Apelin- and VEGF-signaling cooperate to promote Angiogenesis

Annegret Rittershaus & Christian S.M. Helker

Cell Signaling and Dynamics, Faculty of Biology, Philipps-University Marburg, 35043 Marburg, Germany

The G protein-coupled receptor (GPCR) Apelin receptor (Aplnr) and its ligand Apelin (Apln), are expressed in newly growing blood vessels. Mouse and zebrafish knockout animals for Apelin or Apelin receptor exhibit similar vascular defects. The molecular mechanism of how Apelin-signaling regulates angiogenesis and how Apelin-signaling is integrated into other pro-angiogenic pathways is not known.
In zebrafish, mutant embryos for the *aplnr* and for the *kinase insert domain receptor like (kdrl, vegfr2)* phenocopy each other. To analyze if Apelin and Vegf signaling genetically interact, we generated double mutants for *aplnr* and *kdrl*. Double heterozygous mutant embryos for *aplnr* and *kdrl* as well as double homozygous mutant embryos exhibit a more drastic phenotype compared to their single heterozygous or homozygous siblings. However, expression analysis of *aplnr* in *kdrl* mutants and vice versa by *in situ* hybridization showed no significant difference in expression levels in comparison to wildtype siblings. This leads us to speculate, that Apelin- and Vegf-signaling interact on the level of downstream effectors rather than a regulation on the transcriptional level. Based on our findings we conclude that Apelin- and Vegf-signaling genetically interact.