



MELODI Multidisciplinary European
Low Dose Initiative

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Multidisciplinary European Low Dose Initiative

MELODI is an European Platform dedicated to low dose radiation risk research. In 2010 MELODI was founded as a registered association with 15 members. The purpose of MELODI is:

- MELODI will propose R&T priorities for Europe in its field of competence - EUROPE 2020 Strategy.
- MELODI will seek the views of stakeholders on the priorities for research, keep them informed on progress made, and contribute to the dissemination of knowledge.
- MELODI will interface with international partners like WHO and IAEA.

Based on the outcomes of the yearly MELODI workshops a **Strategic Research Agenda (SRA)** is being progressively developed. To assure an open and vivid discussion and development of the SRA the contribution from a large number of scientists and stakeholders is needed. More information about the SRA and the ongoing discussion can be found under SRA.

In parallel to the SRA a statement on a **short- to medium-term research agenda for R&T projects** is developed to improve the scientific basis for radiation protection in Europe giving guidance for pending EURATOM R&T project calls. These recommendations can be found under **MELODI documents**. Comments on the statements are welcome, too.

MELODI Partners

BfS, Germany; CEA, France;
CREAL, Spain; DUTH, Greece;
ENEA, Italy; HMGU, Germany;
HPA, U.K.

Sweden; SBU, Sweden;
Republic; UAM, Spain;
University of Rostock,
Germany; URV, Spain;
Wiv-isp, Belgium

Membership

How to join MELODI?

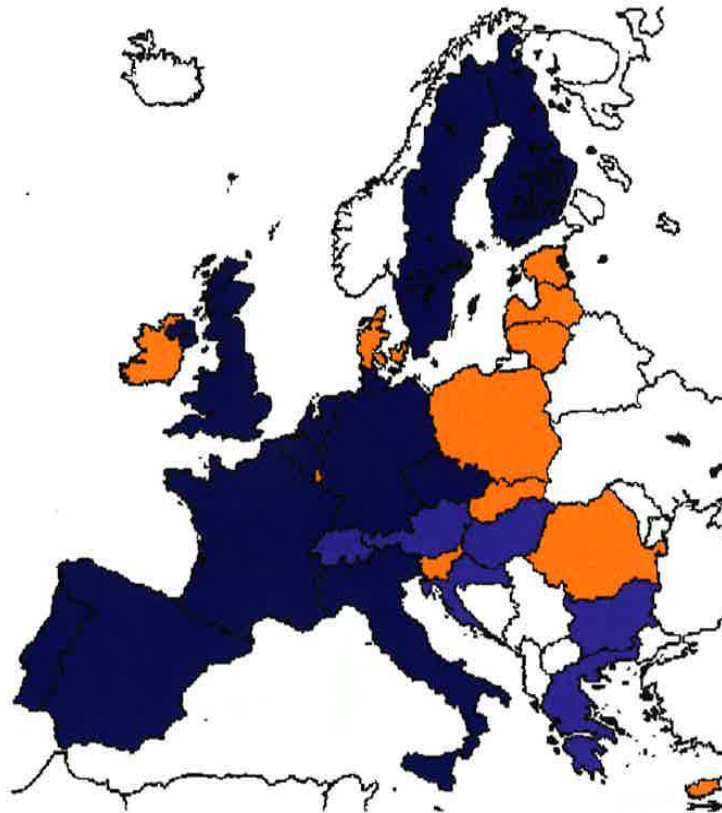
Members Login

Contact

Bundesamt für
Strahlenschutz
Postfach 10 01 49
D-38201 Salzgitter
Germany

**European
platform -
created 2010**

Current MELODI membership



- 11 countries with « founding members »
- 6 countries with MELODI members»
- 11 countries still without MELODI members



Multidisciplinary European Low Dose Initiative

AUSTRIA	MEDICAL UNIVERSITY OF VIENNA
BELGIUM	SCK-CEN, ISP
BULGARIA	NCRRP
CROATIA	IMROH
CZECH REPUBLIC	UNIVERSITY OF SOUTH BOHEMIA
FINLAND	STUK
FRANCE	CEA, IRSN
GERMANY	BFS, HMGU, KIT, KVSF, UNIVERSITY OF ROSTOCK,
GREECE	DUTH
HUNGARY	HUNGARIA ACADEMY OF SCIENCE, NRIRR
ITALY	ENEA, INFN, ISS, UNIVERSITY OF PAVIA
NETHERLANDS	RIVM
PORTUGAL	ITN
SPAIN	CREAL, UAM, URV
SWEDEN	SSM, SU
SWITZERLAND	IRA
UK	PHE, UNIVERSITY OF BELFAST

5th draft of MELODI SRA

- **Michaela Kreuzer (Chair), BfS, Germany**
- **Dietrich Averbeck, IRSN, France**
- **Imre Balashazy, MTA-EK, Hungary**
- **Simon Bouffler, PHE, UK**
- **Elisabeth Cardis, CREAL, Spain**
- **Mats Harms-Ringdahl, SU, Sweden**
- **Peter Jacob, HMGU, Germany**
- **Jean-Rene Jourdain, IRSN, France**
- **Katja Kojo, STUK, Finland**
- **Simona Pazzaglia, ENEA, Italy**
- **Kevin Prise, UK**
- **Friedo Zölzer, Czech Republic**

