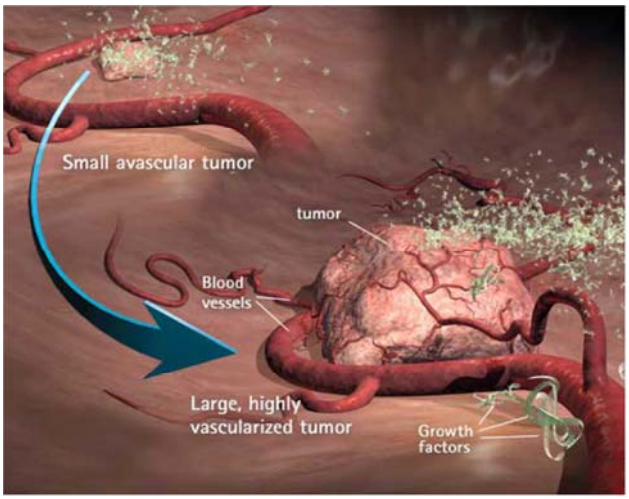
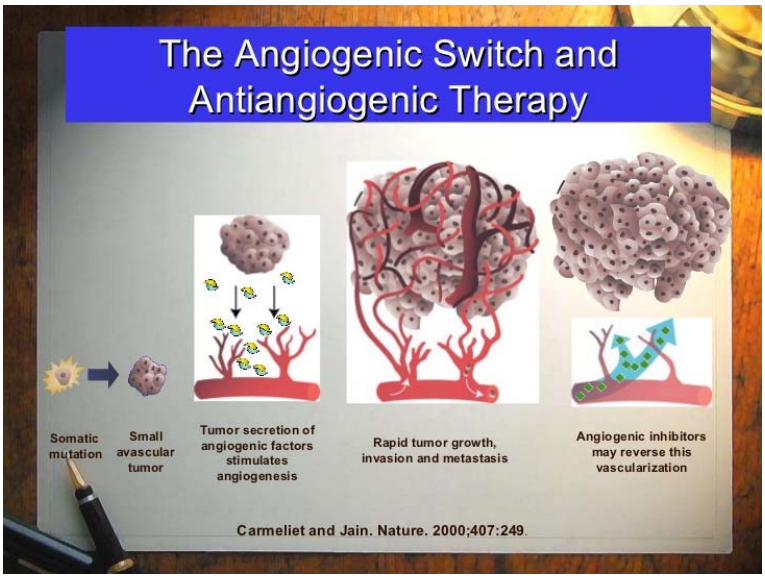


Seminario

Angiogenesi tumorale

http://www.biooncology.com/research-education/vegf/images/Angiogenesis-tumor-growth.jpg



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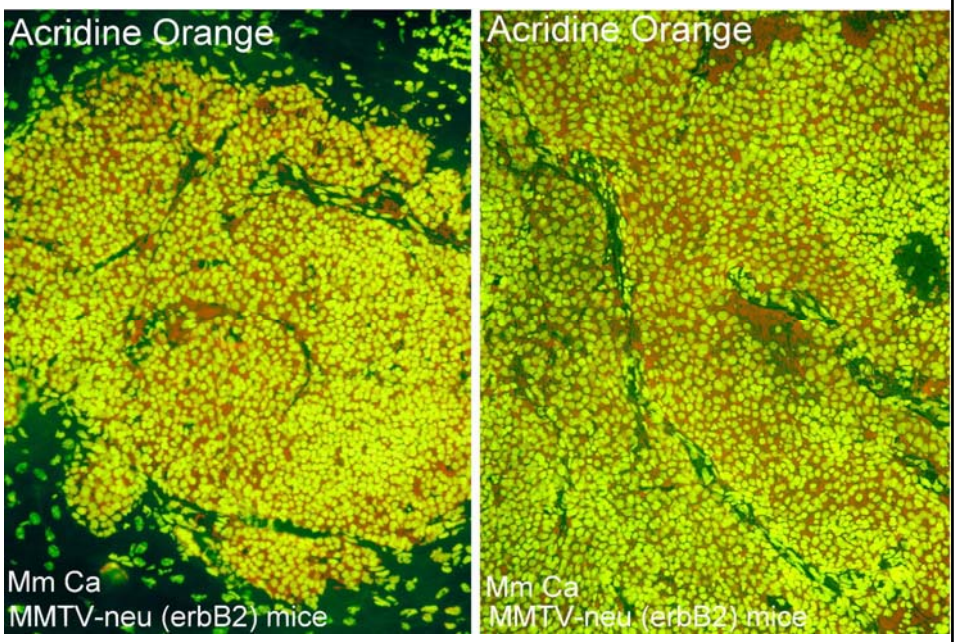
NATURE|Vol 451|14 February 2008

