Title: Are one in four individuals metabolically disadvantaged from conception? Effects of nc886 imprinting

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Abstract
The nc886 locus is the only known polymorphic imprint in humans whose methylation status (imprinted vs. non-methylated) is not determined by genetics. Maternal age has previously been linked to nc886 methylation status of offspring, which has then been linked to their adulthood health traits.
We investigated the association between pregnancy conditions and offspring's nc886 methylation status and how predicted nc886 RNA levels associate with their health in childhood.

We studied how pre-eclampsia and FASD (foetal alcohol spectrum disorder), associate with nc886 methylation status, and how, when combined with a genetic polymorphism to predict nc886 expression levels, they associate with metabolic traits such as levels of insulin, glucose, lipids, and adiposity of the offspring. We utilized two population cohorts (YFS n=3596, GenerationR n=1349), four freely-available FASD cohorts and two pre-eclampsia cohorts.

Children with an unmethylated nc886 locus were overrepresented in FASD and pre-eclamptic pregnancies (results being statistically significant in 4/6 cohorts.)
Moreover, our results suggest that non-methylation of the nc886 locus is associated with sub-optimal metabolic traits, shown by the upregulation of insulin and cholesterol (total cholesterol in GenerationR, LDL and non-HDL in YFS). In girls, there was an association with adiposity. For all results, $p<0.05$ in linear regression.

Our results show that FASD and pre-eclamptic pregnancies result in more children with non-methylated nc886 locus than control pregnancies (Figure1). Children with elevated nc886 RNA levels portray worse metabolic profiles. As the regulators of nc886 expression are stable through life, they might be linking pregnancy complications to later life heath of offspring.

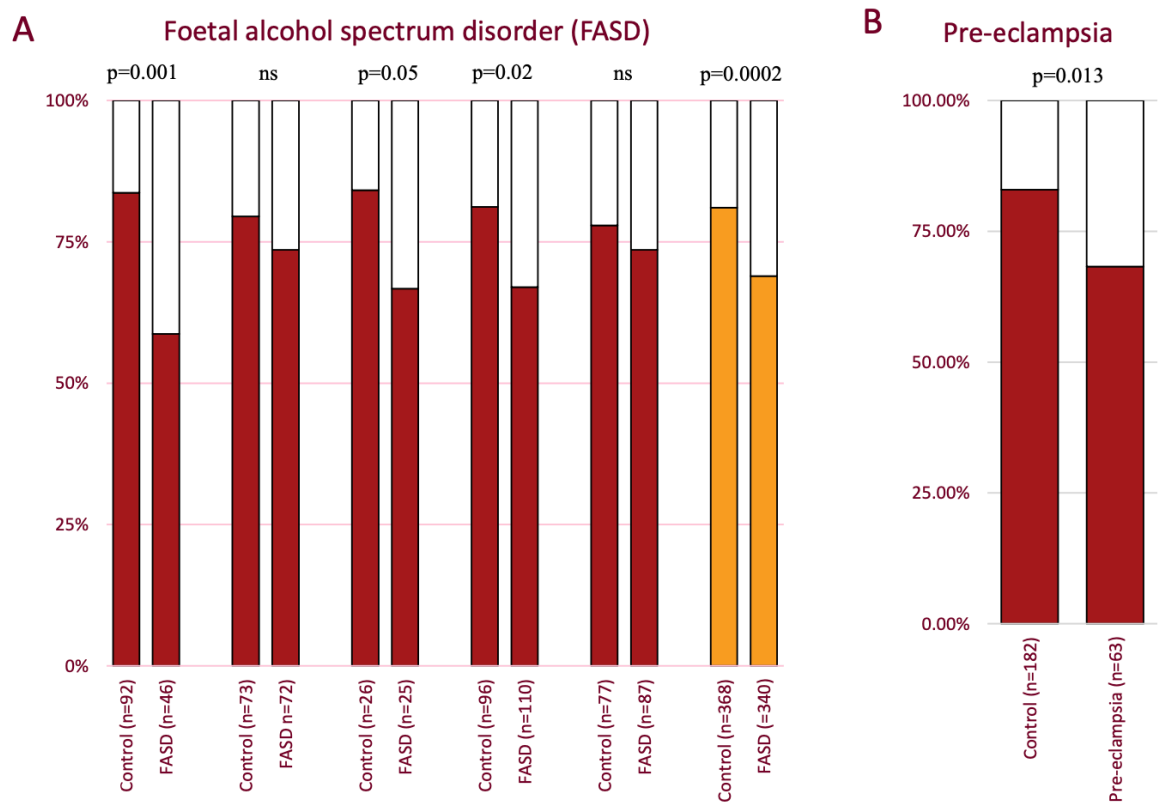

Figure 1 Children with an unmethylated nc886 locus are overrepresented in FASD (A) and pre-eclamptic (B) pregnancies