Unraveling the fate of anticancer gold complexes in cells through HERFD-XAFS

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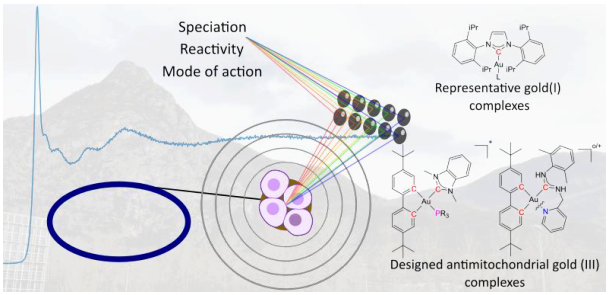
ABSTRACT

Organogold complexes are increasingly studied for their anticancer properties both *in cellulo* and *in vivo*.[1–3] Like any metal complex however, they are susceptible to a wide range of transformations in biological media (redox, ligand exchange) dictated by their structure and reactivity. Determining the speciation of such complexes is therefore key to understanding their mode of action, for which XAFS methodologies have proven very useful. These techniques have been employed to study the fate of Pt(IV),[4] and Os(II)[5] complexes in cell samples. XAFS has also been used to study the reactivity of some gold complexes with proteins[6–8] but has never been employed to monitor their speciation *in cellulo* to date. Taking advantage of the high sensitivity and resolution of cryo-HERFD-XAS offered by the crystal analyzer spectrometer of FAME-UHD beamline (BM16, ESRF), we systematically studied the speciation of a library of representative gold(I) complexes in biological settings. A relationship between their speciation in bulk A549 lung cancer cells and their structure and biological activity was successfully established. Additionally, we could probe the speciation of two new families of biphenyl gold(III) N-heterocyclic carbene (BGC) complexes, and link their speciation to their physico-chemical properties and biological activities. This altogether allowed for a better understanding of the fate of these metallodrugs in cells and provided pivotal information regarding their mode of action.



REFERENCES

1 Y. Lu, X. Ma, X. Chang, Z. Liang, L. Lv, M. Shan, Q. Lu, Z. Wen, R. Gust and W. Liu, *Chem. Soc. Rev.*, 2022, **51**, 5518–5556.
2 M. Salmain and B. Bertrand, *Eur. J. Inorg. Chem.*, 2023, **26**, e202300340.
3 A. Balfourier, J. Kolosnjaj-Tabi, N. Luciani, F. Carn and F. Gazeau, *Proc. Natl. Acad. Sci.*, 2020, **117**, 22639–22648.
4 M. D. Hall, C. T. Dillon, M. Zhang, P. Beale and A. Et., *JBIC J. Biol. Inorg. Chem.*, DOI:10.1007/s00775-003-0471-6.
5 C. Sanchez-Cano, D. Gianolio, I. Romero-Canelon, R. Tucoulou and P. J. Sadler, *Chem. Commun.*, 2019, **55**, 7065–7068.
6 L. Messori, A. Balerna, I. Ascone, C. Castellano, C. Gabbiani, A. Casini, C. Marchioni, G. Jaouen and A. Congiu Castellano, *JBIC J. Biol. Inorg. Chem.*, 2011, **16**, 491–499.
7 A. Jacques, C. Lebrun, A. Casini, I. Kieffer, O. Proux, J.-M. Latour and O. Sénèque, *Inorg. Chem.*, 2015, **54**, 4104–4113.
8 I. J. Pickering, Q. Cheng, E. M. Rengifo, S. Nehzati, N. V. Dolgova, T. Kroll, D. Sokaras, G. N. George and E. S. J. Arnér, *Inorg. Chem.*, 2020, **59**, 2711–2718.