VANADIUM COMPOUNDS INHIBIT CELL PROLIFERATION VIA MAPK AND CELL CYCLE ARREST

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Vanadium compounds demonstrated several biological effects, such as the insulin-like action, the reduction of hyperlipidemia and hypertension, associated to few adverse effects; moreover, evidences suggested that vanadium compounds could be considered as a new class of non-platinum, metal antitumor agents (Evangelou, 2002).

Sgarbossa et al. synthetized and characterized six new vanadyl complexes with acetylacetonate derivatives bearing asymmetric substitutions on the β-dicarbonyl moiety, which inhibited proliferation of both non-tumour (hTERT-HME1 and podocytes) and tumour cell lines (HCT 116 e HT-29): the antiproliferative effect seemed to be correlated to the vanadyl moiety in non-tumour cell lines, whereas tumour cell lines were resistant to vanadyl sulphate and ligands, suggesting a prevalent role of the conjugates (Sgarbossa et al., 2013).

To better characterize the antiproliferative activities of these compounds, complex c and complex d, in which the vanadyl moiety was complexed with naphthalene derivate, were selected because more active in inhibiting proliferation and for their fluorescent properties, which allow us to study their intracellular localization through confocal microscopy. The localization was cellular-dependent: they were prevalently localized in the cytoplasm, and only in tumour cells we could observe some clusters in nucleus, in particular complex d.

Both complexes modified cell cycle: particularly complex d induced cell cycle arrest in G2/M, more evident in hTERT-HME1 and podocytes; the effect was lower than that induced by oxaliplatin. The effect on cell cycle could be correlated to the increase of cdc-2 phosphorylation caused by both complexes in non-tumour and tumour cell lines.

Complex c and d modulated MAPKs activation in a time- and cell-dependent manner; the treatment with MAPKs inhibitors just in part modified the antiproliferative effect of the complexes. All together our results evidenced that antiproliferative effects mediated by these compounds are cell type-dependent and involve cdc-2 and MAPKs pathway.

Evangelou (2002). Crit Rev Oncol Hematol. 42(3), 249-65.

Sgarbossa et al. (2013) J Inorg Biochem. 128, 26-37.