

# Assessing Oral Feeding Readiness Through Neonatal Salivary Analysis



Jill L. Maron M.D., M.P.H.  
Professor of Pediatrics  
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**Tufts** Medical Center  
*Mother Infant Research Institute*

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## Disclosures

- I have no financial disclosures or conflict of interests.

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## Objectives

- Identify the challenges associated with assessing oral feeding skills in the newborn
- Assess the current tools available for determining readiness to feed in the neonatal population and their limitations
- Understand the benefits of saliva as a noninvasive diagnostic biofluid
- Assess the diagnostic potential of saliva in determining readiness to feed in the neonate and diagnosing other feeding problems in infancy

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## Objectives

### Main Objective:

- *Challenge our current thinking about oral feeding assessment and treatment strategies in the newborn*

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## Question?

- How often are you confronted with a newborn who cannot successfully feed?
  - As a group we are capable of discerning between successful and unsuccessful oral feeders
  - *Distinct from understanding readiness to feed*
- How many times have you known *why* an infant cannot orally feed?



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## Anecdotes About Feeding

- Various opinions about why newborns can't orally feed
  - *Infants of diabetic mothers are 'pokey'*
  - *Infants with pulmonary hypertension have been 'sick'*
  - *NAS babies are not 'captured'*
  - *Boys are well. . . Boys*
  - *35 week infant who fed well earlier in day is now 'too tired'*

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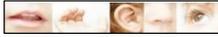
## Complexities of Oral Feeding

- Oral feeding competency relies upon the maturation and coordination of:

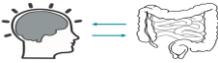
*Suck* → *Swallow* → *Breathe*

- However, the ability to feed is also driven by:

Senses:



Gut – Brain Axis:



Neurodevelopment:



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## Oral Feeding is NOT a One Size Fits All Model

- Multicenter retrospective analysis of a prospective cohort of moderately preterm infants admitted to an NICHD NRN hospital
- Primary Outcomes: Post menstrual age at full oral feeding and at discharge home
- Subjects: 6,146 infants born between 29-33 weeks' gestation between January 2012-November 2013

Brumbaugh et al. for the NRN, 2018 Early Hum Dev

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## Oral Feeding Outcomes

Explanatory (independent) variable	Estimate	95% Confidence limits		p-Value
PMA at first feed (in weeks)	4.49	4.13	4.85	<0.0001
Birth weight (per 100 g)	-0.46	-0.51	-0.40	<0.0001
SGA	0.91	0.24	1.58	0.008
Male	1.31	0.87	1.76	<0.0001
Surfactant exposure	2.43	1.87	3.00	<0.0001
PDA requiring treatment	3.37	0.93	5.81	0.007
Black race	-1.62	-2.44	-0.80	0.0001
Multiple gestation	0.59	0.09	1.10	0.021
Human milk in the first 28 days	0.77	0.11	1.44	0.023

Brumbaugh et al. for the NRN, 2018 Early Hum Dev

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## In Utero Differences

- Sex specific maturation of oral motor function and development has been seen as early as 15 weeks' gestation
- Utilizing ultrasound assessment of oral-upper airway regions in 85 fetuses, investigators concluded that oral-motor and upper airway skills emerged earlier in females



Miller et al., Dev Med Child Neurol 2006

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## Assessing Feeding Development

- How do we determine sensory integration status?
- How do we assess the gut-brain axis?
- How do we assess oromotor skills
- How do we know the baby is neurodevelopmentally ready to begin oral feeding?

### Cue based feeding!

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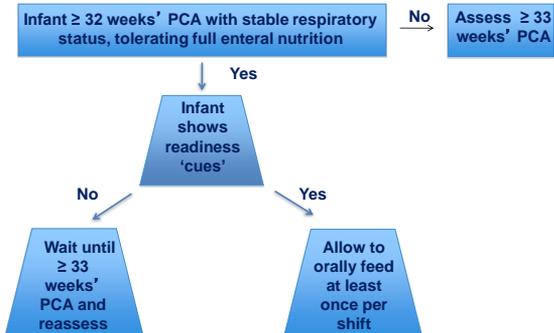
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## Current Cue Based Feeding Tools



Ludwig and Waltzman, Newborn and Infant Nursing Reviews 2007.

