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Chemotherapy effect on Human iPSC-Derived Sensory Neurons

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Human Induced Pluripotent Stem Cells iPSCs represent a revolutionary strategy for the design of new personalized experimental in vitro models [1]. So far, many iPSCs based models have been developed most of them targeting cardiac and Central Nervous System, while few models are currently available for diseases affecting Peripheral Nervous System [2, 3]. This may be particularly interesting since a very disabling side effect of several effective antineoplastic drugs is the induction of peripheral sensory neuropathy, known as Chemotherapy-Induced Peripheral Neuropathy (CIPN), which often causes the anticancer treatment interruption [4]. CIPN mainly targeting Dorsal Root Ganglia and, besides its complexity, a limiting factor for progress is the lack of reliable in vitro human models to screen putative neuroprotective molecules without interfering with the anticancer drugs. In this study, we examine the effect of four chemotherapy agents with established neurotoxic potential, Oxaliplatin, Cisplatin, Paclitaxel, and Bortezomib on iPSCs-derived sensory neurons provided by FUJIFILM Cellular Dynamics (iCell Sensory Neurons). iCells were exposed for 24 hours to different concentrations of each drug, and viability and neurotoxicity were assessed using MTT assay and neurite outgrowth analysis. Our results showed a significant decrease of neuronal survival after the exposure to all the antineoplastic agents. Moreover, all drugs impaired neurite outgrowth in a dose dependent manner. The results reported using FUJIFILM iCell® Sensory Neurons are consistent with findings previously obtained with murine DRG models [5], both in terms of reduction of neuronal survival and of neurite damage, supporting them as a valid human-based model for studying peripheral neuropathy and drug testing.

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