RELEVANCE OF ION TRANSPORT PATHWAYS IN THE RED BLOOD CELL MEMBRANE FOR PATHOPHYSIOLOGICAL PROCESSES

I. BERNHARDT[1], E. WEISS[1], L. KAESTNER[2]

[1]Saarland University, Saarbruecken, Germany;
[2]Saarland University, Homburg, Germany

The red blood cell (RBC) membrane contains ion pumps and a large variety of carriers and channels. The presentation will focus on the $K^+(Na^+)/H^+$ exchanger as well as on the non-selective voltage-dependent cation (NSVDC) channel.

The $K^+(Na^+)/H^+$ exchanger is relevant since the ion flux mediated by this transporter is part of the so far assumed residual ion transport (or leak flux), which is significantly increased in certain hemolytic anemia. From previous work it is known that the $K^+(Na^+)/H^+$ exchanger is remarkably activated in low ionic strength solutions. We show that a newly developed drug (HOE 642, 0.5 mM), originally designed to inhibit Na^+/H^+ exchanger isoforms, inhibits the assumed residual K^+ influx of 40% in physiological solution and 60% in low ionic strength solution. A general conclusion of the findings is that the ground state membrane permeability for K^+ is much smaller than usually supposed. In addition, we provide evidence that the increased K^+ uptake of the RBCs of a patient with cryohydrocytosis is mainly due to an enhanced transport mediated by the $K^+(Na^+)/H^+$ exchanger.

Characterizing the physiological relevance of the NSVDC channel in more detail, we are demonstrating that the channel can be activated by Prostaglandin E_2 (PGE_2). We provide evidence that PGE_2 at physiological concentrations (10^{-10} M) activates Ca^{2+} rises mediated by Ca^{2+} influx through the NSVDC channel in human RBCs. The extend of Ca^{2+} increase varied between cells with a total of 45% of the cells responding. Ca^{2+} enhancement elicited the Ca^{2+}-activated K^+ channel (Gardos channel) in the RBC membrane resulting in K^+ efflux and shrinkage of the cells. From this we conclude that the PGE_2 responses of RBCs reveal a direct and active participation of erythrocytes in blood clot formation.