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## Cue Based Feeding Tools

- Integration of Infant-Driven Feeding<sup>7</sup> protocols are an essential part of our care
- They are designed to answer the important developmental questions related to feeding readiness
  - Waking to feed *surrogate* for a maturing gut brain access
  - Sucking on a pacifier *surrogate* for oral motor readiness
- However, can we do better?

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## Cochrane Review 2012 and 2016

- Reviewed the effectiveness of oral feeding assessment tools:
  - Reducing length of stay
  - Shortening time to establish full oral feeds
- Results: “**No studies met the inclusion criteria**”
- Conclusion: “There is currently **no evidence to inform clinical practice**” and research is needed in this area to develop an instrument to assess feeding readiness in the preterm infant population

Crow et al., Cochrane Database Syst Rev. 2012 Apr 18;4:CD005586.

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## Current State of Affairs

- Infant-Driven Feeding<sup>7</sup> is the current GOLD standard
- Numerous devices on the market to improve feeding outcomes
  - Sensory integration
  - Oral feeding training
- But which infant needs which intervention? And when?

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## Oromotor Maturation

- Ntrainer: Somatosensory training—without feeding



- NFant: Oromotor assessment with feeding



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## Feeding and Sensory Integration

- Pacifier Activated Music Player (or Mother's Voice)



- Breast milk olfactory stimulation



Chorna OD, et al. Pediatrics. 2014;133(3):462-468.  
Davidson J, et al. Breastfeed Med. 2019 May;14(4):230-235.

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## Olfactory Stimulus with Breast Milk

- Infants born between 28 0/7 and 33 6/7 weeks' gestation (n=36) were randomized to receive either MOM or water (sham) stimulus during the learning process of oral feeding
- Clinical and feeding outcomes were recorded
- Statistical analyses examined the effect of stimulation with MOM on feeding outcomes stratified for age and sex

Davidson J, et al. Breastfeed Med. 2019 May;14(4):230-235.

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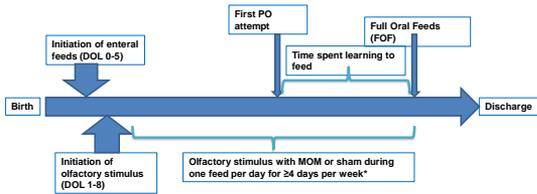
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# Olfactory Stimulation with Breast Milk

## Study Design Schematic



Davidson J, et al. Breastfeed Med. 2019 May;14(4):230-235.

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# Olfactory Stimulus with Breast Milk

- Overall, there was not a significant difference between sham infants compared to MOM infants in mean post menstrual age of full oral feeds (Sham: 35 5/7 vs. MOM 36 0/7; p=0.37)
- Infants born < 31 weeks' gestation who received MOM stimulation learned to feed sooner than controls (p=.06), suggesting an ideal developmental window for the intervention
- There were no sex differences in response to olfactory stimulus.

Davidson J, et al. Breastfeed Med. 2019 May;14(4):230-235.

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# Treatment Strategies

- In order to fully understand which baby needs which intervention(s) when, we must be able to assess their development in real-time
- How do you do that in this highly vulnerable population?



**SALIVA**

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## Saliva as a Diagnostic Biofluid

- Saliva has several benefits over other bodily fluids
  - Noninvasive and relatively easy to obtain
  - Safe acquisition and biohazard profile
- Direct filtrate of blood
  - Electrolytes and cells
  - Proteins, hormones, enzymes, drugs and immunoglobulins
  - Microorganisms
  - Genetic material-DNA and RNA

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## Oral Feeding

- My laboratory has used saliva to objectively monitor multiple developmental systems simultaneously
  - Oral motor control and facial development
  - Sensory integration (olfactory, vision, hearing, taste)
  - Hunger signaling
  - Neurodevelopment
  - Gastrointestinal development

