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Topic 1: Improvement of health risk assessment associated with low dose/dose rate radiation

Measurement of Ionisation Track Structure with Nanometre Resolution

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The effect of ionising radiation in biological tissue depends crucially on the details of the energy deposition in the nanometric and sub-micrometric scale. E.g. the different biological effectiveness of gamma- and neutron radiation at the same absorbed dose for inducing genetic aberrations or cell death is based on their vastly different ionisation pattern at the level of the DNA, but also on long range correlations of ionisation patterns on the chromosomal scale, i.e. in compartments of 1 nm up to several hundred nm in size.

Direct experimental access to ionisation patterns and local cluster size distributions in these relevant length scales is not possible in biological tissue. Therefore, the main tool in describing track structure and correlating it to biological damage is simulation. However, computer modelling is based on a comprehensive knowledge of molecular, atomic and sometimes nuclear data in gaseous and condensed phase or, alternatively, on proven models to predict these data with sufficient quality.

At PTB we are developing different approaches to experimentally access ionisation patterns in all scale ranges relevant for biological effects of ionising radiation. One of the already existing and well characterised instruments is the ion-counting nanodosimeter, which represents simulated sites of the order of 1 – 5 nm in diameter and measures the cluster size distribution in such small volumes. While this classical nanodosimeter represents just one single site of defined size the other instrument is a track structure imaging Time Projection Chamber (TPC), capable of quantitatively measuring 3-dimensional ionisation distributions along electron or ion tracks over sites ranging in equivalent length scales from 30 nm to 1 µm in a single measurement.

In a new project we are now attempting to combine both techniques towards a track structure imaging instrument with 1-2 nanometer tissue equivalent resolution within simulated sites of about 100 nm. Within the frame work of CONCERT we are looking for collaboration with partners interested to collaborate with us in this development, benchmark their track structure simulation results with experimental data and developing models for biological damage prediction based on track structure data.

The infrastructure PTB can provide for this work and for interested partners are the following:

- Nanodosimeter and Particle Track TPC as described before.
- Detector and electronic laboratory, with profound experience in gaseous, scintillation and vacuum detectors for neutrons, X-ray and gammas, ion and electron as well as UV- and visible light detection and imaging.
- Various irradiation facilities for light ions (p, d, α), ranging from a few keV to ca 20 MeV. This includes also the microbeam facility described by U. Giesen in a separate information sheet for this meeting.
- Close in-house collaboration with an atomic and molecular data group, working on measurements and evaluation of data for biologically relevant track structure simulation.
- Support for numerical modelling.

Information Sheet of Weibo Li, HMGU

Application for
Participation in 27th of January, 2016 - Information Day on the 1st OPEN RTD CALL of the 'CONCERT - European Joint Programme for the Integration of Radiation Protection Research' under Horizon 2020

Applicant: Weibo Li
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My name is Weibo Li (Li is my surname). I have been working in Helmholtz Zentrum München, Neuherberg, Germany since 1997. Regarding to the first CONCERT Calls, my research interests can be divided into two areas: (1) Uncertainty in radiation protection and in medical dosimetry and (2) Nanodosimetry in radiation biological application. According to my competences, I would like to be a potential partner in the Topic 1 and Topic 2 announced in the CONCERT preliminary announcement.

(1) Uncertainty study in radiation protection and in medical dosimetry
In the last years, I developed a statistical approach for quantitative evaluation of uncertainties in biokinetic models and internal doses to the occupational workers and to the publics. Meanwhile, this method has been also applied and implemented into internal dose calculation to patients in nuclear medicine. This method can be used to analyze the overall uncertainty of internal dose to workers and to patients. Furthermore, this method can be used to identify the important parameters or factors in the procedure of the dose calculations. This method can also be extended to evaluate the uncertainty of dose to occupational workers in the epidemiological study.

(2) Nanodosimetry in radiation biological application.
I have a strong scientific background in using Monte Carlo radiation transport simulation programs (for example, PARTRAC in cooperation with Dr. Werner Friedland in HMGU and PENELOPE) for studying the physical track structures and chemical radicals and biological effects. Moreover, I am working on mathematical modeling of the cell survival based on the initial physical quantities and DNA damages.

In the following, a brief description of our organization - Helmholtz Zentrum München— German Research Center for Environmental Health (GmbH) for potential partners.

Helmholtz Zentrum München (HMGU) is the German Research Center for Environmental Health. It investigates important common diseases which develop from the interaction of lifestyle, environmental factors and personal genetic background. HMGU is a research institution of the Federal Republic of Germany and the Free State of Bavaria. It is a member of the Helmholtz Association of German Research Centers. The "Research Unit Medical Radiation Physics and Diagnostics" (AMSD) is a member of the "Department of Radiation Sciences" (DRS) in HMGU. The mission of AMSD is to contribute to the protection against man-made ionizing radiation, in particular by optimizing the performance of medical diagnostic procedures and developing innovative medical technologies. Other important research topics in AMSD aim at contributing to a better understanding of internal and external radiation exposures on humans. The AMSD gives advice to politics and stake-holders, cooperates with national and international partners and tries to commercialize own ideas and developments.

CONCERT INFO DAY participants from Istituto Superiore di Sanità (ISS)

Cinzia De Angelis
Sara Della Monaca
Barbara Pascucci
Maria Antonella Tabocchini

Topic 1: Improvement of health risk assessment associated with low dose or dose rate radiation

Research interests

1. investigation of the biological response to low doses/dose rate irradiation of cultured cells of different types and origin, including stem cells and cells with defects in the response to DNA damage, with special emphasis to the dependence on radiation quality
2. characterization of the effects of DNA damage on mitochondrial organization and dynamics by analysis of mitochondrial DNA damage, mitochondrial morphology, mitochondrial biogenesis and mitophagy
3. investigation of metabolic effects by Nuclear Magnetic Resonance spectroscopy: cell clustering based on metabolic fingerprints and identification of specific spectroscopic markers
4. methods of retrospective dosimetry in support to epidemiological studies
5. analysis of the relation of biophysical markers with internal contamination and radiation components (gamma and neutrons)
6. reducing uncertainties and increasing quality of measurements in retrospective dosimetry and dosimetry in medical field through participation to dosimetry networks (participation in EURADOS and RENEB)
7. communication with stakeholders on radiation protection research issues (in particular in the framework of the projects OPERRA and CONCERT)

Topic 2: Reducing uncertainties in human and ecosystem radiological risk assessment & management in nuclear emergencies and existing exposure situations, including NORM

Research interests

1. NORM in building materials:
   a. reducing uncertainties on Rn exhalation modeling to improve evaluation of Rn contribution from NORM containing building materials;
   b. proving modeling reliability in controlled situations
2. NORM industry releases and residue landfills: improving environmental and human health impact assessment taking into account physical and chemical NORM characteristics and human habits
3. communication with stakeholders on dose levels (in particular in the framework of the project SHAMISEN)

Infrastructures:

Irradiation facilities

At the ISS, besides the Gammacell 40 Exactor for acute gamma irradiation, there are irradiation facilities dedicated to continuous exposure of cultured cells in physiological condition, namely: the LIBIS gamma irradiation facility (dose rate range: 2 microGy/h - 20 mGy/h and the alpha particle irradiator (dose rates ranging from a hundred of microGy/h to few tens of Gy/h). Moreover, it is also available the PULEX-Cosmic Silence facility for exposure of biological samples in extremely low radiation background at the Underground Gran Sasso National Laboratory (LNGS) (for more information see AIR2- bullettin – Issue3).