OBITUARY

M. Judah Folkman (1933–2008)

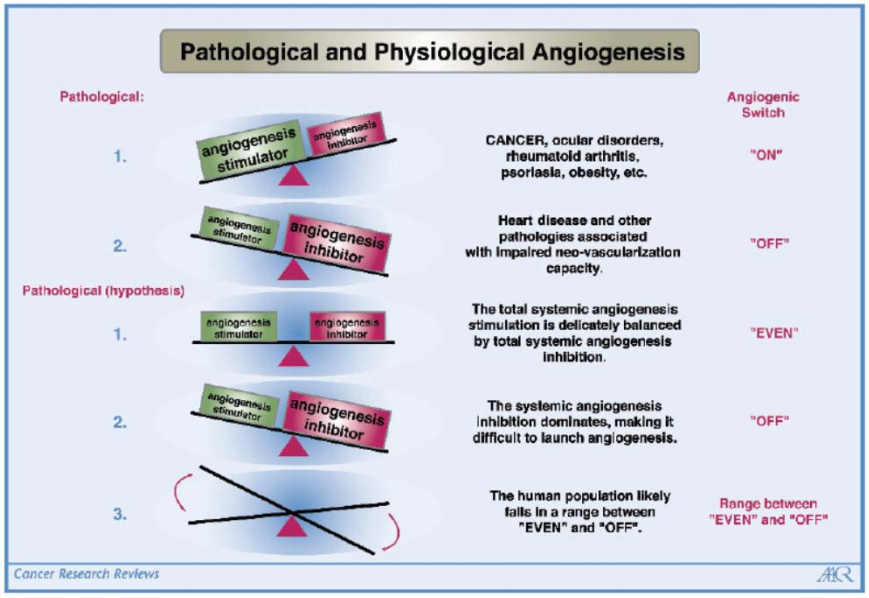
Scientist, surgeon and creator of the field of angiogenesis research.

Int. Symp. "Angiogenesis. Key principles, Science, Technology, Medicine"
St. Gallen, Svizzera, 1991 (foto di I.Freitas)

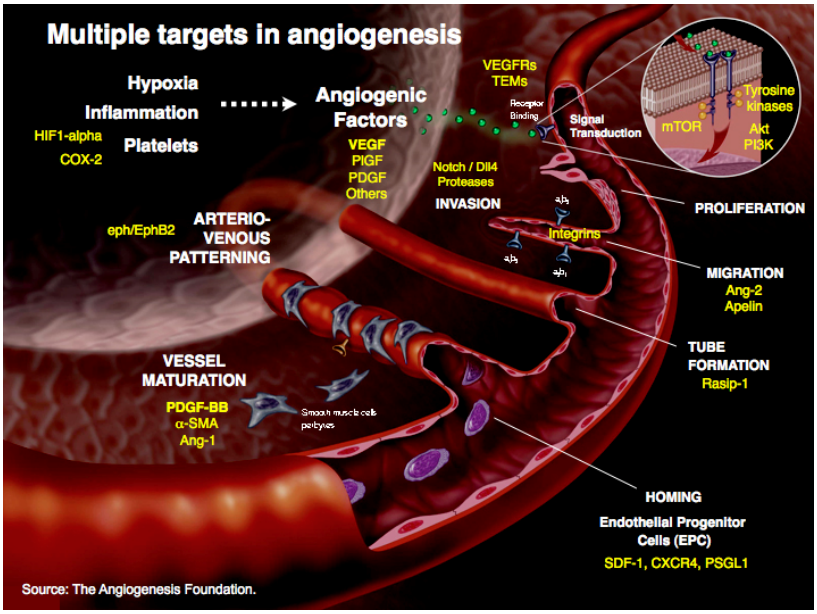


Che cosa è l'angiogenesi?

