

End-of-Mission Report (FrenchBIC co-funding)

Tumor targeting of Pt(IV) conjugates of oxaliplatin and MnSOD mimics: towards anticancer agents with reduced neurotoxicity

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Mission details

- **Type of mission:** Research stay at National University of Singapore (Prof. Giorgia Pastorin laboratory, Faculty of Pharmacy) and Singapore Immunology Network (A*STAR, Prof. Giulia Adriani laboratory).
- **Host institution:** A*STAR (Agency for Science, Technology and Research).
- **Location:** Singapore
- **Dates:** 13/02/2023-07/04/2023

1. Objectives of the mission

The objective of the mission was to perform experiments relative to my PhD project “Development of platinum(IV) conjugates of oxaliplatin and redox modulators as anticancer agents with reduced neurotoxicity”.

Prior to my visit to Singapore, we had synthesized a platinum(IV) prodrug containing a manganese-based superoxide dismutase mimic, in an attempt to prevent oxaliplatin-based peripheral neuropathy (the main side effect of oxaliplatin, a first-line drug used for the treatment of colorectal cancer). The designed molecule (namely **PtC5Mn**) displayed encouraging neuroprotective activities but a decreased anticancer activity in a preliminary in vivo experiment.

The objective of this mission was therefore to **1)** enhance its anticancer activity in vivo by using a nanomedicine approach in which the drug was encapsulated in polyethylene glycol-functionalized lipid micelles and **2)** further study its cytotoxic and antiproliferative activities, as well as that of control compounds (such as oxaliplatin, the superoxide dismutase mimic, and the equimolar combination of both) in a 3D cell culture model (spheroids). Goal 1 was carried out at Prof. Giorgia Pastorin laboratory at National University of Singapore, where they have extensive expertise on nanoformulation strategies

Goal 2 was achieved at Prof. Giulia Adriani's laboratory (A*STAR), a group specialized in the development of 3D cell culture models (spheroids, organoids) and drug screening thanks to microfluidic devices.

2. Activities carried out

During my stay, I got training on micelles (empty and **PtC5Mn**-loaded) synthesis and characterization, as well as on spheroid formation and evaluation of the cytotoxic activity of our compounds employing staining experiments and confocal microscopy.

3. Main scientific outcomes

We successfully encapsulated our Pt(IV) prodrug **PtC5Mn** in PEGylated micelles, characterized this formulation and demonstrated that this was a promising approach to enhance the anticancer activity of **PtC5Mn**, while maintaining the neuroprotective activity, in mouse models.

The results obtained in the context of this mission were published in two open access research articles:

- A. Lopez-Sanchez, H. Chédotal, R. P. K. Muthuramalingam, M. Thomas, J. N. N. Yau, P. R. Sahoo, C. Policar, F. Batteux, K. Medjoubi, A. Somogyi, G. Adriani, C. Nicco, R. Coriat, G. Pastorin, H. C. Bertrand, A targeted redox-active dual-action Pt(IV)-Mn(II) prodrug displays enhanced in vivo anticancer activity, *Advanced Healthcare Materials*, **2025**, *14*, 2501847, doi: <https://doi.org/10.1002/adhm.202501847>
- A. Lopez-Sanchez, R. P. K. Muthuramalingam, M. Thomas, K. Medjoubi, A. Balfourier, C. Rampon, C. Policar, A. Somogyi, G. Adriani, F. Batteux, C. Nicco, G. Pastorin, R. Coriat, H. C. Bertrand, Preventing oxaliplatin-induced peripheral neuropathy with a Pt(IV)-Mn(II) prodrug: toxicity, behavioral and X-ray fluorescence microscopy studies, *Biomedicine & Pharmacotherapy*, **2026**, *204*, 120008, doi: <https://doi.org/10.1016/j.biopha.2026.120008>

The collaboration between our laboratory, NUS and A*STAR also resulted in the publication of two open access review articles in *Chemical Reviews* (doi: <https://doi.org/10.1021/acs.chemrev.5c00041>) and *Journal of Controlled Release* (doi: <https://doi.org/10.1016/j.jconrel.2026.114996>)

4. Impact on my research and career

This mission had an extremely positive impact on my research and career. It allowed me to get to know a new professional environment, familiarize myself with new techniques such as 3D cell culture and the synthesis of polymeric micelles, and expand my networking abilities. I strongly believe that this

international experience was a key asset in my CV and therefore contributed to my obtaining a postdoctoral position at Brooklyn College (New York) and my current Assistant Professor position at Aix-Marseille Université.

5. Acknowledgements

I gratefully acknowledge FrenchBIC for the financial support that made this mission possible. The 500 euros funding obtained from FrenchBIC contributed to pay for travel expenses.

Date: 23/10/2026

Fait à: Marseille

Signature:

A handwritten signature in black ink, consisting of a large, stylized capital 'A' followed by a cursive 'M' and a small dot at the end.