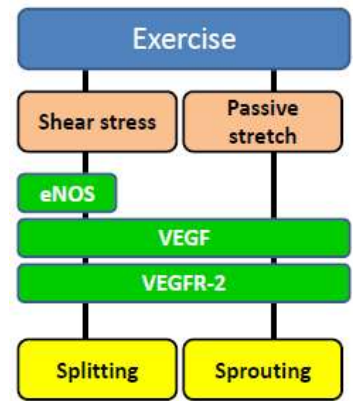


Exercise and angiogenesis in skeletal muscle

- Exercise and the contractile activity of muscle influences capillary growth
- Mechanical stretch and shear stress (flow) stimulate angiogenesis
- VEGF plays an essential role in driving capillary growth
- Shear stress primarily induces longitudinal splitting and this requires eNOS signalling
- Tissue stretch induces angiogenic sprouting
- Passive stretch also stimulates VEGF → sprouting



Pathological Angiogenesis

- Angiogenesis contributes to the pathology of inflammatory diseases and the growth and metastasis of solid tumours
- Tumour growth and hyperplasia in inflammatory disease increases the distance of cells from vessels and hypoxia drives VEGF production
- Chronic hypoxia giving rise to high levels of VEGF and inflammatory cytokines create a pro-angiogenic environment
- Vessel formation is abnormal leading to leaky and poorly perfused vessels and persistent hypoxia
- The leaky vessels facilitate leukocyte extravasation in inflammatory disease
- In tumours/inflammation the vessels aren't very organised because there is constant VEGF. Vessels are also very leaky.

Angiogenesis in Rheumatoid Arthritis

Modulating angiogenesis – inhibiting VEGF signalling

- Monoclonal antibody to VEGF
 - Bevacizumab. Avastin
 - Treatment of cancer and diabetic retinopathy
- Soluble receptor
 - VEGF trap/ aflibercept
- Small molecule inhibitors of VEGFR
 - Cancer treatment
- Antibody blocking binding of VEGF to receptor
 - IMC1C11

Promoting angiogenesis in ischaemic Disease

- E.g. atherosclerosis
- Promoting angiogenesis has the potential to re-vascularise ischaemic tissue.

Assessing angiogenic sprouting – the spheroid assay

Assessing angiogenic sprouting – the co-culture assay

- Fibroblast produce extracellular matrix and secrete VEGF
- Co-culture fibroblasts with endothelial cells, then image tubule formation
- Can add VEGFR-2 inhibitors to see difference.
- FGF-2 is added to the co-culture

Can use a zebrafish to investigate the function of genes in angiogenesis in vivo