Mechano-Regulation of Human Mesenchymal Stem Cells Using Stimulus Responsive Hydrogels and 3D Printed Metamaterials

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Ample evidence has postulated that stem and somatic cells sense and react to both biochemical and biophysical cues from their surrounding environments. Tanaka Lab in Heidelberg (biophysical chemistry) has developed new types of materials that can mechanically stimulate and regulate single cells under interdisciplinary collaboration with clinical hematologists in Heidelberg (A.D. Ho and C. Mueller-Tidow), polymer chemists in Osaka (A. Harada and Y. Takashima), and (bio-)engineers in Karlsruhe (M. Wegener and M. Bastmeyer).

In the first part, M. Tanaka will introduce the somet of our recent achievements in this field, including: (A) development of new hydrogel materials for reversible/periodic stimulation of cells [1-3], (B) mechanical manipulation of single cells in 3D printed micro-scaffolds [4], and (C) *on-demand* mechanical stimulation of human mesenchymal stem cells using supramolecular hydrogels with reversible host-guest crosslinks.

In the second part, N. Munding will introduce an ongoing project that aims the regulation of human mesenchymal stem cell behaviors using 3D printed mechanical metamaterials.

We look forward to exchanging ideas with you, hoping that we can generate a major scientific breakthrough by uniting different expertise.

1. Yoshikawa, H.Y., Rossetti, F.F., Kaufmann, S., Kaindl, T., Madsen, J., Engel, U., Lewis, A.L., Armes, S.P., and Tanaka, M. (2011). Quantitative Evaluation of Mechanosensing of Cells on Dynamically Tunable Hydrogels. Journal of the American Chemical Society *133*, 1367-1374. 10.1021/ja1060615.
2. Hörning, M., Nakahata, M., Linke, P., Yamamoto, A., Veschgini, M., Kaufmann, S., Takashima, Y., Harada, A., and Tanaka, M. (2017). Dynamic Mechano-Regulation of Myoblast Cells on Supramolecular Hydrogels Cross-Linked by Reversible Host-Guest Interactions. Scientific Reports *7*, 7660. 10.1038/s41598-017-07934-x.
3. Hayashi, K., Matsuda, M., Mitake, N., Nakahata, M., Munding, N., Harada, A., Kaufmann, S., Takashima, Y., and Tanaka, M. (2022). One-Step Synthesis of Gelatin-Conjugated Supramolecular Hydrogels for Dynamic Regulation of Adhesion Contact and Morphology of Myoblasts. ACS Applied Polymer Materials *4*, 2595-2603. 10.1021/acsapm.1c01902.
4. Hippler, M., Weißenbruch, K., Richler, K., Lemma, E.D., Nakahata, M., Richter, B., Barner-Kowollik, C., Takashima, Y., Harada, A., Blasco, E., et al. (2020). Mechanical stimulation of single cells by reversible host-guest interactions in 3D microscaffolds. Science Advances *6*, eabc2648. 10.1126/sciadv.abc2648.