- **A. Ottolenghi, L. Sabatier**



Strategic Research Agenda of the Multidisciplinary European Low Dose Initiative (MELODI)

M. Kreuzer, D. [Averbeck](#), I. [Balashazy](#), S. [Bouffler](#), E. [Cardis](#),
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Status : 13 June 2014



Integrating observational and experimental research

Barcelona, 7-9 October 2014

MELODI



Bernard Gagnon, 2009



Jordi Cerdà, 2006



UNIVERSITAT
ROVIRA I VIRGILI



Key questions and cross-cutting issues in European low dose risk research

Radiation exposure/dose

External radiation

- acute
- protracted
- fractionated

Internal radiation

- acute
- protracted
- fractionated

Dose-response relationship

Modification of risk by

- Genetic factors
(individual radiosensitivity)
- Age, sex, lifestyle factors
- Other exposures

Radiation quality

Health outcome

Cancer

- Lung, Stomach, Breast, etc.
- Leukemia

Non-cancer

- Cardiovascular
- Lens opacities
- Neurological dis.
- Others

Tissue sensitivity



Because the magnitude of health risk and biological effects is expected to be low, research at low dose-rates or low doses presents significant challenges in the investigation of both

- radiation-related health effects and
- underlying biological mechanisms,

A multidisciplinary approach is therefore essential.

Three research lines / key questions

- Dose and dose rate dependence of cancer risk
- Non-cancer effects
- Individual radiation sensitivity

At low dose rates or low doses

Three research lines / key questions

- Dose and dose rate dependence of cancer risk
- Non-cancer effects
- Individual radiation sensitivity



Basic mechanisms

Research to improve the understanding of the mechanisms contributing to radiation risk

Three research lines / key questions

- Dose and dose rate dependence of cancer risk
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Basic mechanisms

Research to improve the understanding of the mechanisms contributing to radiation risk



Health risk evaluation

Epidemiological research that integrates – where possible and informative – biological approaches for radiation risk evaluation

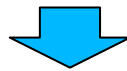
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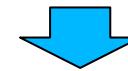
Basic mechanisms

Research to improve the understanding of the mechanisms contributing to radiation risk



Health risk evaluation

Epidemiological research that integrates – where possible and informative – biological approaches for radiation risk evaluation



Impact of radiation exposure characteristics

Research on the effects associated with internal exposures, differing radiation qualities and inhomogeneous exposures

Key question 1: Dose and dose rate dependence of cancer risk

Basic mechanisms

- The nature of the target cells for radiation carcinogenesis
- The contribution of DNA damage / mutational processes
- The contribution of (epi)genetic modifications
- The influence of cell micro-environmental, stem cell, non-targeted and systemic processes

Health risk evaluation

- The shape of the dose-response relationship in humans based on key informative cohorts
- To identify and validate biomarkers of exposure/effects
- To investigate pre-stages of cancer in biological samples of cohort members
-

Models integrating epidemiological and mechanistic data

Key question 2: Non-cancer effects

Basic mechanisms

- To develop *in vitro* and animal models for radiation-associated non-cancer outcomes to clarify which regulatory pathways are involved
- Application of a full range of analytical methods (e.g. ,omics‘) and consideration of the target cells and surrounding micro-environment

Health risk evaluation

- The shape of the dose-response relationship in humans based on key informative cohorts
 - To identify, develop and validate biomarkers for exposure, early and late effects
 - To investigate early stages in the progression of non-cancer effects in biological samples from cohort members

Models integrating epidemiological and mechanistic data

Key question 3: Individual radiation sensitivity

- **Differences in radiation risk may relate to**
 - gender
 - attained age
 - age at exposure
 - state of health
 - genetic or epigenetic make-up
 - lifestyle (e.g. smoking)
 - chemical co-exposures („multiple stressors“)

- We need better knowledge on the extent of the variations in sensitivity in the population, both
 - in the sizes of variations
 - and also in the proportions of the population that are affected

Individual radiation sensitivity

Basic mechanisms

- **To develop a systems model of the acute and long-term responses to low dose radiation**
 - to investigate differences in the response pathways
 - to predict differences in outcome at an individual and population level
- **To identify biomarkers of susceptibility to radiation associated disease**
- **To investigate mechanisms by which these factors may affect radiation risk**

Health risk evaluation

- **To validate candidate biomarkers of individual sensitivity in cohorts of exposed and non-exposed that have developed cancer or non-cancer diseases**
- **To improve key cohorts and determine factors involved in individual sensitivity to radiation-induced diseases**
- **To quantify the variation in risk between different groups and the impact of different factors**

Impact of radiation exposure characteristics

- **Cross-cutting issue: extent to which *internal contamination, radiations of differing qualities and other aspects of dose inhomogeneity* modify dose-response relationship for cancer and non-cancer**
 - Epidemiological studies of internal emitters, incorporating detailed dosimetric assessment and - where feasible and possible - biological samples
 - Experimental studies *in vivo* or *in vitro* to test exposure scenarios, (e.g. localized vs. uniform, acute vs. protracted) to inform biomarker development and risk quantification
 - Epidemiological or mechanistic studies on cancer risk including exposures to different radiation qualities



Multidisciplinary European Low Dose Initiative

QUESTIONS & COMMENTS

Thank you



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