

4th International MELODI Workshop

12-14 September 2012
Helsinki, Finland

Break-out session 2A: Biomarkers and biobanks

Thursday, 13 September at 16-18 hours

Moderator: Sarah Baatout, SCK-CEN

Rapporteur: Ulrike Kulka, BfS

Structure of the break-out session

1. Introduction to biomarkers and biobanks
2. Biomarkers as to the MELODI SRA
3. Discussion
4. 5x poster short presentations
5. Questions / answers

Introduction to Biomarkers and Biobanks (Sarah Baatout)

General considerations:
overview of presentations of the biomarker session

- Definitions of biomarkers
- Classification of biomarkers
- Characteristics of „good“ biomarkers
- Link to biobanks (more characteristics)

MELODI SRA background

Key scientific issues related to biomarkers & biobanks

Research priorities:

- Dose response relationship for cancer
- Individual Radiosensitivity
- Hereditary and transgenerational effects

! Discussion !

Requirement on biomarkers is too high!
(e.g. radiation specificity, biological plausibility)

- ❖ Wish / demand: the „perfect biomarker“
- ❖ Reality: no such biomarker available up to now and in the (near) future;
- ❖ Question: Is there such a thing as the „perfect biomarker“??
- Consequence: more moderate rewording of the paragraphs in the SRA (?)

5x short presentations

1. Micronucleus-centromere test in lymphocytes from currently active uranium miners and radon spa personnel in the Czech Republic (*F. Zölzer*)

Biomarker: Micronuclei (without centromere) in lymphocytes

Comparison of uranium miners – spa personnel – controls

Significant differences between the 3 groups

2. The German Uranium Miners Biobank – current status and perspectives in radiation research

(*M. Kreuzer*)

Molecular epidemiology study, ongoing

Bioprobes: various (DNA, RNA, frozen cells, plasma), origin: blood

Comparison: workers with cancer – healthy workers – children of workers with cancer

5x short presentations

- 3. FANC Belgian study: In vivo gene expression studies confirm differential expression profiles at low doses of ionizing radiation when compared to in vitro ones**

EU EPI-CT project: biomarkers of radiation sensitivity for children (*E. El-Saghire*)

Biomarker: gene expression in human blood

Comparison of response to very low and high dose

Sensitivity of children

- 4. Low dose IR induces gene expression changes via DNA breaks and other pathways (*J. Essers*)**

Biomarker: Gene expression changes and DNA breaks
animal study

5x short presentations

5. Proteomics profiling of low molecular weight plasma proteins from locally irradiated individuals

(R. Nylund)

Biomarker: proteomics and cytogenetic markers

Blood from patients and individuals after accident

Summary:

➤ **“old” and “new” biomarkers are in use (with success)**

➤ **Main source of Biomarkers: blood**

➤ **Careful planning of assays**

Consideration of assay details, e.g. time of exposure and sampling of probes post irradiation, interindividual differences, homogenous conditions

Questions

7 questions

(multiple choice, 1 answer option)

$N = 20$

1. Are there molecular biomarkers that can be validated and used in molecular epidemiology to define radiation exposures, metabolic and pathological impacts and disease? - both cancer and non-cancer

- | | |
|---|-------|
| 1. Yes, such biomarkers exist | 6,3% |
| 2. We are working in this field to establish such biomarkers | 37,5% |
| 3. We are not looking for such new biomarkers ourselves but we would use them as soon as they are established as reliable markers | 31,3% |
| 4. I don't know | 6,3% |
| 5. No, it will not be possible | 18,8% |

2. Can already existing biobanks (STORE, GENEPI etc.) be used in molecular epidemiological studies?

1. Yes, that's a good and realistic approach and I am very interested in using the existing resources 6,3%
2. It seems to be a good approach but one has to be very careful about the quality of data and probes and the legal aspects have to be clarified, first 62,5%
3. Maybe it could be useful but I am not interested in using existing biobanks, most likely the criteria for collecting the probes are out of date by now 18,8%
4. No, in biobanks the variability between the individual probes is too big 12,5%

3. Are there genetic and/or epigenetic modifiers/biomarkers available that allow determination (monitor, predict) of individual sensitivity to radiation, cancer and disease development?

- 1. Yes, there are already modifiers/biomarkers for individual sensitivity to radiation, cancer and disease development that are very reliable 6,3%
- 2. Yes, there are promising biomarkers for individual sensitivity to radiation or cancer or disease development and they could be used as a set of markers 25,0%
- 3. No, but we are working in this field to establish such biomarkers25,0%
- 4. No, but we will use such biomarkers as soon as we are convinced that they are reliable 31,3%
- 5. No, there are not such biomarkers12,5%

4. Can risk assessments for individuals be developed on the basis of molecular indicators for cancer? - leading to genetic profiling of individuals?

- | | |
|--|-------|
| 1. Yes we are working in this field and we are close to reliable results | 6,3% |
| 2. Yes we are working in this field but it still will take many years . | 25,0% |
| 3. Yes, we are not working in this field as researchers but we hope to use the results of such studies | 56,3% |
| 4. No, this will not be possible | 12,5% |

5. Are molecular biomarkers available or may suitable biomarkers be developed for radiation-induced carcinogenesis (molecular signatures) in animals and humans together with sound biological dosimetry?

- | | |
|---|-------|
| 1. Yes, there are already such markers linking carcinogenesis and biological dosimetry | 0,0% |
| 2. Yes, we are working in this field and such biomarkers will be available | 14,3% |
| 3. Maybe; we are not working on the development of such biomarkers, but we will use them as soon as they will be available; | 64,3% |
| 4. No, there are no biomarkers together with sound biological dosimetry | 21,4% |

6. Can biomarkers, gene markers and phenotypic traits indicate specific radiation risks in human individuals? -Ethical problems to be considered

1. Yes, and available biomarkers which can help to indicate a specific individual radiation risk should be used without reservation 6,3%
2. Yes, all available biomarkers which can help to indicate a specific individual radiation risk should be used if an individual asks for it but the information should strictly be private 31,3%
3. In case there are such biomarkes , they should only be used to optimise a medical treatment 31,3%
4. In case there are such biomarkes they should not be used at all 0,0%
5. No, there are no markers , that are specific for radiation 31,3%

7. Are there cohorts that can be used for molecular epidemiological approaches to understand low dose radiation effects (cancer, non cancer)?

1. Yes, there are cohorts with access to bioprobes and we are collecting / using the probes 33,3%
2. Yes there are cohorts and bioprobes could be available but we need someone to collect the probes33,3%
3. I am looking for partners with direct access to such probes 13,3%
4. I don't know but I am interested in such probes 13,3%
5. Bioprobes from cohorts will not help to understand low dose effects 6,7%