AIR²
Access to Infrastructures for Radiation protection Research

Issue 2
November 2015

Editorial

I wish to start the second issue of our Bulletin by thanking all of you for the warm welcome you have given to this publication and for your valuable comments. The aim of publishing 10 issues a year is a big challenge that will involve the willingness and collaboration of everyone. In each issue of the Bulletin, the floor will be given to a member of the Radiation Protection Research Community, and to give credit where credit is due, we are starting with the CONCERT Coordinator, Dr Thomas Jung.

The editorial team eagerly awaits your ideas and contributions to include infrastructures in each of the three categories. AIR² also provides the opportunity to announce future events such as calls for proposals on specific infrastructures, workshops and meetings. Though not exhaustive, AIR² will be filled with your valuable contributions. **Dr Laure Sabatier - CEA**

The floor to...

In addition to the research aims of the EJP CONCERT project (Horizon 2020), it also aims to create optimised use of research infrastructures in Europe, mainly by enhancing the visibility of infrastructures and facilitating access to them. The term "infrastructures" encompasses different elements, which, in brief, can be categorised as: (a) exposure platforms, (b) databases, sample banks and cohorts, and (c) analytical platforms.

CONCERT: Towards optimal use of research infrastructures

An important task of CONCERT is to extend the partners' current knowledge of existing infrastructures, e.g. in terms of availability of access, information and characteristics of the infrastructure, usage costs, legal boundaries related to data protection and intellectual property rights. The research infrastructures will be evaluated by CONCERT Task Groups who will provide recommendations to the CONCERT research partners, in particular to facilitate infrastructure access.

The knowledge and experience gathered in the ERA-PRO project (FP6) led to the development of the data warehouse STORE (FP7), which was further extended in DoReMi. In the future, STORE will be used to build an information and data repository for CONCERT-funded projects. In general, information, data and samples generated from CONCERT-funded projects, will be made available to the scientific community via repositories such as STORE.

Analytical platforms such as RENEB, which handle biological material, are a prerequisite for achieving the best possible analysis of valuable and limited quantities of biomaterial. Other platforms, such as those in the omics field, need to be developed in a similar way.

The CONCERT Work Package "Access to Infrastructures" (WP6) will also play an important role in helping to harmonise practices and protocols (i.e. developing SOPs) and maintaining already existing databases. Moreover, the information on infrastructures that will be collected and annotated in WP6, will provide input for the Education and Training effort (WP7) of CONCERT, as well as for project partners in the forthcoming CONCERT open R&D calls.

The synergistic as well as complementary work done within and across the different CONCERT Work Packages are the basis to make CONCERT as a whole a success

Dr Thomas Jung - BfS
CONCERT Coordinator

© Photo: BfS/R.Kanzliwius

CONCERT CORNER

Future events:

11 Nov 2015 : ExB meeting, Munich, Germany

12 Nov 2015 : MB meeting, Munich

11 Jan 2016: 1st Call launch

WP 6 News:

9 Nov 2015 : WP6 Working Dinner:
19h30-21h30 - Munich at 7th MELODI WS

31 Jan 2016: D6.2
List of recommended infrastructures for radiation protection research

Contents:

Exposure platforms	B3, Animal Contamination Facility
Databases, Biobanks, Cohorts	The Wismut Cohort and Biobank
Analytical platforms	The Genomic Medecine and Bioinformatics Core Facility

Next issue

December 2015

EUROPEAN JOINT PROGRAMME FOR THE INTEGRATION OF RADIATION PROTECTION RESEARCH CONCERT
HORIZON 2020

This project is funded by the Euratom research and training programme 2014-2018 under grant agreement No 662287

B3, Animal Contamination Facility

Actinide behavior following lung or wound contamination

The RadioToxicology Laboratory (LRT) was created in 1961. Since then, numerous experiments have been carried out using a variety of radionuclides. The main focus of activity is on actinides.

