TOBeATPAIN E-Seminar 3, 15th April, 2021

Jeiny Luna Choconta (ESR6) along with Cristiana Dumbraveanu (ESR10) presented the e-seminar 3 for the TOBeATPAIN consortium. The e-seminar titled “Response of immune cells in neuropathic pain”.

Jeiny presented the paper “Spinal macrophages resolve nociceptive hypersensitivity after peripheral injury” authored by Niehaus and colleagues. The paper was published in Neuron in 2021 and is focused on the identity of endogenous cells that resolve spinal inflammation followed by peripheral nerve injury induces long-term pro-inflammatory responses in spinal cord glial cells that facilitate neuropathic pain.

In terms of methodology the group classified the lumbar spinal cord cell types in superficially injured and nerve-injured animals using scRNA-seq.

After experimental procedures they found that spinal macrophages are proliferating, upregulating the level of Cd163 and they are also required for pain resolution in spinal injury animals.

Some key fundamentals of the work of this research group includes,-

- Nerve injury dysregulate the balance between pro-inflammatory microglia and anti-inflammatory spinal macrophages.
- Spinal macrophages can be therapeutically used in a way to resolve microgliosis in terms of long-lasting recovery from neuropathic pain.

To summarise, the key findings from the investigation of the group is spinal macrophages from nerve injury animals support a reduced anti-inflammatory response but can be therapeutically persuade to promote long-lasting recovery of neuropathic pain.

In the other presentation, Cristiana presented the paper “Protective role of neuronal and lymphoid cannabinoid CB2 receptors in neuropathic pain” authored by Cabanero and colleagues. The paper was published in eLife in 2020 and is focused on the cannabinoid receptor 2 (CB2) presents on the peripheral immune cells and in cells with immune function.

For the experiments this group choose CB2 selective agonist, JWH133 with low and high dosage concentration for self-administration by intravenous infusion to mice. The results showed that high dose of CB2 agonist, JWH133 alleviate spontaneous pain and anxiety associated behaviour.

In the second set of experiments, they focused on the specificity of the CB2 agonist to alleviate the pain responses with the mouse model designed as CB2 knockout and wild type. Results showed similar sensitivity on heat and mechanical stimuli on day 6 in wild and CB2 knockout mice. But after 18 days wild type mice had a significant decrease in heat and mechanical nociception, while in CB2 knockout mice, they have a slight decrease in heat nociception but pain threshold was increased.

Previously it was described CB2 receptor is only present on peripheral immune cells, but the group also found that presence of CB2 receptor is also in central nervous tissue that in turn results in

neuropathic pain. Results showed a lack of lacking of CB2 receptors in neuron express anxiety like behaviour.

Some key fundamentals of the work of this research group includes,-

- CB2 agonist, JWH133 is sufficient to promote the drug taking behaviour in nerve injured mice for pain alleviation.
- Selective agonist for CB2 receptor does not induce strengthening effects in wild type animals.
- CB2 receptor expressed on neurons and lymphocytes has protective role on spontaneous neuropathic pain condition.

After the presentation, there was a small discussion with several questions for clarity of the research done by those groups of authors to make the e- seminar interactive. This enhanced the learning skills of the speaker and the people preparing the e-seminar in order to understand questions from an audience taking the question and to right track an answer.

I appreciate the opportunity of hearing Jeiny's and Cristiana's talk and looking forward to upcoming e-seminars for some interesting articles and interesting talks.

-Reviewed by *Anutosh Roy*