Other major research infrastructures:

METAFER platform (for analysis of chromosome aberrations, micronuclei and DNA damage)

Nuclear magnetic resonance (9.4 T)

Magnetic resonance imaging and spectroscopy *in vivo* (4.7 T)

Electron paramagnetic resonance

Proteomics/Mass spectrometry

Mass cytometry

Confocal microscopy

APOTOME

Electronic microscopy (SEM, TEM)

Flow cytometry

James W Marsh

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We are interested in participating in projects under topics 1 and 2.

Topic 1

We are interested in participating in epidemiological studies by calculating doses to worker cohorts. We have developed the internal dosimetry software PLEIADES, which has been used to calculate dose coefficients and bioassay quantities for the International Commission on Radiological Protection (Fell et al. 2007). As part of European projects (e.g. Alpha-Risk, SOUL, CURE) PHE has developed dosimetry protocols and calculated lung and organ doses to uranium miners and plutonium workers (Marsh et al., 2012; Puncher and Riddle, 2016).

Topic 2

We are experts in internal dosimetry and emergency response. We have had experience in dealing with real emergencies (e.g. London Po-210 poisoning incident) and carrying out dose assessments (e.g. UNSCEAR's Fukushima worker assessment). Members of staff were also consortium members of the TMT Handbook project which produced a handbook on 'Triage, Monitoring and Treatment of people exposed to ionising radiation following a malevolent act' (Rojas-Palma , et al., 2009). We also have facilities and equipment for carrying out rapid screening measurements, personal in-vivo monitoring and urine measurements following an emergency.

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Organisation: **Public Health England**
Principle Investigator: **Ken Raj (ken.raj@phe.gov.uk)**
Group expertise: **Cellular Biology and Molecular Biology**

Research Interest: The Cellular Biology Group in the Radiation Effects Department investigates the following areas related to radiation. These include:

(1) The effects of radiation on different isogenic cell types isolated from normal human skin. We routinely isolate keratinocytes, fibroblasts, melanocytes and microvascular endothelial cells from the same tissues and have a growing cryogenic bank of these isogenic cells which we use to determine the differences between cells in regards to how they respond to radiation. Using our newly established chronic irradiator-incubator, we are studying the effects of low dose-rates of ionising radiation on these cells and how they differ from cellular response to acute radiation. We are also able to isolate mesenchymal and dermal progenitor cells from these tissues for use in our investigations.

(2) The effects of radiation on cardiovascular disease. We have demonstrated how radiation can induce pro-atherogenic properties on human endothelial cells through increasing the adhesiveness for monocytes. We are extending this route of investigation into other pro-atherogenic properties (including chronic inflammation) that radiation may also affect and determine the molecular and cellular pathways targeted by radiation to promote these features. We are also investigating whether (a) acute or (b) chronic low dose radiation induces atherogenic properties in human coronary artery endothelial cells. We will determine the magnitude of inter-individual differences and the influence of age in reference to radiation-induced atherogenic characteristics.

(3) The effect of age on cellular response to ionising radiation. We have recently acquired the ability to generate isogenic cells in the laboratory that correspond to different biological ages. Using these cells we are investigating how they differ in their response to ionising radiation and have already observed profound differences and are elucidating mechanisms responsible for these differences.

(4) To investigate non-mutagenic effect of ionising radiation. We plan to ascertain the effects of acute and chronic low dose radiation on DNA methylation and histone modification and its impact on gene expression

(5) To ascertain potential variations in cellular responses of cells from different individuals to ionising radiation; with the aim of quantifying inter-individual variability to ionising radiation

Infrastructure: Chronic gamma irradiator-incubator with dose rates of 0.01mGy/h to 60mGy/h. The incubator is a low-oxygen incubator. X-ray set.

Materials: A bank of primary keratinocytes, fibroblasts, melanocytes and microvascular endothelial cells. The number of donor cells in this bank is constantly growing as we receive normal foreskin tissues weekly.

Laurence ROY
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My topic of interest is biological dosimetry, I have been the head of the IRSN biological dosimetry laboratory during 8 years. This laboratory is the reference laboratory in France in biological dosimetry. It is accredited for the evaluation of a dose based on the scoring of dicentrics. Almost 300 dose evaluations have been performed in 20 years.
The semi automatic scoring of dicentrics has been validated under different exposure situations.

As work package leader in the RENEB program, I was involved in the harmonization process of biomarkers evaluation.

Several others assays are available in the laboratory: translocations, PCC (chemical and fusion), gamma-H2AX and other Histones. Those assays have been applied to different exposure situations including internal contamination in a mouse model (Cesium and Tritium)

In the department we also address low dose exposure, medical exposure, track structure energy deposit via biological evaluations, epidemiology studies in workers or following medical exposures.

Several experimental platforms are also available:

- Animal facility for rodents including internal contamination possibilities;
- Image analysis systems (Metasystems, Olympus), living imaging;
- X-Ray (GeneX and Sarp).

Genomics and Rabiobiology of Keratinopoiesis
(CEA-LGRK, Evry, France)

The team investigates **human skin biology**, in normal and pathological genetic contexts. The research domains include the characterization of the cellular and molecular mechanisms responsible for the specific radiosensitivity of epidermal and dermal cell compartments, notably stem and progenitor cells. Investigation of human skin radiobiology is conducted by LGRK at different levels:

. CEA-LGRK investigates detrimental effects of medium dose, representative of radiotherapy fraction, as well as low-dose effects, down to 10 mGy, representative of exposures for medical diagnostics or nuclear workers, with dose rates down to 1 mGy/min. Cesium sources and X-ray generator are the major types of sources used.

. The team characterizes **normal skin tissue reactions**, and notably keratinocytes and fibroblasts from healthy donors. Its expertise in establishing well characterized banks of human primary cells is well-known. It also investigates patients with genetic diseases, with a current input on the radiosensitive Gorlin syndrome. At the level of **individual radiosensitivity**, it is characterizing at the genomic and epigenomic levels a **radiosensitive patient cohort**, constituted of patients having developed well characterized adverse reactions after radiotherapy (Copernic, Inserm).

