Spheroid-Based *in vivo* Angiogenesis Model

ProQinase
TARGETING CANCER

Angiogenesis

Angiogenesis, the formation of new blood vessels from pre-existing ones, is a physiological process during growth and development. Beyond that angiogenesis is mandatory for tumor growth and is involved in other pathological disorders (e.g. psoriasis, macular degeneration). The complexity of the angiogenic cascade limits cellular approaches towards the study of angiogenic endothelial cells (EC). In turn, both developmental as well as adult manipulatory *in vivo* assays are complex, multicellular and do not include human endothelial cells. The spheroid-Based in vivo Angiogenesis Assay takes advantage of human EC spheroids which form the basis for the development of a functional human vasculature in mice.

Assay procedure

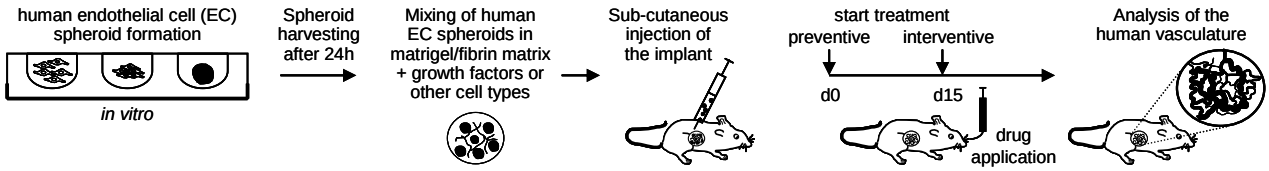
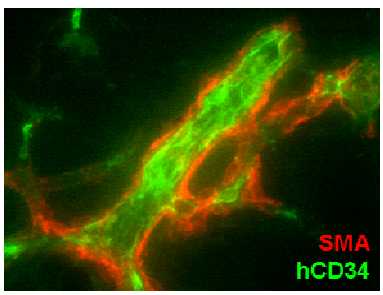


Figure 1: *Assay procedure. Human EC spheroids are mixed in a matrigel/fibrin matrix which is subcutaneously injected in SCID mice. The matrix mixture contains VEGF-A/FGF-2 or fibroblasts/smooth muscle cells (SMC) for human EC stimulation. The treatment may be started directly after implant injection (preventive study) or after a more mature human vasculature is established (interventive study). Finally, the matrix plug is removed and analysed for human microvessel density. Additional readouts like pericyte-coverage or perfusion are possible.*

Assay features

Figure 2: *Assay features. Human EC form a human vasculature that develops anastomoses with the mouse vasculature upon stimulation with VEGF-A/FGF-2 or addition of fibroblasts/SMCs. The first perfused vessels are detectable at day 4 to day 6. After 20 days of in vivo growth a well established vasculature with around 40 - 60 % pericyte-covered and perfused vessels is established [1].*



[1] Alajati, A et al.(2008) Nat Methods. **5(5)**: 439-45

Study example

Figure 3: *Study example. Compound 1 and antibody 1/2 were tested in the cellular Angiogenesis Assay showing a differential inhibition pattern (left). The human microvessel analysis in the spheroid-based in vivo Angiogenesis Assay revealed a similar inhibition pattern with a strong efficacy for compound 1 and antibody 1 and a moderate effect for antibody 2 (right).*