

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-18-00190

Title: Network-centric medicine for peripheral nerve injury: treating the whole to boost endogenous mechanisms of neuroprotection and regeneration

Reviewer's Name: Daoli Zhu

Reviewer's country: China

Date sent for review: 2018-05-10

Date reviewed: 2018-05-20

Review time: 10 days

COMMENTS TO AUTHORS

The merits of the article:

The review paper, written by author David Romeo-Guitart and Caty Casas, is called the network centric peripheral nerve injury medicine: holistic therapy promotes the endogenous mechanisms of neuroprotection and regeneration, and belongs to "peripheral nerve injury and nerve regeneration".

The review is divided into five parts: 1. Introduction is concerned with the recent discovery of NH by means of systematic biology and the use of tools based on artificial intelligence.

2. An experimental model of peripheral neuropathy, the body model is widely used to simulate peripheral nerve damage and has been used to identify factors that regulate axonal regeneration and motor neuron death.

3. The network center has discovered a new neuroprotector: neural repair, when the nerve repair is discovered, uses a technique called the therapeutic performance detection system (TPMS), which allows the use of a machine learning method based on artificial neural intelligence to generate a disease specific mathematical model for drug screening.

4. The neural repair mechanism of neuroprotection and nerve regeneration is that drug discovery is experiencing a paradigm shift from a selective drug ("magic bullet") to a selective hybrid multi target targeting drug ("magic shotgun").

5. Conclusion and summary of the best treatment strategy after peripheral nerve injury is necessary to maintain persistent neuronal activity, enhance axonal regeneration, be beneficial to functional neuromuscular innervation of neuromuscular connection and reduce muscle atrophy.

85 references are cited in this review, of which nearly 1/4 of the literatures in the last three years are published, and top scientific journals such as "Science" and "Cell" are cited.

The shortcoming of the article:

The revision of the nerve repair mechanism of neuroprotection and nerve regeneration in the fourth part of the review needs to be combed clearly. It is mainly about the mechanism of the action mechanism of the peripheral nerve damage signal pathway and the molecular mechanism of the use of drug therapy for the repair of nerve in the appended figure 1.

We hope to carefully modify the science of standardization between "MN" and "MNs", "PNI" and "PNIs".

It is hoped that the authors will seriously modify the relationship between the left side nerve repair (NeuroHeal) of legend 1, and hope that it can straighten out clearly and make it clear at a glance.

**OPEN PEER REVIEW REPORT 2**

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-18-00190

Title: Network-centric medicine for peripheral nerve injury: treating the whole to boost endogenous mechanisms of neuroprotection and regeneration

Reviewer's Name: Shanji Nan

Reviewer's country: China

Date sent for review: 2018-05-10

Date reviewed: 2018-05-19

Review time: 9 days

COMMENTS TO AUTHORS

This is an interesting paper. The authors designed a drug discovery workflow based on a network-centric molecular vision using unbiased proteomic data and neural artificial computational tools. They discovered NeuroHeal, a combination of two drugs which promotes MN neuroprotection. They carried out a complete thought in the process of research and came to a meaningful conclusion.