The LRT houses a radiologically-controlled zone with a dedicated animal house facility where inhalation and other methods of internal contamination using alpha emitter actinides

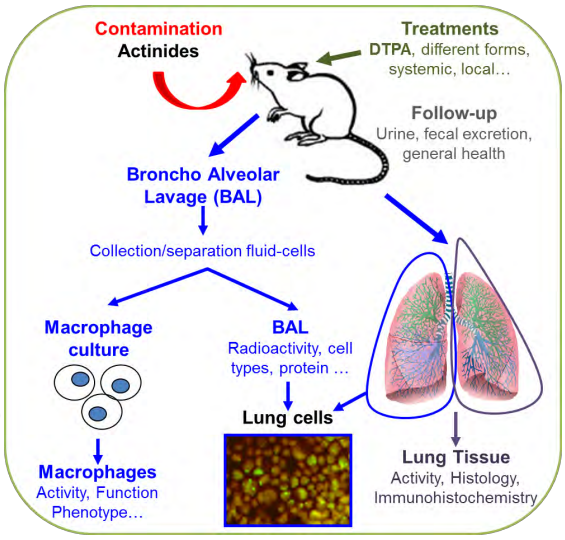


Diagram: CEA/N. Griffiths

Road map for studies after inhalation of actinides

(Plutonium Pu, Americium Am, MOX: Mixed OXide of Uranium U, Pu) are performed. The use of actinides is tightly controlled and requires effective confinement during experimental procedures. The inhalation system to expose animals is within a modified glove box. During inhalation, the animals are conscious and restrained in cardboard tubes with a perforated cover at the head end to allow breathing. This type of exposure is termed "nose-only", and up to 30 rats can be exposed at any one time.

The aerosols created for contamination may be collected and characterized in terms of particle size (cascade impactor). This experimental technique allows simulation of a realistic contamination scenario involving radioactive elements, most likely in an insoluble form, which could be released into the atmosphere (see example of a road map for an actinide inhalation study in figure).

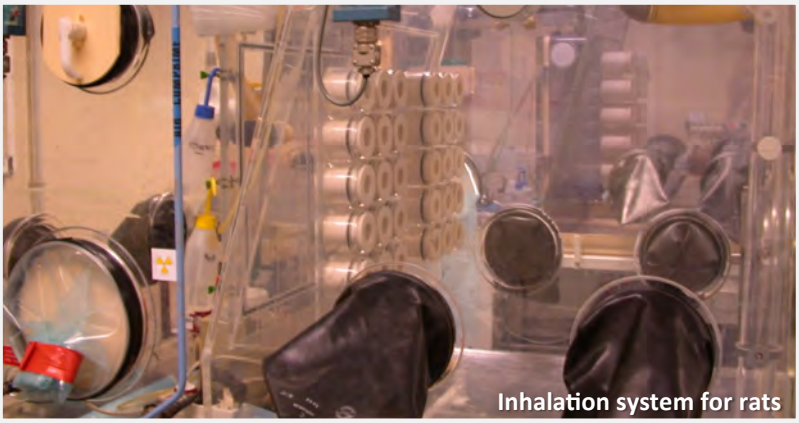
In addition to inhalation studies and lung pathologies with MOX, Pu or Neptunium, the following subjects have been addressed: Pu-induced osteosarcomas, development of a wound model for actinide contamination and evaluation of different decorporation regimens. Tissue samples, mainly paraffin embedded and collected over the decades, have recently been classified, and form the basis of the in-house "Experimental Radiotoxicology Biobank". This bioresource incorporates different tissues, contaminants and routes of contamination.

Photo: P Herpin

Nina Griffiths

LRT also carries out *in vitro* experiments to improve the estimation of dose distribution in human lung epithelial cell monolayers after contamination with alpha emitting radionuclides. Numerical models of cell monolayers can be derived from confocal images. γH2AX foci are markers of radiation-induced DNA damage. This work aims to facilitate assessment of the heterogeneity of dose distribution from alpha particle emitters in cells.

Lastly, LRT performs research *in silico* and is currently developing a unique numerical toolkit to facilitate storage and analysis of the numerous experimental data acquired in the laboratory under various conditions. This toolkit is designed to contribute to a better understanding of actinide biokinetics with particular emphasis on contamination conditions such as the route of intake or the physicochemical form.



Inhalation system for rats

Photo: CEA/DAM/CADAM

ID Card:

Exposure type:
Internal contamination

Source:
Actinides

Dose rate:
To be determined as a function of the radionuclide, radioactive and biological half-life, the administered activity, the duration of the experiment and the potential use of decorporation/ decontamination procedures.

Irradiation type:
Alpha (5000 keV)

Irradiated organism type:
rats, cells

Address:
CEA of Bruyères-le-Châtel,
Domaine du Grand Rué,
BP12 Bruyères-le-Châtel,
91297 ARPAJON cedex , France.

