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Targeting cytoskeletal aberrations to prevent breast cancer metastasis

Michele I. Vitolo
[1]University of Maryland Marlene and StewartGreenebaum NCI Cancer Center, USA
[2]University of Maryland Graduate Program in Life Sciences, Program in Molecular Medicine, USA
[3]Department of Physiology, University of Maryland School of Medicine, USA

Patients diagnosed with triple negative breast cancer (TNBC) develop detectable metastatic disease within an average of only three years, and virtually all women with metastatic TNBC will die of their disease despite treatment. The short time period for developing metastases is due to presence of disseminated disease. Disseminating tumor cells circulate within the bloodstream during an intermediate step of the metastatic cascade. An increase in disseminating tumor cells correlates with disease progression and thus the number of circulating tumor cells are used for diagnostic purposes. However, very little is known about their biology. When in the bloodstream, these tumor cells are in a detached and free-floating state. Recently, we demonstrated that the regulation of the actin cytoskeleton differs in attached versus detached cells, leading to the conclusion that there are crucial targetable cytoskeletal signaling changes specific to detached, disseminating cells. In only detached cells, we determined that PTEN regulates the actin severing protein, cofilin, via a PI3K-independent mechanism. PTEN loss promotes cofilin activation leading to a weakened actin cortex. The weakening of the actin cortex increases cell deformability to enhance both tumor cell survival and cell reattachment. Our objective is to elucidate the mechanism by which PTEN regulates cofilin in detached cells to gain a greater understanding of how disseminating tumor cells control deformability. We hypothesize that PTEN loss weakens the actin cortex which enhances disseminated tumor cell deformability to promote metastatic efficiency. An improved understanding of the biochemical signals which modulate cytoskeletal alterations specifically in detached TNBC cells will provide new insight into the development of pharmacologic approaches for inhibiting metastasis by regulating cell deformability.

Biography:

After attending Franklin and Marshall College, Dr. Vitolo began her career as a laboratory technician. After a few years, she returned to school to obtain her Ph.D. in Biochemistry from the University of Maryland Baltimore where she is currently an Assistant Professor.

Dr. Vitolo has a long-standing interest in the molecular genetics of cancer. Her work focuses on the loss of the tumor suppressor PTEN and the progression of breast cancer. Over the years she has co-authored 29 publications and has acquired funding from numerous sources including the American Heart Association, Susan G. Komen Organization, American Cancer Society, and the National Cancer Institute.