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The Lymphatic Vascular System in Lymphangiogenesis, Invasion and Metastasis: A Mathematical Approach

There are two distinct categories of tumors: benign and malignant. Benign tumors remain confined to the tissue in which they arise and although they may continue to grow, they do not spread to other parts of the body. Unlike benign tumors, malignant tumors grow rapidly, invade and destroy the surrounding tissues and, by exploiting the blood or the lymphatic systems, establish new colonies, a process called metastasis. Metastasis is the predominant cause of cancer death. There are four major routes of neoplastic dissemination: (1) local invasion; (2) direct seeding to body cavities; (3) hematogenous spread; and (4) lymphatic spread, preferentially to regional lymph nodes and later to distant sites.

For a primary tumor to grow, it needs a supply of nutrients, delivered by the blood. The tumor therefore secrets growth factors which induce the formation of new blood vessels, sprouting them from preexisting vessels and directing them toward. the tumor. This is the process of tumor angiogenesis. Targeting angiogenesis, namely, cutting of blood supply, is one off the strategies for blocking tumor growth and dissemination.

A similar, although far less well studied process, also occurs in the lymphatic system and is referred to as lymphangiogenesis or lymphagenesis. Surprisingly, almost all of the published literature focuses on the correlations between angiogenesis, microvessel density, metastatic spread, and tumor prognosis, leaving a missed link between primary tumor and nodal metastases: the lymphatic system.The lymphatic system comprises a vascular network of one-way, open-ended, thin-walled complex network of capillaries and larger vessels, collecting vessels, lymph nodes, trunks, and ducts that transport lymph and cells from body tissues back to the circulatory system.

Various studies have shown that angiogenesis is important for solid tumour growth and, presumably, also in hematogenous metastasis. By contrast, the role of lymphatic vessels and the relevance of lymphangiogenesis to tumor pathology is less clear. Until recently only limited information concerning the molecular mechanisms and pathways involved in tumor lymphangiogenesis and tumor lymphatic invasion have been obtained

Although intensive research in tumor angiogenesis has been going on for the past four decades, experimental results in tumor lymphangiogenesis began to appear only in the last five years. In this paper we propose the first mathematical model of lymphangiogenesis, and obtain numerical results that qualitatively agree with experimental results. In conclusion, we propose the possibility to use the mathematical model presented as a possible lymphangiogenesis assay for better understandingand preventing tumor invasion and tumor lymphangiogenesis