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Metastatic cancer cells with macrophage properties: evidence from a new murine tumor model

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Abstract

Metastasis is the process by which cancer cells disseminate from the primary neoplasm and invade surrounding tissue and distant organs, and is the primary cause of morbidity and mortality for cancer patients. Most conventional cancer therapies are ineffective in managing tumor metastasis. This has been due in large part to the absence of in vivo metastatic models that represent the full spectrum of metastatic disease. Here we identify 3 new spontaneously arising tumors in the inbred VM mouse strain, which has a relatively high incidence of CNS tumors. Two of the tumors (VM-M2 and VM-M3) reliably expressed all of the major biological processes of metastasis to include local invasion, intravasation, immune system survival, extravasation and secondary tumor formation involving liver, kidney, spleen, lung and brain. Metastasis was assessed through visual organ inspection, histology, immunohistochemistry and bioluminescence imaging. The metastatic VM tumor cells also expressed multiple properties of macrophages including morphological appearance, surface adhesion, phagocytosis, total lipid composition (glycosphingolipids and phospholipids) and gene expression (CD11b, Iba1, F4/80, CD68, CD45 and CXCR4). The third tumor (VM-NM1) grew rapidly and expressed properties of neural stem/progenitor cells, but was neither invasive nor metastatic. Our data indicate that spontaneous brain tumors can arise from different cell types in VM mice and that metastatic cancer can represent a disease of macrophage-like cells similar to those described in several human metastatic cancers. The new VM tumor model will be useful for defining the biological processes of cancer metastasis and for evaluating potential therapies for tumor management.

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