

CXCR4/SDF-1 α -chemokine regulates neurogenesis and/or angiogenesis within the vascular niche of ischemic rats; however, does SDF-1 α play a role in repair?

Cell-based treatment of stroke-mediated neuronal progenitor (NPC), and bone marrow stromal cells (BMSC) has shown promise in cerebral ischemia. Transplantation of NPCs after experimental stroke has been demonstrated to improve functional recovery, reduce apoptosis, and enhance angiogenesis and neurotrophic factor release. Furthermore, the stem cells can differentiate into other cells and promote endogenous cell proliferation and axonal remodelling (1, 2). New stroke therapies based on the protective effects of cerebroprotective drugs seem to ameliorate the deleterious inflammatory responses in animal models of focal cerebral ischemia (3). However, how does altered inflammatory response contribute in balancing the interplay between neurodegeneration and regeneration?

Notable advances have been made in understanding the basic cellular mechanisms through which chemokines (chemotactic cytokines) recruit leukocytes to damaged areas of the central nervous system; new roles for these cytokines as neuropeptides and/or neuromodulators are emerging (4). Chemokine stromal cell-derived factor (SDF-1 α) the ligand for CXCR4 α -chemokine receptor is expressed by glia and neurons and has a dual role in neurodegeneration and/or neuroprotection (4). It can potentially promote neurogenesis within the neurogenic zones (neurovascular niches) to counteract local damage in the penumbra area after cerebral ischemia (5). After the initial ischemic response, hypoxia activates

CXCR4 in endothelial and microglial cells in the brain. In these conditions, CXCR4/SDF-1 cell signalling pathways promotes neural progenitor migration toward peri-infarct areas several days after the injury (1, 6). The resulting angiogenesis might promote neural plasticity and enhances vascular re-growth after experimental stroke, inducing repair (1) and improving functional outcome via SDF-1/CXCR4 chemokines (6, 7). Interestingly, a cross-talk between angiogenesis and neurogenesis SDF-1/CXCR4 dependent levels may enhance BMSC entry into the ischemic brain (6–8). Cerebroprotective drugs such as simvastatine improve functional outcome by increasing SDF-1/CXCR4 chemokine levels after stroke and would allow neurogenic and angiogenic responses within damaged areas in ischemic rats that are simvastatine and/or BMSC treated (6, 8). These neurogenic effects are in consonance with new reports in which systemically transplanted BMSCs promote SDF-1 α /CXCR4-mediated migration toward the ischemic brain lesion in a rat model (9).

One common factor in the different environments where vasculogenesis is believed to occur is the presence of a hypoxic stimulus and progenitor homing in response to hypoxia-inducible factor 1 (HIF-1)-regulated hypoxia; HIF-1 regulates SDF-1 α level mediating progenitor cell recruitment to injured tissue (10). Recent evidences are important from a translational viewpoint as the transplanted neural stem cells express HIF-1, a cue molecule involved in regeneration and neovascularisation, and induce behavioral recovery in the rat stroke model (11). In addition, CXCR4 expression is important for cell migration and recruitment, suggesting that the expression levels of CXCR4 may be correlated with the functional activity of implanted cells to promote neovascularisation (9). These observations are in consonance with Li *et al's* (5) studies. These authors reported neurovascularization with MsCh bone de-

rived by CXCR4+ progenitors that differentiate into endothelial cells capable of inducing vascular repair after arterial injury (6). Consequently, CXCR4 expression levels could be a predictive marker of endothelial colony forming cell therapy in injured arteries (9). As such, ischemic tissue may be a conditional stem cell niche, in which recruitment and retention of circulating progenitors by SDF-1 α would be regulated by hypoxia (6–7, 10). It could be suggested that hypoxia may be a fundamental requirement for progenitor cell trafficking and function as endothelial expression of SDF-1 acts as a chemotactic signal, indicating the presence of tissue ischemia and its expression is directly regulated by HIF-1 (10, 11). A recent study by our research group has shown brain protective strategies based on stem cell delivery (12) or cerebroprotective approaches (EPO and/or porcine brain-derived peptide) may promote neuroplastic and antiapoptotic effects by regulating CXCR4/SDF-1 α -chemokines in the injured cortex of ischemic rats (6–7, 13). Further studies will analyze whether porcine brain-derived peptide effects may promote neural progenitor cell migration and/or regulate neuroblast migration toward damaged areas in the ischemic cortex through CXCR4/SDF-1 cell signalling in a rat model of embolic middle cerebral artery occlusion. Consequently, the promotion of novel self-repair strategies based on stem cell recruitment by SDF-1 α may counteract cell death and improve recovery in the injured cortex of ischemic rats (6, 13, 14)

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Conflict of interest: None declared.