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## Development of Oral Feeding Assay

- Goal is to develop diagnostic assays to:
  - 1.) Assess an infant's readiness to orally feed
  - 2.) Identify developmental delays limiting oral feeding success
  - 3.) Personalize our approach to treatment strategies based upon an individual's salivary profile

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## Background

- For over a decade, my laboratory has attempted to understand the molecular mechanisms and developmental pathways involved in oral feeding
- **Genomic** – DNA—mutations within specific genes
- **Transcriptomic** – RNA—Real-time gene expression of the developmental status of the infant *in the moment*
- **Proteomic**—Proteins—Real-time mechanisms of action\*

\*Not discussing proteomic data today, see Khanna et al, Front Pediatr 2017

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## Genomics of Feeding

- Collaboration with Dr. Emily Zimmerman, speech pathologist, at Northeastern University



Dr. Emily Zimmerman

- Forkhead box protein 2 (*FOXP2*)
  - *FOXP2* was the first gene to be implicated in a developmental disorder of speech and language
  - *Molecular studies of 15 individuals in the 'KE' family who suffered from speech language disorders*

Fisher et al., Nat Genet 1998 18(2):168-170.

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## Case Report

- “I came across your name while researching my son’s recent diagnosis.”
- My son “was born via c-section at exactly 35 weeks because I had preeclampsia. He suffered no trauma during pregnancy or labor.”
- “He was in the NICU for 42 days for ‘suck, swallow, breathe’. We tried breast feeding, formula, thickened formula, different nipple sizes, spot feeding etc.”

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## Case Report

- “We had no explanation for why he couldn't coordinate SSB. He underwent an ultrasound of both his brain and his heart and he had an MRI. All findings were normal or non-significant.”
- “. . . after failing a swallow test with flying colors, he had a g-tube placed . . . “
- “In an effort to find the cause of the issue, his *neonatologist* ordered a microarray and chromosomal analysis. . . . ~9kb loss within chromosome band 7q31.1 that contains exon 2 of **FOXP2 gene**”

Zimmerman et al. 2016 Cold Spring Harb Mol Case Stud.

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## Genomics of Oral Feeding Disorders

- To our knowledge, this was the first case report linking a deletion in *FOXP2* to oral feeding impairment in the newborn
- However, in December, 2020, we received an email from the Netherlands:
  - *With great interest I've read your case report about an infant with feeding difficulties and a FOXP2 deletion (PMID: 27148578). I'm a pediatrics resident in Wilhelmina Children's Hospital in Utrecht (the Netherlands) and a patient of mine also has a FOXP2 deletion. This one year old boy has feeding difficulties very similar to the case in your article.*
- These cases serve as important reminders to consider genomic testing in infants who cannot successfully feed by term gestation
  - *Particularly those who lack related pathology that may limit feeding success*

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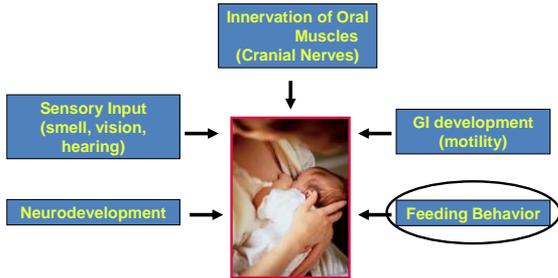
## Transcriptomics of Oral Feeding

- Real-time gene expression (RNA) profiles and infant's feeding status
  - *Successful v. Unsuccessful oral feeding*
- Aimed to gain an understanding of the developmental status of a newborn in the moment
- Conducted this research on saliva samples
- Used various platforms:
  - RT-qPCR, microarrays and RNASeq

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## Oral Feeding

- We were able to **simultaneously** detect genes involved in:



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## Feeding Behavior

- Identification of feeding behavior pathways in newborns learning to feed is novel
- Limited qualitative data are available:
  - Hunger signaling
  - Satiety
  - Neuronal regulation of food intake
  - Hypothalamic regulation of feeding behavior
- The important role of biomarkers involved in feeding behavior makes biological sense in the newborn

