Metal complexes in biological environments: a new frontier in inorganic chemistry

Clotilde Policar

Laboratoire des BioMolécules, LBM, Département de chimie, École normale supérieure, PSL University, ENS-PSL, Sorbonne Université, CNRS, 75005 Paris, France clotilde.policar@ens.psl.eu

Metal complexes are increasingly used for biological applications, as metal-centered probes for imaging or as metal-based drugs.[1,2] To be active a metal complex must reach its biological target that can be embedded in cells or organelles. The metal speciation in low-molecular weight complex, its intracellular quantification and intracellular distribution through imaging, as well as the evaluation of its activity directly in a cellular environment are key steps in the design, study and rationalization of metallo-active bio-molecules. Microfluorescence X is a rapidely developing still state-of-art technique able to image heavy elements, including metal ions,[3] and synchrotrons offer a focus down to subcellular resolution that can be used to map metal complexes.

The talk will first discuss a series of Mn-complexes designed to reproduce the activity of the cell's protective anti-oxidant metalloenzymes, the superoxide dismutases.[4–6] We will show how cellular models can be designed to evaluate the activity of SOD-mimics.[7–9] Two aspects will be developed:

(a) design: Mn-complexes are known to be labile, with fast metal or ligand exchanges and low association constants. We will show how to design complexes with improved inertness (slower metal exchange).[6]

(b) analyses in cells: their bio-activity has been studied in cellular models of oxidative stress. Their quantification in cell lysate will be described.

In a second part, we will focus on application of metal-based probes and their use for multimodal imaging.[10–12] More specifically, probes consisting of a central metal-CO core, called SCoMPIs (for single core multimodal probes for imaging), can be mapped using unconventional imaging techniques such as IR and X-fluorescence imagings. Several examples, including a SOD mimic conjugated with a $Re(CO)_3$-based probe (and vector),[13] $Re(CO)_3$-based organelle trackers.[14,15]

These topics have been chosen to exemplify a range of approaches at this new cellular frontier in bological inorganic chemistry.

[1] E. J. Anthony, E. M. Bolitho, H. E. Bridgewater, O. W. L. Carter, J. M. Donnelly, C. Imberti, E. C. Lant, F. Lermyte, R. J. Needham, M. Palau, P. J. Sadler, H. Shi, F.-X. Wang, W.-Y. Zhang, Z. Zhang, *Chem. Sci.* **2020**, *11*, 12888–12917.

[2] N. J. Farrer, P. J. Sadler, in *Bioinorganic Medicinal Chemistry* (Ed.: E. Alession), Wiley-VCH, Weinheim, Germany, **2011**, pp. 1–47.

[3] J. H. Lovett, H. H. Harris, *Curr. Opin. Chem. Biol.* **2021**, *61*, 135–142.

[4] C. Policar, J. Bouvet, H. C. Bertrand, N. Delsuc, *Current Opinion in Chemical Biology* **2022**, *67*, 102109.

[5] R. Bonetta, *Chem. Eur. J.* **2018**, *24*, 5032–5041.

[6] I. Batinic-Haberle, I. Spasojevic, *J. Porphyrins Phthalocyanines* **2019**, *23*, 1326–1335.

[7] E. Mathieu, A.-S. Bernard, N. Delsuc, E. Quévrain, G. Gazzah, B. Lai, F. Chain, P. Langella, M. Bachelet, J. Masliah, P. Seksik, C. Policar, *Inorg. Chem.* **2017**, *56*, 2545–2555.

[8] A. Vincent, M. Thauvin, E. Quévrain, E. Mathieu, S. Layani, P. Seksik, I. Batinic-Haberle, S. Vriz, C. Policar, N. Delsuc, *J. Inorg. Biochem.* **2021**, *219*, 111431.

[9] A.-S. Bernard, C. Giroud, H. Y. V. Ching, A. Meunier, V. Ambike, C. Amatore, M. Guille Collignon, F. Lemaitre, Policar, *Dalton Trans.* **2012**, *41*, 6399–6403.

[10] D. J. Hare, E. J. New, M. D. de Jonge, G. McColl, *Chem. Soc. Rev.* **2015**, *44*, 5941–5958.

[11] S. Clède, C. Policar, *Chem. Eur. J.* **2015**, *21*, 942–958.

[12] S. Hostachy, M. Masuda, T. Miki, I. Hamachi, S. Sagan, O. Lequin, K. Medjoubi, A. Somogyi, N. Delsuc, C. Policar, *Chem. Sci.* **2018**, *9*, 4483–4487.

[13] E. Mathieu, A.-S. Bernard, E. Quévrain, M. Zoumpoulaki, S. Iriart, C. Lung-Soong, B. Lai, K. Medjoubi, L. Henry, S. Nagarajan, F. Poyer, A. Scheitler, I. Ivanović-Burmazović, S. Marco, A. Somogyi, P. Seksik, N. Delsuc, C. Policar, *Chem. Commun.* **2020**, *56*, 7885–7888.

[14] G. Schanne, L. Henry, H. C. Ong, A. Somogyi, K. Medjoubi, N. Delsuc, C. Policar, F. García, H. C. Bertrand, *Inorg. Chem. Front.* **2021**, *8*, 3905–3915.

[15] S. Clède, F. Lambert, C. Sandt, Z. Gueroui, M. Réfrégiers, M.-A. Plamont, P. Dumas, A. Vessières, C. Policar, *Chem. Commun.* **2012**, *48*, 7729.