Inhibition of Filamin-A Reduces Cancer Metastatic Potential

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Abstract:

Filamin-A cross-links actin filaments into dynamic orthogonal networks, and interacts with an array of proteins of diverse cellular functions. Because several filamin-A interaction partners are implicated in signaling of cell mobility regulation, we tested the hypothesis that filamin-A plays a role in cancer metastasis. Using four pairs of filamin-A proficient and deficient isogenic cell lines, we found that filamin-A deficiency in cancer cells significantly reduces their migration and invasion. Using a xenograft tumor model with subcutaneous and intracardiac injections of tumor cells, we found that the filamin-A deficiency causes significant reduction of lung, splenic and systemic metastasis in nude mice. We evaluated the expression of filamin-A in breast cancer tissues by immunohistochemical staining, and found that low levels of filamin-A expression in cancer cells of the tumor tissues are associated with a better distant metastasis-free survival than those with normal levels of filamin-A. These data not only validate filamin-A as a prognostic marker for cancer metastasis, but also suggest that inhibition of filamin-A in cancer cells may reduce metastasis and that filamin-A can be used as a therapeutic target for filamin-A positive cancer.

Key Word:
Filamin-A, ABP-280, migration, invasiveness, metastasis, biomarker.