Genetic Polymorphisms to Improve Interpretation of Contaminant Exposure and Risk in Inuit – Year #1 Summary

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INTRODUCTION

- Inuit communities are exposed to some of the highest levels of mercury and other contaminants worldwide (1)
- The ability of humans to process such contaminants is reliant upon environmentally responsive genes (2)
- Environmentally responsive genes are polymorphic and thus their activity varies tremendously across individuals and ethnicities (2)
- Genetic variability may affect the susceptibility of individuals or populations to the effects of pollutants in the environment (2)
- Little is known about gene-contaminant interactions amongst Inuit communities

OBJECTIVES

•In collaboration with the Inuvialuit Settlement Region (ISR) and using archived samples from the 2007-2008 International Polar Year Inuit Health Survey (IHS), specific aims were to:

1. characterize polymorphisms in environmental responsive genes
2. Relate polymorphisms with existing data on blood contaminant levels

•long-term objective of our research program is to better understand how Inuit process contaminants so that dietary exposure assessments and linkages to health can be improved

METHODS

•Leverage biospecimens and information from n=288 ISR community members who participated in the 2007-2008 International Polar Year Inuit Health Survey (IHS)

•Select and then genotype single nucleotide polymorphisms (SNPs) in n=360 environmentally responsive genes (e.g., metallothionein, glutathione) at McGill-Genome Quebec Innovation Center using the Sequenom iPlex platform

•Descriptive methods to compare genetic variation of ISR with other ethnicities (via 1000 Genomes Project database)

•ANOVAs and regressions to relate polymorphisms with existing data on blood Hg, Pb, Cd, and Se

RESULTS

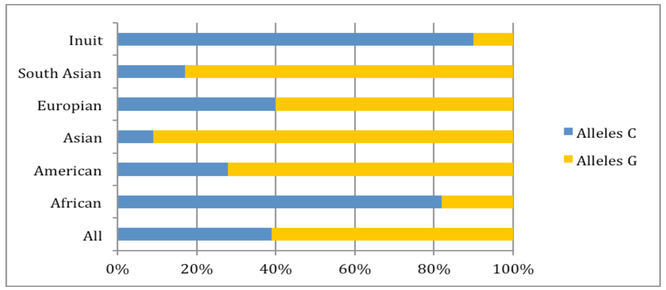
1) Demographic Characteristics of ISR Study Population

Demographic	(n)	mean (SD) or %	range
Age (years)	281	44.73 (16.02)	18.00 to 90.00
Male (%)	281	33.8	
Nutritional			
Body mass index (BMI)	235	30.40 (6.65)	17.3 to 58.3
Hemoglobin (g/L)	234	13.70 (1.51)	7.6 to 17.0
Blood Hg (µg/L)#**	249	4.64 (9.31)	0.05 to 55.00
Blood Cd (µg/L)#**	249	1.31 (1.72)	0.02 to 7.30
Blood Se (Hg) (µg/g)#**	249	304.36 (32.18)	150 to 1300
Blood Pb (µg/L)#**	249	32.18 (33.36)	4.50 to 210.00
Estimated average MeHg intake from fish µg/kg/day	236	4.53 (7.67)	0.01 to 68.23
Estimated average Se intake from fish µg/kg/day	236	10.68 (17.19)	0.02 to 109.82

GM (SD) reported instead due to distribution of the variable.
**Geometric means are reported, but SDs are arithmetic SDs

2) Example of Genetic Variation Across Ethnicities

- 146 SNPs (of 360) successfully studied from 281 participants
- Below is representative data on SNP rs1056836 (CYP1B1)



3) Genetic Polymorphisms and Blood Metals

Category	Gene symbol	SNP	Blood Hg: Main Effect	Blood Hg: Genotype * Ln Fish Hg Intake	Blood Cd: Genotype	Blood Cd: Genotype * Ln packs year
Oxidative Stress	*TXNRD2*	rs1139793				
	TXNRD2	rs5748469				
Selenoprotein	*SEPHS2*	rs1133238				
	SELS	rs7178239				
	GPX3	rs8177412				
Transporter	*ABCB1*	rs1128503				
	ABCC1	rs212090				
	ABCG2	rs2231142				
	ABCB1	rs3842				
Xenobiotic Metabolism	*NAT2*	rs1041983				
	CYP2D6	rs1080985				
	CYP2D6	rs16947				
	AHR	rs2066853				
	PRDX2	rs33942654				
	CYP24A1	rs6022987				
			Legend:		Positive Beta	Negetive Beta
			Not Significant	p>0.05		
			Nominal	p<0.05		
			More Significa	p<0.01		
			Bonferonni Co	p<0.0003		

DISCUSSION

- Many environmentally responsive genes are polymorphic amongst study participants
- Frequency of several polymorphisms are different than in other ethnic groups
- Carriers of certain genetic variants have different levels of blood metals including mercury, cadmium and lead
- These type of results are similar to what is being found in other populations worldwide
- Results such as these are expected to improve interpretation of dietary exposure and biomarker relationships, exposure-disease relationships, and ultimately improved risk assessments and guidance for Inuit communities
- Additional work is underway to: A) conduct more detailed epidemiological analyses; and B) perform a similar study with Inuit from Nunavik who participated in the 2004 Qanuippitaa Survey

REFERENCES

1.Chan, H.M. plus many others. 2012. Inuit Health Survey 2007-2008: Contaminant assessment in the Inuvialuit Settlement Region. Report.

2.Basu, N., Goodrich, J., Head, J. 2014. Ecogenetics of mercury: From genetic polymorphisms and epigenetics to risk assessment and decision-making. Environmental Toxicology and Chemistry. 33: 1248-1258.

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