Cytotoxicity and induction of cell cycle arrest in SCL-II cells after transfection with I-125 labeled Triplex-Forming Oligonucleotides.

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Introduction: Triplex-forming oligonucleotides (TFOs) 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. TFOs posses also a therapeutic potential e.g. as a carrier molecule for Alpha- or Auger-Electron-Emitter (AEE) to target specific DNA sequences in tumor cells. We established a method for the effective labeling of TFOs with the AEE iodine-125 (I-125) and studied the influence of labeled TFOs in transfected SCL-II cells with regard to cell survival, appearance of DNA Double-Strand-Breaks (DSB) and the induction of cell cycle arrest.
Methods: The TFOs employed were a single binding site TFO, specific for *GAPDH* and two multi-binding TFOs with several thousand binding sites in the human genome. 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.
Results: All three tested TFOs induced a pronounced cytotoxic effect on SCL-II cells. The broadest effect was found for the TFO employing the highest target number in the genome. Furthermore an increased frequency of DSB and a significant cell cycle arrest in G2/M phase 8 h post-transfection could be detected.
Conclusion: I-125 labeled TFOs with multiple binding sites as well as single binding TFOs do induce a pronounced cytotoxic effect and increase the DSB frequency in SCL-II cells. Additionally there is strong evidence that I-125-labeled TFOs can influence the cell cycle course in transfected SCL-I cells.

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