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A preclinical overview on gold (III) compounds in the forefront of the targeted anticancer therapy

Chiara Nardon[1,2], Leonardo Brustolin[1], Mauro Coluccia[3] and D Fregona[1,2]
[1]University of Padova, Italy
[2]A.R.TE.M.O. Association for the Research of Targeted Therapies in Oncology, Italy
[3]University of Bari "Aldo Moro", Italy

In the last four decades the drug cisplatin has been widely used in oncology despite of its toxicity, in particular nephrotoxicity, due to the high affinity of the soft metal center Pt(II) toward renal sulfur- and selenium-containing enzymes, thus affecting their catalytic processes. Taking into account the severe toxicological profile of cisplatin and the peculiar chemical properties of Pt (II), a number of metal compounds with encouraging antitumor activity and reduced toxicity compared to the reference drug have been recently designed, synthetized and biologically studied. In designing these coordination compounds, we replaced the Pt(II) and the two ammonia ligands were replaced with Au(III), Cu(II) or Ru (III) and a dithiocarbamato (DTC) moiety, respectively. Among all the studied complexes, our Au (III)-based potential chemotherapeutics showed a particularly promising chemotherapeutic index. On the other hand, the bidentate DTC ligand is able to widely stabilize metal ions owing to its electron-donating capability, thus hindering the ligand-metal decomposition that could give rise to non-specific metal reactivity in healthy tissues. Furthermore, the presence of sulfur donor atoms in the DTC ligand prevents the metal from interacting with thiol-containing biomolecules (trans effect), resulting in reduced or even absent side-toxicity. So far, researches on gold(III)-dithiocarbamato derivatives of aminoacids and oligopeptides have been carried out. These compounds generally showed higher antitumor activity than cisplatin and no cross-resistance to the reference drug on several human tumor cell lines. *In vivo* studies, on breast cancer MDA-MB-231 and prostate cancer PC3 xenografts, showed a reduction of 53% and 70% in tumor volume respectively, with neither decreased activity nor weight loss. The *in vivo* acute toxicity by i.v. and oral administration routes recording remarkable results. No signs of toxicity have been observed during the study in any of the treated animals. It is worth highlighting that body weight for any mouse was constant or increased during the 14-day observation period. Along with the antiblastic activity against breast cancer, a transcriptomic study has been performed to yield a deep mechanistic understanding of what biochemical pathways, crosstalks and feedbacks are affected by our gold(III) compounds.

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Biography

Chiara Nardon completed her PhD (2013) at the University of Padova (Italy) during which she spent 6 months at Karmanos Cancer Institute in Detroit (USA). Her research interests are mainly focused on studying new metal-based anticancer agents. She has been awarded with several Italian and international prizes and fellowships including being worldwide selected among the 600 final participants in the 63rd Meeting of Nobel Laureates. The magazine Scientific American has defined her among the young scientists who represent the future of chemistry. She is member of ACS, SCI and CIRCMSB societies and co-guest Editor of the *Journal of Nanoscience and Nanotechnology.*

chiara.nardon@unipd.it