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## Neonatal Feeding Behavior

- On average, a newborn infant gains **200%** of his/her birth weight by 1 year of age
  - A preterm infant may gain **> 300%** of his/her birth weight
- Newborn must consume **80-150 kcals/kg/day**
- Caloric intake of a newborn is equivalent to an adult diet of **7,000 to 10,000 kcals/day**



~ 3800 kcals

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## Hypothalamus and Neonatal Feeding

- One of our first successful 'transcriptomic hits' related to oral feeding in the newborn involved hunger signaling and a maturing gut-brain axis
- The gene, *NPY2R*, is a known modulator of feeding behavior
  - + expression = satiety
  - - expression = hunger



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## NPY2R as a Biomarker

- In neonatal saliva, *NPY2R* performed in a binary fashion
  - +/- detection
- Amplification of *NPY2R* in neonatal saliva had a 95% positive predictive value in determining that an infant cannot sustain full oral feeds
  - Infants did NOT have a mature gut-brain axis driving feeding
- However, the negative predictive value of the assay was only 27%
  - Infant may be hungry, but still not know how to feed

Maron et al., *PLoS One* 2012; 7(5):e37870.

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## Background

- This research led to the need to identify a more diverse gene panel for the prediction of oral feeding readiness in the premature newborn
  - Genes needed to be representative of a diverse range of biological functions required for successful oral feeding



Hunger Signaling  
*NPY2R, AMPK*



Sensory Integration  
*PLXNA1, NPHP4*



Facial Development  
*WNT3*

Maron et al. *J Pediatr* 2015

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## Positive Gene Expression



### •AMPK:

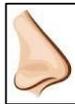
- Regulates whole body energy balance
- Activation of gene in the hypothalamus induces feeding and weight gain



AMPK = Hunger

### •PLXNA1:

- Controls axon guidance
- Increased expression in mature compared to developing olfactory sensory neurons



PLXNA1 = Olfactory maturation

McIntyre et al., J Neurosci Res 2010 88:3243-3256.

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## Negative Gene Expression



### •NPY2R:

- Down-regulated expression of this gene induces hyperphagia



NPY2R = Hunger

### •WNT3:

- Embryologic gene involved in lip, palate and tooth formation



WNT3 = Facial Development

### •NPHP4:

- Involved in retinal development and visual behavior



NPHP4 = Vision

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## Successful Feeders

Genes	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Odds Ratio	Odds Ratio 95% CI	p value
PLXNA1	85.05	22.75	56.12	56.72	2.89	(1.47, 5.67)	0.002
AMPK	96.36	8.38	55	66.67	3.21	(1.09, 9.48)	0.03
WNT3	17.01	72.46	41.77	42.91	0.59	(0.33, 1.07)	0.09
NPY2R	39.18	52.69	49.03	42.72	0.71	(0.36, 1.0)	0.05
NPHP4	58.25	35.33	51.13	42.14	0.60	(0.34, 1.03)	0.06
Age	-	-	-	-	1.43	(1.25, 1.63)	<0.001
Sex (Female)	-	-	-	-	1.75	(0.99, 3.06)	0.05

Maron et al., J Pediatr 2015 166(2): 282-288.

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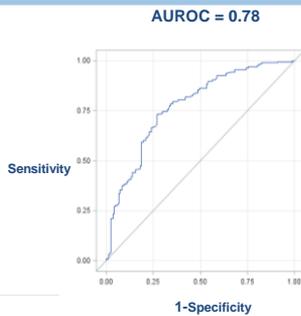
## Results

- Data suggest again that there is no **single 'magic bullet' biomarker** for determining readiness to orally feed in the newborn
- How predictive are the biomarkers in combination?
  - Combine the 5 genes
  - Randomly select samples from the data set to generate a ROC curve

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## Background

• The combined expression profile of these genes, along with an infant's post-conceptual age and sex, demonstrated 78% accuracy in predicting feeding maturity



Maron et al., J Pediatr 2015.

