An in vitro model of dorsal root ganglion neurons to investigate the molecular mechanisms of chemotherapy-induced peripheral neuropathy.

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Keywords : dorsal root ganglion neurons, patch-clamp, electrophysiology, oxaliplatin, peripheral neuropathy

In our laboratory we have established an *in vitro* model to study neuronal activity modulation and neuropathy. F-11 is a hybrid cell line of embryonic rat dorsal root ganglion (DRG) neurons and mouse neuroblastoma N18TG-2 cells, which can be differentiated in DRG neurons by means of different approaches. Electrophysiological characterization of differentiated F11 cells has not been documented yet. Recently we have demonstrated that morphologically mature neurons could be obtained by maintaining the culture for 14 days in low serum medium.

Electrophysiological recordings, performed by the patch-clamp technique in the whole-cell configuration, showed that cells which exhibited neuritic-like processes and expressed neuronal marker NeuN were able to generate spontaneous electrical activity, demonstrating that differentiated F-11 cells were functional mature neurons. Moreover they showed properties of DRG neurons: they were responsive to acetylcholine and their activity was modified by glutamate, capsaicin and substance P (Pastori *et al.*, 2019, *PeerJ* 7:e7951).

Since differentiated F-11 cells are a good model of DRG neurons, we started studying the effects of oxaliplatin (OHP), an anti-cancer molecule known to cause peripheral neurotoxicity as the most common side effect. We tested the drug (7,5 µM for 24 and 48 h) on differentiated F-11 cells to investigate the molecular targets of the neuropathic symptoms manifested in treated patients.

Electrophysiological recordings showed effects of OHP on voltage-gated sodium channels, concerning current density and both activation and inactivation properties. Moreover, we reported for the first time an effect of OHP on ERG (*ether-à-go-go-related gene*) potassium channel. These effects on both sodium and potassium channels could explain the membrane depolarization and the change in the electrical activity we recorded in OHP-treated cells, which are consistent with OHP-induced toxicity and support differentiated F-11 cells as a good model to study neuropathy mediated by voltage-gated ion channels.