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 vasculization, 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.

**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 tissues during wound healing. Angiogenesis in normal tissues is a carefully regulated process, coordinated by pro- and antiangiogenic factors such as vascular endothelial growth factor receptor (VEGF) 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, its 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 altered blood flow and differing permeability. In addition, factors such as a tumor’s p53 status, can affect physiological angiogenesis, producing poorly formed blood vessels with altered blood flow and differing permeability. When a tumor develops, its 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 altered blood flow and differing permeability.

**Tumor Vascularization**

Transforming growth factor receptor (TGF β), initiates transcription of HIF-1α, which in turn activates the expression of HIF-1α, hypoxia-inducible factor 1. Hypoxia inducible factor 1 (HIF-1) undergoes prolyl hydroxylation, which facilitates ubiquitination and its breakdown. A primary trigger for the growth of new blood vessels in a tumor is hypoxia. Hypoxia inducible factor 1 (HIF-1) undergoes prolyl hydroxylation, which facilitates ubiquitination and its breakdown.

**Tumor Vascularization – Therapeutic Targets**

Matrix metalloproteases (MMPs) are also secreted from tumor cells and from circulating endothelial progenitor cells. Platelet-derived growth factor receptor (PDGFRβ) 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 cell proliferation and their sensitivity to VEGF. Finally, Notch signaling plays a key role in differentiating and shaping the new vascular network.

**Inhibition of VEGF2 Signaling**

- Block growth factor binding
- Directly block VEGF binding site
- Inhibit VEGF2 phosphorylation

**Inhibition of HIF**

- HIF inhibitor: prevents transcription

**Inhibit Pericyte Attachment**

- Small molecule
- Antibody

**Hypersprouting**

- Blood supply stimulates further proliferation and growth

**Hypoxic environment**

- HIF-1α is stabilized

**Angiogenesis in Cancer**

- Pathogenesis and Drug Targets

**Angiogenesis**

- Matrices metalloproteases (MMPs)
- Tumor angiogenesis

**Products available from Tocris**

- Small molecule
- Antibody

**Angiogenesis antibodies from our sister brands**

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