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Gold(I)-NHC complexes containing selenium as alternatives to conventional chemotherapeutics

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Considered as the second cause of death on a global scale in the context of non-communicable diseases, cancer still continues to represent one of the most urgent public health challenges, reinforcing the need for more effective and safer treatments[1]. Due to the limitations of conventional chemotherapy with platinum-based drugs – such as adverse effects and cellular resistance – the choice of other transition metals has been used as one of the strategies to overcome this problem. In this scenario, gold-based compounds have gained attention as they are a promising alternative, due to their interactions with different biological targets (such as TrxR)[2]. In particular, organo-golds with the N-carbene-heterocyclic (NHC) class of ligands – like imidazole ionic liquids – form strong bonds with metal atoms, presenting themselves as stable and diverse structures, in addition to being biologically active. On the other hand, selenium (Se), as a sulfur analogue, has greater reactivity due to its lower pk_a and greater nucleophilic character, also acting as a cofactor in selenoproteins responsible for protecting oxidative stress[3]. In this study, the synthesis of three gold(I) complexes was performed with imidazole ionic liquids containing selenium, characterized by IR spectroscopy, UV-VIS, ^{1}H and ^{13}C NMR, mass spectrometry, elemental analysis (CHN) and X-ray crystallography. In fluorescence studies, the results of interaction with bovine serum albumin (BSA) showed that the complexes induced a suppression up to 50% of the protein fluorescence, calculated through the Stern-Volmer constants, a moderate interaction. DNA-intercalation studies with ethidium bromide (BE) indicated that the compounds were not able to displace BE and, therefore, the intercalation-type interaction is not predominant. The evaluation of the effect of the complexes on cell viability was carried out in triple-negative breast cancer cell lines (MDA-MB-231 and 4T1), using the mean inhibitory concentration (IC_{50}) values. To define selectivity effects (SI), the normal breast cell line MCF-10 was used under the same conditions. The results showed greater cytotoxicity and selectivity (SI) of the complexes in relation to the ligands, demonstrating the importance of the coordination of the gold metal center in the cytotoxic activity (**Figure 1A and 1B**). Tests of compounds with reduced Glutathione (GSH) show an interaction with the tripeptide. Due to the promising results, new derivatives and tests are in preparation.

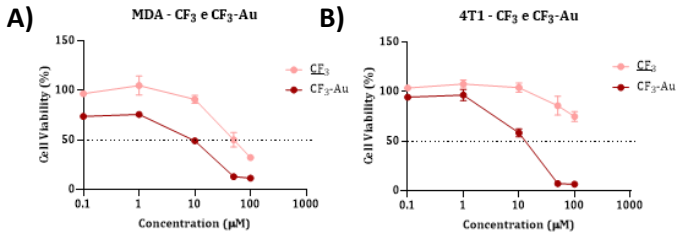

Figure 1: A) cell viability curves of CF_3-Au in MDA **B)** and 4T1 cells.

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