. The CEA-LGRK know-how includes the sorting by flow cytometry of cell subpopulations corresponding to different immaturity statuses (i.e. stem cell-enriched or progenitor cell-enriched), as well as different functional assays at the tissue level, including clonal and long-term 2D cultures, *in vitro* **3D skin reconstruction models**, and *in vivo* xenograting of bio-engineered human skin grafts. Research approaches developed by LGRK are also based on different functional genomics technologies and tools, including transient gene down-modulation by siRNA, generation of stable gene knock-down contexts using lentiviral vector driving shRNA permanent expression. Due to tight connections with the French CEA National Genotyping Center (CNG), LGRK is developing different massive sequencing approaches, including DNA and RNA-Seq, which will allow the characterization of original genomic variations related to individual radiosensitivity. A major current interest of the group is **epigenomics**, which is studied at the level of DNA methylation changes and miRNAs, and will be developed for non-coding RNAs (LcRNAs).

. Concerning the target genes and pathways of interest at CEA-LGRK, we have a long-lasting success story concerning the cytokine **TGFb1**, and we are currently investigating the role of this network in skin stem cells. Another important pathway is Sonic hedgehog, including **Patched1** receptor.

Taken together, these different complementary approaches aim to identify new molecular effectors involved in the control of radiation-related cellular and tissular responses, and the cells at risk.

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Organisation: Oxford Brookes University (OBU)
Principle Investigator: Munira Kadhim (mkadhim@brookes.ac.uk)
Group expertise: Genomic Instability, Radiation Biology, Non-Targeted Effects, Molecular Cell Communications

Research Interest: The remit of the Genomic Instability Group's research in the Department of Biological and Medical Sciences at Oxford Brookes University, is to investigate the delayed effects of radiation i.e. Genomic Instability (GI) and Bystander Effects (BE).

The main focus of their work includes investigation into:

1- The mechanisms underlying radiation-induced genomic instability in irradiated, as well as un-irradiated cells (bystander cells) in mammalian cell / tissue systems, including: primary human fibroblasts, endothelial & lens epithelial cells and murine haemopoietic stem cells.

2- Establishing mechanistic links between the irradiated and the un-irradiated bystander populations by determining the influence of radiation quality and dose/dose rate, individual genetic differences, cell/tissue type differences and tissue/cellular microenvironment signalling molecules such, cytokines, reactive oxygen species (ROS) and microvesicles (MV) / exosomes.

3- Investigation into the role of sub-cellular components such as lysosomes and mitochondria in the induction of GI and BE.

The groups' recent research focuses on MVs/exosomes which carry various signalling components and how this changes with following radiation exposure of different types doses and dose rates. This includes the phenotypical/morphological characterization of MV/exosomes as well as their signalling potential based on the cargo, these could become novel biomarkers for radiation exposure or predictors of radiation response.

On a wider scale, these projects will help guide and identify practical health and risk implications for other processes such as ageing , initiation and progression of cancer, environmental, occupational and medical risks of radiation exposure. Ultimately it may impact on legislation for radiation exposure limits and personalised medicine through response prediction.

Infrastructure and material: The Genomic Instability (GI) Research Group is sited within the Faculty of Health and Life Sciences which has been recognized in the latest government Research Excellence Framework exercise where the majority of research was judged to be world leading or of international standing. State of the art equipment including numerous imaging facilities and platforms and microarray facility with bioinformatics support. This is in addition to up to date modern equipment for all cellular biology and molecular biological techniques. Within the laboratory we also have start of the art "Tuneable Resistive Pulse Sensing" equipment (TRPS) for accurate quantification and profiling of exosomes, we have tight links with the company /manufacturer who are also based in Oxford. We also have strong links with collaborators at Oxford University who are involved with the physics aspect of our work.

NRPA information sheet – Topic 1: Improvement of health risk assessment associated with low dose/dose rate radiation

The Norwegian Radiation Protection Authority (NRPA) is the competent authority in radiation protection and nuclear safety in Norway. It also participates extensively in national and international research projects. It has been a partner in numerous EU projects since FP 4 and is one of the main partners in the Norwegian Centre of Excellence, CERAD.

NRPA's research interests in relation to topic 1 of the CONCERT call include epidemiological, dosimetric and radiobiological research. Examples of potential contributions are as follows:

Health risk assessment in uranium workers and in the populations living near uranium mining in Kazakhstan – The NRPA has experience in epidemiological research on exposed populations from Kazakhstan, the world's largest uranium producer, with 20 active uranium mines. Currently, more than 30,000 workers are involved in the uranium industry activities in South Kazakhstan, and the operating companies conduct dosimetry surveillance for workers involved in nuclear activities. A group of Kazakh researchers has conducted an epidemiological study in a subset of workers and surveys in populations living in the uranium mining regions. The group aims to extend epidemiological investigations and are seeking European collaborators.

Epidemiological assessment of cancer risk and other health risks from low-dose ionising radiation exposure in the medical field – The NRPA has expertise in large scale harvesting of medical exposure data from medical databases, as well algorithm based dosimetry on large sets of medical exposure data. This comprises dosimetry at organ level and for different body sizes, as well as Monte Carlo modeling of dosimetric uncertainties. The NRPA also has expertise in assessment of inhomogeneous dose distributions and dose-response modelling.

Computational dosimetry for radiobiological research – The NRPA is the Norwegian Secondary Standard Dosimetry Laboratory for the units Gy, Bq, and Sv, and has a well-equipped dosimetry laboratory that is also used in calibration of radiobiological research, to ensure accurate and traceable dosimetry. Furthermore, the NRPA is actively developing Monte Carlo dosimetric models for radiobiological research, including dosimetric uncertainty estimates.

For further information, please do not hesitate to contact: Dr. Åste Søvik, Head of Section form Radiation Research at aste.sovik@nrpa.no or +47 67 16 25 06.

Financial note: The NRPA is the Norwegian POM in CONCERT. However, as a non-EU country, the NRPA does not request EU funding for its participation in CONCET – NRPA participation in EU projects is funded by the Research Council of Norway.

Participant: Octávia Monteiro Gil

Institution: Instituto Superior Técnico - Campus Tecnológico e Nuclear

Description of Institution:

Instituto Superior Técnico (IST) is the leading university of Engineering, Science and Technology in Portugal. The Association of Instituto Superior Técnico for Research and Development (IST-ID) is a private not-for-profit institution, which primarily aims at carrying out Science and Technology activities, fostering knowledge transfer and promoting the involvement of national and foreign researchers in RD&I projects in their areas of expertise.

The IST-ID carries out RD&I activities in major areas, which are associated with challenges with a strong impact on society. These are strongly interdisciplinary areas in nature and cut across different fields of engineering, science and technology and architecture, comprising not only fundamental aspects but also projects with a strong applied component. The areas of intervention are Basic Sciences, Applied Life Sciences, Information and Communication Technologies, Energy, Environment and Mobility, Materials, Nanotechnologies and Nanosciences, Nuclear Reactors and Accelerators, Nuclear Safety and Radiological Protection. IST¬ID commits to providing the above referred support to the Research Centre for Nuclear Sciences and Technologies (C^2TN) aiming at carrying out the proposed R&D activities as a crosscutting structure with proven expertise in several research areas with access to specialized equipment and infrastructures, unique in the country.