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## Predictive Modeling: Feeding Success

35 week ♂

		AMPK		PLXNA1			
		-	+	-	+		
NPZR	NPY2	NPY4	-	14%	32%	35%	60%
			+	9%	22%	34%	48%
+	-	-	9%	22%	24%	48%	
		+	6%	14%	16%	35%	
+	+	-	9%	22%	24%	48%	
		+	6%	15%	16%	35%	
+	+	-	6%	15%	16%	36%	
		+	3%	9%	10%	25%	



Predictive modeling of successful oral feeders based upon age, sex and gene expression profiles

Maron et al., J Pediatr 2015 166(2): 282-288.

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## Background

- Data analysis also reinforced 2 important aspects of feeding maturation in the newborn:

- Importance of age

- *If you wait long enough, infants will feed*



- Importance of sex

- *Females learn to feed earlier than males*



**GIRLS RULE**

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## Needed Additional Studies

- There still remains a knowledge gap regarding the essential molecular mechanisms required for oral feeding maturation
- We hypothesized that the RNA Seq platform would:
  - *Improve our understanding of oral feeding competency*
  - *Identify novel pathways related to oral feeding success not previously seen*
  - *Allow for the development of personalized approaches to improve feeding outcomes*

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## RNASeq

- *Hypothesis discovery platform*
- Unlike approaches that quantify only a select number of known genes, RNASeq allows the investigator to quantify all the genes being expressed at a given time point
- Comparisons between expression profiles are then made between groups (i.e. cases vs. controls) to identify genes that may be involved or causing a condition
- Allowing the investigator to generate a hypothesis of the pathophysiology

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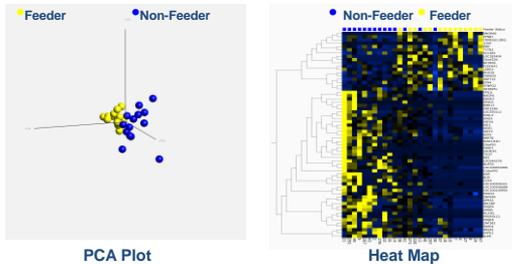
## Methods

- Performed RNASeq on saliva samples collected from both successful and unsuccessful oral feeders
- Every attempt was made to match cohorts by gestational age, post-conceptual age, sex, and ethnicity
- Performed comparative and systems biology analyses of differentially expressed genes between
  - Successful and unsuccessful oral feeders
  - Males and females

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## Results

- Overall, **63** genes were differentially expressed between feeders and non-feeders
  - 59 mapped to a known gene function; 4 genes were unmapped



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## Results

- In our combined analysis, the RNA Seq platform identified novel networks involved in oral feeding maturation
  - Nervous system
    - Memory, myelination
  - Facial structural maturation
    - Palate
  - Sensory Integration
    - Vision and smell

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## Nervous System Development

- Genes mapping to cranial nerve development and sensory integration were *the most statistically significantly* differentially expressed



Abnormal Morphology of CN III & IV  
Formation of retinal ganglion cells  
Abnormality of aqueous humor



Size of olfactory bulb (CN I)

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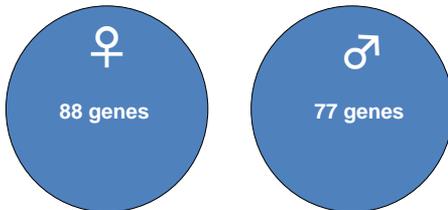
## Networks of Interest

- Analysis highlighted other areas of biological relevance including disruption in:
  - Palatal shelf formation
  - Maturation of circadian rhythms
  - Abnormal morphology of hindgut and mesenchyme
  - Development of the abdomen

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## Sex Matters

Independent analyses of males and females highlighted the unique differences in oral feeding maturation between the sexes



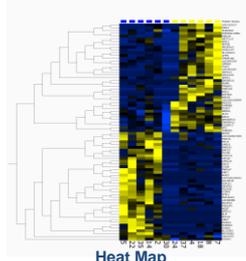
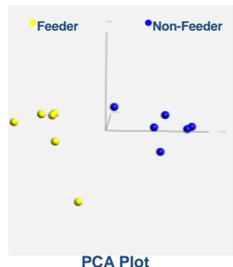
**NO OVERLAP**

