## Reg. No: 2021/41/B/NZ4/04424; Principal Investigator: dr hab. Michał Marek Godlewski

It is several decades since the concept of nanotechnology, or the use of matter of nanometre size, emerged in the World. Although initially, the development of this field was not impressive due to technological constraints, it is now flourishing. We often do not even realise that we come into contact with nanomaterials in everyday life. As defined by the European Union, nanomaterials are materials that in at least one of their three dimensions are between 1 and 100 nm. The most common nanomaterials are nanoparticles, which are limited in size in the three dimensions. They have found applications in industries such as the food industry as a food additive and in food packaging, in the cosmetics industry in numerous body care products, toothpaste, and sunscreens. The clothing industry has also found applications for nanoparticles in the form of pigments or pigment stabilisers. In addition, they are used in many components in electronics and agriculture in pesticides. Medicine, however, remains the most critical area of application for nanoparticles. Currently, nanoparticles are used in dental components. However, research is also being conducted into their use as drug carriers for the early detection and treatment of cancer or in supplementation in the case of deficiencies of various micronutrients in the body. Over the years, the number of products containing nanoparticles has increased dramatically. As we reduce an object with known properties to smaller and smaller size, at some point, its physicochemical properties change significantly, which is the reason why nanoparticles have been so widely implemented. Early in the history of nanoparticle research, nanoparticles were often compared to their macro-scale counterparts, which led to incorrect assumptions about many of their properties and a postponed the relevant toxicological studies. In addition, the novelty of nanoparticles has delayed the introduction of legislation. New ways of modifying and producing nanoparticles are expanding their possibilities as well as the risks associated with them. There is now a significant accumulation of nanoparticles in the environment, resulting in increased exposure to them, both in animals and in humans. It has been proven that nanoparticles can enter the body through the digestive system with food, through inhalation and are able to penetrate the skin. When they enter the bloodstream, they reach the main organs, including the liver, kidneys, spleen, pancreas and brain. Furthermore, nanoparticles have been shown to be able to cross the placental barrier, thereby potentially compromising embryonic and foetal development. Currently, the effects of nanoparticles on embryonic development only have been studied in very sensitive models such as fish, which are difficult to relate to humans. As a result, we still have a very limited knowledge on the toxicology of nanoparticles and the safety of their use, and it is essential to undertake further research in this area to find answers to current research questions.

This project aims to verify the hypothesis that selected nanoparticles (ZnO, ZrO<sub>2</sub>, Y<sub>2</sub>O<sub>3</sub>, HfO<sub>2</sub>) in doses not exceeding the doses generally considered as typical environmental impact, will not significantly impair the development of the key organs at the embryonic stage. For research purposes, we will use chicken embryos, a model commonly used in toxicology and with results transferable to humans. In the first stage of the project, dose-dependent toxicity will be evaluated, and the impact of the site of exposure on the nanoparticle distribution in embryonic tissues. This data will be used in all subsequent stages. The second stage of the project will investigate impact of single dose of nanoparticles (model of acute exposure) on embryonic development and formation of key organs. In a final stage, the effects of cumulative nanoparticle exposure (chronic model, of 4 consecutive daily expositions) on embryonic development will be studied. On all stages of the project we will assess morphological, pathological and genetical changes in the embryo and embryonic tissues. Resulting data will serve to fill knowledge gaps in the toxicology of nanoparticles and their potential embryotoxicity. This will help define more accurate standards in the future to improve public safety.