New Research Bodes Well for Radionuclide Treatment of Tumours

Study examines biological effectiveness of Auger electron emitter $^{123}$I in human lymphocytes

Auger electrons (AE) are low energy electrons emitted by radionuclides that decay by electron capture. The energy is deposited over a fraction of a distance (nano- to micrometre range) in a high energy linear transfer (LET), making them ideal in the treatment of certain cancers and other diseases due to their limited damage to normal, non-diseased tissue.

AE emitters, such as iodine-123 ($^{123}$I – a radioactive isotope of iodine), are produced in South Africa by NRF-iThemba LABS and can be targeted into the DNA of tumour cells in order to destroy them. Radionuclide therapy with AE emitters, as opposed to external beam therapy or brachytherapy (where a radioactive source is placed next to or inside the area requiring treatment), almost exclusively uses the energetic electrons from the particle emitting isotopes. The limited range of these electrons means that high doses can be delivered to tumours with minimal damage to surrounding healthy tissue.

A new research project conducted by scientists from the Department of Physics at Stellenbosch University, NRF-iThemba LABS and the SA Nuclear Energy Corporation, with funding from the NRF, has taken the concept of using Auger electron emitters for radionuclide therapy further by studying the biological effectiveness of $^{123}$I in human lymphocytes.

While $^{125}$I is the more commonly used radioisotope in studying in vivo and in vitro Auger electron induced DNA damage, $^{123}$I was chosen for this study due to its relatively short half-life (13.2 hours as opposed to 59.4 days for $^{125}$I) which allows it to deposit biologically detectable amounts of radiation over a short time period.

The short range of the Auger electrons (1nm – 2nm) coincides with the 2nm diameter of the DNA helix. Hence, one decay of $^{123}$I incorporated into the DNA of tumour cells will result in one DNA double strand break (DSB). In addition, Auger electron emitters can damage cells indirectly via the radiolysis of water and the production of free radicals, potentially causing complex and multiple DSB to tumour cell DNA.

Blood samples from three male volunteers were used in the study and, once prepared, were exposed to graded doses of $^{123}$I ($0, 0.19, 0.37, 0.56, 0.74, 0.93, 1.9$ and $3.7$ Megabecquerels (MBq)) in the form of $^{123}$IUdR. The Geant4 Monte Carlo toolkit was used to calculate the dose delivered to the cells. The dose rates for the exposures were relatively low (0.02Gy/min at the activity level of 3.7MBq).

The results of the experiment proved promising with a high biological effectiveness of $^{123}$I to kill tumour cells, adding to a relatively new area of cancer treatment research. The study found a linear increase in micronuclei (MN - small extranuclear bodies resulting from chromosome breaks) induction with increasing $^{123}$I activity, indicating the high potential of AE emitters to create dense patterns of DNA DSBs, which contribute to tumour cell killing. This is one of the first studies to evaluate chromosomal damage induced by DNA incorporated $^{123}$I, increasing the potential for $^{123}$I to be used as a theranostic radionuclide (where diagnosis and specific targeted therapy are combined to achieve a personalised treatment approach).