Research interests:

- Radiation Protection
- Radiological and nuclear emergencies
- Biological dosimetry
- Biological effects of ionizing radiation
- Thyroid cancer patients - effects of the different doses of 131 I treatment
- Exposure to low doses of ionizing radiation
- Radiobiology
- Cytogenetic methods

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The laboratory of Research on Transcription in Stem cells (LRTS) is part of the DSV/CEA and is located at Fontenay-aux-Roses (France). This laboratory has several research projects on the effects of low doses of radiations on normal hematopoiesis and on hematopoietic stem cells. Recently, we have shown that that adult hematopoietic stem cells (HSC) are hyper-radiosensitive to dose of γ-irradiation as low as 20 mGy. This hyper-radiosensitivity is not associated with activation of the DNA Damage Response pathway but with immediate production of Reactive Oxidative Species (ROS) that leads to autophagy up-regulation, phosphorylation of p62 and activation of Nrf2. We have also shown that the activation of Nrf2 protects HSC against low doses of γ-irradiation. Twenty□□□□ to HSC causes long-term oxidative stress, decreased self-renewal capacity and a myeloid bias, all of which can be reversed by pretreatment with ROS scavenger NAC. Finally, we show that Total Body Irradiation at 0.02 Gy after mobilization of HSC decreases their self-renewal capacity. These results show that very low doses of γ-rays have detrimental effects on HSC and suggest that low-dose radiation exposure might have adverse effects on somatic stem cells.

Key words

Adult hematopoietic stem cells, low doses of radiation, epigenetics of hematopoietic stem cells, energetics and mitochondria in adult hematopoietic stem cells, low doses of radiation and oxidative stress.

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Research background:

- Member of EURADOS WG6 “Computational dosimetry”
- Member of ICRP Task Group 96 “Computational Phantoms and Radiation Transport”
- Main developer of the HMGU family of voxel phantoms
- Main developer of the ICRP/ICRU adult reference computational phantoms of ICRP Publication 110

Research interests:

- Numerical dosimetry for low dose radiation, especially medical imaging
- Calculation of organ doses for various medical imaging modalities, including radiography, interventional procedures, computed tomography, and nuclear medicine

Tools available:

- Voxel phantoms of various ages, both genders, and various body statures
- Radiation transport code EGSnrc (photons and electrons)
- HMGU irradiation facilities: ^{60}Co and ^{137}Cs sources, x-ray sources (160 kVp and 320 kVp, respectively), 16 slice CT scanner, mammography device

Information for potential partners - 1st RTD Open Call CONCERT

Infrastructure for radiobiology and immunology

Czech Technical University Prague, Faculty of Medical Engeneering,
Sportovců 2311, Kladno, Czech Republic

We propose research topics for 1st call of CONCERT, related to
Topic 1: Improvement of health risk assessment associated with low dose/dose rate radiation

FBME CTU applies practical methods of teaching and preparing specialists in the field of radiology, bioinformatics, crisis management and population protection, cooperates with central and regional government authorities (SUJB, SURO) in training of pre- and postgraduate students, provides expertise, and focuses on innovative processes and technology transfer. The immunological laboratory of FBME, located in Prague, has an SPF animal facility at disposal for small rodents breading and *in vivo* experiments. It is equipped for tissue cultures and for analysis of radiation-induced changes (i.e. phenotype, function, proliferation or cytotoxicity) on cell lines, biological samples and primary lymphoid and neuronal cultures in cooperation with Core facilities for cytometry and microscopy, evaluation of gut microflora (MALDI). We can offer experimental mouse models of cancer and autoimmunity, and novel strains of mice with different sensitivity to radiation. We can perform clinical and immunological examination of humans, due to close collaboration with University hospitals applying radiodiagnostic or radiotherapy of patients (CT, X-ray, ^{60}Co, ^{137}Cs, and proton therapy)

In cooperation with small enterprise (APIGENEX Ltd.) we are developing safe radio-protectives (nor-muramyl lipoglycopeptides) derived from bacterial cell wall peptidoglycans for prevention of leukopenia and restoration of haematopoiesis damaged by radiotherapy. The focus of the company APIGENEX Ltd. lies in research and development for foreign companies (e.g. Novo Nordisk, Pfizer, GSK, Schering Plough) in the development of innovative pharmaceuticals.

Application of nuclear physics methods and procedures can be used in the interdisciplinary fields of research, especially in biology, ecology, medicine, radiopharmacy and materials sciences (Institute of Nuclear Physics ASCR, v.v.i.). The INP ASCR is equipped with MT 25 microtron (cyclic electron accelerator with a Kapitza type resonator) and ^{60}Co-irradiator for small animals. The accelerator applications involve radiation resistance testing and studies under well controlled and monitored conditions for electron and photon beam and for neutron, advanced neutron and photon activation analysis (PAA) procedures, in both non-destructive and radiochemical modes, and their applications in environmental, biomedical, geo- and cosmo-chemical research that allows determination of a large number of elements. (Details will be published in next issue of AIR^2).

Basic and applied research projects:

1. GA14-10100S Utilization of novel mouse strains for investigation of the NK cell regulatory role in development and therapy of cancer
2. GA310/06/0477 NK and NKT cells in the development and pathogenesis of RA
3. IGA MZČR NR/9106 NK and NKT cells in the pathogenesis of primary idiopathic PM/DM
4. GAUK109908/2008 Effects of radiotherapy for prostate cancer on bladder, rectum, and the immune system depending on the radiation dose
5. DINAMO FP7 KBBE 245122 Development of diamond intracellular nanoprobes for oncogen transformation dynamics monitoring in living cells
6. NANOINTEGRATION CZ.1.07/2.3.00/20.0306 Integration of the team for research and development of new principles of nanotechnology in biomedicine for education and medical practice
7. EE2.4.31.0224 Population protection and crisis management and emergencies
8. TA02010760 Development of new generation of antitumor immunotherapeutics
9. 2A-1TP1/055 Development of PET-radiodiagnostics for imaging in oncology and neurology
10. FT-TA5/136 System for finding biologically active substances. Focused combinatorial libraries
11. FT-TA2/054 Discovery libraries of chemical compounds
12. GA205/09/0171 Exposure to cosmic radiation in the vicinity of earth: Effect of space weather and the implications for radiation protection
13. GBP108/12/G108 Preparation, modification and characterization of materials by radiation
14. GA205/09/0171 Optimization of radiation protection of Aircrew

Contact: Anna Fiserova, M.D., PhD: Head of Immunological Laboratory, Department of Health Care Disciplines and Population Protection E-mail: anna.fiserova@fbmi.cvut.cz, phone: +420 724 127 666

Eva Forssell-Aronsson

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Dept of Radiation Physics, University of Gothenburg, Sweden

Topic 1: Improvement of health risk assessment associated with low dose/dose rate radiation

Research interest

- Biological effects of radiation on normal cells, tissues and organisms
- Better understanding of the underlying molecular mechanisms and signalling pathways
- Radiation related biomarkers
- Biological dosimetry
- Influence of other factors on radiobiological effects, e.g. circadian rhythm, chemicals/drugs etc.

