STIFFNESS GUIDED CELL MIGRATION IN 3D HYDROGELS VIA MULTIPHOTON GRAFTING

Peter Gruber[a,e], Marica Markovic[a,e], Lukas Kain[b,e], Orestis Andriotis[b,e], Maximilian Tromayer[c,e], Peter Dubruel[d], Sandra Van Vlierberghe[d], Philipp J. Thurner[b,e], Robert Liska[c,e] and Aleksandr Ovsianikov[a,e]

[a]Institute of Materials Science and Technology, TU Wien, Vienna, Austria
[b]Institute of Lightweight Design and Structural Biomechanics, TU Wien, Vienna, Austria
[c]Institute of Materials Science and Technology, TU Wien, Vienna, Austria
[d]Polymer Chemistry and Biomaterials Group, Ghent University, Ghent, Belgium
[e]Austrian Cluster for Tissue Regeneration

Since tissue cells probe elasticity as they anchor and pull on their surroundings, these mechanical signals can have profound effects that lead to cell death, growth, or differentiation at cellular level [1,2]. The possibility to produce volumetric stiffness patterned hydrogels is very appealing in the field of tissue engineering, as it brings the in-vitro model much closer to the real three-dimensional (3D) environment of natural extracellular matrix (ECM). However, existing methods have a narrow stiffness-tuning range, which limits their applicability. In this study a novel method to modify the mechanical properties of a hydrogel via 2-photon grafting was developed. The utilized chemistry involves the water soluble difunctional azide molecule 4,4′-Diazido-2,2′-stilbenedisulfonic acid (DAS). Upon photoactivation via a near infrared femtosecond laser the azide groups form highly reactive nitrene groups. These species are capable of insertion into C-H bonds of the surrounding methacrylamide-modified gelatin (GelMOD) hydrogel, linking the molecule to the matrix and increasing the crosslinking density locally. This approach can be performed in the presents of living cells to tune the elastic modulus of soft hydrogels by a factor of 50. Our stiffness-tuning approach should provide further insights into the effects of mechanical signals on cell fate.

[1] Discher, D. E., Janmey, P. & Wang, Y.-L. Tissue cells feel and respond to the stiffness of their substrate. Science 310, 1139–1143 (2005).

[2] Vogel, V. & Sheetz, M. Local force and geometry sensing regulate cell functions. Nat. Rev. Mol. Cell Biol. 7, 265–275 (2006).