Imaging angiogenesis

Michal Neeman, Department of Biological Regulation, Weizmann Institute of Science, Rehovot 76100 Israel. Email michal.neeman@weizmann.ac.il

Angiogenesis, the growth of new blood vessels, and lymphangiogenesis, the expansion of lymphatics, are an important component in the development of new multicellular tissues, both normal and pathological. Blood and lymphatic vessels are essential for maintaining tissue homeostasis, and thus angiogenesis is activated during pregnancy at the site of fetal implantation, placentation and fetal development. During post-natal development, angiogenesis accompanies learning and synaptic plasticity in the brain, muscle and bone development in response to training and burden and is induced in the reparative response to injury in wound healing and inflammation. Angiogenesis also accompanies and contributes to diverse pathological processes ranging from diabetes and cardiovascular disease, including atherosclerosis, stroke and infarcts to cancer and metastasis.

The process of angiogenesis utilizes orchestration of multiple growth factors and participation of many cell types, showing large overlap in basic mechanisms between the various angiogenic processes. Due to the need to maintain homeostasis, microenvironmental signals including oxygen and glucose provide important signals for regulating the expression of angiogenic growth factors. Of notable importance is the role of hypoxia in inducing the expression of vascular endothelial growth factor (VEGF) via the stabilization of hif-1. Vascular sprouting and expansion is achieved through proliferation, migration and tube formation by endothelial cells. During this plasticity period the vasculature is hyperpermeable and shows elevated expression of alphaVbeta3 integrins. Alterations of the extracellular matrix include degradation of collagen and hyaluronan and deposition of fibrin. Subsequently, maturation of the vessels occurs via recruitment and association with perivascular contractile mural cells including smooth muscle cells and pericytes, which allow vasoreactivity. During this phase endothelial cells generate adherens junctions through expression of VE-cadherin to help maintain patency of the vasculature.

Imaging tools such as MRI, CT, PET, ultrasound and optical imaging, enable us to probe the vascular bed at all stages of remodeling, providing access to the structure and function of the vessels. Over the last decade new contrast media (CM) were developed also for probing the expression of cell surface markers, the changes in the ECM and the recruitment of cells to sites of angiogenesis. In addition, non invasive imaging provides dynamic functional and anatomical information on the growing vasculature.