Environmental chemicals alter expression of epigenetic factors in the Zebrafish Liver cell Line (ZF-L)

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Background and Aim
Epigenetic mechanisms are responsible for proper spatio-temporal regulation of gene expression in organisms. Chemicals can induce epigenetic changes which may cause disease development, e.g. carcinogenesis, as well as support the transfer of adverse health effects over generations. In this pilot study, we exposed ZF-L cells to selected chemicals and measured gene expression of epigenetic actors. It aimed at providing with preliminary data to 1. address the sensitivity of ZF-L cells to epigenetic disruption and 2. investigate mitotic stability of the observed changes in daughter cells without additional exposure.

Chemical | characteristic
---|---
Vinclozolin | Pesticide
Methoxychlor | Pesticide
Bisphenol A | Plastic monomer
Perfluorooctane sulfonate | Fluorinated surfactant
Perfluorobutane sulfonate | Fluorinated surfactant

Gene | Function
---|---
dnmt1 | DNA methylation
dnmt3ab | DNA methylation
dnmt3ba | DNA methylation
dnmt3aa | DNA methylation
hdac1 | Histone deacetylation
hdac3 | Histone deacetylation
kdm5ba | Histone demethylation
spt6 | Chromatin remodeling factor

Results

Specific effect of vinclozolin on histone demethylation and large-scale effect of methoxychlor.

Specific effect of PFOS on histone demethylation and large-scale effect of PFBS

Bisphenol A impacts DNA methylation and histone deacetylation pathways.

Concluding remarks and outlook
1. Three chemicals selectively impaired the histone deacetylation pathway and 2 chemicals the histone demethylation pathway which suggest that the observed effects are specific.
2. However, tests at lower concentrations must be conducted in order to confirm the absence of aspecific effects related to activation of cell death mechanisms.
3. Are these effects remaining in unexposed daughter cells after several passages?
4. Is there a direct relation to changes in the epigenome, e.g. DNA methylation and histone modifications?

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