MELODI Statement
(October 2011)
on a

Short- to medium-term research agenda for R&D projects to improve the scientific basis for radiation protection in Europe

The following statement of the MELODI governing board provides information on research priorities, which are currently being refined into an extended Strategic Research Agenda of MELODI, elaborated on the basis of the concepts developed by HLEG, of the transitional research agenda of the Network of Excellence DoReMi, of the proceedings of the 1st MELODI workshop (28-29 September 2009, Stuttgart), and of the 2nd MELODI workshop (18-20 October 2010, Paris). This executive statement of the MELODI governing board updates and consolidates the MELODI statement from November 2010.

The research calls by EURATOM for R&T projects have been led by the policy goals to improve radiation protection standards in Europe, and to prioritise and focus European research efforts to achieve maximal impact on scientific knowledge and avoid duplication of research, with a view to consolidating the current scientific basis for the system of radiation protection, as recommended by ICRP and defined in the Basic Safety Standards. These goals are fully supported by MELODI.

The Fukushima nuclear accident has highlighted the necessity to consolidate the scientific knowledge on radiation risk at low doses in a way that emergency response measures especially for the general public in directly effected regions and beyond can be based on the best scientific evidence that conveys to the public the validity of measures taken in order to simultaneously protect public health and ensure the economic and societal continuity in the country.

MELODI recommends the introduction of research projects specifically addressing the situation in Fukushima where Europe could join Japanes efforts to develop suitable cohorts for the purpose of long term research. This could be of interest for cancer, non-cancer, and may be other projects. Apart from demonstrating the solidarity with the Japanes people, this could be a further incentive for European R&D teams to join efforts with Japanese teams.

The present radiation protection system is mainly based on scientific knowledge from epidemiological studies, which have played an important role in assessing the magnitude of radiation risk in the dose range down to about 100 mSv. Epidemiological studies continue to contribute to low dose risk research and particularly on risks of low dose rate chronic exposures, risks from internal emitters and non-cancer risks. However, further refinement of low dose risk estimates will necessitate the close association of epidemiological with experimental mechanistic studies. For example, by

using suitable molecular and cellular biomarkers, the value of future epidemiological studies (molecular epidemiology) for radiation risk research is expected to be maximised. To achieve maximal value, validated and reliable biomarkers are required for exposure, for effects on the cellular and tissue level, individual radiation sensitivity and, most importantly, for in-situ stages of radiation-associated diseases. Any research should include a realistic assessment of the associated uncertainties.

Experimental evidence suggests that both effects in target cell and effects and responses in the tissue environment (microenvironment) contribute to radiation-induced disease. The relative importance of these effects for different radiation qualities, at different dose levels and exposure conditions (acute, chronic, fractionated) in relation to different diseases is currently not sufficiently understood. Experimental work can best contribute by seeking dose levels where disease-associated effects are or are not observed, either in target cells, in the tissue environment or in the interacting system of both (tissue, organ or organism).

The experimental and epidemiological studies require a commitment to collect and sustainable archiving of biological materials and data.

Mathematical and computational modelling of experimental data will allow a better understanding of radiation track structure and mechanisms of radiation effects at the level of the DNA, other intracellular targets, at the level of target cells and the tissue environment. In this context MELODI recommends to include the development of omics-based analysis capabilities in a scope of future multidisciplinary research projects. The modelling efforts together with those using animal and epidemiological data including systems biology approaches will provide further insights into biological effectiveness effects of radiation quality.

According to MELODI, priorities for forthcoming and long-term future research should take into account the need to investigate effects of ionising radiation of different qualities on radiation-induced cancer and non-cancer diseases as well as on individual variation of radiation risks. All efforts should include a careful dosimetric approach. The long-term priorities include the following areas:

(1) for radiation-induced cancers and non cancer diseases

- Identification, establishment and continued follow-up of suitable cohorts of radiation exposed people for epidemiological studies related to cancer and non-cancer effects
- Identification, development and validation of biomarkers for radiation exposure, effects and disease.
- Continuing development of suitable whole animal as well as human cellular models (including somatic stem cells) for radiation carcinogenesis and non-cancer diseases which bear clear relationships to human diseases.

(2) for radiation-induced cancer

- Examination of the impact of low dose and low dose rate radiation effects on pathways/processes contributing to carcinogenesis. This involves the understanding of the relationship between early and late effects, targeted and non-targeted effects as well as the role of delayed genetic instability.

- Identification of the nature and number of target cells at risk for a specific cancer in humans.

(3) for radiation induced non cancer diseases

- Examination of the impact of low dose and low dose rate radiation effects on pathways/processes contributing to non cancer disease such as cardio- and cerebro-vascular disease, cataract of the eye and impaired cognitive function.
- Identification of the nature of target cells at risk for specific non-cancer diseases in humans.

(4) for individual and general health and radiation protection issues

- Understanding the impact of inter-individual variation of radiation risks in relation to cancer and non-cancer diseases, and how this might impact on dose response relationships in populations.
- Clarification of the contribution of radiation effects in target cells as well as radiation effects and responses in the tissue environment and interaction between both target cell and tissue environment at different dose levels to the development of radiation-associated diseases.
- Examination of the impact of low dose and low dose rate radiation effects on immune function.
- Understanding of the effect of age-at-exposure on radiation risk.
- Better understanding of the risks of internal emitters following internal contamination with radionuclides.

As an ongoing process MELODI develops and periodically updates the long-term Strategic Research Agenda (SRA) and makes use of the yearly executive statements to recommend short- to medium-term priorities (funding period 2012/2013). In the years to come priority should be given to:

- Quantification of the role of ionising radiation in the development of non cancer disease such as cardio- and cerebro-vascular disease, cataract of the eye and impaired cognitive function after low dose (< 500 mSv) irradiation.
- Development of suitable biomarkers for exposure, cellular and tissue effects as well as for in situ stages of diseases. The biomarkers should be usable for molecular epidemiological studies.
- Clarification of the role of effects in target cells and in the tissue environment in a dose range with clear focus on low doses. This may include in vivo detection systems as well as suitable in vitro systems.
- Identification and analysis of suitable epidemiological cohorts if available with archived biomaterial to improve low dose radiation risk assessment by reducing uncertainties especially for the age- and gender-dependency of radiation risk and including those uncertainties contributed by exposure assessment. Suitable data and biomaterial banks should be established with a

clear focus on the possibilities to share data, material and knowledge within the scientific and wider radioprotection community.

- Development of guidelines for short, medium and long-term exposure and health risk monitoring in case of a major nuclear accident in Europe. This is to ensure the public that all possible scientific efforts are undertaken to record, document and analyse exposed populations in the scientifically best available way to generate information about health consequences from possible accidents in future in a comprehensive manner.