IJAE
Vol. 118, n. 2 (Supplement): 195, 2013
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Emerging roles of CXCL12-bearing microvesicles in glio-vascular communication during human brain development

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The CXC chemokine axis formed by CXCL12 and its receptors CXCR4/CXCR7 is involved in CNS development enhancing migration and differentiation of neuronal precursors [1, 2]. According to these data, our recent studies have demonstrated that during human cerebral cortex development, radial glia (RG) cells express high levels of CXCL12, which finds its receptor on migrating postmitotic neuroblasts [3]. Moreover, during this first survey we have also revealed the ligand concentrated in RG processes and in astrocyte endfeet in contact with the microvessel wall. Features and distribution of these glio-vascular contacts have been further studied to ascertain the possible involvement of the glial CXC ligand/receptor system in vessel growth and differentiation. The study was carried out on human telencephalon by laser confocal and transmission electron microscopy to detect the expression of chemokine CXCL12 together with specific glio-vascular markers and reveal subcellular details of the identified cell structures. Immunolabelling for CXCL12 showed the highest level of RG CXCL12-enriched vascular contacts in the subcortical layers, where the chemokine concentrated in small swellings that appeared at intervals along the RG fibres. These RG varicosities formed *en passant* vascular contacts or asymmetrical enlargements that were seen to specifically bent and come in contact with the vessel wall. At the highest confocal resolution, both symmetrical and asymmetrical RG varicosities appeared filled with CXCL12 labelled dot-like structures that have been regarded as cell microvesicles (MVs). Their vesicular nature was confirmed by ultrastructural observations that allowed to recognize small membrane-bound MVs gathered in RG perivascular varicosities. Aspects of CXCL12 MV shedding also appeared a common feature of these specialized glio-vascular contacts confirming the hypothesis that RG-derived CXCL12 can be conveyed to the recipient vascular cells participating in glio-vascular communication and coordinating neuro-vascular interactions during cerebral cortex development and vascularization.

References

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Key words
CXC chemokines, cell-cell communication, microvesicles, brain vascularization.