- **Angiogenesi**: reclutamento di cellule endoteliali a partire di vasi pre-esistenti.
- **Vasculogenesi**: attivazione di precursori endoteliali



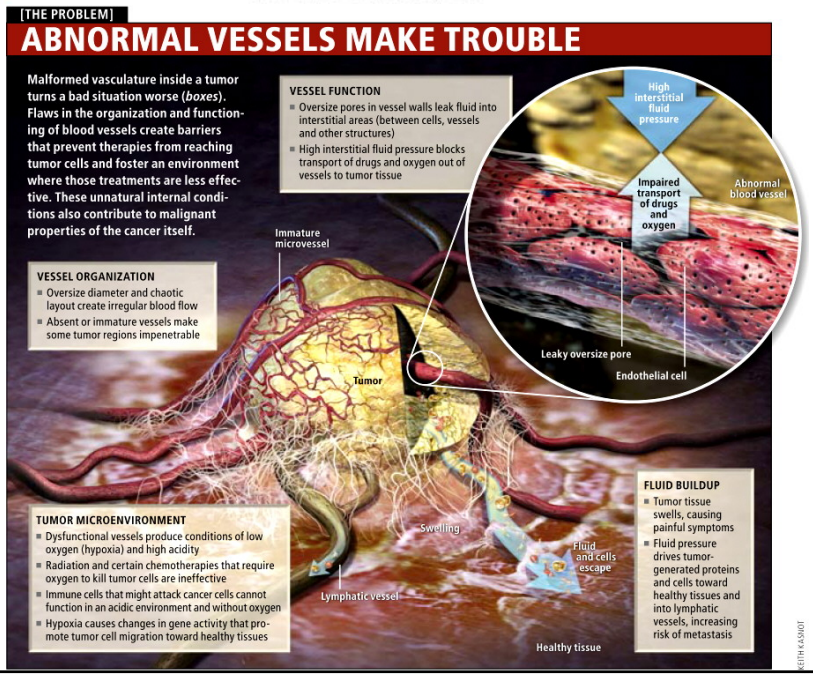
Nyberg P, Xie L, Kalluri R. **Endogenous inhibitors of angiogenesis**. Cancer Res. 2005 May 15;65(10):3967-79.



http://www.angio.org/wp-content/uploads/2013/03/Angiocascade.jpg

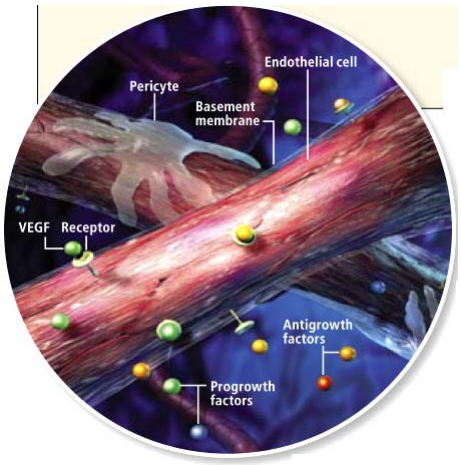
Healthy vessel	Tumor vessel
	
Well organized Defined arterioles and venules Regularly distributed Non-dilated Non-permeable Mature and coated with mural cells Low interstitial pressure Complete basement membrane Endothelial cell and mural cell Appropriate expression of markers Normal rate of blood flow	Disorganized Undefined arterioles and venules Unevenly distributed Dilated Highly permeable Premature and lack of mural cells High interstitial pressure Lack basement membrane Mosaic cells High or low expression of markers Sluggish blood flow

