Angiogenesis

**Angiogenesis** is the generation of new blood vessels from pre-existing vasculature. It is a normal process in growth and development, which is required for the formation of arteries, veins, and capillaries in the embryo. Proliferation of new blood vessels also takes place in adults and is essential for the repair or regeneration of tissue during wound healing. Angiogenesis in normal tissues is a carefully regulated process, coordinated by pro-angiogenic factors such as vascular endothelial growth factor receptor (VEGFR) and endostatin respectively, to produce well-structured uniform vasculature.

### Normal Angiogenesis

Angiogenesis is also a hallmark of cancer and plays a key role in enabling tumor growth, progression and metastasis. When a tumor develops, it is size is limited by the availability of oxygen, glucose and other necessary nutrients from the existing vasculature. As a consequence of their genetic instability, tumors are heterogeneous in nature. Tumor angiogenesis can therefore differ significantly from physiological angiogenesis, producing poorly formed blood vessels with aberrant blood flow and differing permeability. In addition, factors such as a tumor’s p53 status, which regulates angiogenic cytokines, can affect blood vessel formation because p53 regulates angiogenic cytokines.

### Tumor Vascularization

Angiogenesis is a primary trigger for the growth of new blood vessels in a tumor. A hypoxic environment stabilizes HIF-1α expression. Blood flow stimulates further VEGF sensitivity. Blood flow also promotes the expression and secretion of pro-angiogenic factors, which is the most important extracellular matrix (ECM) degradation and pericyte detachment.

**Uniform Vascular Structure**

- **Tip Cells**
- **Stalk Cells**
- **Abnormal and leaky structure**
- **Tumor Cells**

**Proangiogenic proteins** are secreted from tumor cells and from VEGF-stimulated endothelial cells. They help break down the extracellular matrix (ECM) and mobilize proangiogenic proteins from the stroma. Platelet-derived growth factor receptor (PDGFR) activation stimulates the attachment of pericytes along the new vessel branch forming cell-to-cell and gap junctions, followed by basement membrane formation. Pericyte attachment reduces endothelial cell proliferation and induces VEGFR expression, leading to basement membrane degradation and pericyte detachment.

**Angiogenesis in Cancer; Pathogenesis and Drug Targets**

Angiogenesis (also known as neovascularization) is the generation of new blood vessels from pre-existing vasculature. It is a hallmark of cancer and plays a key role in enabling tumor growth, progression and metastasis. This poster discusses differences between normal angiogenesis physiology and tumor vasculature, and highlights therapeutic targets aimed at suppressing angiogenesis. Researchers are now favoring a combination of strategies, which target different stages of angiogenesis in order to prevent tumor growth and expansion.

**Tumor Vascularization - Therapeutic Targets**

A primary trigger for the growth of new blood vessels in a tumor is hypoxia. Hypoxia inducible factor 1 (HIF-1) underpins a key process of hydroxylation, which facilitates ubiquitination and its destruction. In a hypoxic environment the expression of HIF-1 is stabilized, HIF-1α associates with HIF-1β, initiating transcription by binding to the response element of HIF-responsive genes, as well as binding the co-factors p300/CREB and p53, leading to the secretion of proangiogenic factors that encourage new vessel formation. Tumors secrete several proangiogenic factors that induce endothelial cell proliferation and facilitate vessel patterning. Their receptors are very important in angiogenesis research; key targets include vascular endothelial growth factor receptor 2 (VEGFR2) and fibroblast growth factor receptor (FGFR). The most important and commonly studied pro-angiogenic factor is VEGF, which binds VEGFR2 and neuropsin, increasing vasodilation and vascular permeability. Matrix metalloproteinases (MMPs) are also secreted from tumor cells and from VEGF-stimulated endothelial cells. They help break down the extracellular matrix (ECM) and mobilize proangiogenic proteins from the stroma. Platelet-derived growth factor receptor (PDGFR) activation stimulates the attachment of pericytes along the new vessel branch forming cell-to-cell and gap junctions, followed by basement membrane formation. Pericyte attachment reduces endothelial cell proliferation and induces VEGFR expression, leading to basement membrane degradation and pericyte detachment.

**References:**

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