Master thesis project at Radioimmunotherapy group, Norwegian Radiumhospital

BACKGROUND

Radioimmunotherapy is a type of medical treatment of cancer that uses antibodies and radiation. The method uses a radionuclide attached to an antibody (radioimmunoconjugate) to deliver radiation specifically to tumor cells thereby decreasing the dose to normal tissues and the associated negative effects on the patient health. Currently two commercial radioimmunoconjugates are being used for treatment of Lymphoma that target the antigen CD20 presents in the blood cells. The proposals herein presented will take place in close cooperation with Nordic Nanovector. Nordic Nanovector is company founded one year ago that started as a spinoff from research done by the radioimmunotherapy group at the department of Radiation Biology, the Norwegian Radium Hospital. The company is focused on the development of a new radioimmunotherapy drug for Lymphoma treatment called Betalutin™ that targets a different antigen in B-cells. The studies are still in the preclinical stage, and it is expected to begin with Phase I clinical trial in 2012. The master student will work at the Radiumhospital in the Radioimmunotherapy group in close cooperation with a PhD student and a bioengineer, contributing with important research pertinent to the preclinical studies.

PROJECT 1

An important part of the validation of Betalutin is to test its therapy effect in-vitro. In order to do this, extensive work in cell cultures is needed. There are several experiments where the master student can join depending in his/her personal interests. The work with live cells will be done using different lymphoma cell lines that are already in use in the laboratory and different concentrations of Betalutin. The therapy in vivo experiments might begin with the student learning how to conjugate the antibody and radionuclide. Preparation of the cell cultures will be needed, after which the therapeutic amount of
radioimmunoconjugate will be added. The cell growth, viability and radioactivity will be measured at predefined time points. Growth curves will allow estimating the growth rate of the cells for the different treatments. These experiments will allow the research group to assess which Betalutin concentration gives the best therapeutic effect and which cell line is more sensitive to it. The data analysis may include a microdosimetry study in a cell. The student will be supplied with relevant literature and shown how to perform all the relevant experimental techniques and data analysis. Some of the experimental techniques that can be used in this project are: sterile techniques, immunoreactivity fraction assay, cell grow experiments, gamma-detection, etc.

PROJECT 2

Another important part of the validation of Betalutin will be to test its therapy effect in-vivo. In order to do this, extensive work with mice is needed. There are several experiments where the master student can join depending in his/her personal interests. There are plans to perform therapy, toxicology and biodistribution experiments with mice implanted with xenografts of four different cell lines and with different Betalutin treatments. In the therapy experiments the mice are injected with different doses of Betalutin and the evolution of the tumor size and mice weight is followed in time. During the toxicology experiments the mice are injected with different doses of Betalutin and blood samples are taken at regular intervals of time. The blood analysis is done in our own laboratory allowing both hematology and clinical chemistry. In the biodistribution studies the mice are injected with small amounts of radioimmunoconjugate and they are autopsied at predefined time points. The activity in each organ as well as the organs weights are measured and the distribution of radioimmunoconjugate in the different organs is calculated. These tests allow estimating how good the cancer treatment by Betalutin is, how well the organisms tolerate the radioactive dose and which are the main organs to which the radioimmunoconjugate binds. Some experiments using Zevalin (one of the current commercial products used in the clinic) may be performed to compare the efficacy of both products.

PROJECT 3

Any combination of Projects 1 and 2 that might interest the student.
**Contact Person:** Students who might be interested in a master project within one of these topics should contact Dr. Ada Repetto-Llamazares (ada.repetto@rr-research.no, mob. 96820726). Any questions on the project are welcome!