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Study shows salivary biomarkers predict oral feeding readiness in preterm newborns

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Results from a study published online in the *Journal of Pediatrics* hold the potential to substantially improve clinical decision-making to determine when a premature newborn is ready for oral feeding. The study describes developmental salivary biomarkers associated with feeding success in newborns, markers that could lead to development of objective assessment tools for caregivers.

At present, only subjective assessment tools exist to determine oral feeding readiness in preterm infants. Approximately 11.5 percent of pregnancies result in preterm births in the United States, and oral feeding issues affect more than 500,000 newborns each year. Before being discharged from the hospital, each infant must demonstrate mature oral feeding skills in accordance with guidelines set by the American Academy of Pediatrics. Attempting oral feeding before a newborn is ready may result in choking, feeding aversion and poor growth, so accurately determining when these babies are ready to feed could help avoid those complications.

A team of scientists, led by Jill L. Maron, MD, MPH, Associate Professor of Pediatrics at Tufts Medical Center, reports that by combining gene amplification techniques with advanced computational analysis tools they were able to identify and validate salivary biomarkers to predict oral feeding readiness in preterm infants. This biomarker panel is the first to address oral feeding readiness in the newborn.

In the article titled "Computational Gene Expression Modeling Identifies

Salivary Biomarker Analysis that Predicts Oral Feeding Readiness in the Newborn," the scientists describe their two-phase research. In Phase 1, the authors examined the saliva from 12 preterm infants during the learning process of oral feeding to identify potential salivary genes associated with oral feeding success. In Phase 2, they prospectively tested 24 genes identified in Phase 1 on 400 salivary samples from 200 successful and 200 unsuccessful feeders, and analyzed their results to identify genes that could potentially predict oral feeding readiness. The study will appear in The Journal of Pediatrics' February print edition.

They found that the associated genes, alone and in combination, along with sex and postconceptional age, accurately determined oral feeding readiness in 78 percent of the newborns. Postconceptional age is defined as the sum of the number of weeks of pregnancy at the time of birth and weeks of age since birth. They report that female sex and advancing postconceptional age were positive predictors of an infant's ability to feed orally.

Maron explains, "Our work is the first to explore individual limitations to feeding success at a molecular level." By combining salivary gene expression profiles, postconceptional age and sex, this predictive model not only assessed the probability of feeding success, but also, and most importantly, highlighted specific developmental pathways that were likely contributing to feeding immaturity. In order to successfully orally feed, an infant must integrate their sensory, neurodevelopmental, gastrointestinal, facial developmental and hunger signaling pathways. Failure of one or all of these systems to mature limits feeding success. Identifying which infant has which deficit could allow caregivers to develop individualized treatment modalities based on each infant's salivary gene expression profile to improve quality of care.

The study identified five genes predictive of feeding success representing a range of biological systems: sensory integration (NPHP4,

PLXNA1); hypothalamic regulation, a region of the brain that plays a key role in hunger signaling (NPY2R); facial development (WNT3, a gene associated with lip and palate development); and energy expenditure (AMPK, a regulator of whole body energy balance). The team found that a mature pattern of feeding behavior was predicted when three genes were undetectable in neonatal saliva (NPHP4, NPY2R, and WNT3) and two genes were readily detectable in that same saliva sample (AMPK, PLXNA1).

While the team's work does not explain precise biological mechanisms by which these genes affect feeding behavior, it does show biological plausibility that each gene is related to oral feeding and demonstrated a strong association with a gene's expression profile and feeding status.

Maron says, "There is an enormous amount of relative, biological and developmental information in saliva. This biofluid is easily obtainable and with advances in nanotechnology and downstream analyses, there is much we can learn about preterm newborns with this non-invasive approach. Future multicenter trials must now be conducted to determine applicability of salivary gene analysis to predict feeding readiness in preterm newborns across institutions."

Provided by Tufts Medical Center