**Improving Outcomes in Radiotherapy using Novel Biotechnologies: Modification of Tissue Reactions and the Use of Stem Cell Therapeutics**

**Summary:**

During radiotherapy, the most important dose-limiting factor is sensitivity of the normal tissue lying in the radiation field. This can result in organ damage or severe normal tissue reactions. Radiation-induced organ damage is mainly caused by stem cell sterilization and hence leading to a reduced reconstitution of functional cells in the irradiated organ. Replenishment of the depleted stem cell compartment should allow regeneration of irradiated tissues/organs. The major aim of the project is to facilitate and disseminate stem cell research in IAEA Member States to prevent radiation-induced damage to normal tissues/organs. If this approach has proven to be successful in pre-clinical studies, stem cell therapy could be tested in future clinical trials. Moreover, this newly acquired knowledge/expertise could also be used to design new strategies in the treatment of victims of radiation accidents.

**Overall Objective:**

The major aim of the project is to provide the Member States with new and relevant knowledge on stem cell therapeutics (i.e. optimization of techniques) to prevent radiation-induced damage to normal organs/normal tissues. If this approach has proven to be successful in pre-clinical studies, stem cell therapy could be tested in future clinical trials. Moreover, newly acquired knowledge/expertise could also be used to initiate new strategies in the treatment of victims of radiation accidents. The initiation of collaboration between relevant laboratories; establishing of exchange programs and joint applications for additional funding will be stimulated.

**Specific Research Objective:**

Although the first results on stem cell therapy after irradiation look exiting and encouraging, the knowledge about stem cell therapy is not yet sufficient for clinical application. A CRP is proposed to develop new stem cell techniques and/or optimise already available stem cell techniques.

To successfully use stem cell therapy it is important to understand:

- The nature and qualities of different types of stem cells,
- The mechanism by which stem cells differentiate into mature, functional cells and,
- Their capacity to repair damaged (irradiated) tissues/organs in a variety of experimental animal models.

In order to develop experimental protocols for the amelioration of radiotherapy-induced side effects by stem cell therapy a number of specific research questions need to be answered:

- What is (are) the most optimum time-point(s) for stem cell therapy; one or more treatments and when?
- What is the optimum number of stem cells to be transplanted; or optimum drug dose (cocktail of growth factors?); optimum exposure to molecular/viral vectors
- What is the best routing; local administration of the cells/compound/drug or systemic administration (i.e. via IV injections)?
• Which cells/compounds or combinations have the highest potential of reducing radiation-induced tissue toxicity in a specific tissue?

• What are the risks of stem cell therapy; i.e. does stem cell therapy later induce cancer, teratoma’s or other malformations?

**Expected Research Outputs:**

• This CRP will provide new data with respect to the efficacy (usefulness) of different stem cell techniques to repair radiation damage in a variety of normal tissue/organ systems. The tissues of interest will be oral mucosa, skin, gut, salivary gland, as examples of “early responding tissues” and spinal cord, bone, muscle and heart as examples of “late responding tissues”.

• Development of standard methodology (incl. production, delivery storage etc.) for the three different stem cell methods and the different experimental normal tissue/organ models.

• Research progress on this topic (presentations, publications, documents, reports, abstracts etc.)

• Initiation of collaboration between relevant laboratories; establishing of exchange programs and joint applications for additional funding.

**Expected Research Outcomes:**

Provide expertise from preclinical studies to realise clinical trials utilising these novel strategies in the future.

• It is expected that this CRP will lead to improved knowledge and technical expertise in radiobiology stem cell research not only in the participating laboratories but also in the IAEA Member States.

• Modification of irradiation induced normal tissue/organ damage.

• Improving outcomes in radiotherapy (improved cure rates with fewer or less severe side effects).

• Provide technical expertise in the treatment of (accidental) radiation injuries.

**Participating institutions:**

1. ALGERIA: Service de Radiothérapie Oncologie, Centre Pierre et Marie Curie, Centre Hospitalier Universitaire Mustapha (CHU), Alger


3. EGYPT: Misr Oncology Center (MOC), Cairo, Nasr City

4. GREECE: Radiation Oncology Department, University Hospital of Alexandroupolis Dragana, Alexandroupoli.

5. POLAND: Marie Curie-Sklodowska Institute of Oncology, Warsaw.

7. TUNISIA: Institut national de cancer Salah Azaiz, Ministère de la Santé Publique, Tunis, Bab Saadoun

8. CANADA: Wilson Roa Professional Corporation, Edmonton, Alberta (data management)