Infrastructure

- Different laboratories for handling very low to very high amounts of radionuclides. Most types of radionuclides possible, also alpha emitters
- Detectors for measurements of radioactivity using alpha, beta and gamma radiation. Measurement techniques and detectors suitable for both very low to high radioactivity levels
- Laboratories with cell culture facilities, where one is dedicated for use together with radionuclides. Various types of cell lines. Primary cell culture
- Animal facility for small to larger animals, but personal experience of mice, rats and pigs
- Irradiation facilities using radionuclides (emitting alpha particles, electrons and photons), external radioactive sources, X-ray machines and linear accelerators of various types for external irradiation using photons or electrons. Possibilities also for proton irradiation
- Situated at a university hospital, enabling possibilities to include patients or healthy volunteers in studies
- Dosimetric estimations. Internal dosimetry. External dosimetry. Monte Carlo simulations using various codes
- Molecular techniques for studies of effects on genome, transcriptome, and proteome. Microarray techniques, RNAseq, qPCR, Northern blot, Western blot, MS-techniques, ELISA, histopathological techniques, immunohistochemistry, etc. Epigenetics. Programs for analysis, e.g. Nexus, R, IPA. Biostatistics

Competence in the research group

- radiation physics
- radiation biology
- molecular biology
- molecular genetics
- pathology
- oncology
- tumour pathology
- biostatistics
- toxicology
- biochemistry

Paşaportul Laboratorului	Laboratory Passport
Denumirea: Laboratorul ştiinţific Igiena Radiaţiilor şi Radiobiologie **Fondat**: a. 1995 **Statele:** COREŢCHI Liuba, şef laborator, dr. hab. şt. biol., conferenţiar cercetător. (162.01 Genetica, 331.02 Igiena); BAHNAREL Ion, cerc. şt. principal, dr. hab. şt. med. prof. univ. (331.02 Igiena) ROŞCA Andrei, cerc. şt. principal, dr. hab. şt. med, prof. univ. (324.01 Imagistica medicală) GRANACI Vera, cerc. şt. superior; dr. şt. biol, conf. univ. (165.01 Fiziologia omului şi animalelor) COJOCARI Alexandra, cerc. şt., master în radiobiologie VÎRLAN Serghei, cerc. şt., doctorand PLĂVAN Irina, cerc. şt. st., master în radiobiologie CAPAŢÎNA Angela, laborant în med., master CONDREA Larisa, preparator **Direcţia ştiinţifică de bază**: ***Sănătate şi Biomedicină*** **"***Biomedicina, farmaceutica, menţinerea şi fortificarea sănătăţii"* **Domeniile de cercetare**: — Organizarea şi efectuarea cercetărilor ştiinţifico-practice în domeniul Radiobiologiei, Radiogeneticii, Radioprotecţiei şi Securităţii nucleare: — Studierea polimorfismului ADN, efectelor imunologice şi citogenetice la persoane expuse profesional la doze mici de radiaţii ionizante; — Studierea efectelor clinice, imunologice şi citogenetice la descendenţii participanţilor la diminuarea consecinţelor accidentului nuclear de la Cernobîl;	**Name**: Scientific laboratory of Radiation Hygiene and Radiobiology **Foundation**: 1995 y. **Staff:** COREŢCHI Liuba, head of the lab., doctor habilitate, Associate Professor (162.01 Genetics, 331.02 Hygiene) BAHNAREL Ion, Principal researcher, doctor habilitate, Full Professor (331.02 Hygiene) ROŞCA Andrei, Principal researcher, doctor habilitate, Full Professor, (324.01 Medical Imagistic) GRANACI Vera, Senior Researcher; PhD in Biology (165.01 Human & Animal Physiology) COJOCARI Alexandra, Scientist researcher, MD in Radiobiology VÎRLAN Sergey, Scientist researcher PLĂVAN Irina, Junior Researcher, MD in Radiobiology CPAŢÎNA Angela, Analyst in medicine, MD. CONDREA Larisa, preparatory **Basic scientific direction**: ***Health and Biomedicine*** *"Biomedicine, pharmaceutics, health care and strengthening"* **Domains of Research**: – Arranging and conducting scientific and practical research in the field of Radiobiology, Radio genetics, Radiation protection and Nuclear safety: – Studying of DNA polymorphism, cytogenetic and immunological effects of people occupationally exposed to low doses of ionizing radiation; – Study of the clinical, immunological and cytogenetic effects of offspring participants to mitigate the consequences of the Chernobyl nuclear accident;

— Studierea incidenţei prin maladii oncologice şi analizarea corelaţională a asociaţiei acestora cu factorul radiaţional, inclusiv expunerea la Radon;
— Evidenţa şi monitorizarea radiologică a teritoriului republicii cu efectuarea investigaţiilor gama-spectrometrice şi a măsurărilor dozimetrice a obiectivelor mediului ambiant.

Proiecte ştiinţifice:

● 2009-2010 „Stabilirea efectelor medico-biologice ale radiaţiilor ionizante". Nr. înregistrare de stat: 348 INST. (Director de proiect Ion BAHNAREL).
● 2011-2014 „Stabilirea riscului pentru sănătate determinat de poluarea mediului ambiental cu radionuclizi naturali şi tehnogeni cu elaborarea tehnologiilor de bioremediere a solurilor radiocontaminate". Nr. înregistrare de stat: 534 INST. (Director de proiect Liuba COREȚCHI).
● 2010-2011 „Stabilirea corelării dintre tipul solurilor şi concentraţiile de Radon". Nr. înregistrare de stat: 264.IND (Consultant ştiinţific Liuba COREȚCHI).
● 2010-2011 „Evaluation and utilization of natural and mutant germplasm" (Proiect ştiinţific regional RER/5/013 suportat de AIEA). (Director de proiect Liuba COREȚCHI).
● 2014-2015 "Establishing Enhanced Approaches to the Control of Public Exposure to Radon" (Proiect de cooperare tehnică cu AIEA RER/9/127). (Director de proiect Liuba COREȚCHI).

Colaborare ştiinţifică:

● Institutul Oncologic al Republicii Moldova.
● Institutul Mamei şi Copilului
● Instituţiile Medico-Sanitare Publice.
● Agenţia Naţională de Reglementare a activităţilor nucleare şi radiologice.
● Academia de Ştiinţe a Moldovei: Institutul de Genetică,

– Studying the incidence of cancer diseases and correlation analysis of their association with radiation factor, including exposure to radon;
– Records and radiological monitoring of the territory of the gamma-spectrometric investigations and dosimetric measurements of environmental targets.