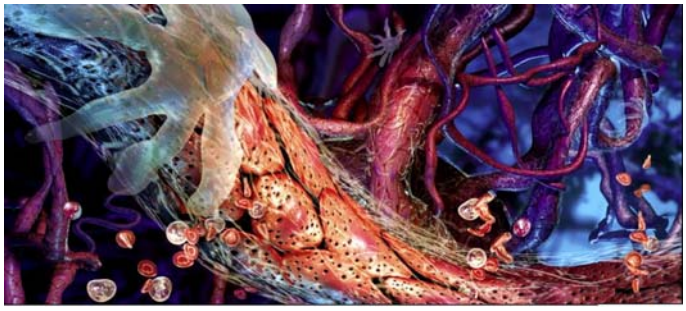
Jain RK, Sc Am, January 2008

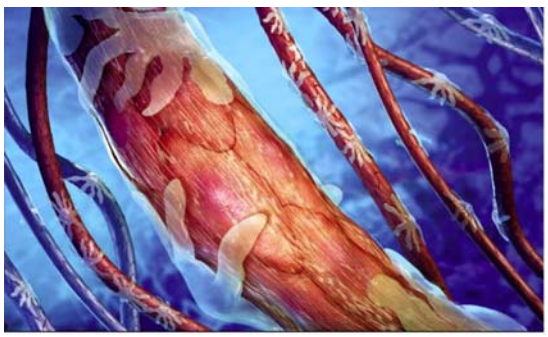


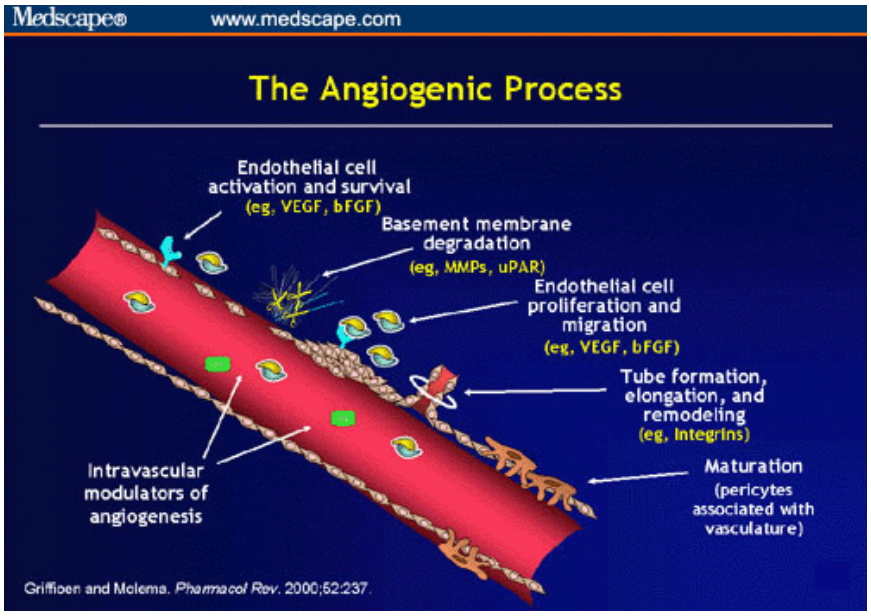
▼ **CRESCITA E MANTENIMENTO DEI VASI SANI**

Le cellule endoteliali formano vasi sanguigni in risposta ai segnali di molecole che stimolano e inibiscono la crescita. I vasi sono sostenuti dai periciti e dalla membrana basale.

