Summary:
Members of the vascular endothelial growth factor (VEGF) family of secreted glycoproteins play critical roles in angiogenesis and lymphangiogenesis (growth of lymphatic vessels) in embryonic development and cancer. A range of mutant mouse models have indicated the importance of VEGFs for development of blood vessels and lymphatics in the embryo, thereby shedding light on several vascular and lymphatic disorders in humans. In cancer, VEGF-C and VEGF-D have been shown to promote lymphangiogenesis and metastasis via the lymphatics in a range of animal tumor models. These growth factors also promote angiogenesis and solid tumor growth when appropriately activated by proteolysis. Furthermore, extensive clinicopathological data generated over the past four years indicate that expression of VEGF-C and VEGF-D in human cancer often correlates with lymphatic metastasis and poor patient outcome. These findings suggest that the VEGF-C/D signaling pathway, that operates via the cell surface receptors VEGFR-2 and VEGFR-3 expressed on the endothelial cells of blood vessels and lymphatics, will be a useful target for development of therapeutics designed to inhibit the metastatic spread and growth of cancer. Development of such reagents and testing in a clinical setting will be high priorities for the future.