

2.

Ms.

No.: NSL-11-1801

Title: Elevated IL-1beta and IL-6 levels in lumbar herniated discs in patients with sciatic pain

Corresponding Author: Dr. Pablo Andrade

Dear Dr Ibarra,

Because of your expertise related to the paper listed above, I would like to ask your assistance in determining whether the above-mentioned manuscript is appropriate for publication in Neuroscience Letters.

The aim of this journal is to provide rapid publication of short papers that add to the literature in neuroscience. Our goal is to publish solid, credible science. In view of our fast publication procedure, I am asking for a brief, constructive review of this manuscript's merit and appropriateness for this journal. For your consideration, the manuscript abstract is included below. In order to ensure a rapid review process, your review would need to be returned to our office within 10 days of accepting this invitation.

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Thank you in advance for your assistance.

Sincerely,

Stephen Waxman
Editor-in-Chief
Neuroscience Letters

REVISIÓN

The manuscript entitled "Elevated IL-1beta and IL-6 levels in lumbar herniated discs in patients with sciatic pain" by Andrade *et al.* attempted to demonstrate the existence of IL-1beta and IL-6 in

lumbar herniated discs (LHD) and to correlate this with sciatic pain. For this purpose paravertebral muscle, annulus fibrosus (AF) and nucleus pulposus (NP) biopsies were intraoperatively-collected from ten LDH patients suffering from chronic sciatic pain and, as painless controls, they biopsied five patients with scoliosis. Gene and protein expression of IL-1beta and IL-6 was assessed by qPCR and Western blot, respectively. The amount of pain was evaluated using a visual analogue scale (VAS); 1 day before surgery, and 6 weeks and 1 year after surgery. The authors found a significant increase in IL-1 and IL-6 concentrations; however, the amount of cytokines did not correlate with the amount of pain. The authors suggest that the acute pain relief obtained by patients could be related to the mechanical decompression, and that the chronic increasing pain could be a consequence of an unresolved neuroinflammatory process.

The findings obtained in the present manuscript contribute little to the general knowledge of sciatic pain and its possible causes. Firstly, the presence of IL-1 and IL-6 at the herniated disc has already been reported by Takahashi H (Spine 1996; 21:218-24). Secondly, the lack of a correlation between the amount of cytokines and the presence of pain further demerits the value of the work since, these inflammatory cytokines, especially IL-1, have been correlated with pain in other works (Eliav E, Brain Behav Immun 2009; 23(4):474-84; Nojonen-Hietala N, Eur J Pain. 2008; 12(8):1018-25). It is important that the authors make more of an effort to explain their contrasting results.

Most of the comments in the discussion section are quite superficial and do not provide a detailed analysis of the study. This reviewer feels that the authors could somehow explain the lack of a correlation. Regarding this, it is only mentioned that IL-6 has been proposed as a cytokine with dual effects. It is a fact that this cytokine induces pain but also inhibits pain (Flatters SJ, Brain Res 2003; 984(1-2):54-62). The inhibitory effect on pain of this cytokine could be a possible explanation of the lack of correlation; however, the authors do not address this issue in detail. Aside from this, the amount of IL-6 is very similar in painful and non-painful patients; thereby, this rationalization does not work. Another problem arises from the illogical and almost arbitrary way of dividing the patients since there is no explanation of the criteria used to divide the painful and non-painful from a VAS of 3.5. Actually, in figures 3 and 4 almost all the patients have a VAS score equal to or greater than 2.5, which indicates pain in patients. Only one patient presented a VAS of zero (no pain). In my opinion, the results of the present manuscript need to be more adequately analyzed and discussed in detail as to justify their relevance.

COMMENTS TO THE EDITOR

The data presented in this manuscript is interesting but represents only a small increment in knowledge and merely consolidates existing data. It requires more analytical work. I do not recommend the publication of this manuscript in its present form.

3. 25-Nov-2011

Dear Dr. Ibarra:

Thank you for agreeing to review the manuscript CM-0570 entitled "Nestin overexpression precedes caspase-3 upregulation in rats exposed to controlled cortical impact traumatic brain injury." for the journal "Cell Transplantation". Please try your