In vivo analysis of collective endothelial cell migration

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Collective endothelial cell migration is a crucial process during vascular development that requires precise intercellular control and coordination. The communication between adjacent cells within a migrating cellular cluster is regulated via cell-cell junction molecules. In this project, we describe the control of cellular guidance by the adherens junction molecule vascular endothelial cadherin (VE-Cadherin) during collective migration of developing blood vessels in the zebrafish embryo. We show that loss of VE-Cadherin function leads to compromised migration directionality accompanied by changes of endothelial cell polarity in the common cardinal veins (CCVs). Furthermore, deficiency in VE-Cadherin results in loss of collective characteristics and represents a switch in migration behavior from a coordinated multicellular behavior to a unicellular individual migrating cell.
Downstream of VE-Cadherin induced guidance signaling we identified the Rho-Kinase ROCK that controls polarized actin polymerization and therefore in turn regulates endothelial migration behavior in the collective. Our experimental setup encompasses live imaging techniques and time-lapse imaging of developing zebrafish embryos. By comparing *in vivo* data from zebrafish to our *in vitro* model using cultured human umbilical vein endothelial cells (HUVECs), we show that the characteristics that define collective cell migration are equally present and required for migration and polarity and equally dependent on VE-cadherin signaling. We are furthermore using FLIM-FRET in order to quantify the activity of the Rho-Kinase ROCK *in vitro* and will apply it to migrating zebrafish endothelial cells in the future. In summary, we present novel mechanistic insights on how adherens junction proteins provide migrative guidance information to single endothelial cells that are part of a collective cluster.