)					48?	
San Diego (reliability of telemedicine)					32	
San Diego (training telemedicine)					15	
Minnesota (application in remote areas)					TBD?	
New Mexico (application in remote areas)					TBD?	
Oxford, England					TBD?	
Rochester					TBD?	
San Diego FASD Research Subject Pool						
Number of subjects recruited					400	
<b>Fraining</b>						
Number of physicians trained					TBD?	
Date of Update:						/

Jones U24 Dysmorphology Core	Overall Goal	May 2018 Goal	May 2019 Goal	May 2020 Goal	May 2021 Goal	May 2022 Goal	Completion Goal Date
In Person Dysmorphology Exams							
Atlanta	120						5/31/22
Minnesota	90						5/31/20
Seattle	120						5/31/22
San Diego	260						5/31/21
Ukraine	180						5/31/22
Vancouver	80						5/31/21
Telemedicine							
Minnesota (convergent validity)	48?						5/31/20
San Diego (convergent validity)	48?						5/31/20
San Diego (reliability of telemedicine)	32						5/31/21
San Diego (training telemedicine)	15						5/31/21
Minnesota (application in remote areas)	TBD?						5/31/22
New Mexico (application in remote areas)	TBD?						5/31/22
Oxford, England	TBD?						5/31/22
Rochester	TBD?						5/31/22
San Diego FASD Research Subject Pool							
Number of subjects recruited	400						5/31/22
Training							
Number of physicians trained	TBD?						5/31/22



Chambers U01 Ukraine	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	Completion Goal Date	
Newly Recruited Mothers							
Exposed mothers					120	5/31/20	
Low/unexposed mothers					80	5/31/20	
Neurobehavioral Testing							
School age exposed					80	5/31/21	
School age low/unexposed					70	5/31/21	
6 mo. old infants exposed					80	5/31/21	
6 mo. old infants low/unexposed					40	5/31/21	
12 mo. old infants exposed					60	1/1/22	
12 mo. old infants low/unexposed					40	1/1/22	
Blood Samples Collected							
Infants exposed					80	5/31/21	
Infants low/unexposed					60	5/31/21	
School age children exposed					40	5/31/21	
School age children low/unexposed					30	5/31/21	
2D Ultrasounds							
Exposed mothers					120	5/31/20	
Low/unexposed mothers					80	5/31/20	
3D Images							
Exposed school age children			·		35	5/31/21	
Low/unexposed school age children					30	5/31/21	
Date of Update:							



Coles U01 Adults	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	Completion Goal Date	
Enrollment							
Number of adult registry enrollees (Atlanta and Seattle)					500	5/31/22	
Completed Questionnaires - De	mograph	ics and Heal	th				
ATL Qs completed - FASD					40	5/31/21	
ATL Qs completed - AE					40	5/31/21	
ATL Qs completed - CON					40	5/31/21	
SEA Qs completed - FASD					40	5/31/21	
SEA Qs completed - AE					40	5/31/21	
SEA Qs completed - CON					40	5/31/21	
Tier 2 (YRS 2-5)							
Medical Record, Urine Sample a	nd NB (N	IH Tool Box	and Q	s)			
ATL MR, US and NB - FASD					40	1/1/22	
ATL MR, US and NB - AE					40	1/1/22	
ATL MR, US and NB - CON					40	1/1/22	
SEA MR, US and NB - FASD					40	1/1/22	
SEA MR, US and NB - AE					40	1/1/22	
SEA MR, US and NB - CON					40	1/1/22	
Date of Update:							

Hammond U01 2D/3D Images	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	Completion Goal Date
2D Images Received						
Web Portal - Foroud						
Atlanta - Coles						
Ukraine - Chambers						
Vancouver - Weinberg						
3D Images Received						
Minnesota - Wozniak						
Ultrasound and 3D Images Rece	eived					
Aiton sample - 135 per year						
Ukraine - Chambers						
Date of Update:						
	1	I				

Foroud U01 Genetics			% Complete	Completion Goal Date			
DiG FASD Aim 1: Develop web portal YEARS 1 and 2							
Develop consent form				1/31/18			
Develop Case Report Form (study questionnaire)				1/31/18			
Develop procedure for collecting prior FASD evaluations for participant	S			2/28/18			
Develop saliva collection system				3/31/18			
Develop assent video				4/30/18			
Finalize data dictionary with CIFASD Informatics Core				4/30/18			
Establish file transfer with CIFASD Central Repository				4/30/18			
Develop protocol, video and interface for collecting 2D facial images				4/30/18	1		
Develop risk score from facial imaging data				4/30/18	1		
Develop study web portal				4/30/18	1		
Final IRB approval for protocol, paper and video consent/assent, HIPA		y materials		5/31/18			
Publicize study through NOFAS, other support groups, FAS-related we				6/30/18			
Develop materials to make participants aware of other CIFASD studies				6/30/18			
Implement FONS (in collaboration with S. Mattson)				10/31/18	1		
Foroud U01 Genetics	Current	Cumulative			Overall	Completion	
	Month	Total	Goa	Goal	Goal	Goal Date	
DiG FASD Aim 2: Whole Exome Sequencing							
CIFASD3 sample genetic analysis completed					N?	1/31/22	
Genetic analyses performed in CIFASD project nominated genes					N?	3/31/22	
Genome-wide genetic tests performed					N?	4/30/22	
Genes of interest shared with other CIFASD projects					N?	5/31/22	
Online Web Portal Participants							
Number of participants enrolled in the Web Portal					2000	7/31/21	
Number of enrollees who provided consent via the Web Portal					2000	7/31/21	
Participants who uploaded 2D facial images					2000	7/31/21	
Participants who returned saliva samples					2000	8/31/21	
Saliva samples sequenced at IU Sequencing Core					700	12/31/21	
Date of Update:							

