

Study describes effects of prenatal environmental stressors on regulation of microRNAs

October 7 2013, by Daniela Weber



In addition to nicotine, there are some 4800 other chemicals found in cigarette smoke, many of which are harmful to health. Credit: Kristin Junge/ UFZ

The Leipzig Helmholtz Center for Environmental Research has gained new insights on the influence of tobacco smoke in utero. For the first time, it could be demonstrated with smoking pregnant women and their children, how exposure to tobacco smoke affects the development of human immune system on molecular level. The focus thereby was on

microRNA – a short, single-stranded RNA molecule that is now recognised as playing an important role in gene regulation.

For some time now, the impact of environmental stressors during pregnancy on allergy risk among new-born [children](#) is a main research topic at Leipzig Helmholtz Center for Environmental Research (UFZ). As part of the long-term study LINA, environmental immunologists from Leipzig have been focussing on tobacco smoke as an environmental stressor. The main objective for Dr Gunda Herberth was to reveal the influence of tobacco smoke on the development of children's immune systems – at molecular level. From the results that were recently published in the *Journal of Allergy and Clinical Immunology*, one thing is certain: "For the first time we were able to describe the effect of prenatal environmental stressors on the regulation of microRNA."

Former studies have already proven that smoking during pregnancy can harm the unborn child: Newborns from smoking mothers have shown low birth weights and impaired lung functions; later on in life respiratory diseases, diabetes type II, asthma or cardiovascular diseases were also more common. However, the exact molecular mechanisms and processes that are behind such developments still struggle researchers.

For this reason, Dr. Gunda Herberth and Dr. Irina Lehmann from the UFZ decided to address the relatively recent research area of microRNA. From the early 1990's these cell components started to become more and more of a focus in molecular and cell biology. In the meantime, for humans more than 1,200 different short, single-stranded RNA molecules have been named, some of them playing an important role in immune response. Among others, they have a considerable influence on the differentiation of regulatory T cells (Treg cells), which in turn prevent an overactive immune system and thus autoimmune diseases. If there are insufficient Treg cells or if their function is

impaired, the self-regulatory function of the immune system will be reduced, possibly resulting in allergies.



It is well-known that smoking can harm the unborn child. UFZ scientists have now discovered which molecular mechanisms are behind it. Credit: zven0/fotosearch

To investigate the relationship between smoking mothers during pregnancy on the one hand and their children's risk of developing allergies on the other, the scientists from Leipzig examined microRNA-223, microRNA-155 and regulatory T cells – not only in the blood samples of [pregnant women](#) (36 weeks pregnant) but also at birth in the cord blood of their babies. At the same time, questionnaires were filled out and urine samples of the pregnant women were tested to

substantiate the effect from exposure to tobacco smoke and/or from volatile organic compounds resulting from smoking. From the pool of mothers participating in the LINA-study, 315 mothers (6.6 percent of whom were smokers) and 441 children were consulted in these investigations.

The focus was on miR-223 and miR-155, because their role in regulating T cells had already been proven. "What we are now interested in finding out", explains Dr. Gunda Herberth, "is whether or not these microRNAs link exposure to smoke, regulatory T cells and the risk of developing allergies."

By measuring the concentration of these microRNAs as well as the number of regulatory T cells in maternal and cord blood it could be shown that a high exposure to inhaled [volatile organic compounds](#) (VOCs) associated with tobacco smoke coincides with high values for miR-223. At the same time it was also found that increased values for maternal and umbilical cord blood miR-223 correlate with low regulatory T-cell numbers. Finally, it could be shown that low regulatory T-cell numbers in umbilical cord blood was an indication that children exposed to [tobacco smoke](#) were more likely to develop an allergy before the age of three compared to those children with normal values for miR-223 and Treg cells. Furthermore, the probability of developing eczema was almost twice as high for these children.

"After already being able to demonstrate the influence of prenatal smoking on regulatory T-cell numbers in cord blood from our LINA study, the current epidemiological investigation delves even deeper into molecular processes", Dr. Gunda Herberth and Dr. Irina Lehmann resume. "Now", the immunologists from Leipzig explicate, "we will know more about the molecular processes that trigger off stressors from smoke during pregnancy." Thus, for the first time the association between prenatal environmental stressors and the regulation of

microRNA is described. In this respect, the current Helmholtz study opens the door to further research on the role of microRNA in terms of how the human [immune system](#) reacts to [environmental stressors](#).

More information: Herberth, G. et al. Maternal and cord blood miR-223 expression associates with prenatal tobacco smoke exposure and low regulatory T-cell numbers, *Journal of Allergy and Clinical Immunology*, 2013 Aug 23. doi:pii: S0091-6749(13)01052-X. 10.1016/j.jaci.2013.06.036

Provided by Helmholtz Association of German Research Centres

Citation: Study describes effects of prenatal environmental stressors on regulation of microRNAs (2013, October 7) retrieved 25 April 2024 from <https://medicalxpress.com/news/2013-10-effects-prenatal-environmental-stressors-micromnas.html>

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