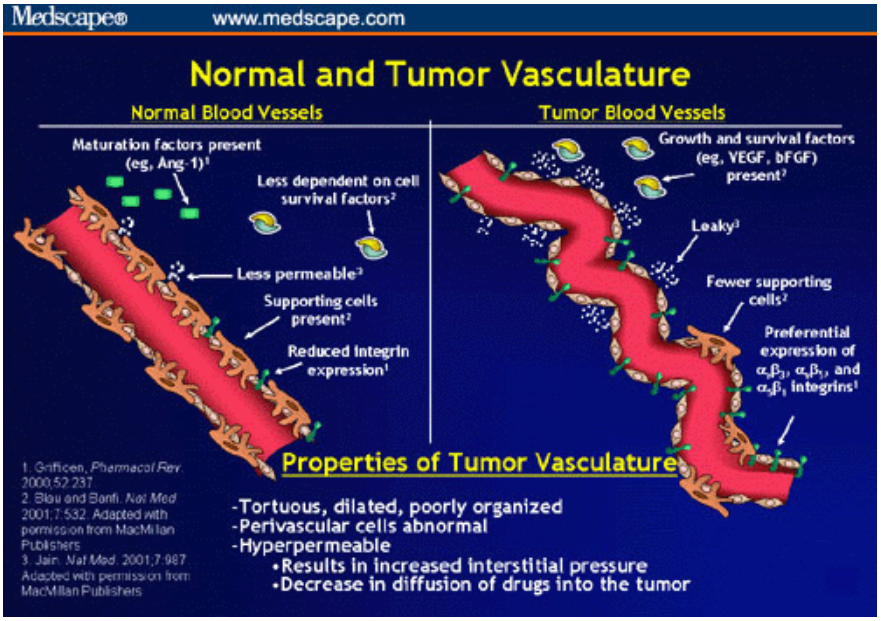






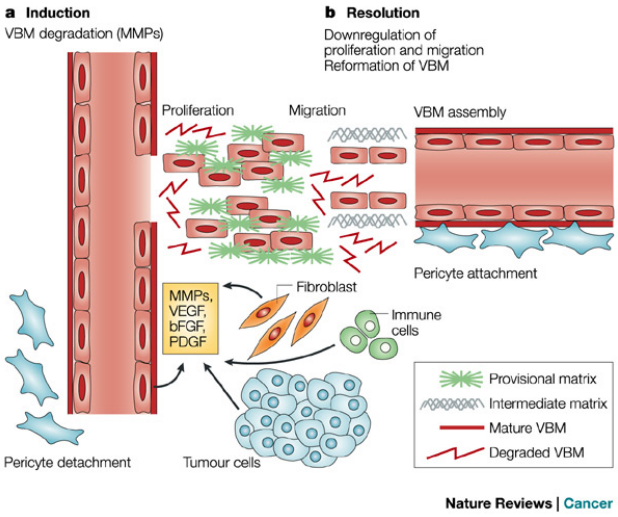


http://www.medscape.org/viewarticle/548836_3



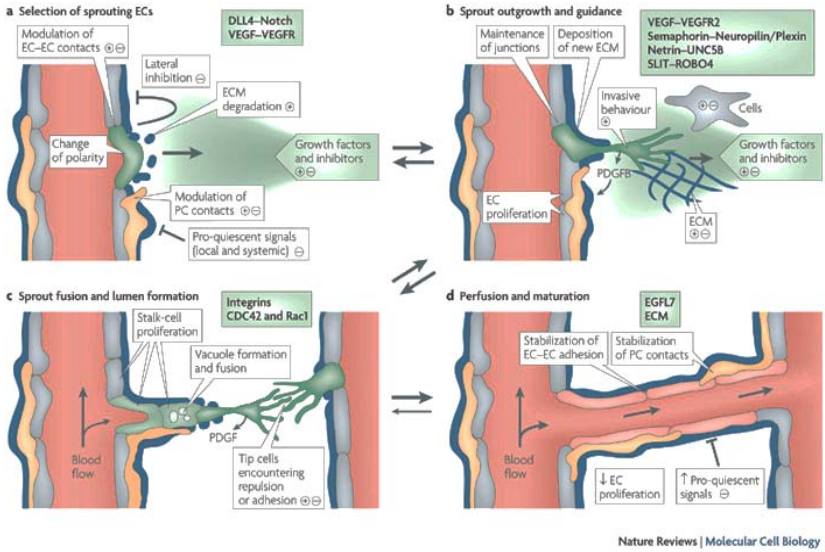
http://www.medscape.org/viewarticle/548836_3

