Our plastic world – what does it mean for our health?

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Plastic is an inevitable material used in different areas of everyday life due to its stability and long lifespan. However, many products are designed for single-use and eventually end up in the environment, polluting even the most remote parts of the world. In the oceans, this causes the formation of enormous islands that consist mainly of plastic waste, which are experiencing steady growth due to the accumulation of garbage. One of these islands, the Great Pacific Garbage Patch, covers an area as large as Mongolia, with 94 per cent of the 1.8 trillion pieces floating around being microplastics (Lebreton *et al.*, 2018).

Microplastics (particles smaller than 500 µm) are capable of being transported over vast distances and can be detected even in Antarctic snow (Aves *et al.*, 2022), affecting various species around the world, such as fish and birds, as well as humans (Clark *et al.*, 2023; Yee *et al.*, 2021). Humans are exposed to micro- and nanoplastics (particles *smaller* than 100 nm) through inhalation, e.g. tyre abrasion and textile fibres in the air, through dermal contact, e.g. through cosmetic products and in particular by ingestion of food contaminated with plastic, e.g. water, salt and fish (Yee *et al.*, 2021). Only around 10 per cent of plastic worldwide can be recycled (Quartinello *et al.*, 2021), as many of the conventional plastic materials are designed to be durable and are not susceptible to easy degradation (Rüthi *et al.*, 2023).

Therefore, it is not surprising that these particles also accumulate in the human body and have already been detected in human blood and placenta (Leslie *et al.*, 2022; Zhu *et al.*, 2023). All of these findings highlight the consequences that plastic pollution can have on our environment and our health, emphasising the importance of evaluating the health risks they pose to us and to future generations.

Can our immune system fight plastic?

Macrophages were described as professional 'eaters', so-called phagocytes, already in the nineteenth century (Mass, 2018). Therefore, it is conceivable that macrophages may be the prime targets for plastic particles that pass our body barriers. Macrophages are already generated during the first days/weeks of development and differentiate into various tissue-specific cells during organogenesis. In many organs, these cells persist throughout adulthood and proliferate within the tissues. Many of the important functions of macrophages can already be performed in the early stages of maturation, including various forms of phagocytosis (Mass *et al.*, 2023). This is particularly important to protect against pathogens and other contaminants that enter the body.

Macrophages have a protective immune function and contribute to homeostasis and inflammation (Ginhoux and Guilliams, 2016). Particularly in organs that act as interfaces to external molecules, such as the lungs, skin and intestine, macrophages are crucial in distinguishing hazardous from harmless substances to trigger immune tolerance or immune reactions. The resident macrophages in the liver, known as Kupffer cells, besides their sensory function, also play an active role in iron and cholesterol metabolism as well as erythrocyte decomposition (Mass *et al.*, 2023). In the brain, microglia, the macrophages of the parenchyma, contribute to the structure and maturation of the brain, especially in the early stages of development. Among other processes, they orchestrate the development of neurons and synapses and contribute to the plasticity of the brain throughout adulthood (Colonna and Butovsky, 2017).

Conversely, besides their role in homeostatic processes, macrophages also contribute to various diseases, especially due to their potential to recruit further immune cells, including monocytes. In inflammatory bowel disease in the gastrointestinal tract, dysfunctional intestinal macrophages can lead to further disease progression. In the liver, oxidative stress and lipotoxic cues can lead to loss of the Kupffer cell niche, resulting in liver cirrhosis. In the brain, mutations of microglia genes can cause the development of Alzheimer's disease (Park *et al.*, 2022). Moreover, tissue-resident macrophages were shown to promote autoimmunity and cancer in their respective tissue and niches (Li and Chen, 2021).

Because of their longevity, effects on other cell types, and role in disease, macrophages are prime candidates for understanding and investigating the consequences of environmental perturbations to human health.

Where in the body does plastic end up?

In the project NanoGlia, we investigate the influence of micro- and nanoplastic particles on different organ systems of the body with a focus on macrophages, especially the brain resident microglia. Previous studies in mice have shown that plastic particles, depending on size and charge, can be found in almost every organ. Recent investigations have shown that micro- and nanoplastic particles can interfere with the intestine's barrier function by disrupting tight-junction proteins that regulate the permeability of the intestinal membrane. Thus, it is hypothesised that digested particles can be absorbed through the intestine into the bloodstream and transported to various organs (Xu *et al.*, 2021). Other results from mammals and invertebrates indicate that micro- and nanoplastic particles can interfere with lipid metabolism (Yang *et al.*, 2020) and lower the regulation of immune cell numbers (Xu *et al.*, 2021).

In addition, micro- and nanoplastic particles were shown to cross biological barriers such as the blood-brain barrier, causing inflammatory responses in the brain, damage to neurons (Shan *et al.*, 2022), and even lead to locomotor impairment in fish (Chen *et al.*, 2017). Additional studies reveal that micro- and nanoplastic particles affect future generations, as maternal exposure can trigger neurodevelopmental abnormalities in the brain in progeny (Jeong *et al.*, 2022).

Using mice as experimental animals, NanoGlia will help evaluate the short-term and long-term effects of micro- and nanoplastic particles on human health and behaviour in a comprehensive and systemic approach.

Similarities in the placental structure of humans and guinea pigs enable us to explore the effect of maternal micro- and nanoplastic exposure during pregnancy on future generations and their brain development.

Summary

NanoGlia will provide the foundation to understand the damaging implications of plastic pollution on humans and their health and to uncover potential consequences for us and future generations during development.

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NanoGlia nanoplastics meet microglia

PROJECT SUMMARY

The interdisciplinary ERC Starting Grant project "Understanding the impact of nanoplastics on the development of neurological disorders (NanoGlia)" studies how plastic particles activate immune cells in the developing and ageing brain, thereby causing neurodevelopmental and neurodegenerational disorders.

PROJECT PARTNERS

The NanoGlia project is based at the LIMES Institute of the University of Bonn, taking advantage of the inter-departmental collaboration in biomedical research ranging from immunology to developmental biology to biochemistry. Collaboration partners include groups from the USA, Belgium, France and the UK.

PROJECT LEAD PROFILE

Elvira Mass, born in 1986 in Semipalatinsk (Kazakhstan), received her PhD in Molecular Biomedicine at the University of Bonn in 2013, and worked as a postdoc in Germany, the UK and the USA. She received an ERC Starting Grant in 2019 to investigate whether nanoplastics can activate the immune system. Since 2022, she has been a full professor at the University of Bonn.

PROJECT CONTACTS

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erc European Research Council

FUNDING

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under grant agreement No. 851257.

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