A NOVEL GAIN OF FUNCTION MUTATION OF PIEZO-1 IS INVESTIGATED IN RED BLOOD CELLS BY HIGH-THROUGHPUT PATCH CLAMP

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During their passage from the bone marrow to peripheral organs, Red Blood Cells (RBCs) experience substantial mechanical forces that trigger RBC volume changes via Ca^{2+} influx through mechanosensitive channels like Piezo-1 (1-3). However, direct electrophysiological proof of Piezo-1 activity in RBCs has been lacking so far as most of the studies come from animal models, were recorded under pathophysiological conditions or via Ca^{2+} imaging (1, 2, 4). In addition, the RBCs' small and variable size and their large heterogeneity in ion channel expression pose a significant challenge for successful patch clamp recordings (5, 7).

Here, we used automated patch clamp technology to study and characterize different ion channels present in RBCs, aiming specifically for Piezo-1 activity. We approached the problem of RBC heterogeneity by upscaling to high throughput automated patch clamp recordings of 384 cells in parallel to separate the cells in Yoda-1 responders and non-responders based on automated quality filtering. Thereby, we functionally characterized RBCs from patients carrying a gain of function mutation in Piezo-1 (8), demonstrating that high-throughput patch clamping can provide assays for drug discovery and personalized treatment of anaemic disorders such as hereditary xerocytosis and the sickle cell disease.

References:

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