FLEXiGUT: Towards a comprehensive understanding of the life-course impact of dietary and environmental exposure on chronic low-grade gut inflammation

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INTRODUCTION

Exposure to dietary and environmental contaminants, such as toxins, man-made chemicals and air pollution, is suspected to disturb gut homeostasis and have a negative impact on human health. Several studies have moreover associated microbiome alterations with common chronic human diseases, such as obesity, diabetes, and colorectal cancer. Gut microbes may either contribute to or benefit from the development of diseases and deciphering whether these associations are in fact cause or consequence is not straightforward. Interestingly, the Bacteroides2 enterotype has recently been linked to gut inflammation as well as to systemic inflammation, revealing the existence of a gut microbiome-inflammatory axis. The gut microbiota appears to play a central role in inflammation owing to its ability to release inflammatory products, which may contribute to biological processes that negatively affect our health, increase the risk of chronic diseases and/or accelerate biological ageing. FLEXiGUT is the first large-scale exposomic study focused on chronic low-grade gut inflammation.

METHODOLOGY

The FLEXiGUT project aims to characterise human dietary and environmental exposure throughout their lifespan to assess and validate its impact on chronic low-grade gut inflammation and related biological processes and diseases. Two Flemish prospective cohorts are used to cover the human life course: the 'ENVIRONAGE birth cohort', a mother-child cohort which provides follow-up from gestation to the age of 10, and the 'Flemish Gut Flora Project longitudinal cohort', a cohort of adults. Available biological samples include blood, urine, saliva, faeces and pregnancy-related samples (placenta and cord blood). Targeted and untargeted analysis of mycotoxins, legacy and emerging contaminants, markers of air pollution and the metabolome, including objective markers of e.g. food intake, ensure a comprehensive assessment of the exposures. The associated biological responses are investigated by applying -omics techniques, including metagenomics, DNA adductomics and metabolomics, as well as assessment of telomere length and measurement of inflammatory markers.

RESULTS

During 2021 and early 2022, 38 mycotoxin biomarkers and metabolites will be analysed in urine and blood by liquid chromatography-tandem mass spectrometry. The data on mycotoxin biomarkers will be combined with DNA adductomics data to provide a direct reflection of the genotoxin exposure, effects and disease risk. Possible links to gut microbiome disturbances will be investigated through microbiome profiles in faeces, enabling quantification of microbial, gene and pathway abundances, and the assessment of enterotypes. Faecal calprotectin and serum C-reactive protein will be determined to respectively assess gut and systemic inflammation. The impact of the exposures and gut inflammation on markers of accelerated biological ageing will be investigated assessing telomere length by quantitative polymerase chain reaction in blood and placenta. An integrative multi-omics data processing approach will be applied to uncover associations between the exposures and diseases, but also provide insights into the mechanisms by which the exposure might be exerting its effects.

DISCUSSION

The selection of the dietary and environmental contaminants of interest is based on previous evidence relating them to gut homeostasis disturbance. The biomonitoring of contaminants and the gathering of -omics data for the biological samples collected at different time points (n=400 mother-child pairs and n=400 adults), complemented with the metadata on dietary intake, lifestyle, location and clinical data, including information on the use of antibiotics, captures the exposome from prenatal life onwards. The multi -omics concept of FLEXiGUT aligns with the technology-driven paradigm change from reactive towards predictive, preventive and personalised (3P-concept) medical services as the medicine of the future benefiting the patient and healthcare at large. The ultimate goal is to develop evidence-based health prevention and intervention strategies regarding chronic low-grade gut inflammation and related diseases.