

“Developing Fascin Inhibitors to Block Tumor Metastasis”

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Abstract: Tumor metastasis is the main cause of death of cancer patients. Tumor cell migration and invasion are critical steps in the process of tumor metastasis. For cell migration to proceed, actin cytoskeleton must be reorganized by forming polymers and bundles to affect the dynamic changes of cell shapes. Individual actin filaments are flexible and elongation of individual filaments per se is insufficient for membrane protrusion which is necessary for cell migration. Bundling of actin filaments provides rigidity to actin filaments for protrusion against the compressive force from the plasma membrane. Currently there are no drugs that specifically target tumor cell migration and invasion. Recently we have identified fascin as a therapeutic target for blocking tumor cell migration, invasion and metastasis. Elevated levels of fascin have been found in metastatic tumors and are correlated with clinically aggressive phenotypes, poor prognosis, and shorter survival. The objective of this research program is to develop fascin inhibitors as therapeutics for treating and preventing tumor metastasis. In this one-year project, we will screen chemical libraries to identify small molecules that inhibit the function of fascin, to start an initial medicinal chemical modification of the identified hits, and to investigate the effects of these inhibitors on tumor cell migration, invasion and metastasis. The fascin inhibitors will provide a first-in-class drug specifically targeting tumor cell migration and invasion.