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Cancer metastasis via lymphatic versus vascular routes from the primary site to the distant sites

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The cancer microenvironment (CM) consisting of fibroblasts, lipocytes, immune cells, lymphatic and vascular vessels and other parenchymal cells. Cancer growth is genetically dependent. Cancer cells tend to spread first through the sentinel lymph node (SLN) in most of the time, which serves as a primary gateway in which the cancer cells proliferate and spread to the distant sites. Patients with negative SLNs but develop distant metastasis later during follow-up represent those that their cancer cells have spread through the vascular system bypassing the SLNs. The cancer-immune interaction is a complex one with variation among different patients. Cancer cells may develop PD-L1 or other molecules to render the immune cells ineffective resulting in cancer growth. The emergence of such resistant cancer clones is akin to Darwin's survival of the fittest clones developing under the selective forces of the CM acting like natural selection to allow the formation of these fittest cancer clone(s) with the ability to metastasize. It is important to understand further the molecular mechanisms of cancer proliferation and metastasis via the lymphatic versus vascular channels to develop better therapeutic strategies.

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