Mechanotransduction: the effect of mechanical properties, topography and shear stress on cell response

L. Papadimitriou[1#], **P. Kavatzikidou**[1], **E. Babaliari**[1], **G. Flamourakis**[1], **A.Kordas**[1], **E. Kanakousaki**[1], **M. Papageorgiou**[1], **A. Parlanis**[1] and **Anthi Ranella**[1]

[1]Institute of Electronic Structure and Laser, Foundation for Research and Technology Hellas, N. Plastira 100, 71110, Heraklion, Crete, Greece

Presenting author: Lina Papadimitriou, email: lpapadim@iesl.forth.gr
* Corresponding author: Anthi Ranella, email: ranthi@iesl.forth.gr

ABSTRACT

Mechanotransduction refers to the ability of a cell to actively sense and respond to mechanical cues of its microenvironment by adapting its behavior accordingly. For a such response the cell activates a series of mechanisms to receive mechanical stimuli from the surrounding extracellular matrix (ECM) or from neighboring cells. These mechanical stimuli are converted intracellularly to biochemicals ones and with their transduction into the nucleus they orchestrate the cell response by regulating gene expression.

The responses to these mechanical cues play key roles in many important cell functions such as the adhesion, survival, migration, proliferation and differentiation, and are therefore of interest in connection with the fabrication of improved biomimetic materials for tissue engineering applications. In **TERMIM Lab** (Tissue engineering, Regenerative medicine & Immuno-engineering Lab) we are study the activation of mechanotransduction mechanisms in response to the mechanical properties of a scaffold, the topography and the shear stress.

Mechanosensing of ECM/substrata stiffness is mediated primarily by focal adhesions (FAs) which influence cell adhesion, spreading, and remodeling of the actin cytoskeleton. The FAs in turn modulate signaling pathways that control cell proliferation and differentiation through YAP/TAZ molecules. Generally, with a stiffer substrate, there is increased cytosol to nuclear translocation of YAP/TAZ substrate, which can be attributed to increased number of FAs per cell, as well as increased tensile force on the stress fibers connecting the FAs that cause the cell to spread over a larger surface area. In the case of bone marrow derived mesenchymal stem cells (BMSCs), increased YAP/TAZ activation on a stiff substrate leads to enhancement of osteogenic differentiation. Laser made micro- and nano-topographies or 3D scaffolds of auxetic metamaterials offer an invaluable non-invasive means of investigating the cell response to mechanical cues, and greater understanding of mechanotransduction at the cell-material interface offering the potential to advance development of tailored topographical substrates and new generation implantable devices. In addition, the investigation of the mechanotransduction in dynamic cultures by introducing shear stress using microfluidic platforms can better recapitulate the complex cellular mechanosensing milieus *in vivo*. Moreover, shear stress combined with substrate topography can provide biomimetic cell growth environments for the improved understanding of cellular mechanotransduction behaviors accounting biomimetic mechanophysical conditions.