Aquaporin-3 and aquaporin-5 modulate cell biomechanical properties and influence cell migration

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Aquaporins (AQPs) are transmembrane proteins that mediate the transport of water, glycerol, and small neutral solutes across cell membranes. AQPs are overexpressed in different types of cancer, being involved in cancer cell proliferation, migration, angiogenesis, and metastasis. Our previous study with AQP3-, AQP5-, and double-silenced human pancreatic ductal adenocarcinoma cells showed morphological alterations and lower cell-cell adhesion, with AQP5 influencing cell stiffness and membrane fluidity. These findings suggest that these AQPs can impact tumor progression by modulating cell biomechanical properties. With this work, we developed a cell-based platform of HEK-293T (HEKT) cells overexpressing individually the isoforms most associated with cancer: AQP3 (water and glycerol channel) and AQP5 (water channel) to investigate how their overexpression can modulate biological processes and cell membrane features. After cell model validation, we assessed their impact on morphological properties through atomic force microscopy (AFM) imaging. AQP5-overexpressing cells exhibited a higher roughness and area, with no differences observed for AQP3-HEKT cells. Using AFM-based force spectroscopy, we evaluated the influence of these AQPs on cell stiffness and cell-cell adhesion. AQP3-HEKT cells showed higher cell stiffness and lower cell-cell adhesion. In contrast, AQP5-HEKT cells demonstrated higher elasticity and cell-cell adhesion. Afterwards, we investigated the effect of AQP3 and AQP5 overexpression on cell migration, proliferation and adhesion. Both AQPs promoted cell migration and impaired cell adhesion to matrix, while no differences were observed for cell proliferation. Further studies are needed to understand the mechanisms underlying the roles of AQP3 and AQP5 on cell membrane properties and their impact on biological processes crucial for tumorigenesis.