Access:
Use of the facility requires specific authorization for people and projects in addition to authorization for animal experiments

Supporting lab:
Radiochemistry, biochemistry, cell culture, microscopy

Internet link:
http://ircm.cea.fr/dsv/ircm/Pages/Equipes/LRT.aspx

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Related to:
EURADOS, MELODI, STORE

PREFERENTIAL DECORPORATION OF AMERICIUM BY PULMONARY ADMINISTRATION OF DTPA DRY POWDER AFTER INHALATION OF AGED PUO(2) CONTAINING AMERICIUM IN RATS. O. Grémy et al., Radiat Res. 2010; 174(5):637-44.
INTERNAL CONTAMINATION BY ACTINIDES AFTER WOUNDING: A ROBUST RODENT MODEL FOR ASSESSMENT OF LOCAL AND DISTANT ACTINIDE RETENTION. NM. Griffiths et al., Health Phys. 2012; 103(2):187-94.

The Wismut Cohort and Biobank

A cohort of nearly 60,000 uranium miners with extensive exposure data

The German uranium miner cohort offers a unique basis for the assessment of health effects associated with inhalation of radon and its progeny and uranium dust, but also effects associated with exposure to low dose external gamma radiation. The cohort includes 58,982 male workers employed between 1946 and 1989 at the East German uranium mining company "Wismut" [1]. Individual information on exposure to radon, long-lived radionuclides and external gamma radiation is available for all cohort members. In addition, absorbed doses to various organs have been calculated with support from the European Commission (Alpha-risk project).

Cumulative exposure to	Mean	Median	Max
Radon progeny [WLM]	280	33	3224
External gamma radiation [mSv]	47	16	909
Long-lived radionuclides [kBqh/m³]	4.1	1.0	132.2

Distribution of radiation exposures among exposed miners (n=50,700)

Strengths of the cohort are the large size, long follow-up period (mean 37 years), large number of total deaths (25,438), wide range of radiation exposures, and availability of information on silica, fine dust and arsenic dust; some information is also available for smoking. Individual data from the cohort are accessible to the scientific community (http://www.bfs.de/EN/bfs/science-research/projects/wismut/wismut-cohort-proposals.html). These data allow investigation of the exposure-response relationship for cancer and non-cancer mortality, different radiation qualities (alpha-radiation, gamma radiation) and low dose or dose rate range. A European pooling of the uranium miner cohort studies (Czech, French and German miners) was performed in the EU alpha-risk project and a worldwide pooling of uranium miner cohorts from Canada, the United States and Europe is currently in preparation.

In addition to the cohort data, a biobank at the BfS contains biological samples from former Wismut employees, which overlap to some extent with the cohort. The biobank consists of three sets of biomaterial: 1) Biomaterial collected from 2009–2012 from miners alive at that time (n=442); 2) Biomaterial from miners who died from lung cancer (biomaterial obtained from the pathological archive) (n=400); 3) Biomaterial from children whose fathers died from lung cancer before the age of 50 (n=81). The biomaterial (lymphocytes, plasma, DNA, RNA, fixed lymphocytes) from the first and third sets was obtained from blood and is of high quality [2], and is stored at -20°C, -80°C or in liquid nitrogen depending on the material. DNA and RNA for the second set are obtained from formalin-fixed paraffin-embedded tumour and normal lung tissue of lower quality.

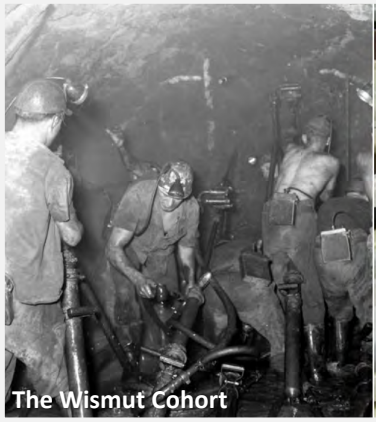
Michaela Kreuzer

For the miners whose material is in the biobank, the same exposure data are available as for the Wismut cohort. Additionally, information on smoking is partly available as are epidemiological and medical data and data for the material from the pathological archive tumour subtype.

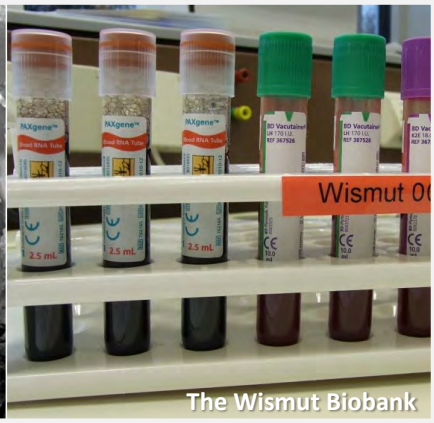
The biobank has already been used:

- To investigate leukemia specific markers
- To detect chronic radiation exposure using miRNA expression and whole genome expression arrays as well as mFISH analysis

Access to the Wismut biobank is restricted to approved proposals. Experimental data will be archived via STORE.



