Birth defects are one of the most important childhood healthcare issues and neural tube defects (NTDs) are among the most common (approximately 324,000 births worldwide and over 100,000 pregnancies in the China, annually), lethal/life-threatening and disabling groups of birth defects. These serious conditions include: craniorachischisis (failure of fusion along the entire body axis), anencephaly (failure of fusion in the cranial region) and spina bifida (failure of fusion of the caudal neural tube). NTDs are among the most common, lethal/life-threatening and disabling groups of birth defects. We have investigated the maternal and embryonic exposomes, that is, the internal chemical environment that is possibly relevant to NTD etiology by measuring targeted analytes and biomarkers using biological samples and epidemiological data in an area known for its exceptionally high NTD prevalence (~10/1000 live birth), extremely heavy pollution, and poor nutritional status in Shanxi Province, China. Previous efforts to identify the gene(s) that predispose the embryo to a neural tube closure failure during development have been challenging. Hypothesis-driven candidate gene studies were not successful in identifying common variants that may be predictive for NTD risk. Re-sequencing of a limited number of candidate genes has yielded few genetic variants, although none of these variants alone is a robust predictor of human NTDs. This leads us to postulate that NTDs, like other complex diseases, may arise from combinatorial effects of rare variants. Using next-generation whole genome sequencing technologies we have begun the analyses of a spectrum of gene variants including single nucleotide variations (SNV), insertion/deletion (Indel) and structural variations (SV) that contribute to the expression of NTDs. The results of our studies should help to clarify relationships among maternal exposures, maternal nutrition, immune responses, maternal/embryonic genetics, and NTD risk.

Selected references:

