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Chitinase-3 like-protein-1 CHI3L1 expression associated with pulmonary inflammation accelerates breast cancer metastasis

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Disseminated metastasis accounts for a majority of breast cancer deaths. Recently, elevated serum levels of a glycoprotein known as chitinase-3 like-protein-1 CHI3L1 has been correlated with poor prognosis in both breast cancer and asthmatic patients. We have combined mouse models of breast cancer and pulmonary inflammation to determine if CHI3L1 associated pulmonary inflammation accelerates metastasis. We found that allergic pulmonary inflammation significantly enhances primary tumor growth in 4T1, 4T07 and 67NR mammary tumors by 10-fold, while decreasing survival. 4T1 tumor bearers with allergic pulmonary inflammation showed a 100-fold increase in metastatic tumor formation. We also assessed CHI3L1 levels and myeloid cells in the lungs of wild type and CHI3L1 knockout mice with allergic pulmonary inflammation and 4T1 mammary tumors. CHI3L1 levels were higher in the lungs of mammary tumor bearers with allergic pulmonary inflammation and correlated with increased metastasis. Wild type mammary tumor bearers with allergic inflammation had higher numbers of myeloid cells in the lungs in comparison to CHI3L1 knockout tumor bearers with allergic pulmonary inflammation. CHI3L1 knockout mice tumor bearers had significantly fewer myeloid cells in the lungs, decreased tumor growth and metastasis, along with increased survival. We propose that increased CHI3L1 in the lungs attracts myeloid cells that promote tumor growth and breast cancer metastasis.