Scientific projects:

● 2009-2010 - „Establishing of the medical biological effects of ionizing radiation". Code 348 INST. (Project Director Ion BAHNAREL).
● 2011-2014 – „Establishing risk to health caused by environmental pollution with natural and anthropogenic radionuclide with the development of bioremediation technologies of radiocontaminate soils". Code 534 INST. (Project Director Liuba COREȚCHI).
● 2010-2011 – „Correlations between soil type and radon concentrations". 264.IND. (Project Director Liuba COREȚCHI).
● 2010-2011 " Evaluation and utilization of natural and mutant germplasm" (RER/5/013 supported by AIEA). (Project Director Liuba COREȚCHI).
● 2014-2015 - "Establishing Enhanced Approaches to the Control of Public Exposure to Radon" (AIEA RER/9/127). (Project Director Liuba COREȚCHI).

Scientific collaboration:

●The Oncology Institute of Moldova.
● Mother and Child Institute.
● Public Health care Institutions.
● National Agency for regulation of nuclear and radiological activity.
● Academy of Sciences of Moldova: Institute of Genetics, Physiology and Plant Protection and Institute of Microbiology and

Fiziologie şi Protecţie a Plantelor, Institutul de Microbiologie şi Biotehnologie.

- Agenţia Internaţională pentru Energie Atomică, Viena, Austria
- Institutul Unificat de cercetări ştiinţifice, Dubna, Federaţia Rusă

Publicaţii (7 cele mai importante):

1. BAHNAREL I..; COREŢCHI L.; MOLDOVAN M. Medical and biological aspects of the Cherobyl nuclear accident influence on the population of the Republic of Moldova. Ch.: Î.S.F.E.-P. „Tipografia Centrală", 2006. – 160 p. ISBN 978-9975-78-176-3.
2. BAHNAREL I..; COREŢCHI L.; MOLDOVAN M. Aspecte medico-biologice ale acţiunii accidentului nulear de la Cernobîl asupra populaţiei Republicii Moldova. Ch.: Î.S.F.E.-P. „Tipografia Centrală", 2005. – 152 p. ISBN 9975-78-405-4.
3. COREŢCHI L. et al. Report on current status of Radon related activities in Member States participating in TC EU RER /9/127 "Establishing Enhanced Approaches to the Control of Public Exposure to Radon", 2015, 131 p. Vienna, AIEA. (TECDOC).
4. ROŞCA A., BAHNAREL I., COREŢCHI L. Optimization of radio-therapeutic treatment and the program of quality assurance in ionizing radiation therapy. In: Curierul medical, vol.58, nr 1, 2005, p.3-7. ISSN 1857-06663.
5. CORETCHI, L.Ş.**;** BAHNAREL, I.N. [et al.]. Health effects of children of the Chernobyl NPP accident consequences liquidation participants. In: Engaging the public to fight the consequences of terrorism and disasters, NATO Workshop, 2-4 June, 2014, NATO Science for peace and Security Series E: Human and Societal Dynamics – Vol.120. IOS Press, 2015, p. 275-285. ISBN 978-1-61499-492-3 (print) ISBN 978-1-61499-493-0 (online) ISSN 1874-6276 (print) ISSN 1879-8268 (online).
6. ROŞCA A., BAHNAREL I., COREŢCHI L., PLĂVAN I. Quality assurance standards in ionizing radiation therapy. In: The XIV International Conf. INVENTICA 2015, June, 24-26, 2015, Iaşi,

Biotechnology.

- International Agency of Atomic Energy, Vienna, Austria
- Joint Institute of Nuclear Research, Dubna, Russian Federation

Publications:

1. BAHNAREL I..; COREŢCHI L.; MOLDOVAN M. Medical and biological aspects of the Cherobyl nuclear accident influence on the population of the Republic of Moldova. Ch.: Î.S.F.E.-P. „Tipografia Centrală", 2006. – 160 p. ISBN 978-9975-78-176-3.
2. BAHNAREL I..; COREŢCHI L.; MOLDOVAN M. Aspecte medico-biologice ale acţiunii accidentului nulear de la Cernobîl asupra populaţiei Republicii Moldova. Ch.: Î.S.F.E.-P. „Tipografia Centrală", 2005. – 152 p. ISBN 9975-78-405-4.
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4. ROȘCA A., BAHNAREL I., COREȚCHI L. Optimization of radio-therapeutic treatment and the program of quality assurance in ionizing radiation therapy. In: Currier medical, vol.58, nr 1, 2005, p.3-7. ISSN 1857-06663.
5. CORETCHI, L.Ş.**;** BAHNAREL, I.N. [et al.]. Health effects of children of the Chernobyl NPP accident consequences liquidation participants. In: Engaging the public to fight the consequences of terrorism and disasters, NATO Workshop, 2-4 June, 2014, NATO Science for peace and Security Series E: Human and Societal Dynamics – Vol.120. IOS Press, 2015, p. 275-285. ISBN 978-1-61499-492-3 (print) ISBN 978-1-61499-493-0 (online) ISSN 1874-6276 (print) ISSN 1879-8268 (online).
6. ROȘCA A., BAHNAREL I., COREȚCHI L., PLAVAN I. Quality assurance standards in ionizing radiation therapy. In: The XIV International Conf. INVENTICA 2015, June, 24-26, 2015, Iaşi,

Romînia.

7. URSULEAN, I.; COREŢCHI, L.; CHIRUŢA, IU.; VÎRLAN, S. Estimation of indoor radon concentrations in the air of residential houses and mines in the Republic of Moldova. *Romanian Journal of Physics*. 2013, Volume 58, Number Suppl., 291-297. First East European Radon Symposium - FERAS 2012 September 2nd - 5th, 2012, Cluj-Napoca, Romania Proceedings - selected papers. ISSN 1221-146X. JCR [IF 2013 0, 745].

Brevete de invenţie:

1. BAHNAREL, I.; SAMOTÎIA, E.; COREŢCHI, L.; MOLDOVAN, M. (MD). Brevet de invenţie C2, MD, A 61 B 5/145. Procedeu de evaluare a statutului imun. Cerere depusă 26.02.2004, BOPI nr.1/2005.
2. COREŢCHI, L.; EMNOVA, E.; BAHNAREL, I.; SPÎNU, C.; CECHIRLAN, N. (MD). Brevet de invenţie nr. 3212 G2, MD, C 12 N 1/14. Tulpină de fungi Mucor vulgaris X Mich. Pentru solubilizarea compuşilor insolubili ai cobaltului. Cerere depusă 15.09.2005, BOPI nr.12/2006.
3. COREŢCHI, L.; BAHNAREL, I.; FRUNZE, N.; COREŢCHI, L.; SPÎNU, C. (MD). Brevet de invenţie nr. 161. 3657 G2, MD, C 12 N 1/14. Tulpină de fungi Penicillium viride 2 pentru solubilizarea compuşilor insolubili ai cobaltului. Cerere depusă 25.12.2007, BOPI, nr.7/2008.
4. BAHNAREL, I.; SPÎNU, C.; COREŢCHI, L.; BÎRCĂ, L.; CHINTEA, P.; VUTCARIOV, V.; SPÎNU, I.; COREŢCHI, L. (MD). Brevet de invenţie 27 Z 2009, MD, A 61 K 31/56. Metodă de tratament a dereglărilor imunităţii celulare provocate de radiaţia ionizantă. Cerere depusă 24.10.2008, BOPI, nr. 5/2009.

