Tumor-induced monocyte adhesion drives pre-metastatic niche formation

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Before cancer cells arrive, future metastatic organs populate macrophages to form a premetastatic niche which enhances homing of circulating tumor cells. For macrophages to form a premetastatic niche in metastatic sites, adhesion to endothelial cells is the most critical step for initiation of subsequent metastatic cascade. However, the mechanisms underlying the adhesion of monocytes and macrophages-mediated pre-metastatic niche are poorly understood. Here, we identify a specific soluble factor, highly expressed in aggressive breast cancer cells, as a major culprit associated with formation of premetastatic niche. We demonstrate that in vivo inhibition of the tumor-derived factor reduced the macrophage recruitment and lung metastasis in the spontaneous metastatic breast xenograft models. Mechanistically, the primary tumor-derived factor induces adhesion molecules ICAM-1, VCAM-1 and E-selectin in endothelial cells, thereby enhancing the recruitment, adhesion and transendothelial migration of monocytes. These findings suggest the tumor-derived factor has a critical role for initiation of macrophage-mediated premetastatic niche and provide the factor as a potential target to regulate cancer metastasis.

Keywords : Tumor associated macrophages, Premetastatic niche, Endothelium, Adhesion molecule, Metastasis
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