Oral Presentations

– 10. Mechanobiology –

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Combined SICM-TFM reveals a subcellular correlation between stiffness and traction forces in living cells

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As cell mechanics play an important role in many physiological processes as well as numerous diseases, a comprehensive understanding of the living cell and its cytoskeleton as an active mechanical system is of major importance. However, the interaction between the passive material properties of the cell and the actively generated contractile forces remains ambiguous. Here, we present combined scanning ion conductance microscopy (SICM) and traction force microscopy (TFM) as a novel method for parallel probing the "passive" material properties in terms of the mechanical stiffness and the "active" contractile forces of living cells with subcellular resolution. We identify a spatial correlation between the local stiffness and the traction force density in living cells. This behavior can be interpreted as local stress-stiffening of the cytoskeleton, recently postulated as the "missing piece in cell mechanics". Interestingly, we found this correlation in healthy breast epithelial cells but not in breast cancer cells, indicating that healthy cells exhibit "normal" stress-stiffening behavior while breast cancer cells do not. This might be a hint for a fundamental difference in mechanotransduction between normal and cancerous cells on the single-cell level and shows that combined SICM-TFM is a powerful method to study the complex interplay between cell stiffness and contractility.

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Dermal fibroblasts and human breast cancer cells differentially stiffen their local matrix

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Bulk ECM stiffness measurements are often used in research on cell mechanobiology. However, past studies by our group have shown that peri-cellular stiffness can span few orders of magnitude and diverges from the bulk properties. Using optical tweezers active microrheology (AMR) we can describe stiffness landscape around individual cells. In this study, we show how different cell lines cultured in 1.0 and 1.5 mg/ml type 1 collagen (T1C) create disparate patterns of peri-cellular stiffness. Dermal fibroblasts (DFs) increase peri-cellular stiffness, when embedded in 1.0 mg/ml T1C hydrogels, but do not alter stiffness in 1.5 mg/ml T1C hydrogels. In contrast, invasive human breast cancer MDA-MB-231 cells (MDAs) do not significantly change the stiffness of T1C hydrogels, as compared to cell-free controls. Results indicate that while MDAs adapt to the bulk ECM stiffness, DFs regulate local stiffness to levels they intrinsically "favor". Further, cells were also subjected to treatments that were previously shown to regulate their migration, proliferation and contractility. Following each treatment, cells established dissimilar stiffness patterns. Stiffness magnitude and extent of anisotropy varied with the cell line, T1C concentration and treatment. In summary, we demonstrate that AMR can reveal otherwise masked mechanical properties of the local ECM, which are known to affect cell behavior.