Title: Preliminary analysis of epigenetic effects on adults conceived by mothers exposed to dioxin.

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The dioxin exposure impact has been studied to be associated with a series of effects on the developmental process that is correlated with reproductive problems particularly on breastfed infants. The Seveso disaster left many adults in the fertile age range exposed to the dioxin, we aimed to investigate the effect of dioxin to child conceived years later by mother exposed to the dioxin.

Epigenome and exposome interaction is an interesting field of investigation, to understand the underlying mechanism of regulation. This study evaluates the effect of dioxin (TCDD) on the DNA methylation on offspring, due a pregnancy done by a mother exposed to the dioxin years before the conception, some of the cases were breastfed.

We used the Illumina 850K (EPIC) array to measure the genome wide DNA methylation in whole blood obtained from 38 adult men exposed and 17 adult men not exposed. The inferred age calculated with the Hannum markers was used as covariate.

The analysis was conducted using two different techniques the first technique addressed the  
differential methylation level between the two groups (exposed and not exposed); the second technique studied epigenetic drift and investigated genomic areas with extreme outlying values of methylation (Stochastic epigenetic Mutations (SEMs))

Differential methylation analysis was performed both at site and region level, the most important signals arised out from the 100 top ranked genes belonging to interesting biological process for the hypermethylated probes, the outcome pointed out to an impact on the angiotensin-renin pathway (confirmed by the literature).

The SEMs analysis revealed that the burden of SEMs resulted significantly higher in the exposed group for the mutations with hyper methylation.

In conclusion outcomes confirm a variation of the DNA methylation of the exposed samples, the differential analysis and the epi stochastic mutation outcomes pointed to a general increase of the epigenetic drift, sign of an altered epigenome.