



# A Response to Article “Hypoxia Effects in Intervertebral Disc-Derived Stem Cells and Discus Secretomes: An in vitro Study” [Letter]

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## Dear Editor

We appreciate the authors who have reported their research in “Hypoxia Effects in Intervertebral Disc-Derived Stem Cells and Discus Secretomes: An in vitro Study”, published in *Stem cells and Cloning: Advances and Applications* 2022;15:21–28. This is very important information about hypoxic preconditioning in mesenchymal stem cells/MSc for degenerative disease therapy.<sup>1</sup>

In this study, the authors reported that 3% oxygen (O<sub>2</sub>) levels could increase the secretion of growth factors, especially fibroblast growth factor/FGF and platelet-derived growth factor/PDGF, meanwhile, increased secretion of transforming growth factor/TGF-β1 needed higher oxygen level (5%). These findings indicated that MSc could secrete various growth factors according to environmental conditions, including oxygen levels or hypoxic preconditioning. This means that O<sub>2</sub> levels can facilitate MSc to produce growth factors according to specific purposes. For example, TGF-β1 acted as an immunosuppressant to overcome inflammation and accelerate cell regeneration.<sup>2</sup> However, if the experiment goal was to increase cell proliferation which is strongly influenced by FGF and PDGF, then hypoxia 3% O<sub>2</sub> is recommended.

Stem cells in this study were isolated from intervertebral disc-derived stem cells/IVDS. Currently, many researchers are interested in the potential of IVDS to address the degeneration problem in the intervertebral disc. Unfortunately, this study did not report the characterization of their stem cells, therefore we could not precisely estimate the purity of stem cells in the cell population. Characterization of stem cells could provide information about the type of stem cells that produced these growth factors (FGF, PDGF, VEGF, and TGF-β1).

Other studies have reported that cytokines and growth factors secretion from MScs originating from gingival, adipose tissue, umbilical cord or Wharton’s jelly tend to increase in a hypoxic microenvironment.<sup>3–5</sup> Upregulation of pro and anti-inflammatory cytokines and chemokines can certainly be used as immunomodulators.<sup>5</sup> Increased neurotrophic factor would be very beneficial for nerve cell regeneration.<sup>3</sup>

More information about the sources of stem cells, and the methods of obtaining the secretome containing cytokines, chemokines, and growth factors, they would be very useful as evidence for translational research from in vitro and pre-clinical research toward clinical trial settings.

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## Disclosure

The authors report no conflicts of interest in this communication.

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