

# How is STUK responding to emerging challenges?

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Research Director

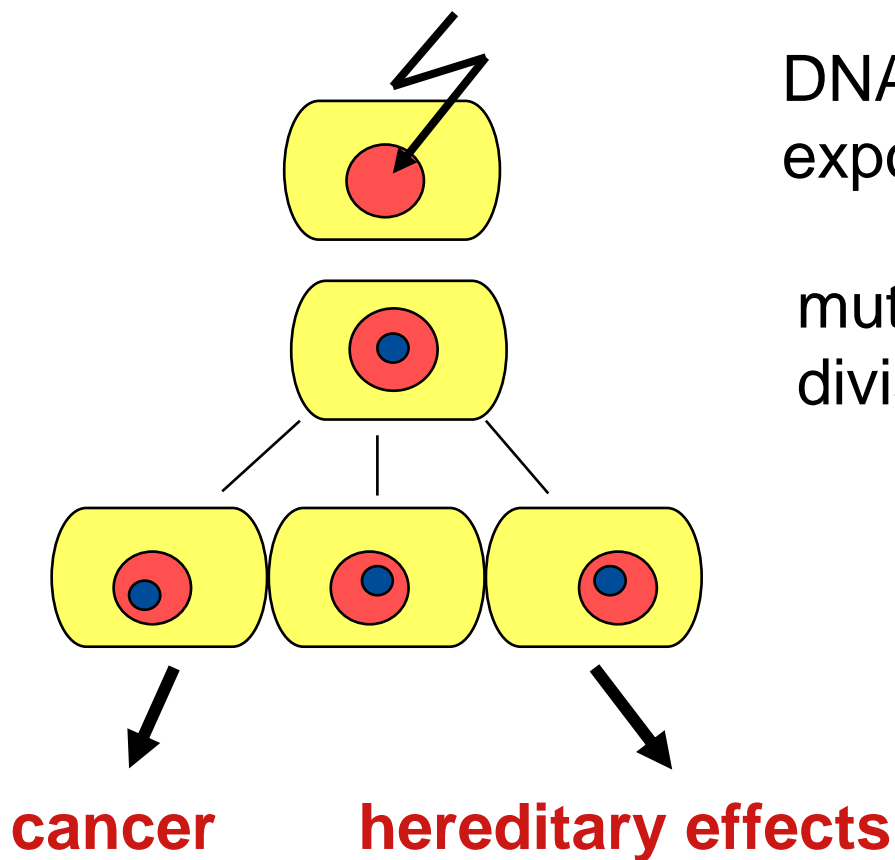
OECD/NEA Committee for Radiological Protection and Public Health Workshop  
Science and Values in Radiological Protection  
Helsinki, 15-17 January 2008

# Activities and milestones in response to emerging challenges

- Lessons from Chernobyl - STUK as WHO Collaborating Centre
  - thyroid cancer in children - a sensitive subpopulation
  - WHO Guidelines on Stable Iodine Prophylaxis
- Scientific breakthroughs on non-targeted effects
  - delayed cell death (Seymour *et al.* 1986)
  - genomic instability (Kadhim *et al.* 1992)
  - bystander effect in vitro (Nagasawa and Little 1992, Prise *et al.* 1998)
  - bystander effect in vivo / 3-D (Watson *et al.* 2000, Belyakov *et al.* 2005)
- Organising international workshops and training courses
- STUK research priorities
- Coordination of international research projects
- Contribution to international research strategy

# The classical paradigm in radiobiology

## - the basis of radiation-induced health effects



DNA damage induced at the time of exposure

mutation fixed in the first cell division (misrepair of damage)

