TITLE: International networking on in vitro colon models simulating gut (INFOGUT)

(Proposal OC-2023-1-26491) https://www.cost.eu/actions/CA23110/

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Abstract

Scientific literature is shedding light on the centrality of GIT (Gastro-intestinal tract) for human health and wellbeing. Indeed, the physiologic effects of nutrients, bioactives and even toxic compounds (including foodborne pathogens) are mediated by their absorption rate in the intestine and by their interaction with gut microbiota and its host ecosystem. Testing food, feed, supplements or drugs in clinical studies gives rise to ethical issues, and the transferability of animal data across species is often problematic because of differences in physiology, metabolism and chemical susceptibilities. According to a recent survey of European Commission (EURL ECVAM, 2021), complex in vitro models (CIVMs) approaches should be adequate not only for regulatory use-contexts, but also for application in the research field provided that standardized CIVMs are developed, enabling a consensus on their use. A new COST Action would fill the knowledge gap on in vitro colon models providing consensus protocols and robust data sets to improve our knowledge of the events taking place in the intestinal milieu, including the complex interactions between the microbiota and the host. Moreover, innovative educational tools will be suggested to increase knowledge on gut models in young researchers and widen to society to avoid any unhealthy consumer choices coming from misleading messages. Bringing together different experts in Gastroenterology, Microbiology, Physiology, Nutrition, Food Science, Biochemistry, Bioinformatics, Biotechnology etc., the new COST Action could represent an effective strategy for the development of healthy food and for the counteraction of diseases.

This initiative will also promote the development of educational tools for young researchers and raise societal awareness to prevent misleading consumer choices related to gut health. With five working groups focusing on the review of existing models, extension to other gut compartments than the colonic one, diseased conditions, data management, and regulatory/education efforts, INFOGUT is positioned to contribute to the development of healthier food systems and the prevention of related diseases while relying less on animal studies.

Working Groups

WG1 Development of harmonized procedures and *in vitro* gut models

- **Task 1.1.** Review and map of the current *in vitro* models (batch, continuous, multi-assays), with the objective of identifying key parameters that require standardization.
- **Task 1.2.** Apply the standardized parameters (inoculum, fermentation medium and control) across the range of *in vitro* colon models to establish the consistency and repeatability of gut microbiota readouts under standardized conditions.
- **Task 1.3.** Review the available protocols and experimental conditions to propose standardized parameters for *in vitro* animal gut models.
- **Task 1.4.** Prepare a peer review publication on the agreed standardized parameters and their application across the available *in vitro* colon models, highlighting the key benefit of their application.

WG 2 Expansion of current *in vitro* models to include other GIT compartments and host interactions

- **Task 2.1.** Connection to upper GI tract: overview of model systems that regionalize gut microbiota along the digestive tract but also integrate mucosal environment.
- **Task 2.2.** Coupling with host cells: identify *in vitro* gut models that can be coupled to host cells (intestinal, liver, pulmonary, brain cells) or 3D cultures to provide a more accurate representation of host interactions.
- **Task 2.3.** Miniaturization: analyze the potential of miniaturizing to enable high throughput screening of dietary or diseased factors or individual fecal samples.
- **Task 2.4.** *In silico* gut models: discuss the application of in silico models for the exploration of human microbiomes.
- **Task 2.5.** *In vitro/in vivo* correlations (IVIVC) : overview of IVIVC studies pivotal to assess the relevance and predictive capabilities of new *in vitro* gut models.

WG 3 Extension to diseased situations

- **Task 3.1.** Provide an overview on *in vitro* models adapted to reproduce gut microbiota dysbiosis associated to most common digestive pathologies (IBD, IBS, colon cancer…). Discuss the current limitations of these models in comparison to *in vivo* situations.
- **Task 3.2.** Extend the potential of *in vitro* gut models to metabolic and non-communicable diseases (including metabolic syndrome, obesity, diabetes, steatosis hepatis, coeliac disease, etc.). The main objective is to maintain *in vitro* microbiota dysbiosis considered as a typical feature of these pathologies *in vivo*. The associated gut parameters should also be adapted to the specific diseased conditions (pH, transit time, bile acids profiles, nutrient availability...)
- **Task 3.3.** *In vitro* gut models can be used to simulate some facets of enteric infection by studying following pathogen inoculation, survival, virulence gene expression and its bilateral interactions with gut microbiota in both upper and lower tract *in vitro* models.

- **Task 3.4.** *In vitro* models can be used to evaluate the impact of acute or chronic exposure to food pollutants (chemical, microplastics, etc.) on gut microbiota composition and activity but also reversely the ability of gut microbes to metabolize compounds and modify their toxicity
- **Task 3.5.** Pharma therapies and non-antibiotic strategies : evaluate the potential of different restauration strategies (of gut microbiota and metabolic perturbations), such as drugs (under various formulations), but also next generation restoration strategies including prebiotics, probiotics, postbiotics, live biotherapeutic products and fecal microbiota transplantation.

WG 4 Data management

- **Task 4.1**. Create FAIR catalogues for the gut omics data and bioinformatics tools: identify and organize relevant omics data repositories and studies for open gut microbiome data.
- **Task 4.2.** Evaluate *in silico* approaches for gut modelling: gather and benchmark the most used AI/ML and bioinformatics tools for gut analysis
- **Task 4.3.** Develop training materials: design, organize, and implement training material for gut data analysis to be used by WG5

WG 5 Regulatory, education, technology transfer, trainings and dissemination

- **Task 5.1.** Support to translational studies of food/feed, ingredients, supplements, drug therapies
- **Task 5.2.** Educational tools (YRIs, consumers, academics, students)
- **Task 5.3.** Transfer to industries and training to professionals