The impact of micro-nanoplastics on female reproduction

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In recent decades, industrial activities have led to a dramatic increase in the global production of plastic, with millions of tons produced every year. Under the action of various physical, chemical, or biological agents, plastic waste breaks down into nano and microplastic particles (NMPs) that spread in the environment, posing a threat to human health. Once absorbed, NMPs migrate from the digestive tract to circulatory systems, reaching organs and cells, including female gonads. However, knowledge of their effects on mammalian reproductive functions is insufficient to allow for an accurate risk assessment and management of potential risks in animals and humans. The purpose of the study was to investigate whether NMPs have effects on ovarian follicles, examining potential intracellular mitochondrial dysfunctions and alterations in the sirtuin pathway in a model of human granulosa cells.
Human ovarian granulosa cells (KGN cell line) were exposed to NMPs of different sizes (40 nm, 70 nm, 100 nm, and 200 nm) at concentrations ranging from 5 to 1000 μg/ml for 24 hours. Using fluorescent NMPs and observation under confocal laser scanning microscopy, we demonstrated that NMPs are absorbed by granulosa cells at all tested concentrations and doses. Exposure to NMPs was associated with a significant decrease in cell viability, regardless of the sizes and concentrations used. Real-time analysis of oxygen consumption in response to mitochondrial inhibitors (MitoStress kit, Seahorse Xfe96, Agilent) revealed altered bioenergetic profiles in cells exposed to NMPs. Then, we assessed the gene and protein expression of key antioxidant enzymes using real-time Taqman PCR and Western blotting, respectively. Gene and protein expression of catalase (CAT), superoxide dismutase 1 (SOD1), and superoxide dismutase 2 (SOD2) was increased in cells exposed to NMPs, while the transcript and protein level of sirtuins (SIRT1 and SIRT3) was decreased. Reduced levels of phosphorylated NRF2, the substrate of SIRT1 that acts as a transcription factor that activates gene expression mediated by antioxidant response elements (ARE), were observed.
In this study, we have shown that NMPs enter human granulosa cells and influence their vitality, altering mitochondrial bioenergetics and sirtuin mediated antioxidant response. Our results contribute to understanding the effects of NMPs on mammalian fertility in order to find possible protective approaches. Considering that the susceptibility level of mammalian granulosa cells to NMPs is still unknown, the current results will improve knowledge on the subject and enable living and working in a healthier environment.