Contractile Cell Forces on Rigid Substrates

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INTRODUCTION: In recent years biomechanical parameters have been evolved as crucial factors for the determination and characterization of cell fate, e.g. for the differentiation of stem cells or the malignant transformation in cancerogenous cells.[1,2] Several methods to evaluate the contractile forces, which cells exert on the underlying substrate, have been developed since the early 1980s. These methods, however, rely on the significant deformation of the substrate and are thus suitable to mimic cell biomechanics on softer substrates. Here, we present results from an approach to determine cell forces on stiff substrates using nanomechanical cantilever sensors that is much more relevant for load bearing implants and cell culture dishes. The technique allows for the quantification of cell forces generated on different substrates and can thus be applied to characterize cell-materials interactions in many biomedical applications, aiding e.g. the development of implant surfaces and investigate fundamental cell characteristics.

METHODS: For the cell force determination cells were cultured on nanomechanical cantilever sensor arrays 500 µm long, 100 µm wide and 1 µm thick, which allow for the detection of forces as small as 10^{-5} N/m. Following adhesion and contractile force generation the cantilever sensors are transferred to the Cantisens Research system (Concentris GmbH, Switzerland) to monitor changes in cantilever bending upon trypsin-mediated release of the cells from the substrate as shown in *Fig. 1*.

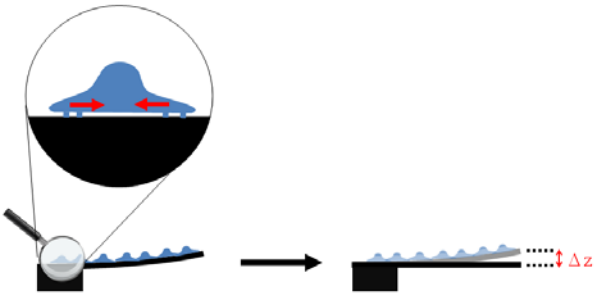

Fig. 1: Principle of the cantilever-based cell force quantification.

RESULTS: For the establishment of the cell force determination standard cultured cell lines where used. When rat2 fibroblasts are seeded on cantilevers they adhere and develop a morphology indistinguishable from that on a standard culture dish. Upon release of the cells from the sensor surface the cantilever relax with an amplitude correlating to the release of contractile cell forces (*Fig. 2*).

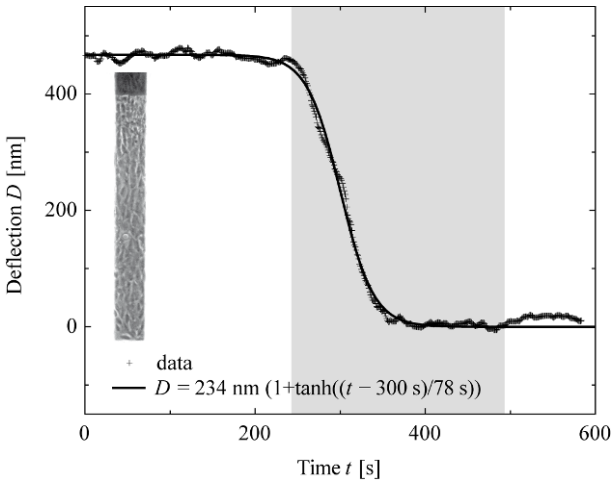

Fig. 2: Cantilever bending signal during the release (grey shaded area) of cells from the substrate.

The release kinetics can be perfectly described using the following empirically determined function:

$$\Delta z = 0.5 z_0 \, (1\text{-}\tanh((t\text{-}t_0)/\tau))$$

where z_0 corresponds to the deflection amplitude, τ denotes the time constant and t_0 relates to the start of experiment.

DISCUSSION & CONCLUSIONS: This communication deals with a method which allows the determination of contractile cell forces on different kinds of rigid substrates with materials properties similar to the ones used for implants and standard cell culture dishes. By modifying the cantilever geometry both single cell measurements and the quantification of forces in organized cell layers become feasible. We expect this method aids to the understanding of fundamental aspects of cell-materials interactions with important implications for future implant design.

REFERENCES: [1] Engler et al. (2006), *Cell* **126**, 677-689. [2] Cross et al. (2007), *Nature Nanotechnology* **2**, 780-783.

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