

# **Dietary and gut microbiome effects on MeHg uptake and elimination rates: a case study of two Malagasy populations**

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Methylmercury (MeHg) is a globally prevalent developmental neurotoxicant associated with impaired cardiovascular health in adults (Karagas et al., 2012; Debes et al., 2016). Among individuals, the same level of external dietary exposure can result in different internal biomarker concentrations reflected by hair, nails, and blood. Understanding toxicokinetic drivers of these differences and variability in MeHg metabolism is important for risk mitigation strategies, such as dietary guidelines. Prior studies show a link between human MeHg metabolism, elimination, and the gut microbiome, which could potentially explain this variability (Caito et al., 2018; Rand et al., 2016).

This study leverages extensive environmental, epidemiological, and nutritional data from the Madagascar Health and Environmental Research (MAHERY) cohorts (Golden et al. 2017; 2019) to examine the relationship among diet, gut microbiome, and MeHg metabolism and elimination. Specifically, we measured biomarkers of mercury exposure in fingernails and feces and sequenced the gut microbiome genome of individuals from an inland rainforest population and a coastal population. These two populations are close in physical proximity (less than 20km apart) but have distinctly different diets (predominantly seafood vs. bushmeat). Total Hg (THg) concentrations in fingernails for 87% of individuals included in coastal populations exceed >400ng/g compared to only 4% of individuals in the rainforest populations. By using dietary intake estimates, toxicokinetic modelling, and paired MeHg, THg, and Hg stable isotope measurements in stool and fingernails together, we examine variability in MeHg metabolism across individuals.