clonal proliferation

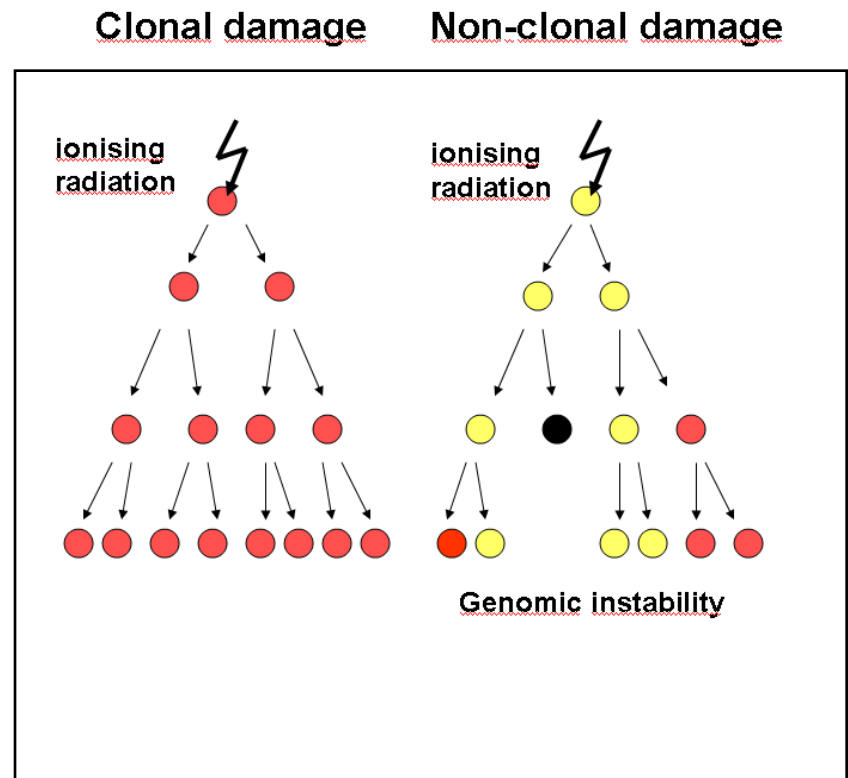
**HEALTH EFFECTS**

# Genomic instability

The progeny of irradiated cells show

- occurrence of new aberrations and/or new mutations
- lethal mutations (delayed cell death)

*These non-clonal effects occur in cells that have never been irradiated*



# **International Workshop on Public Health Aspects of Radiation-Induced Genomic Instability**

Helsinki 25-28 October 1995

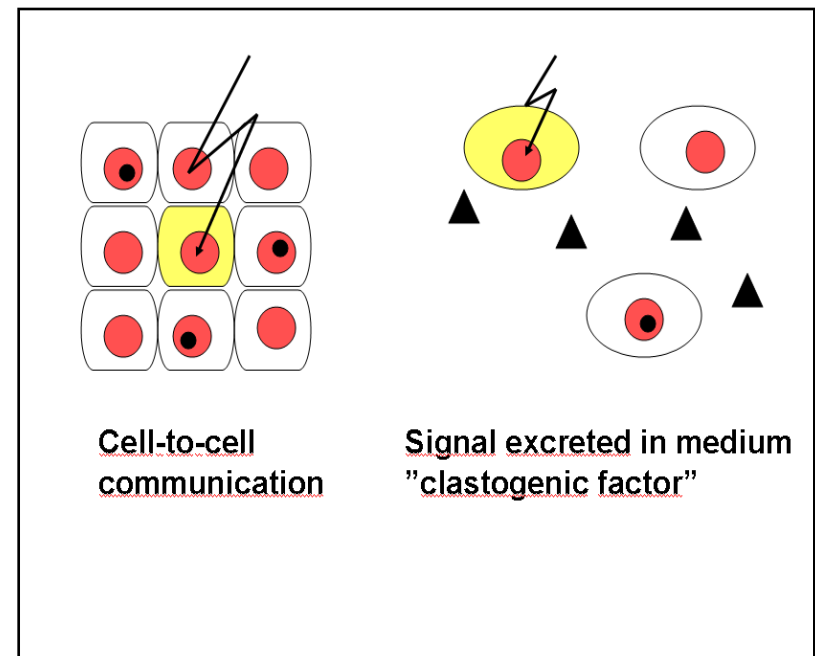
STUK and WHO

# Bystander effect

mutation and cell killing  
seen in cells that were not  
directly hit by radiation but  
were nearby

***These effects occur in  
cells that have never  
been irradiated.***

## Signalling of bystander response



# Minisatellite mutations and biodosimetry of population around the Semipalatinsk nuclear test site (SEMIPALATINSK)

- coordinated by STUK 1998-2000
- INCO COPERNICUS programme
- Kazakhstan, UK, Finland
- transgenerational effects after paternal exposure
- three-generation study
- minisatellites are non-coding DNA repeat sequences; mutations scored as changes in repeat number

