New platinum-based chemotherapeutics: a journey beyond cisplatin

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ABSTRACT

The discovery of cisplatin and its later approved derivatives started a new era in the bioinorganic medicinal chemistry field but the persistence of severe side-effects along with the emerging of drug resistance evoke the need of a new generation of transition metal-based chemotherapeutics. The starting point of this journey was the preparation of diamine ligands derived from variously substituted *N*-methyl-2-aminomethyl imidazoles.[1] By introducing differently-long saturated and unsaturated chains at N1, the lipophilicity and the consequent cytotoxicity of the corresponding Pt(II)-complexes was modulated whereas its substitution with the 1,2,5-oxadiazole moiety selectively introduced the ability to simultaneously interact with DNA and to interrupt STAT3 signalling pathway.[2] Breaking the assumption that bifunctionality is necessary for antiproliferative activity, a series of monofunctional cationic platinum complexes were synthesised showing a potent cytotoxic effect toward triple-negative breast cancer cells and in cancer cell lines partially resistant to cisplatin. Moreover, the prominent stability of this class of platinum complexes suggested also a possible application for MSCs loading to use for advanced cell therapy.[3] Moving forward in this field, the effect of the bidentate ligands on the biological activity was highlighted showing for the Pt-8-aminoquinoline series a different biological profile.[4] In order to gain some mechanistic insights, the interaction of such platinum-based compounds with some model proteins was investigated through ESI-MS analysis.

Since an increasing interest has recently arisen in the development of platinum based theranostic agents, indeed, a series of cyclometalated anionic Pt(II) complexes carrying tetrabromocatechol or alizarine as O^O chelating ligands was developed. This last series of platinum complexes displayed enhanced cytotoxicity toward triple-negative breast cancer (TNBC) and they furthermore resulted emissive in solution.[5] Moreover, fluorescence confocal analysis showed their localization in the perinuclear region of MDA-MB231 cells proving their ability to serve as luminescent theranostic probes.

References:

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