

Respond to reviewer 1:

Dear Reviewer,

Thank you for your friendly review to my manuscript. According to your advice, I have revised my manuscript.

Yours sincerely,

Baogan Peng

“The common causes for chronic low back pain are disc degenerative diseases.” A common cause? I think your comment is correct. I have changed ‘The common causes’ to ‘A common cause’.

“These growth factors acted on the intervertebral disc cells which separated from the circulatory system...” “which are”?

“, and promoted disc cell dedifferentiation and proliferation as well as large-scale extracellular matrix synthesis via signal transduction. This may be the main cause of painful disc fibrosis and degeneration.” “and promote”? Also, why would disc cell dedifferentiation and proliferation, along with extracellular matrix synthesis cause pain? This seems like a major concept which is just thrown out, without adequate explanation. My understanding was that nerve growth into the damaged area, with sensitization of the nerves by NGF was the primary concern. It may be that my understanding is limited; if so, the discussion should be made clear to those of us who are not biochemists. I have revised the sentence as “The cells in normal disc are separated from the circulatory system. These increased growth factors acted on the intervertebral disc cells, and promoted disc cell dedifferentiation and proliferation, as well as large-scale extracellular matrix synthesis via signal transduction.”

Your following discussion of the nerve supply to the disc is excellent.

“MSC” is used without giving the phrase for which it is an abbreviation. Thank you, ‘Mesenchymal stem cells’ has been added.

Respond to reviewer 2:

Dear Reviewer,

Thank you for your friendly review to my manuscript. According to your advice, I have revised my manuscript.

Yours sincerely,

Baogan Peng

‘However, they have not used many of the most recent references including the Institute of Medicine (IOM) study and multiple base studies on which IOM conclusions were based.’ I have added the recent references in the manuscript.

‘In this section they also used some references more than once, such as Manchikanti et al reference 51 and 60, which are duplicative.’ I have deleted the reference 60.

‘Authors also have not used the study by DePalma et al illustrating discogenic pain among the various causes published more recently than the others quoted in this discussion.’ I have added the paper by DePalma et al .

‘With reference to treatment, authors have provided reasonable description, however, they have missed the role of epidural injections in managing discogenic low back pain. There have been multiple manuscripts published recently in managing discogenic pain, not only in lumbar spine with caudal and lumbar interlaminar, but also the cervical spine.’ I have added the discussion about the role of epidural injection.

‘More recent systematic reviews on intradiscal therapies, as well as, study by Kapural et al with biaculoplasty may be included and further discussed.’ I have added the discussion about the role of biaculoplasty.

‘I may be missing something, but these authors also published a manuscript on untreated discogenic low back pain and its continued persistence after several years recently. This should be discussed further.’ I have discussed the role of natural history of discogenic low back pain in the discussion section.

‘Authors should add a section on summary and conclusion at the end to describe in short essential features of this manuscript.’ I have added summary and core tip in the manuscript.

In the abstract, authors may want to add a range of prevalence of discogenic pain rather than 39% derived from only one study. I have added the references about the range of prevalence of discogenic low back pain in the abstract and text.

Respond to reviewer 3:

Dear Reviewer,

Thank you for your friendly review to my manuscript. According to your advice, I have revised my manuscript. Thank you very much.

Yours sincerely,

Baogan Peng