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HIGHLIGHTS AND EDITORIALS

Urgent action is required to increase sustainability in in vitro modelling

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Climate change and the inherent climate crisis require immediate action. Protests such as Extinction Rebellion [1] and Fridays for Future [2], and events like COP26 [3] attract societies' attention and spread the news of climate change outcomes. The 1.5 °C and 2 °C benchmarks are widely recognized as limits where environments will become uninhabitable if temperatures continue to rise [4]. Outcomes of climate change have been visible since 1980: decreased water availability, increased wild fire risks, and damage from floods and storms arise due to rising temperatures due to greenhouse gas emissions [5]. Waste disposal is one of the areas creating pollution through burning materials that cannot be composted, recycled, or sent to landfill. Unfortunately, the healthcare sector; biomedical research; and, in particular, activities like in vitro modelling, where high volumes of single-use plastics are used, contribute heavily to this [6].

Specific data about the direct carbon footprint of in vitro modelling is remarkably scarce. Searching for "in vitro modelling" and "greenhouse gas emissions", "carbon footprint", or "waste" in Google Scholar and PubMed does not return any relevant results to date. However, some data is available regarding the overall emissions of healthcare; in 2005–2006, the NHS produced over 118,000 tonnes of clinical waste [7]. In 2012, bioscience research facilities worldwide produced a total of 5.5 million tonnes of plastic waste [8]. Furthermore, the waste generated via laboratory consumables has accelerated dramatically in the past 2 years, due to the COVID-19 pandemic and the inherent increase in in vitro testing for infections [9]. As a result, there is an increased focus on the healthcare sector's waste production and handling, and consequently the climate change impact [7, 10]. Rightfully so, 8.5% of US greenhouse gas emissions originated in the healthcare sector in 2018, which equates to about 553 Mt CO_2e [11]. In 2021, 5.9 million tonnes of solid waste was reported to be produced as a result of healthcare; this amount increases yearly [12]. However, the healthcare sector is broad, and it is not clear how much of an impact in vitro modelling has within this. In the absence of quantitative data, one can assume that improvements must be made here, given the notable volumes of single-use plastic currently required for culturing cells, which is disposed of via incineration, the popularity of animal-derived reagents like collagens and sera, and the power required for laminar flow hoods and associated equipment. We advocate researchers, institutes, companies, funders, and regulators in the in vitro modelling space to begin regularly monitoring and auditing their sustainability practices moving forward, so that more relevant carbon footprints can be estimated, with a view to setting targets for improvement.

Sterile materials are crucial in in vitro research, and single-use plastics are preferred for simplicity, with virtually no single-use products available that are made with sustainable or recycled materials. Following use, having been in contact with potentially biohazardous waste, these plastics are usually incinerated at the end-of-life cycle; this is currently the preferred safe disposal method for biohazardous waste [12].

However, incineration produces further emissions which impact on both climate and health. Firstly, these contribute to greenhouse gas emissions worsening the climate crisis. Secondly, emissions induce health impacts such as malnutrition, heat stress, or worsening respiratory illnesses such as asthma. Furthermore, these emissions are toxic, resulting in further health implications for the population manifesting in symptoms such as disruption of hormone signalling, reproductive and developmental defects, immunotoxicity, liver damage, wasting syndrome,

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and cancer [13]. Suppliers may offer take back schemes where appropriate and reuse packaging for other orders; however, these steps are typically solely related to packaging, they do not actually reduce the plastic waste from in vitro use.

Animal-derived reagents are commonly used in in vitro models. Researchers can purchase a small range of sustainable in vitro modelling reagents, for example, product from jellyfish collagen, where the production process produces less emissions compared to the more commonly used bovine serum, as the jellyfish are sourced from an area where they exist in surplus causing harm to the environment [14]. Certain sustainable materials have been tested for in vitro models. Wood-based hydrogels show promising results in drug release studies, and petroleum-based plastics could be replaced with cellulose nanofibers and TiO_2-coated mica microplatelets due to their great strength, durability, and thermal stability [15, 16]. Whilst such sources move towards replacing fossil fuel–based materials, there is so far no mention of producing sterile laboratory equipment for in vitro modelling. Sustainable materials and reagents for sterile use in this field are scarce beyond this. We urge suppliers of scientific consumables to bring more products such as this to market.

Another key driver of carbon emissions in in vitro modelling is the power used in typical laboratories. Whilst CO2 emissions can be decreased in climate-friendly practices, i.e., turning off unused equipment, optimizing freezer temperature and water usage, and using reusable packaging, current recommendations are typically limited to such steps [17]. Washing and autoclaving materials for reuse should be considered where possible; whilst such procedures produce greenhouse gas emissions, the overall carbon footprint is lower and can further be reduced by sourcing green energy to power autoclaves [18].

In the absence of available products to replace current unsustainable single-use plastics, we advocate refinement of our experimental design, as a field. As in all fields, research waste should be reduced by careful experimental design, planning, and refinement of protocols. Researchers in the in vitro modelling space should make better use of publicly available data from existing work, prior to and alongside "wet laboratory" research. Beyond this, the use of relevant efficient technologies can be adopted for endpoint analysis of in vitro models, such as large-scale multiplexing and spatial multiomics in lieu of investigating individual targets and smaller panels [19]. The combination of these approaches can reduce overall emissions by refining research questions firstly based on publicly available data, then offering more efficient characterization following culture, ultimately reducing waste. Such measures will not only improve sustainability, but additionally decrease expenses, because less material will need to be purchased, and less material will need to be incinerated, which is typically costed per kilogram of waste [20].

In summary, decreasing carbon emissions and plastic waste in in vitro models is urgently required, not only to reduce the negative impact that our field has on the climate, but also ultimately on the health of the population.

Actions taken can include purchasing reusable products, disposing of waste correctly, conducting sustainability audits from platforms such as LEAF, and subsequently improving practices based on optimizing electricity or water usage [21], lobbying companies for the development of sustainable alternative materials, and improving research design including multiplexing and use of publicly available data.

Data availability Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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