Early-life exposure to endocrine disrupting chemicals affects the development of asthma or overweight in the offspring: role of epigenetic alterations

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Environmental chemicals have been shown to play a crucial role in the development of various diseases like allergies, overweight/obesity or behaviour disorders. In particular, synthetic chemicals interfering with the endocrine system (endocrine disrupting chemicals, EDC) and an exposure during pregnancy and the early postnatal period appear critical for the developmental programming of the immune system thereby altering the disease risk in later life. An exposure to EDCs is ubiquitous since these chemicals are added to many consumer products as e.g. plasticizers (phthalates) or preservatives (parabens) that can enter the body via food and water intake, skin absorption, and inhalation. Epidemiological findings from a prospective birth cohort study showed an association between maternal urinary concentrations of mono-nbutyl phthalate (BBP) and an increased asthma risk in children. Using a murine transgenerational asthma model, we could demonstrate a direct effect of BBP on asthma severity in the offspring with a persistently increased airway inflammation up to the F2 generation. This asthma-promoting effect was mediated by a BBP-induced DNA hypermethylation, and a subsequently reduced expression of genes involved in the differentiation of allergy-relevant T helper 2 cells like the GATA-3 repressor Zfpm1 offering an explanation for the increased allergic immune response. In another study, elevated urinary paraben concentrations in maternal urine did not correlate with an increased asthma risk in the children. However, for butyl paraben (BuP) we observed a positive association to overweight within the first eight years of life with a stronger trend in girls. Consistently, maternal BuP exposure of mice induced a higher food intake and weight gain in the female offspring. The effect was accompanied by an epigenetic modification in the neuronal Pro-opiomelanocortin (POMC) enhancer 1 leading to a reduced hypothalamic POMC expression. Our data demonstrate that chemical exposure of the developing immune or metabolic system leads to an altered epigenetic programming contributing to asthma development or altering weight development in later life.