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## Males

- 77 genes were differentially expressed between feeders and non-feeders

• 72 mapped to a known gene function; 5 genes were unmapped



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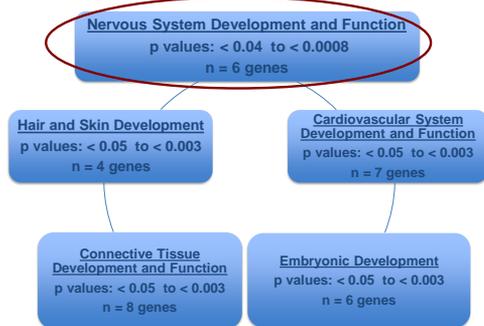
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## ♂ Disrupted Developmental Pathways



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## Nervous System Development

- Disruption in **memory and learning** was only seen in male subjects
  - Abnormal morphology of hippocampal CA1 regions
    - CA1 is required for contextual memory retrieval
    - Re-experiencing detailed episodic memories
- Abnormal myelination and formation of myelin sheath
- Size of forebrain, dentate gyrus, olfactory bulb, and anterior commissure
- Function of central nervous system and oligodendrocytes

Ji et al., Learn Mem 2008  
Bartsch et al., PNAS 2011

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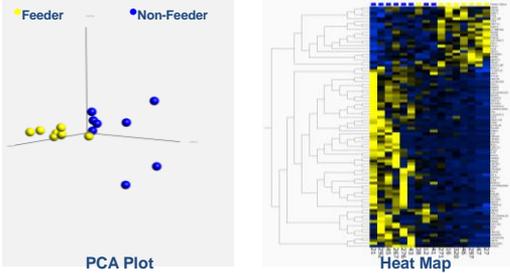
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## Females

- 88 genes were differentially expressed between feeders and non-feeders
- 85 mapped to a known gene function; 3 genes were unmapped



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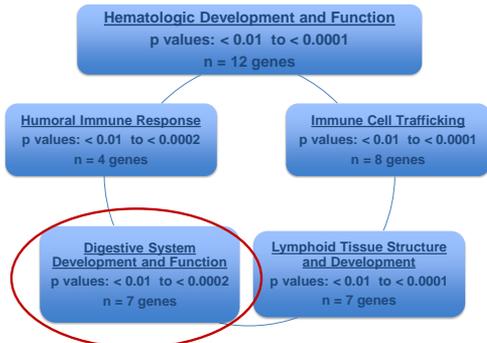
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## Disrupted Developmental Pathways



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## Digestive System Development

- **Structural Development**
  - Abnormal morphology of hard palate
  - Formation of secondary palate
  - Tooth Development
  - Abnormal color and morphology of incisor
- **Intestinal Development**
  - Morphology of intestinal villus
  - Neurogenesis of intestine
  - Development of gastrointestinal tract
  - Length of intestinal villus



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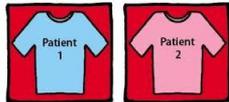
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## Summary

- These data highlight the important impact of sex on acquisition of oral feeding maturation
  - Clinically, we know there are differences between males and females in our NICUs—*outcomes, complications, and milestones*
  - We can now see differences on a molecular level that may help elucidate the findings at the bedside



One size does not fit all.

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## Feeding Next Steps

- In year 5 of an NIH funded multi-center clinical trial to further test the predictive accuracy of the NOuRISH platform in a cohort of infants born < 29 weeks' gestation
- One of the first neonatal salivary diagnostic clinical trials

 U.S. National Library of Medicine

[ClinicalTrials.gov](https://clinicaltrials.gov)

Somatosensory Modulation of Salivary Gene Expression and Oral Feeding in Preterm Infants



Dr. Steven Barlow

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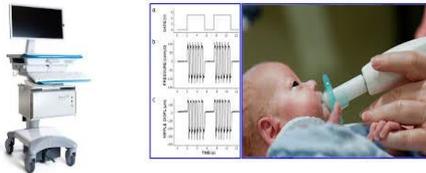
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## Next Steps

- Infants are randomized to receive sensorimotor stimulation with the Ntrainer Feeding Device



- Saliva samples collected throughout treatment and the learning process of oral feeding
- First attempt to understand gene ontogeny and response to treatment

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## Beyond Prematurity

· Can we apply these scientific approaches to a spectrum of infants who have feeding difficulties?

