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The role of astrocytes in tumor metastasis

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Prain metastasis is a defining component of tumor pathophysiology, and the underlying mechanisms responsible for this phenomenon are not well understood. Current dogma is that tumor cells stimulate and activate astrocytes, and this mutual relationship is critical for tumor cell sustenance in the brain. Here, we provide evidence that primary rat neonatal and adult astrocytes secrete factors that proactively induced human lung and breast tumor cell invasion and metastasis capabilities. Among which, tumor invasion factors namely matrix metalloprotease-2 (MMP-2) and MMP-9 were partly responsible for the astrocyte media-induced tumor cell invasion. Inhibiting MMPs reduced the ability of tumor cell to migrate and invade *in vitro*. Further, injection of astrocyte media-conditioned breast cancer cells in mice showed increased invasive activity to the brain and other distant sites. More importantly, blocking the preconditioned tumor cells with broad spectrum MMP inhibitor decreased the invasion and metastasis of the tumor cells, in particular to the brain *in vivo*. Collectively, our data implicate astrocyte-derived MMP-2 and MMP-9 as critical players that facilitate tumor cell migration and invasion leading to brain metastasis.

Biography

Ramani Ramchandran has studied how astrocytes directly influence tumor cell invasion and metastasis *in vivo*. He has authored or co-authored 48 research articles/books. He serves on the editorial board of *Vascular Cell* and *PLoS ONE* journals, and is an expert reviewer for several leading journals including *Cancer Research, FASEB, Journal of Biological Chemistry, Nature, Blood, PNAS, Circulation Research,* and *Nature Communications*. He is a member of the American Association of Cancer Research in addition to other organizations. He has served on numerous review committees for the NIH, including his current membership in the VCMB study section.

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