International Conference on Advanced Optical Technologies
University of Erlangen-Nürnberg, March 13th – 15th 2019

Monitoring of Stretch Activated Ca^{2+} Signaling in Human Endothelial Cells using Fluorescent Calcium Indicators

U. Schöler[1,2], S. Schürmann[1,2], O. Friedrich[1,2]

[1]Institute of Medical Biotechnology, Department of Chemical and Biological Engineering, Friedrich-Alexander-Universität Erlangen-Nürnberg
[2]Erlangen Graduate School in Advanced Optical Technologies (SAOT), Friedrich-Alexander Universität Erlangen-Nürnberg
ulrike.schoeler@fau.de

Calcium ions (Ca^{2+}) play a crucial role in signaling events within living cells and therefore, cell viability is strongly connected to Ca^{2+} homeostasis. Understanding cellular signaling mechanisms related to Ca^{2+} homeostasis strongly depends on the ability to monitor Ca^{2+} distributions and concentrations within living cells [1].
Today, a broad range of fluorescent calcium indicators is available. There are two major classes of fluorescent calcium indicators: chemical calcium indicators and genetically encoded calcium indicators. Calcium sensors of both classes show a significant change in the excitation and / or emission spectrum upon calcium binding.
Changes in the Ca^{2+} level within a cell can result from calcium entry via ligand-gated, voltage-gated, or mechanosensitive ion channels [2]. Latter play a significant role in transducing external mechanical stimuli to intracellular signals in hollow organs such as the cardiovascular system.
In this work, a stretching device developed at our institute, the IsoStretcher, was used to apply defined isotropic mechanical stretch to human endothelial cells attached to an elastic silicon membrane. Previous work was done to optimize the IsoStretcher for microscopic studies [3]. The IsoStretcher can be easily mounted on our commercial epifluorescence microscope and ongoing work is done to minimize the z-shift of the elastic membrane when exposed to stretch.
The simultaneous use of the IsoStretcher to apply mechanical stretch to the endothelial cells and of a fluorescent calcium indicator allowed for monitoring the change in the intracellular Ca^{2+} level resulting from this mechanical stimulus. The use of different chemicals that are known to inhibit mechanosensitive ion channels showed that the Ca^{2+} rise within the cells results from the opening of mechanosensitive channels and not from cell membrane rupture.
Understanding the mechanosensitive properties of cells of the cardiovascular system will give deeper insight into the pathophysiological mechanisms underlying diseases of the cardiovascular system resulting from physical changes such as hypertrophy. Furthermore, pathways within the cell that are influenced by mechanical stress will be studied to identify new starting points for drug development.

References

[1] O. Friedrich, S. I. Head, *Methods Mol Biol* **1601**, 171-193 (2017)
[2] D. E. Clapham, *Cell* **131**, 1047-58 (2007)
[3] S. Schürmann, S. Wagner, S. Herlitze, C. Fischer, S. Gumbrecht, A. Wirth-Hücking, G. Prölß, L. A. Lautscham, B. Fabry, W. H. Goldmann, V. Nikolova-Krstevski, B. Martinac, O. Friedrich, *Biosens Bioelectron* **81**, 363-372 (2016)