Matrix transitions during angiogenesis

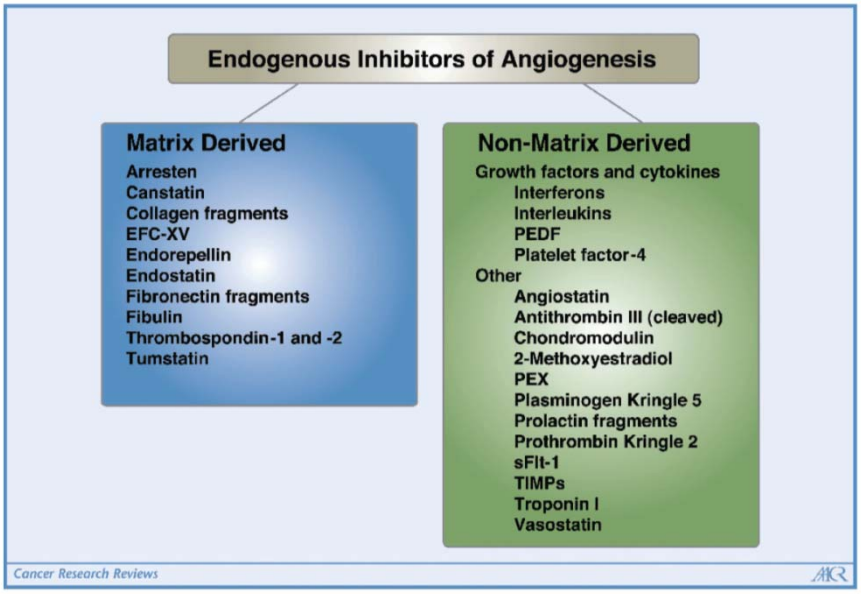


Kalluri R. **Basement membranes: structure, assembly and role in tumour angiogenesis**. Nat Rev Cancer. 2003 Jun;3(6):422-33.

Angiogenesis sprouting

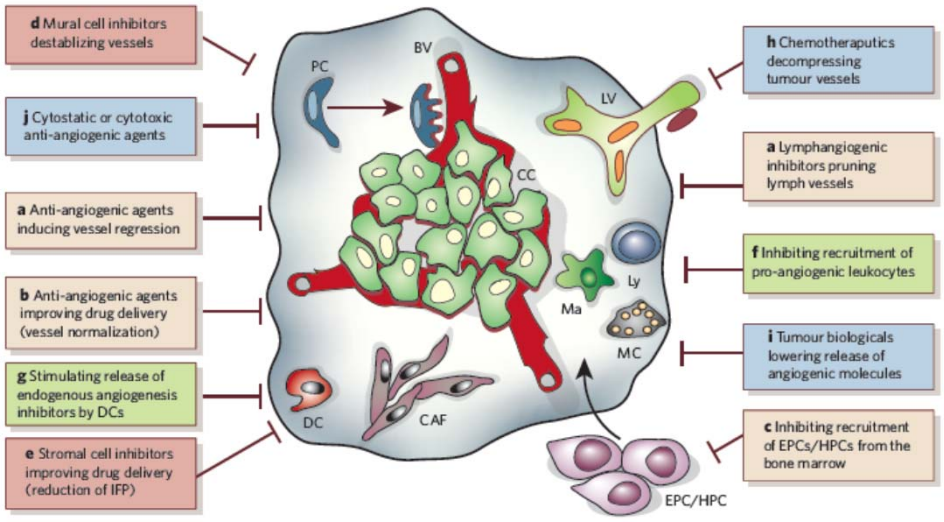


http://www.nature.com/nrm/journal/v8/n6/fig_tab/nrm2183_F2.html
Adams RH, Alitalo K. **Molecular regulation of angiogenesis and lymphangiogenesis**. Nat Rev Mol Cell Biol. 2007 Jun;8(6):464-78.



