127 | Histone H3 levels and modifications in association with gestational particulate matter exposure: the ENVIRONAGE cohort study

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Particulate air pollution is an important environmental health issue with adverse health effects, starting as early as in fetal life (during pregnancy). Epigenetic modifications have been suggested to mediate those effects and may increase disease predisposition in later life. To this extent, histone H3 modifications can influence gene expression by altering the chromatin state. Here, for the first time, the potential prenatal effects of exposure to particulate matter with a diameter less than 2.5 μm ($PM_{2.5}$) exposure on global histone H3 levels and H3K4 and H3K36 tri-methylation in cord blood are explored.

In 630 mother-newborn pairs from the ongoing birth cohort ENVIRONAGE, the levels of global histone H3, tri-methylated H3K4, and H3K36 protein were measured in cord blood by means of ELISA. Linear regression models were used to associate the relative H3K4me3, H3K36me3 and total histone H3 levels in cord blood with different $PM_{2.5}$ exposure windows during pregnancy. H3K4me3 and H3K36me3 levels were normalized against total histone H3 protein.

An inverse association was observed between H3K36me3 levels in cord blood and gestational $PM_{2.5}$ exposure, exposure during the last trimester of pregnancy was most significantly associated with H3K36me3 levels. Similar observations were shown with exposure to black carbon and NO_2 during pregnancy.

Our results suggest histone H3 modifications might play a role in the response to $PM_{2.5}$ exposure during pregnancy.

128 | Family-specific genetic associations with metabolic syndrome in linkage regions

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Specific quantitative traits that characterize the metabolic syndrome (MetS) include body weight, waist circumference, systolic and diastolic blood pressure, triglycerides (TG), high-density lipoproteins (HDL), fasting glucose, and fasting insulin. Using the GENetics of NonInsulin-dependent Diabetes mellitus (GENNID) Study as a resource of multiplex families and genetic data, we previously identified four candidate linkage regions containing putative quantitative trait nucleotides (QTNs) that influence MetS quantitative traits. Using the NimbleGen SeqCap EZ Target Enrichment protocol, these regions were then resequenced in a subset of six European American families (78 subjects) that showed high evidence of linkage. To find associated QTNs in regions of linkage, MERLIN software was used to perform family-based association testing while assuming linkage in a two-point analysis. For each candidate region, selected families were analyzed together as well as individually. The simpleM method was used to correct for testing multiple variants. Family-specific variants and variants shared across linked families were found to be associated with particular MetS quantitative traits. A number of these variants were located in genes with plausible biological functions for MetS traits. With recently developed technology and accessibility of DNA testing, personalized medicine can benefit from family-specific analyses, which allow an individual to identify possible at-risk variants and genes within his or her own family. However, family-specific results should be verified with other established population association results and genetic functional annotation databases.

129 | Likelihood-ratio based approach to select X-chromosome inactivation model

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Analyzing X-chromosomal genetic variants is challenging because of the complexity of the X-chromosome inactivation (XCI) process for female X-chromosome loci. To address such complexity, we previously developed a unified statistical test to assess the association between X-chromosomal SNPs and complex diseases of interest, accounting for different biological possibilities of XCI: