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PADUA DAYS ON MUSCLE AND MOBILITY MEDICINE 2026 ABSTRACT N. 030

BIOLOGY AND PHYSIOPATHOLOGY OF GENETIC NEUROMUSCULAR DISEASES

EXPRESSION OF THE ERG1A POTASSIUM CHANNEL AFFECTS NANOSCALE MEMBRANE CHARACTERISTICS OF CULTURED SKELETAL MUSCLE CELLS

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Rhabdomyosarcoma (RMS) is a rare skeletal muscle (SKM) cancer with an overall incidence rate of approximately 4.5 cases per million in the U.S, this being similar among countries around the world with the exception of East Asia where it is about 2 cases per million [1]. It is generally diagnosed in children and teens and has a five-year survival rate ranging from 30-90%, dependent upon whether it is diagnosed as low, intermediate, or high risk [2,3,4]. There are two key types: 1) embryonic (ERMS) and 2) alveolar (ARMS); the ARMS form is the more aggressive and is less easily treated [2,3,4]. We have reported that the ERG1 voltage-gated K+ channel is detected in RMS cells by immunohistochemistry [5] and our preliminary immunoblots show that the mature glycosylated isoforms are more abundant in the RMS cells than in the control C2C12 cells. Indeed, the ERG1A channel is associated with numerous cancer cell types and, although it is associated with poor prognoses, what role it plays in malignancy is not known [6]. Certain membrane mechanical properties differ in malignant versus normal cells. For example, cancer cell membranes have been reported to exhibit decreased “stiffness” [7,8] as well as altered adhesion [7,8] and deformation [9].We have preliminary atomic force microscopy (AFM) data which show that ERG1A over-expression in C2C12 myoblasts significantly increased membrane adhesion by 6.6 fold ($p<0.02$, $n=19$; Fig. 1). Adhesion is an attractive force that develops between objects dependent upon mechanical forces and electrostatic interactions. It is known to be variably affected in cancer cells relative to appropriate controls and also to vary with stage of the disease [7,8]. Indeed, reports suggest that decreased adhesiveness can increase the potential for cells to metastasize while increased adhesiveness may increase a cell’s potential to form tumors [7-10]. ERG1A overexpression also enhanced Young’s modulus (YM) by 4.2 fold ($p=0.173$, $n=19$) in C2C12 myoblasts. Although not statistically significant, a power analysis revealed that 35 additional cells per group would result in significance at $p<0.05$. YM describes the elasticity (or “stiffness”) of the cell membrane. It is known to be decreased in many cancer cells and this decreased “stiffness” is thought to contribute to cell metastasis; however, there are reports that an increased YM is associated with increased potential of cells to be invasive [7-10]. The effect of YM seems to be cell line and growth stage dependent. Together, the data support our hypothesis that ERG1A alters nanoscale membrane mechanical characteristics of muscle cells and, thus, may contribute to development of malignancy in SKM.

Keywords: *ERG1A Potassium channel, nanoscale membrane characteristics, cultured skeletal muscle cells.*

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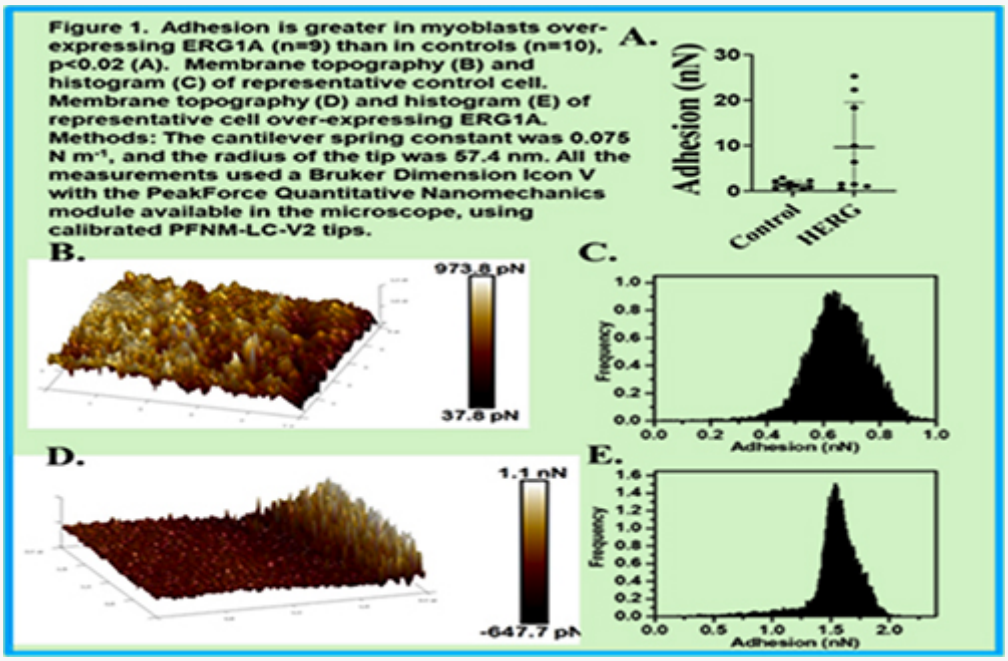

Figure 1. Adhesion is greater in myoblasts over-expressing ERG1A (n=9) than in controls (n=10), p<0.02 (A). Membrane topography (B) and histogram (C) of representative control cell. Membrane topography (D) and histogram (E) of representative cell over-expressing ERG1A. Methods: The cantilever spring constant was 0.075 N m^{-1}, and the radius of the tip was 57.4 nm. All the measurements used a Bruker Dimension Icon V with the PeakForce Quantitative Nanomechanics module available in the microscope, using calibrated PFNM-LC-V2 tips.