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Towards a Gut-on-a-Chip

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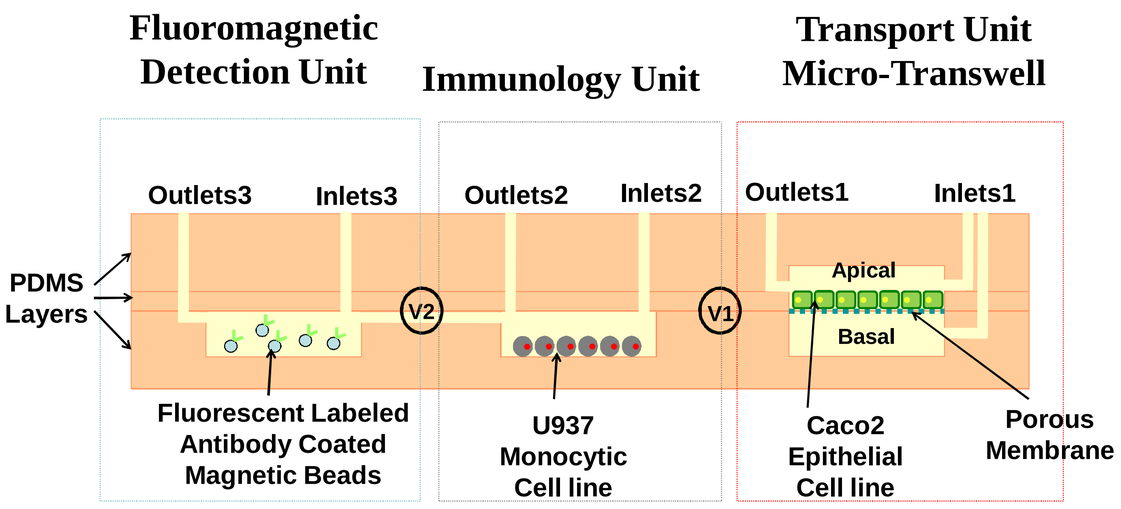
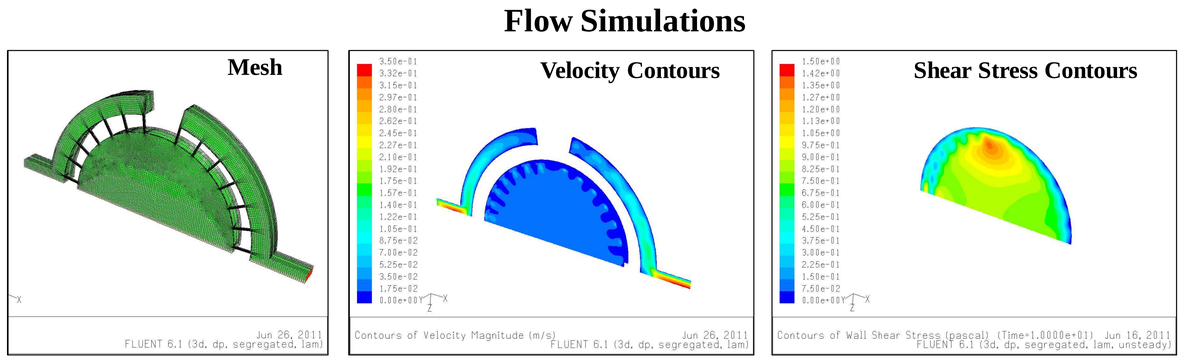
Abstract: **The combination of the transport of the artificially digested nutrients through epithelium and the immunological response of the gastrointestinal system to them can be studied using Gut-on-a-Chip. The two initial cell lines are cultured in the different layers of the chip under controlled micro-environment parameters until they differentiate into intestinal epithelium and macrophages. This sophisticated *in-vitro* model which is miniaturized in this chip can then be used to observe the response of the gut immune system to different nutrients which pass through the epithelium along with the epithelium signals itself. This multilayer bio-microfluidic chip consumes less amount of reagents and power while it is more automated and controllable than the conventional methods. The chip design has predicted different methodologies to study this biological phenomenon, including a transwell on chip to study the transport through the epithelial cell monolayer, fluoromagnetic detection of the cytokines secreted by the macrophages and staining of the membrane proteins which are known to be expressed as inflammatory responses.**

Gut-on-a-Chip Concept Review



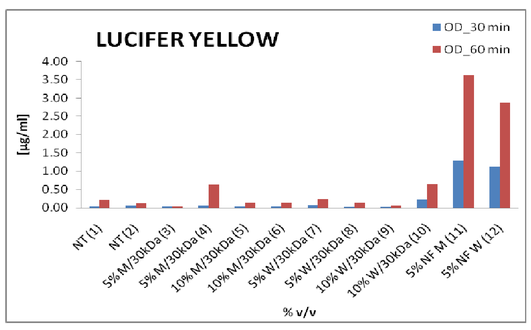
The artificially digested nutrients are introduced on the apical side of the micro-transwell and on epithelial cells. The results of the transport are guided towards the immune cells in the next chamber. Their response is measured in the detection chamber.

