SENSYBILIZOWANE USZKODZENIA FOTOCHEMICZNE I RADIACYJNE W OLIGONUKLEOTYDACH ORAZ KOMPLEKSACH BIAŁKO-DNA

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The main aim of work was to explain and understand the influence of specific interactions between amino acid side chains and nucleobases in sensitized double-starnded DNA/peptide complex to radio- and photodamage of DNA.

DNA, the main target of anticancer therapy, is not sensitive to the near UV photons and hydrated electrons, one of the major products of water radiolysis under hypoxic conditions. A possible way to overcome these obstacles to the efficient radio- and photodynamic therapy of cancer is to sensitize the cellular DNA to electrons or UV light by labeling it with suitable sensitizers.

Radiotherapy, the most common modality for solid cancer treatment, is geared on DNA damage induced by the product of water radiolysis. Under hypoxia, typical for solid cancer cells, the efficacy of hydroxyl radicals (•OH) to trigger DNA damage is significantly lowered as compared to the oxygenated cells while the yield of production of hydrated electrons is equal to that of •OH. However, hydrated electrons (e_{hyd}) are not able to induce a serious damage as strand breaks (SBs) to native DNA [1]. In order to make e_{hyd} harmful one can modify DNA with specifically altered nucleosides (radiosensitizers) so that an irreversible electron attachment to them may lead to SBs and ultimately to lethal effects [1,2]. On the other hand the well described [1] in literature photodame of DNA

It is worth of noticing, that in the cellular environment DNA permanently interacts with proteins via hydrogen bonding between nucleobases and amino acids and these interactions may influence both the primary electron attachment process and the secondary reactions leading to DNA damage [1]. In order to investigate the sensitization processes in environments close the natural ones access to a molecular model, involving a specific DNA-protein complex, is necessary. Here, we will present how a complex of the BrdG/BrdA/BrdC or BrdU-labeled double stranded DNA (dsDNA) with a covalently linked peptide (dsDNA-PEP) can mimic native DNA and serve as a tool for the development of radio- or photosensitizers. The radiolytes (X-ray) and photolytes (260 or 320 nm) of labeled dsDNA-PEP were fully characterized using the HPLC and LC-MS methods. The aquired data reflect the influence of interaction between peptide and DNA on the yiled of radio- and photodamage to the labeled complex.

References:

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