CATAMARAN targeted at innovative radiopharmacy

SCK•CEN explores new medical applications of radioisotopes

In cancer therapy there is a great need for specific treatments: therapies that kill cancer cells selectively without affecting the healthy cells. In the CATAMARAN project (Cancer Targeting Molecules Attached to Radionuclides) SCK•CEN develops, in a preclinical trial, products that deliver the right radiation doses at the right place in the human body. With the new multidisciplinary expertise that has been built up in the project, SCK•CEN is contributing to new medical applications of radiation.

Lutetium-177 + Nanobodies® = Lutebodies

Cancer therapy makes use of radioisotopes with cytotoxic properties, i.e. they are fatal to cancer cells. In order to increase the efficacy of such a therapy, it is important for the radioisotopes to get to the right place, directly to the cancer cells.

/ Treatments with radioisotopes are promising in nuclear medicine, which is continually pushing back its boundaries. With our multidisciplinary research in the field of nuclear physics, radiochemical analysis and molecular biology, we contribute to the radiopharmacy of the future. /

Nathalie Impens and An Aerts

In order to achieve this specificity, vector molecules are used that guide, as it were, the radiotoxic elements to the cancer cells.

The CATAMARAN project is developing radiopharmaceuticals that contain lutetium-177 as a radioisotope, a promising radioisotope in cancer treatment. Nanobodies® are currently used as a vector molecule. They are a new class of innovative therapeutic proteins, derived from fragments of antibodies from camelids, with very interesting pharmacological properties. They have a high affinity, such that they specifically bind to one therapeutic target, they are remarkably stable and relatively easy to produce. These Nanobodies® were originally developed at the Vrije Universiteit Brussel (VUB). Some of them are currently being clinically tested for the treatment of thrombosis, for example. In the CATAMARAN project, Nanobodies® are used that specifically target cancer cells. These Nanobodies®, labelled with lutetium-177, have been dubbed Lutebodies. SCK•CEN is conducting this research in close cooperation with the Vrije Universiteit Brussel (VUB).

Promising

The CATAMARAN project started in 2008 and is proceeding step by step. A different research discipline is involved at each stage, from nuclear physics, radiochemical synthesis and molecular and cellular biology, to medical imaging.
The researchers first of all labelled the antibody fragments with the radioisotope lutetium-177 produced in the SCK•CEN BR2 reactor. This labelling was done by using bifunctional ligands, i.e. chemical molecules that bind to both the

↑ *Radiobiological research for nuclear medicine is a growing field of research at SCK•CEN.*

The CATAMARAN project uses Nanobodies® aimed specifically at cancer cells.

radioisotopes and the Nanobodies®. Once these radiolabelled antibodies have been synthesised, they are exhaustively tested in vitro. The first results are promising: the in vitro tests went according to expectations for both the labelling and the binding to the target cells. Little free lutetium-177 was left, which is important for its application in the human body.

Towards a new radiotherapeutic remedy

In the next few years work will primarily be done on in vivo testing, the reproducibility of the results and the extension to CATAMARAN molecules based on other vector molecules. The aim is to have a new preclinically validated radiotherapeutic remedy. After that, conversion to clinical applications is possible.