Engineered Membrane Systems For Advanced Organotypic Tissues

Simona Salerno[1], Pritam Das[2], Franco Tasselli[1], Patrice Bacchin[2], Loredana De Bartolo[1]

Email: s.salerno@itm.cnr.it

[1] Institute on Membrane Technology, National Research Council of Italy, ITM-CNR, Rende (CS), Italy
[2] Laboratoire de Génie Chimique, Université de Toulouse, CNRS UMR 5503, INPT, UPS, Toulouse, France

The design of a biomaterial that promote cell colonization and tissue regeneration represents a critical aspect and the major challenge in tissue engineering and regenerative medicine. Design approaches aim to reproduce or mimic the *in-vivo* 3D microenvironment, recapitulating the natural niches for hosting cells and promoting cell-cell and cell-matrix interactions, which are essential in the maintenance of cell polarity and differentiated functions. Polymeric micro- and nano-structured membranes provide physical support, mechanical stimuli and biochemical cues able to modulate and affect the cell fate [1]. Moreover, porous semipermeable membranes allow the compartmentalization and the physical separation of cells, ensuring in the meantime their communication by the selective mass transfer of the secreted paracrine factors [2]. In this work, two innovative culture strategies, by using engineered membrane systems for cell compartmentalization and colonization will be presented.

The first one deals with the creation of a vascularized 3D liver microtissue by co-culturing human primary hepatocytes and endothelial cells in a hollow fiber (HF) membrane system. Poly(Ɛ-caprolactone) (PCL) HF membranes were employed for the formation of a liver tissue on the extracapillary surface, and for the compartmentalization of endothelial cells in the lumen. Owing to their intrinsic geometry, the HF membranes provided a wide surface area for the adhesion and growth of cells in a small volume and in a 3D architecture, favoring cell interactions, hepatocyte polarity and endothelial capillary-like structure formation. Moreover, the heterotypic co-culture improved the hepatocytes viability and functional integrity in comparison to homotypic systems, maintaining the stable hepatic human phenotype for prolonged period, which is strictly required for therapeutic purpose and for preclinical drug testing.

The second strategy was to create 3D membrane scaffolds with a double porosity as niches for human mesenchymal stem cells (hMSC). Double porous blended membranes of PCL and chitosan consist of macrovoids easily accessible for the invasion and proliferation of the cells, and interconnected micropores for the mass transfer of nutrients, oxygen and growth factors between the macrovoids and throughout the scaffolds [3]. The scaffolds created a permissive environment for hMSC adhesion and invasion and ensured an adequate diffusive mass transfer of nutrients and metabolites, which are essential for the long-term maintenance of cell viability and functions. These properties make the membranes suitable to open new possibility for stem cell based tissue engineering.

Ultimately, both the engineered membrane systems can provide selective cell co-culture models for different tissues where cells can adhere on the surface and simultaneously can be compartmentalized or entrapped in macrovoids, ensuring the biochemical cross-talk, which is necessary for recapitulating physiological functions.

References:

[1] S. Salerno, A. Messina, F. Giordano, et al. *Mater Sci Eng C Mater Biol Appl*. (2017) **71**: 943
https://doi.org/10.1016/j.msec.2016.11.008
[2] S. Salerno, E. Curcio, A. Bader, et al. *J Membrane Sci.* (2018) **563**: 694
https://doi.org/10.1016/j.memsci.2018.06.029
[3] P. Das, S. Salerno, J.C. Remigy, et al, *Colloid Surface B-Biointerfaces* (2019) **184**: 110493
https://doi.org/10.1016/j.colsurfb.2019.110493