

Mesenchymal stem cells protect sensory neurons, but not cortical neurons, from the chemotherapeutics-induced neurotoxicity

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Mesenchymal stem cells (MSCs) have been often proposed for the therapy of several neurological diseases, due to their manifold peculiar properties. In particular, since it has been previously demonstrated that these cells are able to increase the survival of untreated sensory neurons [1], in this work we evaluated their possible protective effect on sensory neurons previously exposed to toxic agents. This could be particularly relevant to design a supportive therapy to counteract the peripheral neuropathy, a very common side effect of several chemotherapeutic agents, such as platinum and taxanes compounds, which often represents their dose limiting factor [2]. Several strategies have been suggested to reduce drug neurotoxicity without affecting the antineoplastic potential, but up to now results were not encouraging [3]. Here we demonstrated that Cisplatin (CDDP) and Paclitaxel-treated sensory neurons are protected by the co-culture with MSCs, but in two different manners: through a direct contact able to block apoptosis for CDDP-treated neurons, and by the release of trophic factors (including glutathione) for Paclitaxel-treated ones. In addition, the MSCs' effectiveness was also verified on cortical neurons, since the recent advances in targeted drug delivery allowed to drive chemotherapeutic drugs also to the central nervous system. We verified that cortical neurons are more vulnerable to the toxic action of the drugs, and overall that MSCs fail at all to protect them. All these data demonstrated that MSCs are potentially useful to limit the peripheral neuropathy onset for their protective effect on injured-sensory neurons, but they also identified for the first time a different susceptibility of cortical and sensory neurons to MSC action.

References

- [1] Scuteri et al. (2006) Adult mesenchymal stem cells rescue dorsal root ganglia neurons from dying. *Brain Res* 1116: 75-81.
- [2] Cavaletti et al. (2015) Chemotherapy-induced peripheral neurotoxicity. *Curr Opin Neurol* 28: 500-507.
- [3] Marmioli et al. (2016) Drugs for the treatment of peripheral neuropathies. *Expert Opin Pharmacother* 17: 381-394.

Keywords

Chemotherapeutic induced peripheral neuropathy, mesenchymal stem cells, sensory neurons, cortical neurons, neuroprotection