– Infants of Diabetic Mothers

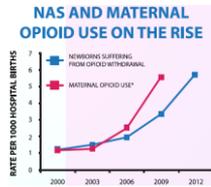
– Persistent Pulmonary Hypertension

– Neonatal Abstinence Syndrome (NAS)

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## Feeding and NAS

- Oral feeding issues do not just affect the premature infants in our care
- Infants exposed in utero to illicit drugs exhibit aberrant feeding behavior:



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## Feeding and NAS

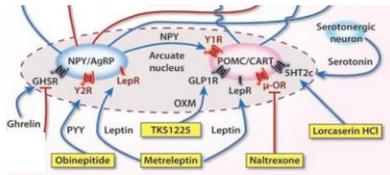
- Infants with NAS have a unique feeding phenotype:
  - 1.) Uncoordinated or ineffective feeding
  - 2.) Hyperphagia
    - Term infants consume 80-120 kcal/kg/day
    - Infants with NAS can consume 150-220 kcal/kg/day. . .or more
    - Excessive caloric intake has often been attributed to increased caloric demand due to withdrawal symptoms

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## Arcuate Nucleus of Hypothalamus

Is food replacing narcotics in a disrupted reward circuitry in NWS infants. . . .

Has food become the drug?



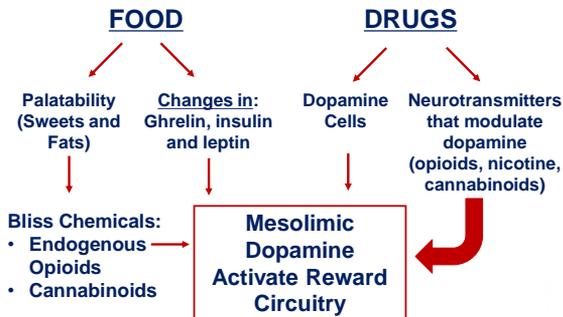
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## Hypotheses

- *In utero* exposure to illicit drugs results in an imbalance between homeostatic (energy-driven) and hedonistic (reward-driven) pathways
- Salivary gene expression profiles will differ between case (infants with illicit drug exposure) and control cohorts (sex-and age-matched infants), as well as between male and female infants.
- Salivary gene expression profiles will correlate with total intake volume in infants with NAS.

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## Reward Circuitry Similarities



Volkow et al, 2018

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## Targeted Gene Analysis

- **FOOD:**
  - *NPY2R*
    - Hunger signaling
    - ↓ Decreased expression increases appetite
  - Proopiomelanocortin (*POMC*)
    - Hunger signaling
    - ↓ Decreased expression increases appetite
  - Leptin Receptor (*LEPR*)
    - Hunger signaling
    - ↓ Decreased expression increases appetite
- **DRUG:**
  - Dopamine D2 Receptor (*DDR2*)
    - Reward signaler
    - ↑ Expression

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## Pilot Study



Dr. Liz Yen

- Prospective, case-control, observational study
- Saliva samples are collected from subjects within 48 hours of birth, prior to any pharmacological interventions.
- Salivary RNA is extracted, pre-amplified, and quantified with commercially available pre-designed quantitative reverse transcription PCR assays of the four designated genes
- Reference genes are used for quality assurance and relative quantification
  - *GAPDH*, *YWHAZ*, and *HPRT1*
  - Data analyzed using the  $\Delta\text{Ct}$ —threshold cycle