Culture Chamber Design for Cell Trapping and Perfusion Feeding

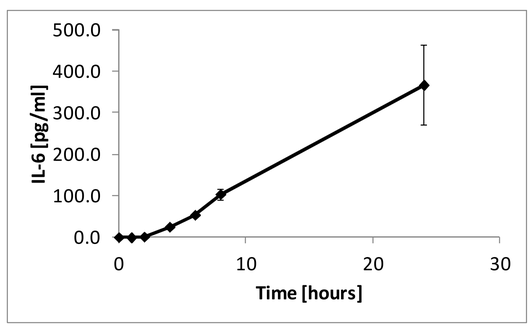


Adapted from Hung et al, BIOTECHNOLOGY AND BIOENGINEERING, VOL. 89, NO. 1, JANUARY 5, 2005

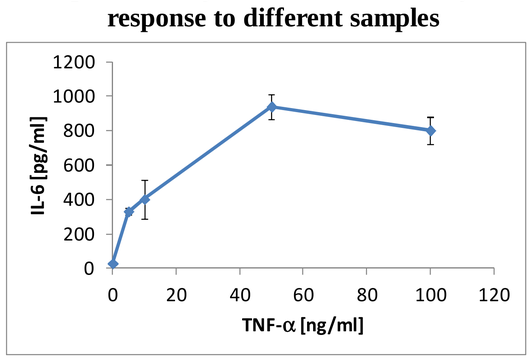
Experiments off-Chip



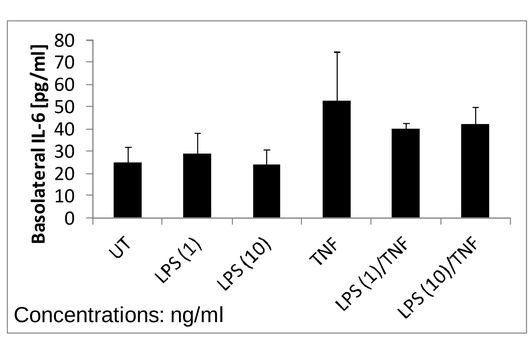
The permeability of the Caco2 monolayer in response to different samples



U937 Il-6 secretion in response to LPS (5nl/ml)



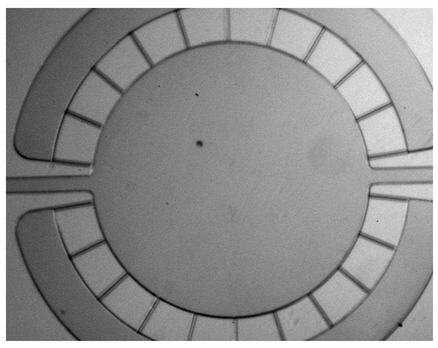
Caco2 Il-6 secretion in response to TNF-a



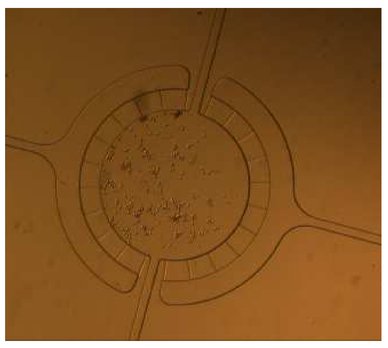
Il-6 secretion response of the co-culture system in response to LPS/TNF-a

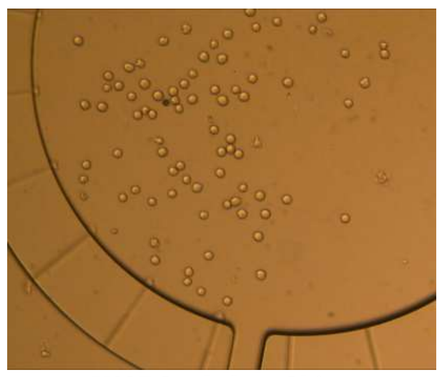
Cells On Chip

Culture chamber in PDMS chip

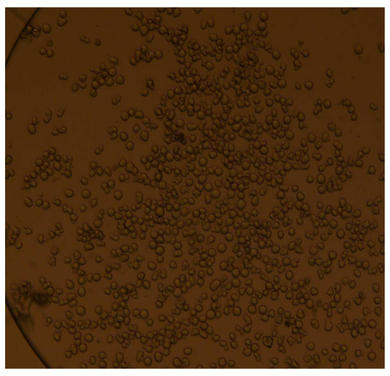


Culture chamber loaded with cells





U937 Seeded on Chip



U937 on Chip after 12 hours incubation

Summary

A PDMS microfluidic chip, with the capability of trapping cells inside the culture chamber with perfusion flow feeding, has been developed for studying the different diary products effects on the inflammatory response of the gastrointestinal system. The design of the chip is based on the minimum flow rate needed for perfusion cell culture on chip and the critical maximum shear stress on cells due to flow rate. Every aspects of this study including the transport through membrane, inflammatory response of the epithelium, inflammatory response of the tissue resident macrophages and also the combination of all these in a co-culture system can be investigated on-chip as it has been done off-chip.