

Gc-protein derived macrophage activating factor (GcMAF) counteracts the neuronal damage induced by oxaliplatin

Gabriele Morucci¹, Jacopo J. V. Branca¹, Massimo Gulisano¹, Marco Ruggiero², Ferdinando Paternostro¹, Alessandra Pacini¹, Lorenzo Di Cesare Mannelli³, Stefania Pacini¹

¹Department of Experimental and Clinical Medicine, University of Firenze, 50134 Firenze, Italy

²Department of Clinical and Biomedical Experimental Sciences, University of Firenze, 50134 Firenze, Italy

³Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Firenze, 50134 Firenze, Italy

Oxaliplatin-based regimens are effective in metastasised advanced cancers. However, a major limitation to their use is represented by neurotoxicity leading to peripheral neuropathy (Wolf et al., 2008). In this study we evaluate the effects of an immunotherapeutic agent (Gc protein-derived macrophage activating factor, GcMAF) in preventing oxaliplatin-induced neuronal damage and in restoring microglial activation. The effects of oxaliplatin was studied in human neurons (SH-SY5Y) and microglial cells (c13-nj). Cell density, morphology and viability as well as production of cAMP and expression of vascular endothelial growth factor (VEGF), markers of neuron regeneration and markers of microglia activation were determined. GcMAF reverted the damage inflicted by oxaliplatin on human neurons and preserved their viability; it also increased cAMP production, VEGF and neuromodulin expression. GcMAF did not revert the effects of oxaliplatin on microglial cell viability. However, it induced microglial activation resulting in an increased expression of a specific marker without any increase in cell number. Our results demonstrate that GcMAF may significantly contribute to neutralize the neurotoxicity induced by oxaliplatin, at the same time concurring to an integrated anti-cancer effect.

References

- [1] Wolf et al. (2008) Chemotherapy-Induced Peripheral Neuropathy: Prevention and Treatment Strategies. *Eur J Cancer*; 44: 1507-1515.

Keywords

Oxaliplatin, human neurons, human microglia, vitamin D, cancer, immunotherapy, GcMAF.