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International Research Visit Report

Deliverables Related to Learning Outcomes:

Learning Outcome 1)
Interrogate mitochondrial DNA methylation and copy number in dendritic cells at birth and in peripheral blood from home visits conducted as part of the Kingston Allergy Birth Cohort.

In the Baccarelli lab I successfully measured mitochondrial DNA copy number and DNA methylation at the 3 mitochondrial genes we set out to examine; mitochondrial transfer RNA phenylalanine (MTTF), mitochondrially encoded 12S RNA (MTRNR1), and the D-loop structural/regulatory region.

We are now in the analysis and publication-writing stages of the project. We have examined the following research questions:

1. Does prenatal smoking affect mitochondrial copy number, MTTF, MTRNR1 and D-loop methylation in cord blood?
2. Does mode of delivery affect mitochondrial copy number, MTTF, MTRNR1 and D-loop methylation in cord blood?
3. Does maternal allergy affect mitochondrial copy number, MTTF, MTRNR1 and D-loop methylation in cord blood?

Approach:
We ran three consecutive models for each question (**Table 1**):
Model 1. Unadjusted model
Model 2. Model adjusted for gender of child, and median household total income
Model 3. Model adjusted for gender of child, and median household total income, and gestational age

We found that mode of delivery and maternal allergy were not associated with the mitochondrial biomarkers I measured. However, MTTF and D-loop methylation in cord blood were significantly associated with maternal smoking (**Table 1**).

Table 1. Association between prenatal maternal smoking and cord blood mitochondrial biomarkers (smoking=1 is the reference).

	Model 1		Model 2		Model 3	
Outcome	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**
Mitochondrial Copy Number						
	0.12 (-0.59; 0.82)	0.75	0.20 (-0.57; 0.96)	0.61	0.20 (-0.57; 0.96)	0.61
MTTF DNA methylation						
	-1.28 (-2.17; -0.39)	0.006	-1.33 (-2.27; -0.39)	0.007	-1.33 (-2.27; -0.39)	0.007
MTRNR1 DNA methylation						
	-4.46 (-10.52; 1.60)	0.15	-4.96 (-10.84; 0.93)	0.10	-4.96 (-10.84; 0.93)	0.10
D-loop DNA methylation						
	-3.46 (-6.61; -0.32)	0.03	-3.39 (-6.64; -0.15)	0.04	-3.39 (-6.64; -0.15)	0.04

Next steps will include an analysis of whether the mitochondrial biomarkers associated with prenatal smoke exposure persist to age 2, and whether the mitochondrial biomarkers are associated with the development of allergies in children. Thus, learning outcome 1 was successful, and will lead to the submission of a collaborative publication in the coming months.

Learning Outcome 2)
Correlate mitochondrial DNA methylation and copy number in dendritic cells isolated from children's blood collected during home visits to the levels of phthalates and polycyclic aromatic hydrocarbons (PAHs) measured concurrently in the children's bedrooms.

I successfully completed all the hands-on benchwork related to this outcome while I was at Harvard University. The levels of phthalates and PAHs will be provided soon by Dr. Miriam Diamond's laboratory. The samples have been prepared for GC-MS and analysis is ongoing.

As soon as the environmental chemical data becomes available I will merge it with the mitochondrial biomarker data I generated and begin statistical analysis.

How the research visit enhanced my research and academic training:

This research visit enhanced my research training by providing me with specialized skills in mitochondriomics that can only be obtained in a few laboratories in the world. I had the opportunity to work with, Dr. Baccarelli, one of a handful of pioneers working on mitochondrial epigenetics. I also collaborated electronically via skype with Dr. Hyang-Min Byun, a former Post-Doctoral Fellow from the Baccarelli lab who is now at the Institute of Cellular Medicine at Newcastle University, United Kingdom. She is an expert in mitochondrial epigenetics and was the lead author on the first paper relating those biomarkers to human environmental health. I also had the wonderful opportunity to work with Dr. Marco Sánchez-Guerra, and learned from him how to carry out mitochondrial copy number assays.

Dr. Baccarelli's group was an amazing conglomerate of multi-talented people. He mentors students and post-docs in bioinformatics, epidemiology and basic sciences and leads multidisciplinary projects that bring them together in innovative ways. Dr. Baccarelli also took a keen interest in providing opportunities for professional development for his students and post-docs. He actively polls them during lab meetings to discover what soft-skill additional training or opportunities they could benefit from. Dr. Baccarelli also spent more time present in the laboratory than I initially expected a professor at his stage of career to be. While he does travel extensively to give talks and attend conferences, he really works hard to maximize the time he spends in the lab and makes himself to his trainees. I was inspired by the data science capabilities of the Baccarelli and I would like to learn more about epidemiology and R programming for statistics in the future.

This research exchange helped me to identify novel epigenetic biomarkers that correlate with maternal smoking. The work experience I gained at Harvard helped me to secure my current position as a post-doctoral fellow at the University of Toronto. It is estimated that the first publication from my work in the Baccarelli lab will be submitted in early 2016. Having the opportunity to publish highly novel work by relating mitochondrial epigenetics to environmental exposures in the homes of the children of known allergic status will enhance my competitiveness for the next stage of my career, which will be applying for faculty positions. The knowledge and expertise I gained through this international research visit will be formative in helping me develop an independent research program.