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### Modeling human-derived in vitro barriers for environmental toxicology

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*In vitro* modeling of cell cultures is widely used in pharmaceutical, medical, food/nutrition and toxicology science. These constructed growth environments support tissue differentiation and mimic tissue-tissue, tissue-liquid, and tissue-air interfaces in a variety of conditions. In toxicology, human-derived in vitro culture models are attracting increasing interest because of the numerous benefits; (1) decreasing the use of in vivo models, (2) rapid and cost-effective experimental methodologies, and (3) the simulation of human physiology and biochemistry in a controlled situation such as (i) the recreation of healthy and disease conditions (e.g., inflammation) and (ii) the coculture with bacterial cells to study host-cell interactions. Therefore, our research group has focused on the modeling of in vitro barrier tissue interfaces for its use in environmental toxicology, concretely, to study the interaction, fate, and effects of engineered nanoparticles (ENPs), and micro- and nano-plastics (MNPLs), recently coined as emergent contaminants. To study the effects of ENPs and MNPLs, three different in vitro systems have been already developed, characterized, and tested: (1) the Caco-2/HT29/Raji-B model that mimics the small intestinal environment, (2) the air liquid interface epithelium of Calu-3 as the bronchial epithelium, (3) and the HUVECs monolayer that closely recreates the endothelium of veins and capillaries. All three models were established in porous transwells® using static conditions. In general, these models have permitted us to visualize and quantify the ENPs (TiO<sub>2</sub>NPs) and MNPLs (e.g., polystyrene, polyethylene, polylactic acid, etc.) cell internalization, nuclei interaction, and their bio-persistence in tissues, to measure oxidative, genotoxic, and structural damage, and to study the response modulation through batteries of gene expression.

Moreover, successful co-exposures to gut-derived microbiota (*L. rhamnosus*) and ENPs demonstrates the protective role of symbiotic bacteria against contaminants. In conclusion, these models have served us to rapidly test a vast number of actual and potential food and environmental contaminants and provide trustable data to regulators and policymakers. Although some limitations such as the incapacity to perform long-term (>1week) studies were detected, the use of dynamic systems (e.g., microfluidics) could potentially help to the tissue replacement.

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