Project Details	
Project Code	MRC23IIARBr Weavers
Title	Does microplastic exposure cause immune dysfunction and impact our health?
Research Theme	Infection, Immunity, Antimicrobial Resistance and Repair
Summary	Humans are estimated to consume millions of microplastics (MPs) each year, but exactly how MPs impact our health is alarmingly unclear. In this project, we will identify the molecular consequences of MP uptake on cells and tissues, and explore whether prolonged MP exposure even weakens immunity. We will integrate in vivo animal models with in vitro analyses of human cells and state-of-the-art imaging, and engage with chemists to test novel bioplastic alternatives.
Description	Background Microplastics (MPs) – microscopic plastic particles smaller than 5mm – are increasingly prevalent in our environment and are now recognised as a growing threat to human and marine health. Recent studies have suggested that humans consume over 10,000 MPs a year, predominantly through ingestion and airborne routes. Strikingly, MPs have been found in a huge variety of human and animal tissues, suggesting that once consumed, they disseminate widely throughout the body. However, the exact impact of MP exposure on our cells, tissues and overall health remains immensely under-explored. In vitro studies are beginning to reveal that MPs can readily enter many human cell types (particularly the cells that make up our immune system) and can even cross the blood brain barrier and the placenta. Initial studies have suggested that MPs have the potential to trigger extensive cellular damage, with genotoxicity, mitochondrial defects and even cell death. However, it remains unclear exactly how our cells interact with MPs and what the downstream effects of MP uptake are on tissue function as well as long-term health. There is a clear need for cutting-edge research to investigate the effects of MP exposure at multiple scales – from the biochemical effects at the cellular level through to their effect on whole tissues and host longevity. Proposed Plan of Research This is an inter-disciplinary project integrating in vivo animal models with in vitro studies of mammalian (including human) cells, along-side synthetic chemistry. It builds on exciting data from the lab showing that MPs accumulate within specific cell types and cause substantial tissue damage, which negatively impacts on animal health. Our data suggests that MPs preferentially accumulate within immune cells (e.g. macrophages), which are highly specialised for clearing foreign invaders (such as pathogens). We are particularly eager to explore how MPs interact with cells of the immune system and whether excessive MP uptake causes immune suppression (including problems fighting infection). In fact, there is some evidence that suggests MPs even exacerbate antimicrobial resistance. In this project we will investigate: 1. Exactly how MPs disseminate in vivo and what the downstream consequences are to cell and tissue health 2. How cells of the immune system (e.g. macrophages or microglia) interact with MPs at the molecular level 3. Whether the cellular effects of MPs are dependent on polymer composition and if novel sustainable (e.g. bioderived and degradable) polymers can offer a safer alternative? There are extensive opportunities for the student to steer the project, including selection of the specific cell types and MP (or

	bioplastic) materials to be investigated. The student will learn skills in experimental in vivo and in vitro cell biology, as well as quantitative biology and bioinformatics. They will also learn fundamentals of synthetic polymer chemistry and have the opportunity to be trained in polymer synthesis techniques. The in vivo studies will involve state-of-the-art live imaging, genetic manipulation, omics and molecular biology within Drosophila, and be complemented by cutting-edge in vitro assays using mammalian and human cells. By synthesising our own bespoke MPs (including commercial bioderived plastics or novel sugar-based polymers developed at Bath), we will explore exactly how polymer material and particle size influences the downstream biological effects. Ultimately we aim to use our models to test whether newly developed sustainable polymers offer a biologically safer alternative.
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