



Mechanobiology of Cancer Summer School · 17-21st September 2019

Andrew Ewald – 20th September 9.00

Novel roles of cell adhesion in breast cancer metastasis

The majority of cancer mortality is attributable to metastasis, the process by which cells escape from the primary tumor, access the systemic circulation, and colonize distant organs. Our work in normal development revealed that mammary epithelial cells have a high capacity for migratory behavior and can readily be induced to disseminate out of the epithelium through changes to either the microenvironment or the signaling state of the cell, without need for mutations. We next demonstrated that metastasis can be accomplished by cancer cells that retain an epithelial phenotype while transitioning between distinct phenotypic states specialized for either proliferation or migration. Our recent publications demonstrated that proliferative breast cancer cells acquire migratory and invasive potential through the expression of basal genes, such as keratin 14 (K14) and p63. This transition occurs specifically at the tumor stroma border. These K14+ cancer cells collectively invade and intravasate as adherent groups of cells, through microenvironments defined by aligned, fibrillar collagen I. Upon arrival at the distant site, these predominantly K14+ clusters transition to predominantly K14-growing metastases. We have developed 3D culture models of invasion past the myoepithelium, intravasation, and metastatic colony formation. We are currently exploiting these models to define the molecular drivers of transitions between proliferative and migratory epithelial states. We are also working on defining the role of epithelial cell adhesion programs in collective strategies for metastasis, on the role of the myoepithelium in restraining invasion, and on the mechanisms by which clusters of cancer cells gain access to the venous circulation. Our ultimate goal is to develop novel concepts for anti-metastatic therapies.

Andrew Ewald is a Professor at Johns Hopkins University, School of Medicine, Baltimore, MD at the Department of Cell Biology, he is also Co-Director at the Cancer Invasion and Metastasis Program Sidney Kimmel Comp. Cancer Center. He received his BS from Haverford College, his PhD from California Institute of Technology, and his postdoctoral training from the University of California San Francisco. Dr. Ewalds investigation line is focused on cellular and molecular mechanisms of epithelial growth, invasion and metastasis; how clusters of cancer cells disseminate from the tumor, traverse the systemic circulation, and cooperate with resident stromal cells to colonize distant organs. His studies show how cells build organs and how these same cellular processes can contribute to breast cancer metastasis.