# Genomic instability and radiation-induced cancer (RADINSTAB) 2000-2003

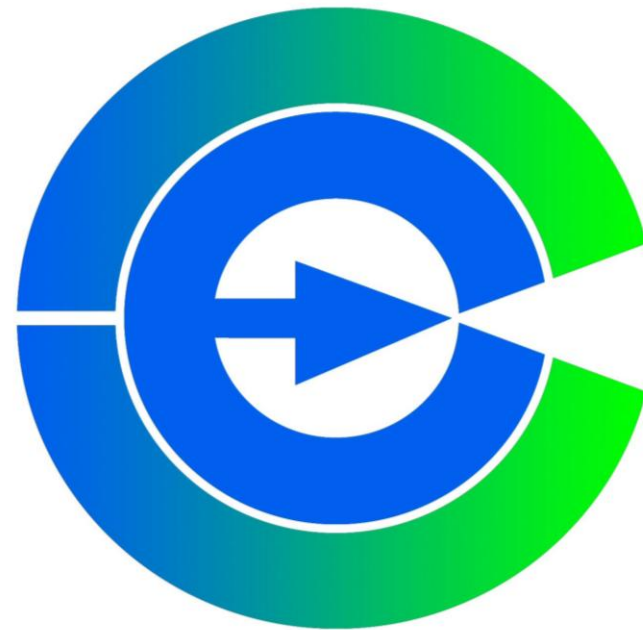
- coordinated by STUK
- 5th Framework Programme, Euratom
- 9 European partners from Finland, UK, France, Germany, Sweden, Ireland
- induction and transmission of genomic instability
- relationship to radiation dose and quality
- delayed gene expression
- genotype differences



# **RISC-RAD Training Course: Non-targeted effects of ionising radiation**

**14-16 February, 2005  
Helsinki**

# Non-targeted effects of ionising radiation Integrated Project, 2006-2010



**NOTE**  
- TOWARDS A NEW PARADIGM

# General information

- Start date of the project: 1 September 2006
- Duration: 48 months
- 22 partner organisations
- Coordinating organisation: STUK - Radiation and Nuclear Safety Authority
- Project coordinator: Prof. Sisko Salomaa
- EURATOM Specific Programme for Research and Training on Nuclear Energy, 6<sup>th</sup> Framework Program
- Total eligible costs: 11.89 M€
- EC contribution: 6.33 M€

# System of radiation protection

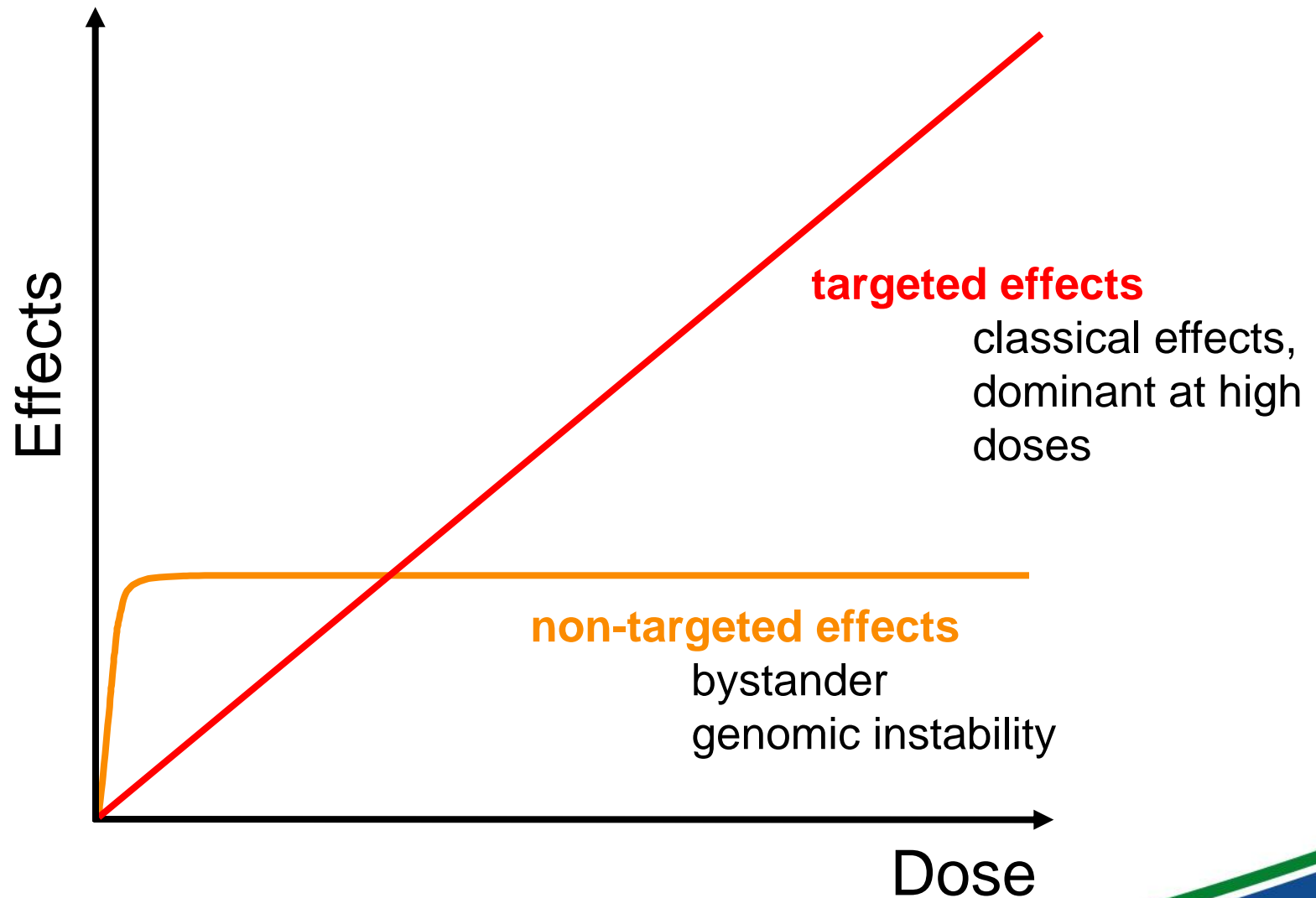
- Knowledge of radiation risk is based on direct epidemiological evidence, as well as scientific study of radiation biology
- The system is designed to protect against both deterministic and stochastic effects
- A linear, non-threshold (LNT) dose-response relationship is used for all long-term health effects (e.g. cancer, genetic effects)
- A dose and dose-rate correction factor is used to relate the effects of acute exposures to chronic exposures (DDREF)
- Radiation dose is used as a surrogate for risk
- The effects produced by different types of radiation are qualitatively the same
- Doses can be summed to predict overall risk

