# Metabolomics assessment in a mice model of Oxaliplatin-Induced Peripheral neurotoxicity.

### Submission No:

1341

### Submission Type:

Abstract

### Preferred Means of Presentation:

Oral and Poster Presenter


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### Presenter:

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### Introduction:

Chemotherapy-induced peripheral neurotoxicity (CIPN) is one of the most common dose-limiting side-effects of oxaliplatin (OHP) treatment. Nevertheless, the mechanisms underlying the pathogenesis of such complication are still not clear. The definition of biochemical markers of nerve damage might indeed be helpful for an appropriate management of chemotherapy regimen.

### Methods:

Forty male CD1-mice were randomized to either oxaliplatin treatment (6 mg/kg, 2 times/week for 4 weeks) or control group. Neurophysiological and dynamic tests were performed to investigate nerve damage. Skin biopsies from sacrificed animals were examined for intraepidermal nerve fiber (IENF) density assessment. Blood samples were collected for metabolomics analysis.

### Results:

A statistically significant reduction both in caudal and digital sensory nerve action potential (SNAP) ($p<0.01$) was observed at the end of the treatment, while nerve conduction velocity (NCV) did not significantly differ between the two groups. After the last administration, OHP-mice developed mechanical allodynia ($p<0.01$) and presented reduced IENF density ($p<0.0001$), which persisted at the 4th follow-up week. Metabolomic analyses identified 407 metabolites in mouse plasma samples. PCA analysis revealed a clear metabolic distinction of samples treated with oxaliplatin for 4 weeks from controls. Samples collected after eight weeks (4 weeks of recovery) from both the control and the oxaliplatin-treated group clustered closely together indicating that the treatment effects were mostly reversed during recovery. Oxaliplatin-induced changes were mostly observed for complex fatty acids, triglycerides, various amino acids and amino acid metabolites as well as citric acid metabolites in plasma.

### Conclusions:

CD1 mice treated with oxaliplatin for 4 weeks developed mechanical allodynia and showed reduced IENF density indicative of sensory neuropathy. Metabolomic analyses demonstrated significant oxaliplatin-mediated changes in plasma hinting to increased TCA activation and turnover of lipids, which almost completely resolved after 4 weeks of recovery.

### Biology:

Other - DRG

### Categories:

Toxic neuropathies

### Clinical:

Toxic

### Techniques:

Biomarkers (exclude antibodies)

## Additional Information

### Would you like your abstract to be considered for the Clinical Case Presentation Session during the Saturday Education Course on Saturday, 27 June, 2020? If selected, your abstract will not be considered as a platform presentation for the PNS General Session.

No

### Would you like your abstract to be considered for the Clinical Trials Session on Tuesday, 30 June? If selected, your abstract will not be considered as a platform presentation for the PNS General Session.

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### Would you like your abstract to be considered for a platform presentation during the new "Basic Science Highlights" concurrent session on Tuesday, 30 June? If selected, you will be required to attend the PNS Annual Meeting until 19.00 on Tuesday, 30 June.

Yes, I would like to be considered.

### Grant Support (Optional): Please list any grant support for this study.

Mundiphama Research Ltd., Cambridge, UK

### Field

Scientist

## Author Approval

### No Identifying Features in the Abstract.

I confirm that I did not embed any identifying features such as names of hospitals, medical schools, clinics or cities in the title or text of the abstract.

### Abstract Published as Submitted.

I acknowledge that all accepted abstracts will be **published as submitted** in the PNS 2020 Abstract Supplement and the *Journal of the Peripheral Nervous System(JPNS)*.

### Abstract will be Presented.

I acknowledge that it is PNS's expectation that all accepted abstracts will, under all usual circumstances, be presented at the meeting. If the presenting author is unable to present an abstract, a co-author is eligible to present on their behalf. I understand that failure to present an accepted abstract may cause the author(s) to be ineligible for abstract submission at next year's annual meeting.

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Junior PNS Member

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Arthur K Asbury - The abstract must pertain to GBS/CIDP/Inflammatory.

## Keywords

### Keyword 1

CIDP

### Keyword 2

Oxaliplatin

### Keyword 3

Metabolomic

### Keyword 4

Biomarkers

## References

### I have references I'd like to disclose.

Yes

### Please list your abstract references. Reference One:

Argyriou, A. A., Polychronopoulos, P., Koutras, A., Iconomou, G., Iconomou, A., Kalofonos, H. P., & Chroni, E. (2005). Peripheral neuropathy induced by administration of cisplatin- and paclitaxel-based chemotherapy. Could it be predicted? Supportive Care in Cancer, 13(8), 647–651. https://doi.org/10.1007/s00520-005-0776-9

### Reference Two:

Argyriou, A. A., Bruna, J., Marmiroli, P., & Cavaletti, G. (2012, April). Chemotherapy-induced peripheral neurotoxicity (CIPN): An update. Critical Reviews in Oncology/Hematology. https://doi.org/10.1016/j.critrevonc.2011.04.012

### Reference Three:

Argyriou, A. A., Kyritsis, A. P., Makatsoris, T., & Kalofonos, H. P. (2014, March 19). Chemotherapy-induced peripheral neuropathy in adults: A comprehensive update of the literature. Cancer Management and Research. https://doi.org/10.2147/CMAR.S44261

### Reference Four:

Argyriou, A. A. (2015, May 29). Updates on oxaliplatin-induced peripheral neurotoxicity (OXAIPN). Toxics. MDPI AG. https://doi.org/10.3390/toxics3020187

## Travel Grants

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### I meet the criteria listed above to apply for the 2020 PNS Travel Grant.

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### Are you from a country where it is very difficult, or impossible to receive a letter of support from a current PNS Member? Would you like the letter of support to be waived?

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