**General guideline for Peer Review process:**

This journal’s peer review policy states that **NO** manuscript should be rejected only on the basis of ‘**lack of Novelty**’, provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(http://www.sciencedomain.org/page.php?id=mdi-general-editorial-policy#Peer-Review-Guideline)
# Review Comments

<table>
<thead>
<tr>
<th>Reviewer's comment</th>
<th>Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</th>
</tr>
</thead>
</table>
| **Compulsory REVISION comments** | Main recommendation  
The latest article cited to support the idea and statement by the author is published five years ago, in the year 2010 (Ref 6 and Ref 8). Therefore, some important progresses achieved from 2010 to 2015, such as the exhaustion of intervertebral stem cells and the degeneration-inducing effects from the harsh disc microenvironment, are missing. The following comprehensive reviews might provide cues to these important issues and guide as a model for comprehensive reviewing.  

---

**SDI Review Form 1.6**

**PART 1:** Review Comments
**Minor REVISION comments**

| Line 29, “starts sooner that the degeneration of other” should be “starts sooner than that…” Line 49, the expression “extracellular matrix, accounting or the most of the disc structure” is not clear. You mean the extracellular matrix account for the most of the disc structure or volume? Please make it clear. Line 54, “between the annulus of the intervertebral disc and its nucleus becomes” should be “between the annulus of the intervertebral disc and its nucleus becomes” Line 59 to Line 66, these important contents are stated without references, please cite the original articles that lead to these conclusions. Line 75, “Serum proteins an cytokines diffuse into the matrix, affect the cells and accelerate the process of the degeneration”. This statement is quite controversial given that the cartilaginous layer of endplate allows perfusion of small molecular, such as oxygen and glucose, attenuating the macro-molecular like growth factors and cytokines. See reference 18. Line 77, “With the matrix degeneration is connected also” is expression is not clear. Line 81, please check “fybronectin” Line 107 “pulpous nucleus” should be “nucleus pulpous” Line 145, “although at the moment of writing still in the experimental” should be changed to “although most of them still in the experimental” |

---

**Optional/General comments**

| This is a brief narrative review that concerns the pathological process and contributing factors that lead to intervertebral degeneration. As we know the degenerative intervertebral disc disease is so huge a topic that no single review, comprehensive or brief one, is able to cover so enormous information that accumulates from epidemiological, mechanical, pathological, and cytohistological researches. Briefly, |
this work starts with an ambitious topic, advances with scattered and abstractive conclusions, and ends with simplified expectations, the regenerative therapy using growth factors and cytokines inhibitors. Although this present review has summarized some major background knowledge about the intervertebral disc and its age-related and stress-accelerated degenerations, it failed to provide a current state of art of the researches, findings, as well as debates in the field of degenerative intervertebral disc disease.

Reviewer Details:

<table>
<thead>
<tr>
<th>Name</th>
<th>Xiao-Tao Wu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department, University &amp; Country</td>
<td>Department of Spine Surgery, Medical School of Southeast University, China</td>
</tr>
</tbody>
</table>