# Concept of dose as surrogate of risk

## LNT and radiation protection

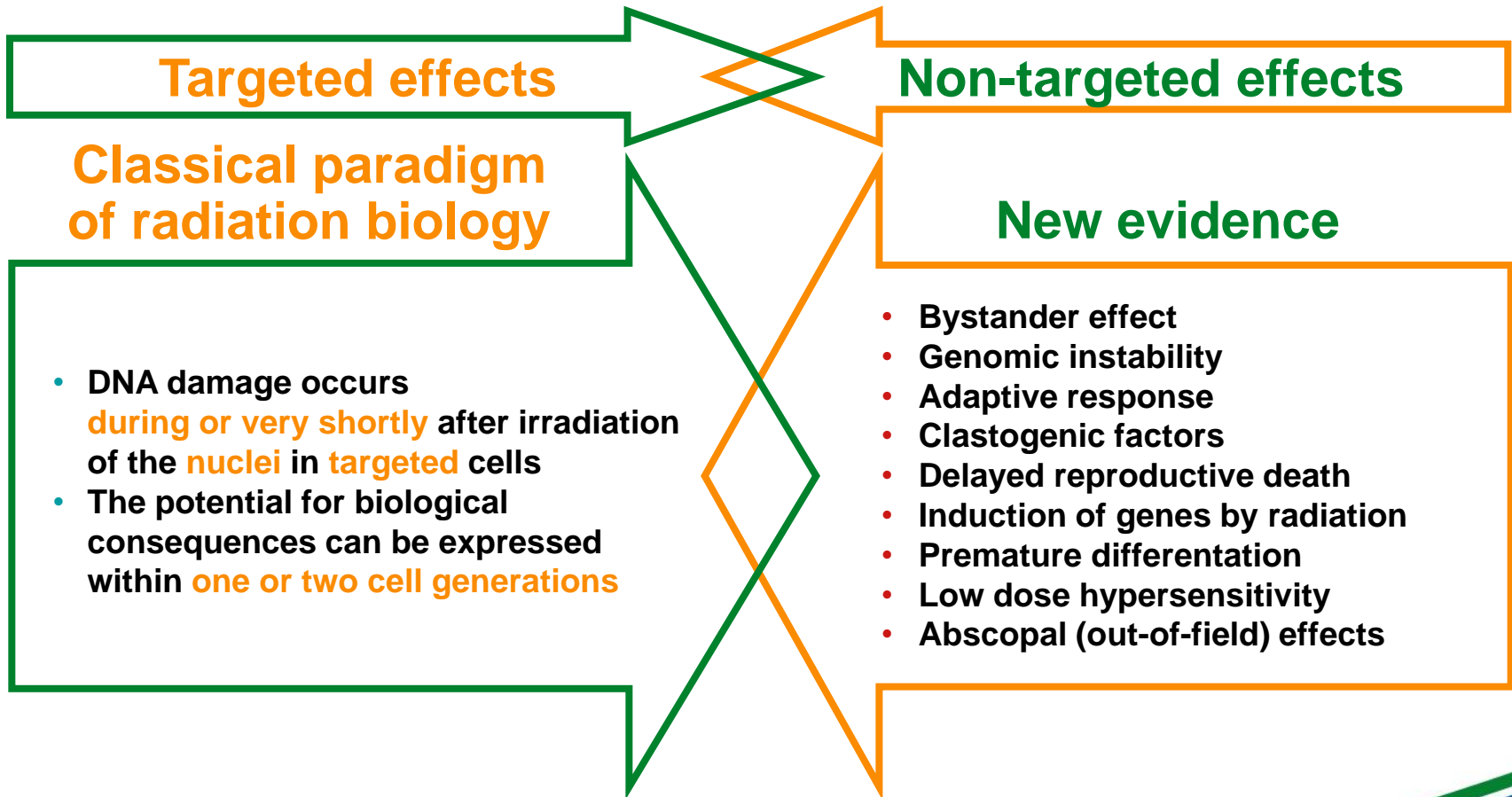
- a linear dose response means that every increment of dose and the associated risk can be assessed separately, irrespective of prior or future doses, as long as doses are below deterministic effects
- a fixed dose increment is always associated with the same additional risk
- doses received by an individual at different time points can be summed up (cumulative dose)
- (collective dose can be used to predict risk at the population level)