Romînia.

7. URSULEAN, I.; COREŢCHI, L.; CHIRUŢA, IU.; VÎRLAN, S. Estimation of indoor radon concentrations in the air of residential houses and mines in the Republic of Moldova. *Romanian Journal of Physics*. 2013, Volume 58, Number Suppl., 291-297. First East European Radon Symposium - FERAS 2012 September 2nd - 5th, 2012, Cluj-Napoca, Romania Proceedings - selected papers. ISSN 1221-146X. JCR [IF 2013 0, 745].

Patents:

1. BAHNAREL, I.; SAMOTÎIA, E.; COREŢCHI, L.; MOLDOVAN, M. (MD). Brevet de invenţie C2, MD, A 61 B 5/145. Procedeu de evaluare a statutului imun. Cerere depusă 26.02.2004, BOPI nr.1/2005.
2. COREŢCHI, L.; EMNOVA, E.; BAHNAREL, I.; SPÎNU, C.; CECHIRLAN, N. (MD). Brevet de invenţie nr. 3212 G2, MD, C 12 N 1/14. Tulpină de fungi Mucor vulgaris X Mich. Pentru solubilizarea compuşilor insolubili ai cobaltului. Cerere depusă 15.09.2005, BOPI nr.12/2006.
3. COREŢCHI, L.; BAHNAREL, I.; FRUNZE, N.; COREŢCHI, L.; SPÎNU, C. (MD). Brevet de invenţie nr. 161. 3657 G2, MD, C 12 N 1/14. Tulpină de fungi Penicillium viride 2 pentru solubilizarea compuşilor insolubili ai cobaltului. Cerere depusă 25.12.2007, BOPI, nr.7/2008.
4. BAHNAREL, I.; SPÎNU, C.; COREŢCHI, L.; BÎRCĂ, L.; CHINTEA, P.; VUTCARIOV, V.; SPÎNU, I.; COREŢCHI, L. (MD). Brevet de invenţie 27 Z 2009, MD, A 61 K 31/56. Metodă de tratament a dereglărilor imunităţii celulare provocate de radiaţia ionizantă. Cerere depusă 24.10.2008, BOPI, nr. 5/2009.

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RADRISK GbR
Dr. Natalia Semioshkina

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Christelle ADAM-GUILLERMIN

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Interest : Topic 1 but could also contribute to topic 2.

Research interests :	Infrastructures :
-Radioecology and ecotoxicology -Low doses/dose rates -Genotoxicity -DNAseq, RNAseq -Proteomics -Protein carbonylation -Epigenetics -Biomarkers -zebrafish -daphnids -nematods -cell culture -in situ experiments (Chernobyl, Fukushima) -DEBtox modelling -Population dynamic modelling	-Gamma irradiator (up to 50 mGy/h) -Radioactive contamination facility (gamma, alpha and beta emitters) -Microcosm experiments (aquatic/terrestrial compartments) -Cell culture laboratory -Microscopy (Transmission Electronic Microscope + EDAX probe ; apotome ; confocal microscope) -RT-qPCR -Flow cytometer -Chemical analysis (ICP-MS/HPLC ; ICP-OES…) -Gamma spectrometry/scintillation

Research Interests and Infrastructure for Information Day of CONCERT
27th Jan 2016, Munich, BfS

Jochen Graw, Research Group Eye Diseases, Institute of Developmental Genetics, HMGU

In our research group we investigate mouse mutants affecting eye development and the health status of ocular tissues (cornea, lens, retina, optic nerve). The mice are being characterized in a functional, morphological and molecular manner. Based upon our experience with hereditary congenital cataracts in mouse, we also identified mutations underlying congenital hereditary human cataracts, in cooperation with different clinics in Germany, Canada and India. An overview of our work can be found on our web page (http://www.helmholtz-muenchen.de/en/idg/research/neuropsychiatric-diseases/eye-disease/research/index.html).

The lens of the eye is recognized as one of the most radiosensitive tissues in the human body, and radiation-induced cataracts are well recognized. Although much work has been carried out, the mechanisms of radiation-induced cataractogenesis are still not fully understood. In particular, the question of the threshold dose for cataract development is not answered. Therefore we performed a Lifetime Study in mice after whole-body irradiation with doses of 0.5 Gy and below to provide a dose-response-curve for lens densities over a period of two years (the lifespan of a mouse). Within this study we collected several organs at different time points. For better understanding of radiation-induced DNA-repair processes in mouse lenses, we use primary lens epithelial cell culture techniques.

We received funding from the DoReMi NoE (low dose research towards multidisciplinary integration) and are supported by the German Federal Ministry of Research and Technology (FKZ 02NUK045A) both for analyzing the effects of low doses of ionizing radiation on cataract formation.

We are running also the vision screen within the German Mouse Clinic (GMC http://www.mouseclinic.de/index.php?id=11636). Here we use sensitive instruments for non-invasive *in vivo* examinations of the mouse eye, such as Scheimpflug imaging (cornea, lens), Optical Coherence Tomography (OCT; retinal fundus and retinal layers), Laser Interference Biometry (eye size parameters), optokinetic drum (vision test), and Electroretinography (ERG; retinal function).

For the morphologic and molecular analyses eyes are embedded in plastic medium or paraffin. Thin sections are stained for histology or immunohistochemistry and evaluated with a light microscope or a confocal scanning microscope.

References:

Ainsbury, E.A., Bouffler, S.D., Dörr, W., **Graw, J.**, Muirhead, C., Edwards, A.A., Cooper, J.: Radiation cataractogenesis – a review of recent studies. Rad. Res. 172, 2009, 1-9.

Bannik, K., Rössler, U., Faus-Kessler, T., Gomolka, M., Hornhardt, S., Dalke, C., Klymenko, O., Rosemann, M., Trott, K.-R., Atkinson, M., Kulka, U., **Graw, J.**: Are mouse lens epithelial cells more sensitive to γ-irradiation than lymphocytes? Rad. Environ. Biophys., 52, 2013 279-286.

DARBA DROŠĪBAS un VIDES VESELĪBAS INSTITŪTS
Institute of Occupational Safety and Environmental Health
RĪGAS STRADIŅA UNIVERSITĀTES aģentūra
Riga Stradins University agency

Summary of situation and proposals for low-dose radiation impact assessment LATVIA

Extensive epidemiological and clinical research on Chernobyl nuclear power plant clean-up workers' health conditions has been done in Latvia during more than 20 last years. Previous studies conducted by researchers from the Centre of Occupational and Radiation Medicine (Pauls Stradins Clinical University Hospital) and Institute of Occupational Safety and Environmental Health (Riga Stradins University) included the analysis of late aftereffects of prolonged exposure to low doses of ionizing radiation after nuclear power plant disaster, e.g.:

- immunological evaluation of changes in the immune system (including immunosenscence),
- biochemical studies of oxidative stress and other molecular disturbances followed the exposure,
- retrospective biodosimetry (from teeth enamel),
- morphological features of thyroid gland diseases,
- electroneurological and psychological evaluation,
- genetic studies (telomere length analysis),
- cause specific morbidity and mortality of CNPP clean-up workers from Latvia compared with general Latvian population.