Funding: This work was supported by a grant from Ramon and Cajal Research Program to J. J. M. (Spain).



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DOI: 10.1111/j.1747-4949.2011.00651.x

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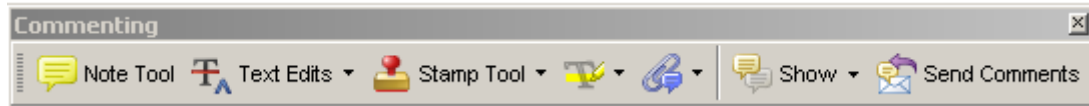
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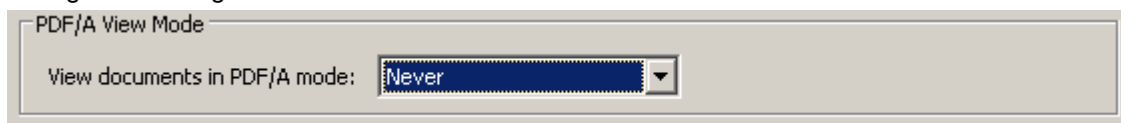
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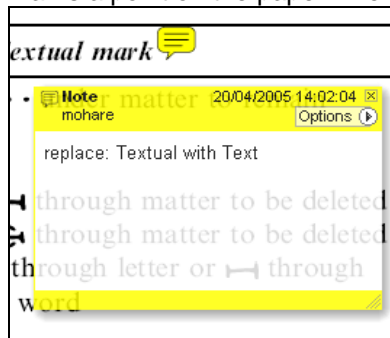
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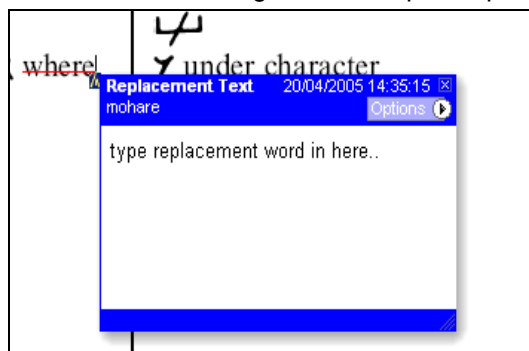


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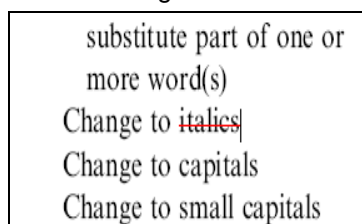


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How to use it:

1. Select cursor from toolbar
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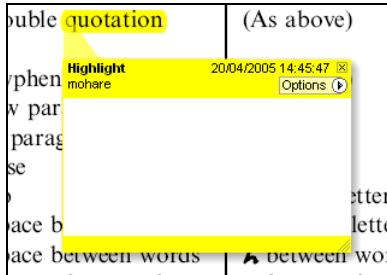


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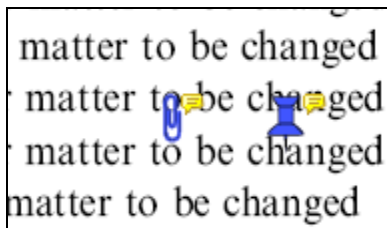


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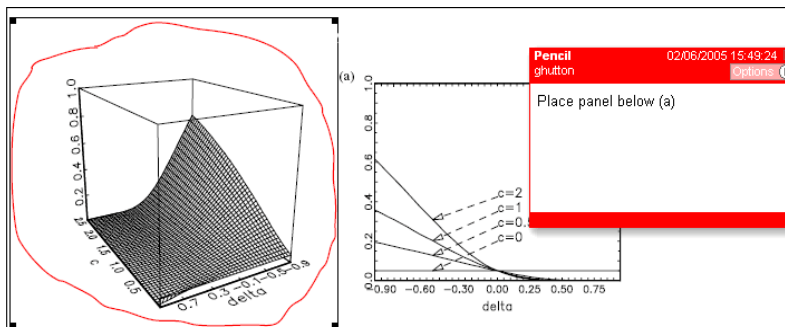


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