

Allergic diseases have reached epidemic scale affecting nearly 30% of the world's population and they are still on rise. Despite scientific efforts and progress in diagnosis and treatment of allergies, we are still lacking of effective ways of their prevention. It has been proposed that allergy increases as countries become more 'western', urban, and 'cleaner'. Recently new key links between environmental exposures, epigenetic modifications and allergy occurrence have been proposed. Epigenetic changes are modifications to DNA that affect changes in gene expression (but do not cause permanent changes in nucleotide sequence). It is postulated that epigenetic patterns may be potential markers of atopy, help diagnose it, and provide therapeutic targets and targets for disease prevention strategies.

Ten years ago we took advantage of the 'natural experiment' afforded by the rapid changes in Polish village life after accession to EU in 2004. Due to economic and social transformation, the Polish villages have significantly changed their character. We examined whether, in the course of a single generation, the loss of typical farm exposures (farm animals, consumption of unpasteurized milk etc.) influenced the protection against atopy and allergies in the previously surveyed population at all ages. We showed a steep increase over a period of just one decade in the prevalence of atopy among villagers. Interestingly, the increase was evident at all ages and eliminated distinct contrast between villagers and townspeople that was evident in 2003. On the other hand, there was little change in the prevalence of asthma symptoms, or diagnosed asthma. Our findings indicate that the atopic state is more plastic than many believed and that the importance of early-life exposures may have been overstated.

Now, after two decades from the original survey, we aim to test if the prevalence of atopy and asthma has changed or is stable in our population. We would also like to investigate the connection between atopy, environmental changes (the loss of the 'farm effect') and epigenetic modifications, precisely DNA methylations.

At first, we will conduct, for the third time, cross-sectional epidemiological study of the current inhabitants of a part of small town Sobótka and seven nearby villages previously surveyed in 2003 and 2013 year (total of about 1700 participants). We will evaluate the prevalence of atopy, allergic rhinitis and asthma in village and town population in different age groups and in the respect to environmental exposures using exactly the same methodology as previously (questionnaires, skin prick tests, blood sampling, nasal swabs). Then we will undertake testing of DNA methylations of the whole blood. We will focus on atopy as the main outcome, as it is objectively measurable. Moreover, in our previous survey, we observed a steep increase of atopy in rural population at all ages due to environmental changes. In an epigenetic study, we plan to incorporate stepwise approach with Human Methyloome Panel to identify CpGs throughout the whole epigenome significantly associated with atopy in limited number of individuals as a first step, followed by a replication of candidate CpGs in larger cohort. Subsequently, we will analyze the associations to farm exposure (and its loss) in at least two points in time in the blood of individuals who took part in the first and repeated surveys (DNA from the first survey (2003) and from second (2013) and/or third survey). This approach will allow us to study the link between atopy, farm exposures and DNA methylations in adult cohort and would be, according to our knowledge, the first study of its kind in the world.

We believe that our project will help disentangle the puzzle of the role of epigenome patterns on the development of atopy and allergic diseases and their correlation with the protective environmental exposure (such as farm living). We also hope to find the answer to the question about the potential role of DNA methylations as a predictive biomarker of atopy and allergy.