## Low-dose effects



Non-targeted effects may be important  
**modifiers of risk at the low dose region**

# A new paradigm of Radiation Biology





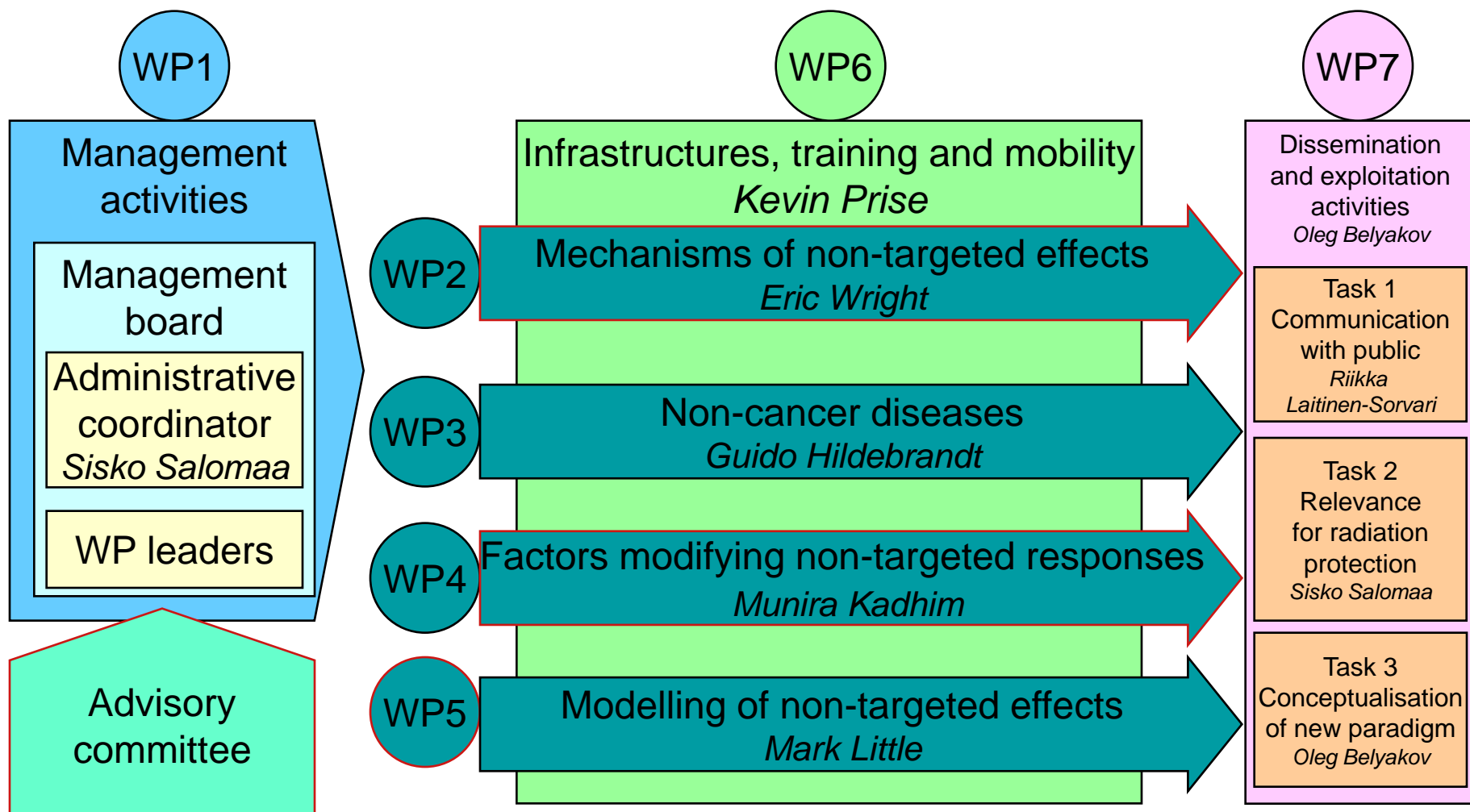
# Paradigm shift

## Classical paradigm

- **DNA-targeted**
- **cells considered as isolated units**
- **clonal effects**
- **linear / linear quadratic dose response**
- **classical radiation biology (effects on DNA)**
- **physics, biophysics**

## New evidence

- **non-targeted**
- **cells are communicating**
- **tissue responses**
- **non-clonal effects**
- **plateau-like dose response (on/off)**
- **need for new methodological approaches**
- **biology, biochemistry**



# General objectives of the NOTE IP ...


- To investigate the **mechanisms of non-targeted effects**, in particular, bystander effects, genomic instability and adaptive response
- To investigate if and how non-targeted effects **modulate the cancer risk in the low dose region**
- To investigate if ionising radiation can cause **non-cancer diseases** or **beneficial effects** at low and intermediate doses
- To investigate **individual susceptibility** and other factors modifying non-targeted responses

# General objectives of the NOTE IP

- To contribute to the conceptualisation of **a new paradigm in radiation biology** that would cover both the classical direct (DNA-targeted) and non-targeted effects.
- To assess the **relevance of non-targeted effects for radiation protection** and to set the scientific basis for a modern, more realistic, radiation safety system

# NOTE website

<http://www.note-ip.org>

**NOTE – TOWARDS A NEW PARADIGM**

Non-targeted effects of ionising radiation  
Integrated project 2006-2010

UTC time: 2007-6-18 7:48:30 Local time: 2007-6-18 10:48:30

