Palbociclib Treated MDA-MB-231 Breast Cancer Cells Exhibit Increased Invasive Behavior in Zebrafish Xenograft Model

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During the progression of metastatic cancer, peripheral cells break away from the primary tumor and acquire the ability to intravasate into the circulatory and lymphatic systems. These invasive cells have mechanisms for subsequent extravasation into secondary sites where they may initiate additional tumors. Previous research using a simple in vivo invasion model in the roundworm nematode C. elegans demonstrated that the anchor cell must be in a G1/G0 arrested state to invade into the vulval epithelium during larval development. Given these results in C. elegans, this investigation sought to ascertain whether the dichotomy between proliferation and invasion exists during cancer metastasis. To determine whether pharmacologically induced G1/G0 arrest acts as a causative factor in the metastatic capabilities of tumors, palbociclib-treated and control MDA-MB-231 breast cancer cells possessing both a fluorescent nuclear cell-cycle state indicator (FUCCI) and a cytoskeletal probe (Lifeact::mCerulean) were injected adjacent to the duct of Cuvier of 48 hours post fertilization (hpf) kdrl:RFP-CAAX zebrafish embryos, which exhibit fluorescent vasculature. Palbociclib treated MDA-MB-231 cells demonstrated a 3.5-fold increase in vascular extravasation as compared to control cells, suggesting G1/G0 arrest as a prominent factor in the acquisition of invasive phenotype. Furthermore, extravasated cells were observed to recommence cycling following their escape from vasculature. This evinces the possibility that antiproliferative pharmaceuticals may have the unintended consequence of enhancing the metastatic potential of disparate tumor types.

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