Investigating cardiomyocyte rigidity sensing with nanopillar arrays

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Abstract:

Mechanical properties are cues for many biological processes in health or disease. In the heart, changes to the extracellular matrix composition and cross-linking results in stiffening of the cellular microenvironment during development. Moreover, remodeling after myocardial infarction, or in cardiomyopathies lead to fibrosis and a stiffer environment. Previous studies established a direct relationship between rigidity and the contractile forces of cardiomyocytes. However, it is still elusive how cardiomyocytes sense matrix stiffness. In contrast to previous studies using micropillars or traction force microscopy, we use here nanopillars, which enable high spatial and temporal resolution, while having only minor effects on cell morphology and behavior. For reliable measurement of cardiomyocyte forces we developed a protocol to label nanopillar surfaces with quantum dots to avoid optical artefacts caused by the cardiomyocyte thickness, high optical density and semi-crystalline arrangement of the myofibrils.

By combining nanopillar arrays, PDMS gels with defined stiffness and FRET molecular tension sensors, we identify a fundamental mechanism for cardiomyocyte rigidity sensing that employs a combination of non-muscle myosin and muscle myosin contractions and is regulated through PKC and Src. Together, our results demonstrate how chemical and mechanical signals can both shift a finely tuned system towards aberrant mechanosignalling.

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