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NOTE is supported by the [European Commission](#) under the [Euratom](#) specific programme for research and training on nuclear energy, 6<sup>th</sup> Framework Programme

## What is NOTE




The NOTE (Non-targeted effects of ionising radiation) project aims to expand the current understanding of health effects caused by low-level doses of ionising radiation. The key focus of the research programme is the possible health consequences of exposures to small radiation doses which have not been investigated sufficiently so far. [Read more](#)

The four-year European Integrated Project NOTE started 1 September, 2006 and is coordinated by STUK - Radiation and Nuclear Safety Authority, Finland. [All participants](#)

## Press releases

8.9.2006 12:00:00  
➔ NOTE research project to examine the health effects of low doses of radiation  
.....

## What's new



Welcome to updated NOTE website.

NOTE Newsletters will consist of NOTE-related new materials intended for members of the general public, scientific community, radiobiologists and radiation protection specialists. You can join [newsletter mailing list](#).

**1<sup>st</sup> NOTE newsletter** was published on 31 May 2007.

Maintained by STUK

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# Key questions from the radiation protection policy point of view

- For cancer risk: is there a deviation from LNT at low doses?
  - Can ionising radiation cause non-cancer diseases or modify their risk at low / intermediate doses?
  - Are there differences in the radiation sensitivity between individuals?
- International collaboration is essential to solve these issues (Europe, US, Japan, Canada...)

# OECD Nuclear Energy Agency Committee on Radiation Protection and Public Health

## Science and Values in Radiological Protection

**Helsinki, Finland  
January 15 -17, 2008**