OPERA OPEN PROJECT FOR EUROPEAN RADIATION RESEARCH AREA

HelmholtzZentrum münchen
German Research Center for Environmental Health

Workshop Radiation Biomarkers

Monday April 20th 2015

Munich; HMGU, Ingolstaedter Landstrasse 1, 85764 Neuherberg, GERMANY

Introduction

The workshop was held with 35 participants in the Helmholtz-Zentrum Munich on the 20th of April 2015. The students of the DoReMi course Radiation Carcinogenesis attended among others the lectures. Of 35 participants, more than half (51%) were not Helmholtz employees. The majority of participants were female.

A total of 10 lectures were held covering variousaspects of ionizing radiation biomarkers that could potentially be used in epidemiological studies. Of these, four were held were by Helmholtz staff, three by staff from other DoReMi partners, and three by invited external experts (Bundeswehr Institute of Radiobiology, Technical University Munich and Federal Office for Radiation Protection).

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Programme
Workshop Radiation Biomarkers 20.4.2015,
Seminar Room 52, Geb 57, HMGU

speakers time	Name	Title	Institute
MODERATION: Mike ATKINSON (HMGU)			
9:30-10:10	Soile Tapio	Use of proteomics in search for biomarkers of radiation exposure	HMGU
10:10-10:50	Valerie O´Leary	PARTICLE - a long non-coding RNA modulator of cellular methylation in response to low dose irradiation	HMGU
10:50-11:30	Harry Scherthan	Gamma-H2AX, a radiation biomarker for external and internal ionizing radiation exposure	Bundeswehr
11:30-12:10	Gabriele Multhoff	Hsp70 in radiation oncology: a novel marker for theranostics	TUM
12:10-13:10	LUNCH		
13:10-13:50	Janet Hall	Biomarkers of individual radiosensitivity: do they exist?	INSERM
13:50-14:30	Roel Quintens	Gene and exon signatures as radiation biomarkers	SCK-CEN
14:30-15:10	Siamak Haghdoost	Biomarker of oxidative stress and it´s application for determination of individual radiosensitivity	Stockholm University
15:10-15:30	COFFEE		
15:30-16:10	Maria Gomolka	Increased radiation sensitivity in new-borns and children under 5 years of age compared to adults after in vitro CT exposure	BfS
16:10-16:40	Simone Mörtl	MicroRNAs: a new source of biomarkers in radiation response?	HMGU
16:40-17:00	**Conclusion**	**Mike Atkinson**	HMGU

If you are interested, please register by sending an e-mail to: mandy.birschwilks@helmholtz-muenchen.de

Figure 1: The flyer of the Radiation Biomarker workshop

Workshop lectures

Prof. Dr. Atkinson opened the workshop. He introduced the objective of the DoReMi network to promote multidisciplinary interaction of European researchers to develop large scale biomarker epidemiological studies. He pointed out that the current workshop Radiation Biomarkers aimed to review the progression and limitations in the same concept.

Dr. Soile Tapio as first speaker introduced the available knowledge about radiation biomarkers. She classified the radiation biomarkers in four categories: Biomarkers of exposure, biomarkers of susceptibility, biomarkers of late effects and biomarkers of persistent effects. She emphasised that these definitions were important for suitable designs and sampling procedures in molecular epidemiological studies. She discussed the characteristics of good biomarkers and currently known radiation biomarkers. She also presented proteomics approach on tissues and cells as a tool for finding biomarkers after low-dose radiation exposure.

Dr. Valerie O´Leary introduced the novel biomolecules affected by irradiation including a new long non-coding (nc) RNA called PARTICLE. She reviewed the methodology of long ncRNA analysis. Her study showed that these molecules can be used as potential candidate biomarkers in the plasma of radiotherapy patients.

Prof. Dr. Harry Scherthan discussed current application of gamma-H2AX as a radiation biomarker for external and internal ionizing radiation exposure. He showed that DNA damage foci (gH2AX +53BP1) can be used as biomarkers due to their high sensitivity around few mGy, and rapid read out (<6h). He concluded that the method was appropriate for dose reconstruction under defined conditions.

The presentation of Prof. Dr. Gabriele Multhoff was given by Dr. Thomas Schmid. He talked about heat shock protein 70 (Hsp70) in radiation oncology as a novel marker for theranostics. He reviewed the multiple roles of Hsp60 in normal and tumour tissues and presented recent studies on membrane (m)Hsp70. He showed that radiation-induced increase of the selective expression of a (m)Hsp70 on the surface of tumour cells can act as a recognition structure for activated natural killer cells with a great clinical relevance.

Dr. Janet Hall´s lecture dealt with the question whether biomarkers of individual radiosensitivity exist in general and at low doses in particular. She mentioned that there is a need to validate potential biomarkers of exposure, susceptibility, and late and persistent effects at low doses. She presented a variety of biological samples that can be used as for biomarker search in epidemiological studies. She emphasised that there are different definitions and properties for biomarkers in the cancer and non-cancer effects of irradiation.

Dr. Roel Quintens presented gene and exon signatures as putative radiation biomarkers. He introduced a European platform applying the gene expression analysis on blood samples to estimate dose in irradiated individuals. An intercomparison study was performed between different laboratories to determine the efficiency and accuracy of gene array in order to correctly estimate the radiation dose. He concluded that gene expression signatures are stable considering multiple variables including individual variation in donors, sample types, distinct time points, and array protocols/platforms.

Dr. Siamak Haghdoost´s talk focussed on the DoReMi supported subproject Radsens. He presented background for the project and discussed the relationship between individual sensitivity to radiotherapy and individual response to oxidative stress. He presented two cohorts of patients that were used in the study: breast cancer patients with extreme skin reaction and head and neck cancer patients with osteoradionecrosis. The results of oxidative stress measurements together with proteomics and miRNA analyses were presented and discussed. He suggested that a combination assay based on proteomic, miRNA and oxidative stress markers might be used as a fingerprint of individual radiosensitivity.

Dr. Maria Gomolka presented data from international cohort study called EPI-CT. The project aims at studying the cancer risks and the underlying biological effects in an international cohort study with a special focus on children. In this frame BfS conducted a pilot study to investigate the effects of CT exposure in different age groups using the chromosomal aberration assay (dicentric chromosomes) and gamma H2AX foci asssay. Blood samples from three different healthy age groups (umbilical cord blood, young children, adults) were collected and investigated in vitro after CT scan. Blood cells of young children (<5 years) showed an 1.5 increased aberration frequency in dicentrics compared to adults after 1 Gy exposure. The gammaH2AX assay did not resolve any age related sensitivity neither in the initial radiation damage nor after 24 h repair.

Dr. Simone Mörtl talked about microRNAs as a new source of biomarkers in radiation response. She gave an outline about the potential of different classes of miRNAs (cellular, circulating and exosomal miRNAs) as biomarkers. She presented *in vitro* data to demonstrate miRNAs as regulators of radiation sensitivity. Based on samples of radiotherapy patients it was shown that cellular as well as plasma-based circulating miRNA profiles are promising markers for prognosis and therapy monitoring.

Conclusion

The speakers reviewed different features of potential radiation biomarkers and highlighted the necessity of radiation biomarker development. They emphasised that the optimal design for a radiation biomarker study needs to consider both logistics and ethics of biological sampling, processing and storing as well as availability and feasibility of related bioassays. In general, it was concluded that multi-marker assay was preferable compared to single biomarkers. Intensive interaction and integration of available biological assays including "omics" technologies in molecular epidemiology studies to search biomarkers especially at low radiation exposure was recommended.