

## CXCR4: A Potential Chemokine Receptor for Future Regenerative Therapeutic Target

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### Summary

Understanding the molecular mechanisms in regeneration could help the stem cell therapists to improve the clinical practices and could be considered a major milestone in the translation of stem cell research to clinics. Chemokines have been described as one of the most significant signaling networks in stem cells homing and regeneration of damaged organs. CXCR4/CXCL12 has been known as a key player in this regard. Expression of CXCR4 has been observed in a number of cells such as mesenchymal stem cells, epithelial cells etc and plays crucial and unique role in the migration of cells towards a cytokine gradient and regulating stem cells trafficking as well as tissue/organ regeneration and embryogenesis.

**Keywords:** Chemokine, CXCR4, Stem cell therapy, Regenerative Medicine

### Dear Editor...

Damaging of tissues and organs by traumatic injuries and various diseases is a current big challenge for clinical researchers and practitioners to deal with it. Considerable developments in regenerative medicine have been seen in last decade as the researchers focused their attentions toward regenerative protocols for lost or damaged organ (Mao and Mooney, 2015).

A number of signaling pathways are involved in regeneration and development among which CXCR4/CXCL12 has been described as a key pathway in leukocyte trafficking, angiogenesis, inflammatory disorders, cancer and HIV pathology. Interaction between CXCR4 and its chemokine CXCL12 induces different downstream signaling such as cell survival, proliferation and chemotaxis (Vidaković et al., 2015). Therefore, due to the significance of CXCR4, targeting this cytokine for clinical research could create a hope for regeneration of damaged tissues. In contrast to other chemokine receptors, CXCR4 primarily functions in the immunity and regulation of inflammation through its expression in leukocytes (Hauser et al., 2002).

CXCR4 is also expressed in a variety of mesenchymal stem cells and epithelial tissues and plays crucial and unique role in the migration of cells towards a cytokine gradient and regulating

stem cells trafficking as well as tissue/organ regeneration and embryogenesis (Naderi-Meshkin et al., 2015a). Stem cells have been described as the key agents of regenerative therapies but their escape after transplantation is a continuous challenge being faced. Stem cell homing is a multistage process similar to the leukocytes migration towards injury sites (Kucia et al., 2004). CXCR4/CXCL12 pathway plays role in the repair of different damages by promoting the migrational stem cells, such as attracting stem cells to the burnt injury sites and injured liver, accelerating wound healing to skin injury sites, repairing infarcted hearts and promoting repair of the injured kidney (Ghieh et al., 2015; Li et al., 2015a; Li et al., 2015b; Ling et al., 2016). It has been described that CXCR4 expression and cells homing to repair damaged tissue decreased following culture (Naderi-Meshkin et al., 2015b).

Dear editor, so far various therapeutic strategies such as treatment with chemical compounds, hypoxia, cytokines, growth factors and genetic modifications have been used to enhance the expression of CXCR4 to get enhanced efficacy in stem cells homing (Naderi-Meshkin et al., 2015a). Stem cell therapy has attracted researchers around the world, and a huge work has been done in this regard, however, but there is very rare clinical trials

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investigating the role of CXCR4 in tissue regeneration focusing its role in stem cells recruitment to the sites of injury and their maintenance. Considering the current reports mentioned in this letter, it could be concluded that CXCR4 is going to be the next therapeutic target but its efficiency and safety in regenerative therapy, has not been approved due to the lack of clinical data. Therefore, focusing CXCR4 in clinical trials of regenerative therapies will open the windows of possibilities to replace lost or damaged organs

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