Immune Dysregulation in FASD: Programming of Health and Neurobehavioral Outcomes

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Presenter Disclosure

• No commercial interests or conflicts of interest
Biomarkers

• Historically, biomarkers for prenatal alcohol exposure were developed to detect alcohol to confirm that was in the person’s system
  • These tell us only what happened on a particular day – i.e., the day of delivery in this case, but not what occurred over the longer term of pregnancy

• CIFASD studies aim to identify biomarkers underlying unique brain/behavioral/physiological/cellular changes → signatures that not only identify alcohol exposure but predict or are associated with child outcome
Biomarkers (cont’d)

miRNAs - Miranda

Epigenetics – Hashimoto-Torii / Torii

fNIRS - Kable

Brain imaging - Wozniak

Genetics – Foroud/ Eberhart/Parnell

Facial imaging – Suttie/Hammond

Microbiome – Blanchard/ Mooney

Immune/inflammation - Weinberg

Neurobehavioral performance Chambers

Weinberg FASD 2019
Our CIFASD research focuses on the Immune System

A complex network of specialized cells, tissues, and organs that recognizes and defends the body from foreign substances, primarily disease-causing microorganisms such as bacteria, viruses, parasites, and fungi.
Inflammation – to ignite, set alight

- Acute inflammation is a normal part of the immune response
  - First line of defense against injury, infection
  - Body initiates inflammation to protect itself, remove harmful stimuli, begin healing
- Chronic or prolonged inflammation can be harmful or damaging
• But sometimes inflammation can be “invisible”
• Chronic or low-grade inflammation may play a role in many diseases and disorders
Cytokines in plasma of pregnant women

Plasma samples collected at intake (2\textsuperscript{nd} trimester) and during 3\textsuperscript{rd} trimester from pregnant women who consumed alcohol or were abstinent (low-no consumption)

Part of Tina Chambers ongoing longitudinal study in Western Ukraine

Assessed inflammation by by measuring 40 cytokines as markers of immune function/inflammation

Cytokines are proteins that modulate or regulate the immune system response

Cytokines also play a role in brain development
Further subdivision of results based on child outcome (Bayley score at 6 and 12 months):

- Women in control group (C)
  - Typically-developing child (TD)
  - Child with neurodevelopmental delay (ND)

- Women in alcohol-consuming group (A)
  - Typically-developing child (TD)
  - Child with neurodevelopmental delay (ND)
Maternal cytokine profile differed in alcohol-consuming vs control women and was associated with child outcome.

Each column is a cytokine, each row represents a maternal condition (alcohol/no alcohol), in relation to child outcome (affected/unaffected).

- C/TD (Control women – typically developing child)
- C/ND (Control women – child with neurodevelopmental delay)
- A/TD (Alcohol consumption – typically developing child)
- A/ND (Alcohol consumption – child with neurodevelopmental delay)

Bodnar, Raineki, et al., Brain Behav Immun, 2018
Additional analysis identified 2 networks or groups of cytokines that act together.

**NETWORK 1 – 10 CYTOKINES:**
- Low expression in controls but high expression with alcohol consumption.

**NETWORK 2 – 7 CYTOKINES:**
- Contrasting patterns of expression in controls vs alcohol-exposed women whose children show delay.

In maternal plasma, cytokine patterns can distinguish if child neurodevelopmental delay is due to alcohol or independent of alcohol.
Cytokines in plasma from alcohol-exposed and unexposed children: Child cytokine profile differs depending on whether or not they were exposed to alcohol and whether or not they show neurodevelopmental delay

Bodnar et al., in preparation
Analysis of child plasma to identify groups or networks of cytokines that act together

- **NETWORK 1 – 4 CYTOKINES:**
  - Cytokines suppressed with alcohol exposure but activated/show no grouping in controls

- **NETWORK 2 – 5 CYTOKINES:**
  - In alcohol-exposed children, distinguish typically developing from those with neurodevelopmental delay

- **NETWORK 3 – 4 CYTOKINES:**
  - Contrasting patterns of cytokine activation between C/ND and A/ND
  
  Can distinguish neurodevelopmental delay due to alcohol or independent of alcohol
What happens in adulthood?

- Our new project is extending our study of the immune system in individuals with FASD into adulthood.
- We are recruiting adults with FASD and adults with no prenatal alcohol exposure in Vancouver.
  - Working closely with Dr. Claire Coles and Dr. Therese Grant who are recruiting adults in Atlanta and Seattle.
- We need you!
- **Come to our Table in the Exhibit area to get information and to sign up for our study!**
PARTICIPANTS NEEDED

ADULT HEALTH STUDY
A Collaborative study led by Drs. J. Weinberg, T. Oberlander, and C. Loock

Investigating the role of the immune system in health of adults with FASD

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DiG FASD
*Dissecting the Genetics of FASD*
Tatiana Foroud, Leah Wetherill, et al

- Everyone with FASD has a different experience and different struggles, and we think genetics might play a role in these differences.
- But each gene has a small effect, so we need gene information from hundreds of people – that’s why we need YOU!
- If we understand how genes make FASD different, we can use that information to help improve treatments and interventions.
- We are sharing a table in the Exhibit area with Tatiana and Leah who are running this study. **Come by to sign up!**
Conclusions

- This is the first clinical study in the FASD field to identify the immune profile/phenotype that occurs with alcohol consumption/exposure
- Our findings hold promise for the potential development of immune biomarkers or immune signatures that might help us predict:
  - Which children may be at risk for neurobehavioral problems
  - What maternal factors may be protective
  - Whether neurodevelopmental delay is due to alcohol or not
- Implications beyond health outcomes to functioning of the children in multiple domains (e.g., attention, cognitive function, adaptive function)
Acknowledgments