Personalized in vitro extracellular matrix models using nanoparticles or cell-derived matrices.

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The question of how exactly cells sense their environment (including the extracellular matrix and neighbouring cells) and respond to it has fascinated scientists for decades. Indeed, we know that environmental inputs can drive cells into distinct paths such as division, differentiation, and even malignancy, representing a paramount regulator of cell function in a myriad of physiological settings. Therefore, by deepening our fundamental understanding of cell-matrix interactions, researchers also contribute to the development of therapies or devices to tackle injury and disease across our bodies.

Since cells exist in the micro-world, their interactions with the surrounding matrix take place primarily at the nanoscale. Protein receptors at the cell membrane bind to ligands present in extracellular proteins; these adhesions have intracellular repercussions and regulate parameters such as cell shape, cytoskeletal organization, or gene expression. Therefore, it is relevant to study the ECM architecture in patients' tissues and to identify biomarkers useful for their diagnosis, prognosis, and guidance of therapeutic intervention. The role of ECM fibrillar organization is increasingly investigated and analysed through the various imaging techniques and associated quantification tools. In this work we will focus on one part to produce nanopatterns of cell-binding ligands and employ them as in vitro platforms for mesenchymal stem cells, in culture media inducers of differentiation towards cartilage, tendon or bone. We analyse cell movement dynamics, the formation of early tissue structures and their mechanical properties and stability, intercellular communication, and cell differentiation to each of the lineages. In a complementary way, we examined the properties of ECM fibres and fibril bundles in patients' and model tissues obtained from cell derived matrices. We focused on Collagen VI related muscular dystrophies (COL6 RMD) because these pathologies present a clear link between altered ECM architecture and patients' outcome. The results obtained confirm that unveil fundamental cell-matrix interactions that drive the development of musculoskeletal tissues can be exploited at clinical level