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Tunneling nanotubes as mediators of Neuron-Mesenchymal Stem Cell interaction

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During the last two decades Mesenchymal Stem Cells (MSCs) have been proposed for the treatment of several neurological diseases, such as Alzheimer's disease or Parkinson's Disease [1], initially with the aim to replace the damaged neuronal cells, and later to cure, rather than to replace the neuronal cells. In particular, previous studies demonstrated that MSCs directly co-cultured with sensory neurons were able to strongly increase the neuronal survival, and to protect them from different toxic stimuli [2; 3], thus theoretically being useful to really change the course of all the diseases affecting sensory neurons. Anyway, it is mandatory to understand the mechanisms involved in such an interaction. Aim of this work is to investigate the different interaction manners, and the identification of the molecules used by MSCs and neurons to communicate.

In particular, by Immunofluorescence and Electron microscopy analysis, we observed the formation of gap junctions and tunneling nanotubes, cellular structures potentially allowing the flow of cellular stuff (4). In addition, with the diffusible fluorescent dye Calcein, we demonstrated the flux direction from MSCs to neurons. We then analyzed the nature of the exchanged materials, and we observed an involvement of exosome and more in general vesicular structures, and even subcellular components as mitochondria. All these molecules and structures may be used by MSCs to cure neurons. As a proof of concept, we will expose neurons to the putative protective MSC-derived molecules, to determine if they are sufficient to achieve a positive effect.

On the basis of the identified interactions and the pivotal molecules exchanged, it will be possible to enhance the MSC protective effect on neurons by exploiting the identified key molecules.

References

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Key words

Tunneling nanotubes, gap junctions, mesenchymal stem cells, sensory neurons, mitochondria, neuroprotection.