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## Red blood cells: ion transport, role in thrombus formation, and interaction with artificial surfaces and nanoparticles

Key words: red blood cells, K<sup>+</sup> and Na<sup>+</sup> fluxes, thrombus formation

The talk will focus on three topics of our investigations of red blood cells (RBCs). (i) The identification and characterization of a so far unknown K<sup>+</sup>(Na<sup>+</sup>)/H<sup>+</sup> exchanger in the RBC membrane and its role in certain diseases, e.g. cryohydrocytosis.

We investigated the so called low ionic strength (LIS) effect on the residual  $K^+$  and  $Na^+$  fluxes of RBCs. This effect was under investigation for about 100 years. On the basis of experimental data as well as theoretical calculations we were able to demonstrate that the so far assumed residual monovalent cation fluxes are only possible to explain on the basis of a novel carrier mechanism.

(ii) The role of RBCs in thrombus formation.

In current models the contribution of RBCs in the process of thrombus (clot) formation is assumed to be purely passive. However, we were able to demonstrate that RBCs can play an active role in thrombus formation.

The enhancement of the intracellular  $Ca^{2+}$  content of RBCs induced by lysophosphatidic acid (LPA, substance released by activated thrombocytes) results in the exposure of phosphatidylserine (PS) on the outer leaflet of the cell membrane due to the activation of the scramblase. In addition, it leads to cells shrinkage due to the activation of the  $Ca^{2+}$ -activated K<sup>+</sup> channel and the resulting KCl loss.

To study whether the  $Ca^{2+}$  uptake of RBC results in an enlargement of the mechanical cellcell interaction, measurements applying holographic optical tweezers as well as single-cell force spectroscopy have been carried out. It was possible to demonstrate that after LPA treatment in the presence of  $Ca^{2+}$ , a pronounced adhesion of the RBCs could be observed. In control experiments (without LPA) it was only possible to detect a weak interaction between the cells.

(iii) The interaction of RBCs with artificial, e.g. nano-structured, surfaces.

To study the interaction of cells with surfaces in real time a new method, the digital holographic microscopy, allowing a focus trekking of the cells during sedimentation will be presented. In addition, the effect of nanoparticles on the Ca<sup>2+</sup> content and the intracellular pH of RBCs based on fluorescence microscopy and FACS measurements will be shown.

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