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Characterization of pathological angiogenesis in the KLEIP knockout mouse model

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Pathological angiogenesis forms the basis for a wide range of diseases, including cancer and sight-threatening corneal infections. KLEIP, or KLHL20, is an intracellular protein contributing to VEGF-mediated endothelial cell sprouting and corneal epithelial phenotype regulation. In this thesis, I investigated two different aspects of pathological angiogenesis in KLEIP deficient mice. First, I performed an allograft tumor assay and assessed microvascular density in tumors grown in KLEIP$^{-/-}$ and KLEIP$^{+/+}$ mice. I could show that although KLEIP is known to be indispensable for VEGF-mediated endothelial cells sprouting *in vitro*, it is not needed for tumor vascularization *in vivo*. To analyze tumor vessels in histopathological sections, I wrote an automatic image-analysis algorithm which could also be used in the clinic.
Second, I investigated molecular mechanisms of corneal neovascularization in KLEIP$^{-/-}$ mice. KLEIP knockout yields a corneal epithelial and stromal phenotype in mice, which is associated with corneal neovascularization and, ultimately, blindness. Using immunohistology and microarray analysis, I discovered a previously unknown miR-204 – angiopoietin-1 pathway that promotes corneal neovascularization independently of VEGF. This novel pathway could be used for targeted, VEGF-independent anti-angiogenic treatment, which is urgently needed for the treatment of patients.