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Influence of I-125 labeled TFO in SCL-II cells on cell survival, cell cycle and DSB induction

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Triplex-forming oligonucleotides (TFO) are able to bind DNA in a sequence specific manner and are a promising tool to manipulate genes or gene regulatory units in a cellular environment. TFO posses a therapeutic potential e.g. as a carrier molecule for Alpha- or Auger-Electron-Emitter (AEE) to target specific DNA sequences in tumour cells. We established a method for the effective labeling of TFO with the AEE Iodine-125 (I-125) and studied the influence of labeled TFO in SCL-II cells with regard to cell survival, appearance of DNA Double-Strand-Breaks (DSB) and the induction of cell cycle arrest.
The TFO employed in this study were two multi-binding TFO with several thousand binding sites each in the human genome and a single binding site TFO, specific for GAPDH. TFO labeling with I-125 was performed using the primer extension method. Cell survival and DNA DSB frequency in I-125-TFO transfected SCL-II cells were analyzed with the Colony-Forming-Assay and the 53BP1 Assay. Analysis of cell cycle was done after 7-AAD staining by flowcytometry.
I-125-labeled TFO were shown to induce a pronounced decrease in cell survival and an increase of DSB. TFO targeting multiple sites differing in the total target number showed a significant different cell killing per decay that was in good accordance with the observed induction of DSB per decay. Single gene targeting I-125-labeled TFO significantly decreased cell survival and induced DSB as well. All three investigated TFO induced a significant cell cycle arrest in G2/M phase 8 h post-transfection.
I-125-labeled TFO with a single binding site as well as TFO with multiple binding sites cause massive cell killing and increase substantially the DSB frequency in SCL-II cells. All investigated TFO induce a pronounced G2/M arrest at rather low numbers of accumulated decays. I-125-labeled TFO might be a very useful tool for basic DNA repair research.

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