

## **Dietary and air-borne carcinogens and risk of childhood cancer**

**Jos C, Kleinjans**

Department of Toxicogenomics, Maastricht University, the Netherlands

j.kleinjans@maastrichtuniversity.nl

Prenatal exposure to adverse environmental agents as a consequence of maternal exposure during pregnancy, either through inhalation or via dietary intake, may induce adverse birth outcomes, as well as diseases such as childhood leukemia in later life. Investigating molecular response patterns in umbilical cord blood cells in newborns in association with endogenous exposure analysis may disclose adverse mechanisms of action for the purpose of evaluating disease risks already initiated during the fetal stage.

From the NewGeneris project microarray-based global gene expression results on 111 newborns will be presented; these have been followed up by targeted PCR analysis of approximately 1200 newborns. Furthermore, selected carcinogenic food ingredients were analyzed in these cord blood samples. In addition, from the ENVIRONAGE 142 newborns were similarly assessed for transcriptomic responses in umbilical cord blood cells, in association with estimated maternal PM<sub>2.5</sub> exposure levels during pregnancy.

In short, the NewGeneris project has demonstrated that upon maternal dietary intake foodborne carcinogens are indeed capable of passing the placental barrier. Fetal exposure to such carcinogens may induce gene expression patterns which can be linked to genes expressed in leukemia and lymphoma as reported in the literature. Induction of leukemia-related gene expression in particular in association with exposure to dioxin-like compounds, was shown to be highest in newborn boys, which is in compliance with earlier reported gender specificity with respect to developing leukemia in later childhood.

The ENVIRONAGE project confirmed gender-specific differences in umbilical blood cell transcriptomics patterns in association with estimated traffic-related air pollution exposure of the mothers during pregnancy. In neonatal boys, maternal PM<sub>2.5</sub> exposure during pregnancy appeared associated with gene expression patterns indicative for molecular mechanisms related to neurodevelopment. In particular, in relation to maternal PM<sub>2.5</sub> exposure during of the last month of pregnancy among newborn boys, transcriptomic pathways related to synaptic transmission and mitochondrial function were observed.

From these results it is obvious that the placenta does not effectively protect the fetus against toxic risks imposed by adverse environmental agents. Maternal inhalatory and oral intake of carcinogenic chemicals appears to induce molecular mechanisms in the fetus which may cause disease in later childhood. Most interestingly, gender-specific response patterns have been demonstrated.

References

- Kleinjans J, Botsivali M, Kogevinas M, Merlo DF; NewGeneris consortium (2015). Fetal exposure to dietary carcinogens and risk of childhood cancer: what the NewGeneris project tells us. *BMJ*. 351:h4501
- Winckelmans E, Vrijens K, Tsamou M, Janssen BG, Saenen ND, Roels HA, Kleinjans J, Lefebvre W, Vanpoucke C, de Kok TM, Nawrot TS (2017). Newborn sex-specific transcriptome signatures and gestational exposure to fine particles: findings from the ENVIRONAGE birth cohort. *Environ Health*. 16:52