**Lay summary**

We investigated the effects of glucose on both breast cancer cells (MDA-MB-231) and macrophages. In the case of breast cancer cells, the study found that high extracellular glucose levels (>11 mM) caused the cells to become stiffer in a concentration-dependent manner, without a change in cell size. This increased stiffness was associated with higher cell migration and invasion. Interestingly, non-tumorigenic epithelial cells did not show changes in mechanics with different glucose levels. The study further confirmed that these changes were related to glucose metabolism by inhibiting glycolysis, which reversed the cell stiffening effects.

The research also delves into the molecular mechanisms underlying these changes in cell mechanics. Phosphorylation of MLC2, a key regulator of cell contractility, was found to be influenced by the Rho-Associated Coiled-Coil Kinase (ROCK) pathway in response to high glucose. Inhibition of ROCK and suppression of RhoA protein expression confirmed their roles in cell stiffening. Additionally, activating RhoA led to increased cell stiffness, supporting the connection between glucose availability and cell deformability.

In the case of macrophages, the study used mouse primary bone marrow-derived macrophages and observed how different glucose concentrations affected M0, M1, and M2 types. The results showed distinct responses to low glucose availability, with changes in glycolysis rate, oxidative phosphorylation rate, and cell mechanics. Notably, M1 macrophages did not show changes in stiffness and contractility with varying glucose levels, unlike M0 and M2 types. The study also investigated functional changes in macrophages, including alterations in chemokine secretion and phagocytic activity in response to low glucose.

The findings led to the hypothesis that in low glucose conditions, M0 macrophages become more deformable and less contractile, enhancing phagocytosis through the cAMP-RhoA-ROCK axis. Our study suggests that understanding these glucose-mediated effects on cell mechanics and functions could contribute to insights in cancer cell behavior and immune response modulation.