Petrenko/Tapparello U01 Intervention		Cumulative			Overall	Completion	
Focus Group Enrollment - YEARS 1 and 2	Month	Total	Goal	Goal	Goal	Goal Date	
Number of participants enrolled					20*	2/28/19	
Number of groups conducted					6	2/28/19	
Initial Feasibility Test - YEARS 1 and 2							
Number of participants enrolled					5	5/31/19	
Number of interviews completed					5	5/31/19	
Date of Update:							
Petrenko/Tapparello U01 Intervention	%	Completic					
	Complete	Goal Dat					
FMF Connect App Development Major Milestone	Complete	Goal Dat and 2					
FMF Connect App Development Major Milestone Design interface programmed	Complete	Goal Dat					
FMF Connect App Development Major Milestone Design interface programmed Family Forum programmed	Complete	Goal Dat l and 2 1/31/18					
FMF Connect App Development Major Milestone Design interface programmed Family Forum programmed Psychoeducational content written & programmed	Complete	Goal Date 1 and 2 1/31/18 5/31/18					
FMF Connect App Development Major Milestone Design interface programmed Family Forum programmed	Complete	Goal Dat l and 2 1/31/18 5/31/18 7/31/18					

Wozniak U01 Neuroimaging	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	Completion Goal Date
MRI Scan #1						
MRI Scan #1 - PAE			15		45	5/31/20
MRI Scan #1 - CON			15		45	5/31/20
Cognitive Evaluation (Mattson N	NB Batte	rv)			,,,	5,51,25
Cognitive evaluation - PAE		[	15		45	5/31/20
Cognitive evaluation - CON			15		45	5/31/20
MRI Scan #2						
MRI Scan #2 - PAE			0		30	1/1/22
MRI Scan #2 - CON			0		30	1/1/22
Date of Update:						

Mattson U01 Neurobehavior	Current Month	Cumulative Total	May 2018 Goal	% to Goal	Overall Goal	Goal Date	
Aim/Source							
eTree Validation & Subjects							
1a: CIFASD Ukraine - AE, CON	0	0	250	0.0%	250	5/31/18	
1a: CoFASP San Diego - AE, CON	0	0	994	0.0%	994	5/31/18	/
1b: UCSD FASD - AE	0	0	40	0.0%	260	5/31/22	
1b: Psych Clinic - CON [YRS 3 & 4]	n/a	n/a	n/a	n/a	50	5/31/21	
1b: Dev'l BX Psychiatry - CON [YRS 3 & 4]	n/a	n/a	n/a	n/a	50	5/31/21	
1b: CIFASD MN - AE	0	0	23	0.0%	45	5/31/19	
1b: CIFASD MN - CON	0	0	23	0.0%	45	5/31/19	
Validation subjects YRS 1-5							
1c/2b: CBT San Diego - AE	0	0	5	0.0%	50	5/31/22	
1c/2b: CBT San Diego - T-CON	0	0	5	0.0%	50	5/31/22	
1c/2b: CBT San Diego - B-CON	0	0	5	0.0%	50	5/31/22	
Online FONS YRS 2-5							
2a: WebPortal	0	0	0	#DIV/0!	2000	5/31/22	
Date of Update:	6/15/18						

#### **Actions Steps**

- Jill will email each project their current CIFASD4
   Progress Tracking table in Excel by tomorrow (Saturday)
   night... or the whole sheet and just update your tab.
- Update it as you see fit.
- Be sure to include CUMULATIVE Year End Ns for each YR (May 2018-2022) and the Overall N for each measure.
- Enter your project's actual Ns and completion percentages for data collected and tasks completed through May 31, 2018 in the current month column.
- Email Jill your revised CIFASD4 Progress Tracking table in Excel no later than <u>Tuesday</u>, <u>June 26<sup>th</sup></u>, <u>2018</u> so she can prepare all tables for discussion during the June 27<sup>th</sup> monthly meeting.

Or else... you meet this Jill. ©





# Spreadsheet Table/Chart Format FOCUS

- Table/chart should <u>QUANTIFY</u> each deliverable, be visually simple and easily point to progress (per aim, monthly, etc.)
- Clearly state the flow chart for shared samples and include timelines that are easy to monitor
- Include collaborations and timelines
- Keep it clean and clear
  - Eliminate redundancies
  - Rungs in the ladder steps are not needed