



**MELODI Statement  
(18 November 2010)  
on a**

**Short- to medium-term research agenda for R&T 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 a first edition of the 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 1<sup>st</sup> MELODI workshop (28-29 September 2009, Stuttgart), and of the 2<sup>nd</sup> MELODI workshop (18-20 October 2010, Paris).*

The research calls by EURATOM for R&T projects (Research and Training) 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 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, robust and reliable biomarkers are required for exposure, for effects on the cellular and tissue level and, most importantly, for radiation-associated diseases. The research should always 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. These 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 cardio-vascular disease.
- Identification of the nature of target cells at risk for specific non-cancer diseases in humans.
- Examination of the impact of low dose and low dose rate radiation effects on pathways/processes contributing to cerebro-vascular disease and cognitive function.

(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 be-

tween 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.

MELODI is currently in the process of structuring all these priorities within a Strategic Research Agenda (SRA). In view of the most recent developments, MELODI recommends that short- to medium-term priorities (funding period 2011/2012) should be given to:

- Quantification of the role of ionising radiation in cardio-vascular and cerebro-vascular disease development after low dose (< 500 mSv) irradiation.
- Development of suitable biomarkers for exposure (immediate post radiation as well as long term after exposure), for cellular and tissue effects and for radiation associated leukaemia, solid cancers and non-cancer diseases. The biomarkers should be usable for molecular epidemiological studies of cancer risk below a cumulative dose of 100 mSv and for non-cancer risk studies below 500 mSv, respectively.
- 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 includes the development of suitable tissue, organ and animal models for the identification of target cells and the interaction between target cells and tissue environment as well as the utilisation of stem cell approaches.
- 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. These may include cohorts exposed to internal contaminations.