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Induction of immunogenic cell death increased antitumor effect of a novel ruthenium complex against murine mammary adenocarcinoma 4T1

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Some cancer chemotherapeutics can induce Immunogenic Cell Death (ICD) while others cannot. Changes in the composition of tumor cell surface as well as release of soluble mediators occur in a defined sequence during ICD. These signals activate receptors expressed by dendritic cells, and activation of the immune system to induce a tumor-specific response may determine the long term success of anticancer therapies. We verified that two novel ruthenium compounds, *trans*-$[Ru(SO_4)(NH_3)_4(ImN)]^{3+}$, or $RuSO_4ImN$, and the NO-donor *trans*-$[Ru(SO_4)(NH_3)_4(ImN)]^{3+}$, or RuNOImN, (ImN=imidazole), showed antitumor effect in syngeneic preclinical models. Induction of ICD by ruthenium compounds in the murine breast carcinoma 4T1 was compared to oxaliplatin (an ICD inducer) and cisplatin. Tumor cells were treated *in vitro* with the chemotherapeutics, administered subcutaneously on female Balb/c mice, and after 8 days animals were challenged on mammary fat pad with viable 4T1 cells. Primary tumors developed similarly on all groups, but oxaliplatin and $RuSO_4ImN$ groups showed significantly reduced numbers of lung metastatic nodules and increased survival compared to cisplatin and RuNOImN groups. FACS analysis using splenocytes showed increase in $CD3^+/CD4^+$ cells on Oxaliplatin group, while increase in $CD49b^+$ Natural Killer cells was observed in $RuSO_4ImN$ group. These results suggest that the induction of a tumor-specific immune response increased antimetastatic effect of ruthenium compounds, and that different drugs may induce different immune responses.

Biography

Samanta Lopes Tomaz graduated in Pharmacy at University of Mogi das Cruzes, São Paulo, Brazil, in 2010. She is currently a Ph.D. student at the Department of Microbiology, Immunology and Parasitology, Paulista School of Medicine, Federal University of São Paulo. She works with preclinical models of breast cancer and immunogenic cell death.

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