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Mechanosensing Dynmics of Red Blood Cells

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Abstract: Piezo proteins (Piezo1 and Piezo2) are recently identified mechanically activated cation channels in eukaryotic cells and associated with physiological responses to touch, pressure, and stretch. In particular, human RBCs express Piezo1 on their membranes, and mutations of Piezo1 have been linked to hereditary xerocytosis. To date, however, physiological functions of Piezo1 on normal RBCs remain poorly understood. Here, we show that Piezo1 regulates mechanotransductive release of ATP from human RBCs by controlling the shear-induced Ca2+ influx [1]. We find that, in human RBCs treated with Piezo1 inhibitors or having mutant Piezo1 channels, the amounts of shear-induced ATP release and Ca2+ influx decrease significantly. Remarkably, a critical extracellular Ca2+ concentration is required to trigger significant ATP release, but membrane-associated ATP pools in RBCs also contribute to the release of ATP. Our results show how Piezo1 channels are likely to function in normal RBCs and suggest a previously unidentified mechanotransductive pathway in ATP release. Last, we showed *in vivo* using two photon imaging that the change of RBC mechanical properties in piezo1 KO mice and with changes of local oxygen tension [2] and how it affects microcirculation in the brain.

Keywords: Piezo1 channels red blood cells; microfluidics; *in vivo* two photon imaging; cerebral microcirculation.

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References

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