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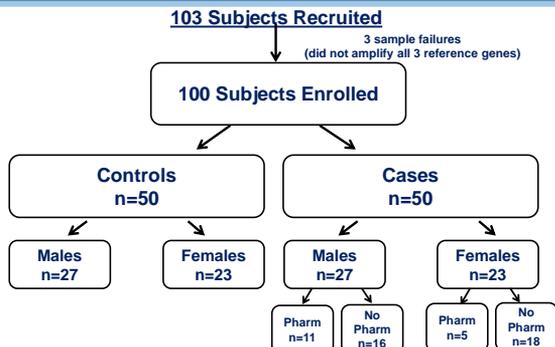
## Subjects

INCLUSION CRITERIA	EXCLUSION CRITERIA
≥34 weeks post-gestational age	Infants of diabetic mother
Maternal and/or neonatal toxicology positive for opioids and/or cannabinoids	Infants whose mothers were on antidepressants (SSRIs)
Sex- and gestational age-matched controls	Congenital anomalies, CNS abnormalities

Two hospitals, IRB approval at both sites

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## Subjects



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## Results

- **Case vs. Control:**
  - **No difference** in gene expression
- **CASE: Treatment vs. No Treatment:**
  - **No difference** in gene expression  
**BUT . . . .**
- **Males vs. Females:**
  - Expression of *DRD2* (reward gene), was significantly differentially expressed between male and female case infants (higher expression in males)  $p = 0.006$
  - True if infant required treatment ( $p = 0.03$ ) for NAS or not ( $p = 0.02$ )

Yen et al., J Pediatr, 2019

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## Intake and Gene Expression in NAS

- Expression of *DRD2* (reward gene) also correlated with volume intake:
  - Infants who expressed the highest levels of *DRD2* on days of life 2 and 7, took in the greatest volume
- Expression of *POMC* (feeding driver gene) correlated as well:
  - Infants who expressed the highest levels of *POMC* on day of life 2, took in the greatest volume

Yen et al., J Pediatr, 2019

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## NAS Summary

- These pilot data suggest that the hyperphagia often seen in infants with NAS may be due to developmentally disrupted reward signaling pathways
  - *Food becomes the drug*
- Sex specific differences in these pathways may provide a molecular basis for the clinical outcomes we see in infants with NAS

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## NAS Next Steps

- Dr. Yen has been recently funded to compare functional and structural brain MRI studies on newborns exposed to *in utero* opioids with sex and gestationally-aged matched controls
- Images are acquired directly after a feed to better assess response to food
- Dr. Yen is also exploring the role of inflammation on the developing brain in infants exposed to opioids in utero through salivary gene expression analyses
- Will ultimately perform long-term follow-up on infants to assess development, feeding behavior and addiction

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## Other Areas of Investigation

- **Infants of Diabetic Mothers**
  - Large for gestational infants born to diabetic mothers often have poor po intake after birth -- “pokey” eaters
  - Some require NICU admission and NG feeds
  - Studies have suggested that these infants have immature neurodevelopment
- **Alternative Hypothesis:**
  - ‘Overfed’ state in utero and increased insulin levels result in disruption of gut-brain axis, feeding and fat regulating genes (i.e. leptin)
  - In response to these in utero exposure, infants down-regulate appetite in order to normalize their growth curve within the first year of life

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## Infants of Diabetic Mothers

- Conducting an ongoing, prospective observational study
- Comparative analysis of term infants born to diabetic and non-diabetic mothers
  - Body composition
  - Feeding intake
  - Salivary profiles

*Stay tuned...*

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## Summary

- Feeding is **complicated**:



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## Summary

- The molecular basis for oral feeding difficulties is informative and relevant for the both short and long term outcomes of our infants



- **Why** an infant cannot feed should inform treatment strategies to improve outcomes
  - Males appear to be on a distinct developmental time course compared to their female counterparts.

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## Conclusions

- We need to be able to monitor and assess **multiple** biological systems **simultaneously**, in real time, to truly understand the mechanisms underlying oral feeding maturation and oral feeding difficulty in the newborn
- We must recognize the importance of sex on development – it matters!
- Advanced genomic platforms can aid caregivers in determining **specific** areas of delay or disrupted development that may be prohibiting feeding success
- Important opportunity to individualize care plans and feeding strategies

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