Peer Review Report

Review Report on The role of TGF-β in the electrotactic reaction of mouse 3T3 fibroblasts in vitro

Original Research, Acta Biochim. Pol.

Reviewer: Anna Polak
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EVALUATION

Q 1 Please summarize the main findings of the study.

Chronic wounds (venous ulcers, pressure sores, cancer wounds, etc.) are a difficult clinical problem that many millions of people around the world struggle with. The healing of chronic wounds in humans is generally long-lasting and complicated. Therefore, it is extremely important to search for and develop modern methods that will increase the effectiveness of wound treatment and shorten the duration of treatment.

Fibroblasts play an important role in the wound healing process. Therefore, understanding the mechanisms that promote the attraction of fibroblasts to the wound area and then the mechanisms of activating fibroblasts in wounds is extremely important in order to develop the most effective methods for treating chronic wounds in humans.

The authors conducted an in vitro study aimed at obtaining knowledge about the role of TGFβ signaling in the electrotactic reaction of 3T3 fibroblasts.

In my opinion, this study was very well planned and conducted. The authors observed that inhibition of both canonical and several non-canonical signaling pathways associated with the activated TGF-β receptor did not impede the directional migration of 3T3 cells to the cathode. Furthermore, silencing the expression of the TGF-β receptor failed to eliminate the directional migration of 3T3 cells in the electric field. Additionally, there was no redistribution of the TGFβ receptor under electric field conditions. At the same time, the study confirmed an important role for PI3K kinase in electrotaxis, but its activation was probably related to the action of factors other than TGFβ.

Q 2 Please highlight the limitations and strengths.

Strengths of the study
Probably the migration of fibroblasts to the wound area and their activation in the wound area depend on many factors that are activated in different conditions and at different stages of wound healing. Understanding these factors will allow the development of effective methods to stimulate fibroblasts and thus stimulate wound healing.

It is commonly believed that one of the growth factors that stimulates the migration and activation of fibroblasts in wounds is TGF-β (in the form of various TGF-β1-3 isoforms). The strength of the study conducted by the authors is the demonstration of the stimulating effect of PI3K kinase on the migration of fibroblasts in an electric field. This result is important because it shows that PI3K kinase plays an important role in the process of fibroblast stimulation and at the same time shows the possibility of using an exogenous electric field in wound treatment.

Limitations of the study
My scientific experience is primarily related to the assessment of the possibility of clinical use of various types of methods for treating chronic wounds in humans (including electrostimulation). I am not an expert in

planning and conducting in vitro tests, therefore I do not have the appropriate competences to demonstrate the weaknesses of the in vitro tests conducted by the authors.

Q 3 **Please comment on the methods, results and data interpretation. If there are any objective errors, or if the conclusions are not supported, you should detail your concerns.**

As I mentioned above, I am not an expert in the field of in vitro tests, therefore my competences do not allow me to express a clear opinion on the correctness of the in vitro test methods used by the authors.

However, the description of the research methodology as well as the results and conclusions of the study are fully understandable to me and I believe that these chapters were well written. The introduction and discussion are also interesting and well-written.

The study results are important for understanding the biological mechanisms that determine wound healing. They also show the influence of an exogenous electric field on the mechanisms involved in wound healing, which is important from a clinical point of view, because electrotherapy is one of the methods recommended in the treatment of chronic wounds in humans (including stage II-IV pressure ulcers).

Check List

Q 4 **Please provide your detailed review report to the editor and authors (including any comments on the Q4 Check List)**

In my opinion, the study is very well planned, justified, conducted and described. The study results provide significant knowledge regarding the biological mechanisms involved in the wound healing process and at the same time show the possibilities of influencing and using exogenous electric fields in wound treatment.

I would only suggest that authors:
1) The title stated that it was an in vitro scientific study;
2) At the end of the discussion, they pointed out the strengths of the study and the limitations of the study;
3) They indicated further directions of scientific research in the topic they described (including in vitro research and possibly in vivo research and clinical trials);
4) If, in the authors' opinion, the results of their study have an application that can be used in clinical settings, it would also be good to emphasize this in the manuscript;
5) Include a separate chapter at the end of the manuscript, titled "conclusions", unless the journal's requirements for conclusions from in vitro studies do not require a "conclusions" chapter.

Q 5 **Is the English language of sufficient quality?**

Yes.

Q 6 **Is the quality of the figures and tables satisfactory?**

Yes.

Q 7 **Does the reference list cover the relevant literature adequately and in an unbiased manner?**

Yes.

Q 8 Are the statistical methods valid and correctly applied? (e.g. sample size, choice of test)

Yes.

Q 9 Are the methods sufficiently documented to allow replication studies?

Yes.

Q 10 Are the data underlying the study available in either the article, supplement, or deposited in a repository? (Sequence/expression data, protein/molecule characterizations, annotations, and taxonomy data are required to be deposited in public repositories prior to publication)

Yes.

Q 11 Does the study adhere to ethical standards including ethics committee approval and consent procedure?

Not Applicable.

Q 12 Have standard biosecurity and institutional safety procedures been adhered to?

Yes.

QUALITY ASSESSMENT

Q 13 Originality

Q 14 Rigor

Q 15 Significance to the field

Q 16 Interest to general audience

Q 17 Quality of the writing

Q 18 Overall quality of the study