Vascular endothelial growth factor A

Vascular endothelial growth factor A (VEGF-A), also known as Vascular Permeability Factor or VEGF165, is a potent mitogenic and angiogenic disulfide-linked homodimer responsible for angiogenesis in several organs including the CNS. VEGF-A has been shown to increase extravasation of proteins from tumor associated capillaries, thus the monicker Vascular Permeability Factor. VEGF-A is part of the VEGF family of proteins which includes VEGF-B, VEGF-C, VEGF-D, and placental growth factor.

VEGF-A expression is increased by reduced blood flow and ischemia, and is involved in the growth and expansion of tumors in a cycle where tumor growth results in ischemia, which increases VEGF-A expression resulting in angiogenesis and further tumor growth. Furthermore, VEGF-A is secreted from tumors, which has made it a primary objective for development of the VEGF-A antagonist bevacizumab (Avastin, Roche). Bevacizumab is used as an adjuvant chemotherapeutic agent in the treatment of metastatic colon cancer, advanced non-squamous, non-Small-cell lung cancer, metastatic kidney cancer, and glioblastoma. VEGF-A has also been shown to play an integral part in exudative age-related macular degeneration, where choroidal neo-vascularization results in blood and protein leakage below the macular and subsequent vision loss. Exudative age-related macula degeneration is also treated with anti-VEGF-A.

This gene is a member of the platelet-derived growth factor (PDGF)/vascular endothelial growth factor (VEGF) family and encodes a protein that is often found as a disulfide linked homodimer. This protein is a glycosylated mitogen that specifically acts on endothelial cells and has various effects, including mediating increased vascular permeability, inducing angiogenesis, vasculogenesis and endothelial cell growth, promoting cell migration, and inhibiting apoptosis. Alternatively spliced transcript variants, encoding either freely secreted or cell-associated isoforms, have been characterized.

VEGF-A shows prominent activity with vascular endothelial cells, primarily through its interactions with the VEGFR1 and -R2 receptors found in prominently on the endothelial cell membrane. Although, it does have effects on a number of other cell types (e.g., stimulation monocyte/macrophage migration, neurons, cancer cells, kidney epithelial cells). In vitro, VEGF-A has been shown to stimulate endothelial cell mitogenesis and cell migration. VEGF-A is also a vasodilator and increases microvascular permeability and was originally referred to as vascular permeability factor.

During embryonic development angiogenesis is initiated as mesoderm mesenchyme cells are specified to differentiate into angioblasts, expressing the Vascular Endothelial Growth Factor Receptor (VEGFR-2). As embryonic tissue utilizes more oxygen than it receives from diffusion, it becomes hypoxic. These cells will secrete the signaling molecule vascular endothelial factor A (VEGFA) which will recruit the angioblasts expressing it's partnering receptor to the site of future angiogenesis. The angioblasts will create scaffolding structures which form the primary capillary plexus from where the local vasculature system will develop. Disruption of this gene in mice resulted in abnormal embryonic blood vessel formation, resulting in underdeveloped vascular sructures. This gene is also upregulated in many tumors and its expression is correlated with tumor development and is a target in many developing cancer therapeutics. Elevated levels of this protein are found in patients with POEMS syndrome, also known as Crow-Fukase syndrome which is a hemangioblastic proliferative disorder. Allelic variants of this gene have been associated with microvascular complications of diabetes 1 and atherosclerosis.