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SYNERGISTIC INTERACTIONS BETWEEN INVASIVE CANCER CELLS AS A MEASURE FOR METASTATIC RISK

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Summary: The main cause (90%) of cancer-related deaths is due to metastasis, spreading of cancer to distant sites in the body. Metastasis requires cells to detach from the tumor and invade through neighboring and distant tissues, composed of cells and matrix. To do that, the cell needs to reshape itself, modify its environment, and apply forces to push through narrow regions. The Weihs lab has recently correlated the ability of cells to apply invasive forces outside of the body with the metastatic risk in patients, concurrently revealing novel mechanisms of synergistic force application by the cancer cells. The origin and mechanisms underlying these synergistic interactions are the focus of the current talk, and will be addressed experimentally and through finite elements modeling.
We have previously shown that a subpopulation of single, metastatic breast cancer cells from cell-lines will rapidly (<2 hours) and forcefully indent an elastic, synthetic, impenetrable gel to depths of 1-10mm, whereas benign breast cells do not indent. Interestingly, when the cancer cells are in high density, close to many neighbors, they are able to synergistically interact and indent more deeply. Specifically, we observe a bimodal distribution of indentation depths, overlapping single cell capabilities and at larger depths. This synergistic phenomenon/capability is lost when cells are treated with chemotherapy, undergo mechanical perturbation, or are seeded on gels with stiffness outside their preferred range; the stiffness range varies with cancer type. To determine the mechanisms leading to this synergistic interaction we combine experiments and finite element modeling of indenting cells on different gels and with varying environmental cues. In this talk we will discuss the cues and mechanisms that are available to the cells, and how that will affect the ability to predict the metastatic risk and to potentially negate it.