Nyberg P, Xie L, Kalluri R. **Endogenous inhibitors of angiogenesis**. Cancer Res. 2005 May 15;65(10):3967-79.

Strategies targeting endothelial and non-endothelial cells to inhibit tumour angiogenesis

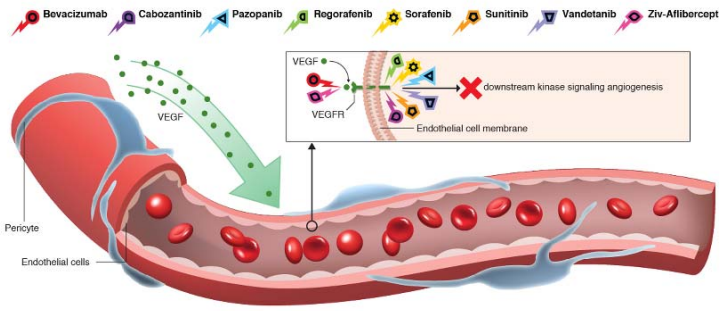


Carmeliet P. **Angiogenesis in life, disease and medicine**. Nature. 2005 Dec 15;438(7070):932-6.

Strategies targeting endothelial and non-endothelial cells to inhibit tumour angiogenesis

Tumour angiogenesis has classically been inhibited by anti-angiogenic agents that affect ECs directly. Alternative anti-tumour angiogenesis strategies target other cell types in tumours (mural and stromal cells, haematopoietic cells and tumour cells), which stimulate angiogenesis indirectly. The yellow boxes show agents (such as VEGF inhibitors, metronomic chemotherapy and other compounds) that target endothelial (progenitor) cells (EPCs); they inhibit (lymph)angiogenesis (**a**), induce vessel regression (**a**) and normalization (**b**), and block recruitment of EPCs (**c**). The red boxes show agents (such as PDGF inhibitors) that target mural and stromal cells and destabilize vessels (**d**), reduce the release of pro-angiogenic factors or progenitor cytokines, and lower the interstitial fluid pressure (IFP), which improves drug delivery (**e**). The green boxes indicate agents (such as VEGFR-1 inhibitors, chemokine antagonists and so on) that target haematopoietic cells and reduce the infiltration of pro-angiogenic bone-marrow-derived precursors and mature leukocytes (**c**,**f**), and stimulate the release of endogenous angiogenesis inhibitors in dendritic cells (**g**). The blue boxes show agents targeting cancer cells (chemotherapy, radiation, tumour-cell-targeted biologicals) that improve drug delivery by decompressing tumour vessels (**h**) and decrease the release of (lymph)angiogenic factors (**i**); some anti-angiogenic agents are also cytotoxic for tumour cells (**j**). BV, blood vessel; CAF, carcinoma-activated fibroblast; CC, cancer cell; DC, dendritic cell; LV, lymph vessel; Ly, lymphocyte; Ma, macrophage; PC, pericyte; MC, mast cells.

Carmeliet P. **Angiogenesis in life, disease and medicine**. Nature. 2005 Dec 15;438(7070):932-6.



In the U.S., there are currently thirteen approved anti-cancer therapies with recognized antiangiogenic properties in oncology. These agents, which interrupt critical cell signaling pathways involved in tumor angiogenesis and growth, comprise of three primary categories:

1) monoclonal antibodies directed against specific proangiogenic growth factors and/or their receptors; and
2) small molecule tyrosine kinase inhibitors (TKIs) of multiple proangiogenic growth factor receptors;
3) inhibitors of mTOR (mammalian target of rapamycin).

In addition, at least two other approved angiogenic agents may indirectly inhibit angiogenesis through mechanisms that are not completely understood. Finally, in the field of dermatology, there are several agents used for neoplasms of the skin.

http://www.angio.org/learn/angiogenesis/