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CXCL12/CXCR4/CXCR7 axis regulates microvessel growth in human developing cerebral cortex

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Chemokine CXCL12 (also called stromal-derived factor-1, SDF-1) together with its cognate receptors CXCR4 and CXCR7 represents a well characterized chemokine system in developing and adult CNS, being involved in axonal pathfinding and neuronal regeneration [1]. Moreover it has been recently demonstrated that a distinct subpopulation of glioma cells express high levels of CXCR4, which promote tumor angiogenesis and vasculogenesis and correlates with an advanced state of the disease [2,3]. We have disclosed cell expression and localization of this chemokine ligand/receptors system in human foetal cerebral cortex during vessel growth and blood-brain barrier differentiation. Stem vessels, which penetrate the future cerebral cortex by sprouting from the perineural plexus, grow radially into the tissue and start to branch by angiogenic mechanism in the subcortical layers. During both vascular sprouting and elongation, high levels of CXCL12 and CXCR4/CXCR7 are detected on glio-vascular components of developing brain. CXCL12 is expressed by radial glia cells, perivascular astrocytes, and angiogenically activated CD105+ endothelial cells, which also express the receptor CXCR7. A detailed analysis of sprouting microvessels reveals CXCL12+/CXCR7+ stalk endothelia together with endothelial tip cells enriched in CXCL12 and CXCR4. This receptor also prevails on tip-associated pericytes, whereas CXCR7 is preferentially expressed by pericytes accompanying endothelial stalk cells. These findings of a cell-specific expression of CXCL12 and its receptors by perivascular glial cells and sprouting microvessels indicate that activation of the ligand/receptor signalling axis may account for an autocrine/paracrine differential control of endothelial proliferation/migration and pericyte recruitment and stabilization.

References

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