

## Abstract of Contribution 627

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Poster Abstract Submission

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### **Paclitaxel Alters Drg SGCs in Animals with Peripheral Neuropathy**

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Chemotherapy-induced peripheral neurotoxicity is one of the most common dose-limiting toxicities of several anticancer drugs, including taxanes such as paclitaxel (PTX) and no effective treatments are available to counteract it.

In this work, PTX-induced peripheral neurotoxicity (PIPNe) development will be explored focusing on the study of DRG (dorsal root ganglia) satellite glial cells (SGCs) and their interaction with sensory neurons.

For the study adult female Wistar rats were treated with PTX or vehicle for 4 weeks, and half of them were monitored for additional 6 weeks (follow up). All animals underwent morpho-functional evaluations including neurophysiological and behavioural assessment as well as neuropathological investigations to verify the features of PIPNe both at the end of PTX treatment and follow up. In addition, localization and expression analyses of the marker of glial activation (GFAP) and proteins involved in the signaling pathway between SGCs and/or SGC-neurons (i.e. L1CAM, P27XR, Kir4.1) were conducted in DRG by immunohistochemistry and immunoblotting. Transmission electron microscopy (TEM) analysis was also performed to thoroughly characterized ultrastructural alterations.

PTX determined an extensive upregulation of GFAP demonstrating a glia activation that persisted at the end of follow up period, when the painful component of neuropathy, but not the nerve damage, was resolved. Moreover, significant upregulation in L1CAM and P27XR expression was observed after PTX treatment, suggesting an increment of interactions between SGCs and SGC-neurons, confirmed also by TEM analyses which demonstrated an increase in the intimate contact between SGCs and their associated neurons with a complex and peculiar pattern of glial cytoplasmic projections. By contrast, at the end of the follow-up, when mechanical allodynia resolved, a reduction in L1CAM and P27XR expression was observed.

This work suggests that SGCs are involved in the pathophysiology of PIPNe, paving the way for the identification of new therapeutic targets for its treatment and prevention.