PRE-CLINICAL PROTEIN SCREENING IN BIOENGINEERED INTESTINAL TUBULES

P.G.M. Jochems[1], J. van Bergenhenegouwen[1,2], P.C.S. Rietveld[1], R.M.C. Ariëns[3], S. Bastiaan-Net[3], H.J. Wichers[3], J. Garssen[1,2] and R. Masereeuw[1]

[1] Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands
[2] Nutricia Research, Global Center of Excellence Immunology, Utrecht, The Netherlands
[3] Wageningen Food & Biobased Research, Wageningen University, Wageningen, The Netherlands

The increasing world population goes hand in hand with an increase in food demand. Therefore, the need for sustainable nutrition grows. In the search for novel foods, safety and efficacy testing are of at most importance. After oral ingesting, the first organ system foods directly interact with is the gastrointestinal tract. The small intestine plays a key role in the selective absorption and first line of defense via its epithelial barrier. For pre-clinical screening, we recently developed bioengineered intestinal tubules. These make use of Caco-2 cells cultured on hollow fiber membranes resulting in an advanced model with key features of the small intestine: a 3-dimensional tube structure, formation of a functional epithelial barrier, differentiation in the main small intestinal cell types and villi-like structures. Our model was used to screen 14 different *in vitro* digested proteins of different origins. The model was either exposed to only protein digest (3hr) or a barrier disruptive challenge (24hr) prior to protein digest (3hr) exposure. Thereafter, the leakiness of the epithelial monolayer was evaluated via inulin-FITC leakage and quantification of zonula occludens-1 immunostainings. Furthermore, cell viability and alkaline phosphatase activity were determined. The latter is known to decrease the toxicity of LPS and an increase is therefore considered beneficial. In the supernatant, immune modulators (e.g. IL-6 and IL-8) and nitric oxide were quantified as markers for inflammation and tissue repair. Our findings together show the applicability of the bioengineered intestinal tubules as pre-clinical screening device for novel proteins.