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"Effects of Low Glucose on Cell Motility and Invasiveness in Oral Squamous Cell Carcinoma (OSCC) In Vitro"

Oral cancers, quick spreading malignant tumors associated with high mortality and a poor 68% 5-year prognosis average, have seen a rise since the mid-2000s. They typically occur in individuals over 40 years of age and have a higher incidence in men than in women. Oral cancer can present in various initial forms, including a sore, thick patch, or swelling in or around the mouth. Most oral cancers are squamous cell carcinomas, comprised of epithelial cells that typically line various organs like the mouth. Though there are many factors in developing oral cancer, such as smoking or drinking history, the rise in oral cancer has been linked to an increase in human papillomavirus (HPV) associated oral cancers. HPV is a prevalent sexually transmitted disease that millions of Americans contract every year. Certain strands of HPV can be cancer-causing, leading those who catch it to be at higher risk of oral cancer. Despite higher morbidity, those with HPV typically have a better prognosis. The reason for this is not fully clear. As cancers metastasize and spread, prognosis usually worsens. Cell motility and migration are hallmarks of cancer metastasis. The tumor microenvironment (TME) and extracellular matrix (ECM) play a large role in cancer prognosis. Cell movement and the remolding of the ECM within the TME are regulated through cell communication and cytokines. The cells have different types of receptors that regulate signaling pathways that help navigate ECM stiffness and remolding. These mechanisms are often fueled by glucose, which is broken down to create energy for the cell in the form of adenosine triphosphate (ATP), a needed component for cell growth and function. Described as the Warburg effect, some types of cancer cells have been shown to utilize glycolysis over oxidative phosphorylation for energy production, despite it being less efficient because of its lower ATP output. The reason cells prefer glycolysis is still unclear. Understanding the role glucose has on cells' motility and invasiveness can be used for future treatment and therapeutic targets.

Our objective was to observe oral cancer cell lines in low glucose environments and measure the output of cell motility and invasiveness of OSCC HPV negative and positive cells. Cal 27 HPV negative and SCC 090 HPV positive cells were used in two assays, the wound healing assay, which measures cell motility, and an invasiveness assay that measures the cell migration through 1% agarose matrices simulating ECM stiffness. Both cell lines were cultured in regular medium that contains 4g/ml of glucose and then challenged in a low glucose environment with 1 g/ml. For the motility assay, cells were seeded in a 6-well plate and wound closure was measured over a 24-hour period, at 0-, 6-, and 24-hour time points. For the invasiveness assay, cells were seeded in a 24-well plate and were challenged with low glucose for 7 days, and migration was measured as the area of migration through a 1% agarose matrix.