Rat Bone Marrow Mesenchymal Stem Cells Conditioned Medium Induces Excitotoxic Cell Death in Organotypic Hippocampal Cultures

Horn A.P.[1], Frozza R.L.[1], Grudzinski P.B.[1], Bubols G.B.[1], Chagastelles P.[2], Nardi N.B.[2], Lenz G.[3], Salbego C.G.[1]

[1] Departamento de Bioquímica, ICBS, Universidade Federal do Rio Grande do Sul, [2] Departamento de Genética, IB, Universidade Federal do Rio Grande do Sul, [3] Departamento de Biofísica, IB, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil

Cell therapy using bone marrow-derived mesenchymal stem cells (MSC) seems to be a new alternative for the treatment of neurodegenerative diseases. In spite of several good and promising results about the use of these cells, their side effects are still unknown. Previous results from our group have shown that MSC conditioned medium is toxic to hippocampal slice cultures and that this toxicity seems to be selective to CA1, CA2 and CA3 areas. In an attempt to understand why hippocampus is dying in response to MSC, we investigated whether classic receptors such as AMPA, NMDA and GABA are involved in this toxic effect. For this purpose rat organotypic hippocampal cultures from 6-8 old male Wistar rats were exposed to rat bone marrow-isolated MSC conditioned medium for 24h. Cultures were exposed to the conditioned medium from MSC and/or the channel antagonists (MK801, CNQX), agonists (GABA) or the calcium blocker nimodipine. Propidium iodide was used as a marker of cell death and we observed that MK801 (30µM), a NMDA antagonist, CNQX (100µM), an AMPA antagonist, nimodipine (10µM), a calcium voltage-dependent channel blocker, and GABA (100µM) were able to protect from cell death the hippocampus that was exposed to MSC conditioned medium. The results obtained in this work suggest that classic mechanisms such excitotoxicity leading to calcium toxicity are involved in the cell death induced by MSC conditioned medium. *Supported by CNPq.*