Endogenous metabolites role in regulation of metastasis

Metastasis is frequently deadlier than the original tumor ultimately, reducing the risk or occurrence of metastasis could effectively cure or at least manage human cancer. My laboratory has carried out research that could significantly contribute to the control of malignant progression, involving the use of endogenous metabolite that is released from the extracellular matrix, which is both an endogenous angiogenesis inhibitor and anti-metastatic molecule. The signaling mechanism(s) underlying the influence of these metabolites on regulation of tumor angiogenesis is known, where as regulation of tumor metastasis are not yet known. We identified that one of the endogenous metabolite binds to different cell surface integrins, inhibits different cellular signaling in a manner distinct from that of other metabolites studied to date. Treatment of endothelial cells with this metabolite specifically inhibiting k-elastin mediated phosphorylation of FAK, Akt, mTOR and PI-3K signaling. In addition different in-vitro and in-vivo studies, we found that this metabolite possibly binding to Laminin D-III and D-IV domains and inhibits Laminin degradation by the matrix metalloprotease-14 (MMP-14), and thereby reduces the generation of different sized Laminin peptides that can bind to the EGF receptor and promote cancer metastasis, in addition to its integrin(s) mediated signaling. Our findings suggest that this metabolite interacting with different cell surface integrins and cross talking with othermolecules and inhibiting tumor angiogenesis and tumor metastasis both in-vitro and in-vivo.

Biography

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