



SODIUM-CALCIUM EXCHANGER NCX2 ROLE IN OXALIPLATIN-INDUCED PERIPHERAL NEUROTOXICITY DEVELOPMENT

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Category

Abstract Category: Scientific Research Abstract

Topic & Theme selection

Main Topic: B.2.c: Calcium channels

Secondary Topic: D.8.d: Chronic pain

Abstract Body

Abstract body: Oxaliplatin (OHP) is the cornerstone drug for colorectal cancer, hampered by OHP-induced peripheral neurotoxicity (OIPN). OIPN is characterised by an acute and chronic syndrome. Acute OIPN mirrors a transient axonal hyperexcitability at each cycle, whereas chronic OIPN corresponds to persistent axonal damage (AxD) causing sensory loss and neuropathic pain, affecting the quality of life of cancer survivors. The putative link between acute and chronic OIPN could be the Na⁺/Ca²⁺ exchanger 2 (NCX2): acute OIPN might lead to increased intraneuronal Na⁺ levels triggering NCX2 reverse mode; thus, Na⁺ is exchanged with Ca²⁺ potentially leading to chronic AxD. We investigated NCX2 contribution to OIPN in an in vitro setting. Primary cultures of mouse dorsal root ganglia neurons were treated with OHP to trigger neurotoxicity. First, NCX2 protein expression was characterised via Western blot, while NCX2 localization via immunofluorescence. Then, as a tentative neuroprotection strategy, NCX2 expression was selectively downregulated via siRNA technology. Neurite elongation and viability were the outcome measures to detect neuroprotection. OHP treatment was associated with changes in NCX2 protein expression compared to control conditions. Immunofluorescence analyses tentatively suggested an alteration in NCX2 distribution in sensory neurons and satellite cells that surround degenerating neurons. Moreover, siRNA-mediated NCX2 silencing significantly reduced neurotoxicity. NCX2 might play a relevant role in preventing OIPN, thus, targeting NCX2 might represent a promising strategy to treat this condition and more: a similar pathogenetic cascade (an upstream event - axonal hyperexcitability - and a downstream event - consequent Ca²⁺ neurotoxicity) were described in other peripheral neuropathies.

Keywords

Keywords: Yes

Keyword 1: Peripheral Neuropathies

Keyword 2: Oxaliplatin

Keyword 3: Sodium-calcium exchanger

Keyword 4: siRNA-mediated silencing

Keyword 5: CIPN

Poster Group Code

Poster Group Code: Lab_Cavaletti_ENU

Virtual Poster Submission

I would like to submit a virtual poster to make my poster available online, free of additional cost: Yes

Early Career Training Programme (ECTP)

I am interested in receiving information on the ECTP via the provided email address Yes

Travel Grant

Do you meet all the below listed eligibility criteria? Yes

Do you want to apply for a FENS Travel grant? Yes

Country of residence: Italy

Nationality: Italy

Career status: PhD student (minimum 2nd year)

Year PhD started: 2023

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Presentations and posters: 1. PNS Annual Meeting 2024 (22-25/06/2024, Montréal, Quebec, Canada) - Poster presentation: Refinement of Dorsal Root Ganglia Neurons Morphometry

2. PNS Annual Meeting 2025 (17-20/05/2025, Edinburgh, UK) - Poster presentation: Sodium-calcium exchanger 2 (NCX2) role in an in vitro oxaliplatin-induced peripheral neurotoxicity model

Have you participated in international conferences before? Yes

Please mention which conferences and the respective dates: 2024 and 2025 PNS Annual Meetings (Montréal, 22-25/06/2024 and Edinburgh, 17-20/05/2025)

Publications: Tarasiuk, O., Invernizzi, C., & Alberti, P. (2024). In vitro neurotoxicity testing: lessons from chemotherapy-induced peripheral neurotoxicity.

Pozzi, E., Serra, M. P., Boi, M., Canta, A., Chiorazzi, A., Capelli, C., Invernizzi, C., Ballarini, E., Rodriguez-Menendez, V., Kraus, M. F., Quartu, M., Cavaletti, G., & Alberti, P. (2025). Molecular characterization of Oxaliplatin-Induced peripheral neurotoxicity: the complex spectrum of painful manifestations. *Journal of the Peripheral Nervous System*, 30(4), e70078. <https://doi.org/10.1111/jns.70078>

Motivational statement : I would love to attend this FENS Forum since this is my last year of PhD and I am not sure if it will be possible to participate to this kind of congress in the next years. I am very interested in Neurosciences and I think this Forum could be a great opportunity to meet other groups from other countries working on topics related to my PhD project, but I am also curious about other fields which could be interesting for my future career. I have never attended to a Forum like this one, the congresses I have been to were very focused only on peripheral nervous system or morphology, and even though I have always found them engaging and impressive, I think this occasion is unique to find collaborators and new ideas for our project.

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I have obtained consent from my supervisor to share their data Yes

Affirmations
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