Kinase suppressor of Ras-2 regulates endothelial cell migration and angiogenesis

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The Ras/Raf/MEK/ERK pathway is required for endothelial cell function during angiogenesis. In particular, *in vitro* and *in vivo* studies implicate ERK1/2 in endothelial cell survival, migration and angiogenesis. KSR (kinase suppressor of Ras) was originally identified as a novel protein kinase evolutionarily conserved in Drosophila and Caenorhabditis elegans that function between Ras and Raf in the Ras signalling pathway. At the present two distinct isoforms of KSR are described (KSR-1 and KSR-2). Both proteins act by forming a complex with Raf and ERK1/2 that is necessary for Ras signal transduction, however certain differences have been identified. KSR-1 has been described to be important in immune system, adipogenic differentiation, replicative senescence and tumor growth, and KSR-2 is reported to interact with the protein phosphatase calcineurin, to promote tumor cell transformation by AMPK activation and to induce calcium mediated ERK 1/2 activation. In this work we investigated the role of KSR-2 in endothelial cell migration. Deletion of KRS-2 in endothelial cells resulted in decreased cell migration and sprouting formation. AlphaV/betaIII integrin and Focal Adhesion Kinase were expressed at lower levels in endothelial cells lacking KSR-2, leading to defects in the organization of the cytoskeleton and in cell motility. Our data suggest that KSR-2 might play a role in the molecular and functional effects of angiogenic growth factors.

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