

Angiogenesis or the development of intrinsic blood supply is the essential mechanism for tumors to grow to sizes beyond 0.5 mm.

Pro-angiogenic factors are VEGF, PDGF, FGF-beta, TGF-alpha, TNF-alpha, Angiogenin, Pleiotropin, G-CSF

Anti-angiogenic factors are Angiostatin, Endostatin, Vasostatin, Interferon-beta & alpha, TGF-beta, Thrombospondin,

Anti-angiogenic agents in clinical use are:

- (1) Anti-VEGF MAb → Bevacizumab
- (2) Matrix Metallo Protease inhibitors
- (3) Thalidomide, Lenalidomide
- (4) Interferons

*Mechanism of invasion, angiogenesis & metastasis:*

Oncogenesis/ Tumorigenesis



Angiogenesis



Clonal dominance & development of invasive phenotype



Proteolysis of extracellular matrix (downregulation of E-cadherin & production of MMPs)



Penetration of vasculature



Circulating tumor cells



Tumor cell trapping & extravasation at secondary site (independent of protease activity)



Angiogenesis at metastatic foci & evasion of immune response



Growth of metastatic tumor