There were a number of successful studies conducted in collaboration with foreign scientists.

In parallel data of occupationally exposed population (e.g., radiologists and other medical staff exposed to ionizing radiation) were analysed to assess oncological morbidity among them.

The comprehensive data on health observations in Chernobyl NPP clean-up workers from Latvia (approximately 6000 people) were collected since the disaster time (1986) till now in the State Register of Persons Exposed to Ionizing Radiation in Chernobyl Accident. It is important to notice that before the works in Chernobyl and after return to Latvia these people were living in relatively radiologically uncontaminated area. Chernobyl NPP clean-up workers regularly undergo medical check-ups and receive treatment in the Centre of Occupational and Radiation Medicine. The data and experience collected may be used for future epidemiological and clinical studies to evaluate in details the late consequences of nuclear disaster.

In the future collaboration study molecular epidemiologic evaluation is planned to compare populations from different countries previously exposed to ionizing radiation (e.g., Chernobyl accident clean-up workers from Latvia, Lithuania and Estonia, A-bomb survivors in Japan). The evaluation will include retrospective biodosimetry based on the analysis of immune and genetic parameters supported by epidemiological data from previous health observations and data bases (special attention will be paid to chronic inflammatory conditions, chronic degenerative disorders, history of cancer and radiation therapy, additional radiological examinations). The immune parameters measured in blood will include various inflammation-related biomarkers to determine the presence/or absence of radiation-related persistent inflammation. The analysis of DNA samples will reveal risk markers, which will help to determine whether or not individual differences in radiosensitivity affect the onset of disease after radiation exposure. Epidemiological data on oncological morbidity and cause specific mortality in whole exposed population will be analysed in details too.

The selection of age and gender matched people non-exposed to excessive ionizing radiation (except natural background) from general population living in corresponding country is planned as the control group. Additionally other groups of occupationally exposed persons may be added to the analysis for comparison (e.g., medical staff, defectoscopists, pilots, etc.).

This study proposal is expected to develop biomarkers useful for long-term monitoring of populations afflicted by future nuclear accidents as well as ethnic-/individual-specific assessment of risk of developing radiation-related diseases after radiation exposure.

List of current publications and summaries of PhD thesis will be available for the Information Day.

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Dzirciema str. 16
LV 1007, Riga
Latvia

The most important publications on radiation research from Latvia:

1. Eglite ME, Zvagule TJ, Rainsford KD *et al.* Clinical aspects of the health disturbances in Chernobyl Nuclear Power Plant accident clean-up workers (liquidators) from Latvia. *Inflammopharmacology* 2009;**17**(3):163–9.
2. Kalnina I., Kurjane N., Reste J., Zvagule T., Kirilova J., Kirilovs G. Assessment of Blood Plasma Albumin and Lymphocyte Subpopulations in Patients with Gastrointestinal Cancer // RSU Collection of Scientific Papers 2010: Research articles in medicine & pharmacy – Rīga, RSU, 2011 – Pp. 128-133.
3. Kurjane N, Bruvere R, Shitova O *et al.* Analysis of the immune status in Latvian Chernobyl clean-up workers with nononcological thyroid diseases. *Scand J Immunol* 2001;**54**(5):528–33.
4. L.Matisāne, L.Carpenter, K.Venables. Female All Cancer Incidence in Medical Radiation Workers in Latvia, 1982-2002. RSU 2004. gada Zinātniskie raksti; 2004; Rīga, RSU, 199.-202.lpp.
5. Mironova-Ulmane N, Pavlenko A, Zvagule T et al. Retrospective dosimetry for Latvian workers at Chernobyl. Radiat Prot Dosimetry 2001; 96(1-3):237–240.
6. Petukhov V.I., Dmitriev E.V., Kalvinsh I., Baumane L.Kh., Reste E.D., Zvagule T., Skesters A.P., Skalny A.V. Metal-Ligand Homeostasis in Epidermic Cells of Chernobyl Accident Liquidators // Vitamins & Trace Elements, 2011; 1:2 (ISSN: 2167-0390 VTE, an open access journal http://dx.doi.org/10.4172/2167-0390.1000102)
7. Reste J, Kurjane N, Zvagule T *et al*. Mortality analysis in Chernobyl clean-up workers from Latvia. 14th International Congress of Radiation Research, ICRR 2011, 28 August - 1 September 2011, Warszawa, Poland, 2011,120-1.

8. Reste J, Kurjane N, Zvagule T *et al*. Oncological morbidity pattern of Chernobyl accident workers from Latvia. International Proceedings of IFEH 12th World Congress on Environmental Health, Vilnius, Lithuania, 22-27 May 2012. Bologna: Medimond, 2012,105–9.
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27 January, 2016-Information Day on the 1st OPEN RTD CALL of CONCERT

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Topic 1: improvement of Health risk assessement associated with low dose/dose rate radiation.

Recently, an emerging consensus highlights that different cell types secrete bioactive factors as microvesicules that mediate proximal as well as distant cell-to-cell signalling. Cell-cell communication has proven to be even more complex than previously thought since the discovery that extracellular vesicles serve as containers of biological information on various pathophysiological settings. Extracellular vesicles are classified into exosomes, microvesicles/microparticles, or apoptotic bodies, originating from different subcellular compartments. The cellular machinery controlling their formation and composition, as well as the mechanisms regulating their extracellular release, remain unfortunately much unknown. Their biomarker potential has raised significant because the vesicle composition and microRNA content are specific signatures of cellular activation and injury. More than simply cell dust, extracellular vesicles are capable of transferring biological information to neighboring cells and play an active role in inflammatory diseases, apoptosis and senescence. The molecular interactions regulating these effects involve specific receptor activation, proteolytic enzymes, reactive oxygen species, or delivery of genetic information to target cells.
More importantly, the concept of a specific microenvironment or "niche" that is required for Stem Cells SCs to function emerged more than three decades ago. SCs reside in specific local microenvironments that provide structural support and molecular signals to regulate SC quiescence, self-renewal, and activation for tissue maintenance. The different functions of distinct SC populations appear to depend largely on extrinsic influences. More importantly, different signals from the vascular niches are generated to induce SC activation for tissue turnover and repair, confirming the importance of external inputs in regulating SC function. .
Our major objectives are to determine how SC niches function how they are altered after irradiation exposure**.** We propose a comprehensive and resourceful approach to characterize the nature and the regulation of the **angiocrine factors (microvesicles)** released by the vascular niche as well as to assess their roles in tissue homeostasis under low dose exposure. This new vascular paradigm may offer major novel insights into the development of innovative therapeutics strategies.

I am a radiopathologist with a particular interest for radiation-induced vascular dysfunction and radiation induced microvesicles regulation.