

## ABSTRACT

The „omics“ is a concept of biological disciplines that globally characterizes and quantifies biomolecules involved in the key functions of an organism. The „omics“ methods are used e.g. in molecular epidemiology, where they help to evaluate potential biomarkers that identify the impact of environmental factors for human health. In this thesis, the „omics“ methods were applied in samples collected from newborns born in localities of the Czech Republic mostly differing by pollution levels from industrial sources. The principal aim was to determine whether environmental changes during prenatal development can affect gene expression and its regulation in newborns. The thesis further aimed to evaluate the level of air pollution at the time of biological samples collection. Using the whole genome approach, differentially expressed genes (DEGs) in newborns from districts Karvina and Ceske Budejovice (CB) were identified. In a pilot study of a small group of newborns from districts Most and CB, differentially methylated CpG sites in DNA were assessed. These sites attenuate gene activity and could be responsible for long-term changes at the genetic level. Finally, the aim was to find differentially expressed small non-coding RNA (DE miRNA) in newborns from Most and CB.

Samples of umbilical cord blood from 230 newborns were obtained after delivery and further processed in the Institute of Experimental Medicine Czech Academy of Sciences. “Omics” methods were used to analyze whole genome gene expression and genome-wide gene-specific DNA methylation on a microarray platform (iScan, Illumina); miRNA expression was evaluated using next generation sequencing (MiSeq, Illumina). Statistical processing of gene expression, methylation and sequencing data was performed in RStudio using own scripting and Bioconductor packages.

The highest concentrations of particulate matter of aerodynamic diameter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) and benzo[a]pyrene (B[a]P) were observed in Karvina, especially in the winter season. In all study seasons, the annual air pollution limits of the pollutants were exceeded in this locality. In contrast, no differences in air pollution levels were observed between Most and CB. The highest number of DEGs was identified in samples from Karvina in the winter season, while the effect of season played a key role in both localities. The DEGs identified in Karvina samples are mostly involved in the cellular defense against oxidative and electrophilic stress and the immune response. The DEGs participating in T- and B-cell receptor pathways were found for a comparison between both seasons in Karvina. A different profile at the epigenetic level was also observed for a comparison between newborns from Most and CB. Here, the CpG sites targeting genes and processes that are involved mainly in T-cell pathways, immune response, as well as asthma and allergies were found. The most significant DE miRNA detected in these samples may regulate the activity of genes that are associated with chronic obstructive pulmonary disease, or some atopic and autoimmune diseases (eczema, psoriasis).

This work demonstrates that a different gene expression profile and epigenetic pattern of DNA methylation and miRNA expression can be observed in newborns at delivery. The results suggest that the beginning of life in a different environment, regardless of the current level of air pollution, may be associated with alterations in the immune system, increased susceptibility to allergies, asthma and dysfunction of biochemical processes affecting the healthy development of the individual. The level of expression of different genes can be also modulated by a birth season, provided that the difference between the seasons is associated with different levels of air pollution.