
Epigenetic Alterations and Stress among New Mothers and Neonates in the DRC: A Biocultural Investigation of the Intergenerational Effects of War

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It has been known for decades that a mother's health impacts the health of her children. Moreover, it is known that a mother's experiences while she is pregnant (i.e. peri-natal experiences) affect her children's health, both when they are born and throughout their lives. What is unknown is how information about the mother's health is transmitted to the developing fetus and, furthermore, how this information impacts children's health throughout their lives. This project is one of the first to test the possibility that extreme environmental or psychosocial stressors may result in altered health outcomes, possibly in a heritable, multigenerational manner.

With Nikki Rodney (2013 UF anthropology PhD), we are testing if epigenetic changes, which are **inherited** changes in **gene expression** that do not affect the underlying DNA sequence, translate the impact of stress and trauma to mothers into altered health outcomes in newborns. We are working in Goma, in eastern Democratic Republic of Congo, where ongoing civil war and the use of rape as a weapon has created one of the most stressful and traumatic environments for women on the planet. Through extensive ethnographic interviews, Nikki has developed culturally relevant measures of maternal stress. We tested these data against patterns of epigenetic variation detected in DNA samples collected from mothers and their newborns. Cutting-edge DNA sequencing techniques were used to generate the largest epigenetic dataset ever on a unique set of mother-newborn samples.

Our first results from 25 mother-neonate dyads collected in 2010 were published last year (Mulligan et al. *Epigenetics*, 2012, 7:853-857). We showed that increased maternal stress was correlated with increased methylation at the glucocorticoid receptor (*NR3C1*, associated

with birthweight) and decreased birthweight. These results are consistent with the developmental origins of health and disease hypothesis in which events in early life, such as pre-natal maternal stress, may modify offspring biology, in this case via an epigenetic mechanism. We also have a manuscript in review in which we present genome-wide methylation data at over 400,000 sites. These data show that methylation in both mother and newborn is correlated with maternal stress indicating that stress has a more generalized effect that is manifest throughout the entire genome at over 600 genes.

Based on these initial, intriguing results, I was successful in obtaining NSF funding to expand the study. This past summer, Nikki returned to Goma to train a team of collaborators at HEAL Africa to conduct interviews, collect samples and oversee the project over the long-term. This expanded collaboration has resulted in a fabulous, unprecedented set of samples and data to address the long-term, possibly heritable, effects of stress. Our HEAL Africa colleagues are collecting information on

stress exposures as well as information on post-partum depression and anxiety, blood samples from mother, placenta, cord blood and newborn for DNA and RNA analysis, and saliva and hair samples from mother and baby to measure cortisol as a biological indicator of stress and stress reactivity. We have also recently expanded the study to include follow-up samples from the infants at birth, Day 1, Month 1, Month 6 and Year 1. Felicien Maisha, who is director of the HEAL Africa team, recently visited the U.S. for the first time – he hand-carried the samples to UF and also started the process to apply to our graduate program in medical anthropology.

We believe this research will improve our understanding of the link between stress and health and has broad implications for the increasing prevalence of stress-related disorders in the US. Our project takes a broad, interdisciplinary perspective that integrates human genetics, cultural anthropology and sociology, biology and psychology, as well as political realities and public health policy.

Connie J. Mulligan is professor of anthropology, associate director of the UF Genetics Institute, and a Center for African Studies affiliate. Her research is supported by a NSF grant from the Program in Biological Anthropology. The UF team for this project includes Alyson Young and Lance Gravlee (anthropology) and Darlene Kertes (psychology). The HEAL Africa team includes Luc Malemo Kalisya and Justin Paluku Lussy, Felicien Maisha, Georgette Kanate, Bernard Kitumaini, Bisho Malungule, Chantel Meba, and Anne Marie Rutega.

