Real-time Analysis of an Invasive Ductal Carcinoma Using 3D Paper-based Cultures

Cellular invasion is one of the mechanisms by which cancer cell populations metastasize, or move to other areas of the body. One factor promoting cancer cell movement is the development of an unfavorable environment (low pH, nutrients, oxygen, etc.) on the interior of enlarging tumors, encouraging movement up the gradient, to avoid deprivation. The poorly understood HIF/HGF signaling pathway enables cells to read oxygen gradients and elicits cell movement within and sometimes out of the tumor microenvironment. Previous research has monitored cellular invasion in purely oxygen deprived (hypoxic) environments by mammary cells, but it is not known how different cell components respond and migrate when cultured together in various hypoxic and normoxic environments. Current methods to study 3D invasion like the Transwell assay, multicellular spheroid invasion assay, and microfluidic-based culture assay are expensive, difficult to engineer, and ineffective in gradient remodeling. Here, we modeled the tumor microenvironment in vitro using a 3D paper-based culture, to study the responses of both fibroblasts and mammary cells to varying accessibility to oxygen. We developed a platform that uses cell-laden paper enclosed in an acrylic holder, which enabled manipulation of oxygen availability to each cell population. Our 3D paper-based culture technique is simple, inexpensive, easily adopted, highly adaptable and provides a powerful approach to studying co-cultures. Our ongoing work with this novel assay is aimed at real-time monitoring of oxygen-dependent migration from fibroblasts and adenocarcinoma mammary cells.