The Wismut Cohort



The Wismut Biobank

Photo left to right: Wismut GmbH, BfS/S. Hornhardt

Bundesamt für Strahlenschutz

ID Card:

Data base topic:
Male Uranium miners

Data owner:
BfS

Description:
Cohort study with individual data on exposure to radon, external gamma radiation and long-lived radionuclides

Biobank available:
GUMB - The German Uranium Miners Biobank

Sample type:
Blood: DNA, RNA, lymphocytes (cultured as well as fixed), plasma
Tumour tissue: DNA, RNA
Normal tissue: DNA, RNA

Sample storage condition:
-80°C (DNA, RNA, plasma) or liquid nitrogen (lymphocytes/plasma)

Access:
External scientists interested in the cohort data or biobank material may send a proposal to the BfS

Contact:
For cohort data:
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+49 30 18333 2250
For biobank material:
Maria Gomolka:
mgomolka@bfs.de
+49 30 18333 2211

Related to:
Research: MELODI, EURADOS

[1] COHORT PROFILE: THE GERMAN URANIUM MINERS COHORT STUDY (WISMUT COHORT), 1946 – 2003. M. Kreuzer, et al. Int J Epidemiol 2010; 39:980-7.
[2] ASSESSMENT OF mRNA AND microRNA STABILIZATION IN PERIPHERAL HUMAN BLOOD FOR MULTICENTER STUDIES AND BIOBANKS. DG. Weber, et al. Biomark Insights. 2010;5:95-102.

The Genomic Medicine and Bioinformatics Core Facility

Hungarian Genomics Research Network

The Genomic Medicine and Bioinformatics Core Facility (http://genomics.med.unideb.hu) was established in the year 2000 to provide access to cutting edge genomics technologies and foster collaborations between basic science and clinical research groups, as well as small and large pharma companies in the area of clinical genomics. The Centre now has 20 staff members working in the areas of biobanking, gene expression profiling, epigenetics, next generation sequencing and bioinformatics. The Centre is a national leader in the field of genomics. It is a designated key national infrastructure, coordinator of the Hungarian Genomics Research Network, and leader of the National Genomics Technology Platform (http://www.genomika.net/gntp/home.html).

Photo: UD/Sandor Nagy

Standardized epigenetics workflow based on robotics

The main research infrastructure comprises:

- Next Generation Sequencing (Illumina HiScan) (Exome Sequencing, RNA-Seq, ChIP-Seq, RNA-Seq)
- Microarray Technologies (Affymetrix and Illumina Arrays, gene expression, genotyping and cytogenetics)
- Biobanking system, sample processing using robotics (Qiagen), LN_2 storage and -70°C storage for over 20,000 samples
- Pipetting robots for sample preparation and processing (Tecan, IPStar)
- UNIX server for data analysis and storage

The Centre's long-standing technology and twinning partner in the MOLMEDREX project is the Gene Core at EMBL, Heidelberg. This partnership consists of regular bidirectional visits and transfer of know-how from GeneCore (EMBL). In addition, the Centre has been involved as an external partner (access user) in the European Sequencing and Genotyping Infrastructure Project (ESGI: http://www.esgi-infrastructure.eu/) and was invited to undertake continued collaboration on the project.

Photo: UD/Sandor Nagy

Laszlo Nagy

To date, the Centre has successfully completed projects for pharma and biotech companies such as Pfizer Global Research (EUR 340 K), Richter Hungary (Schizo Biobank EUR 2,900 K) and Csertex (EUR 1,000 K). Besides the pharma contacts, the Centre has provided services to dozens of Hungarian research groups, as well as groups from Poland, Romania, Lithuania, Taiwan, Greece, etc.

The Genomic Medicine and Bioinformatics Core Facility is located in the "In Vitro Diagnostic Building", together with the Laboratory of Medicine, the Molecular Diagnostic Laboratory and Microbiology Institutes. The Molecular Diagnostic Laboratory performs DNA analysis for monogenic disorders using sequencing, targeted mutation analysis, MLPA, trinucleotide repeat analysis, next-generation sequencing on the Roche Junior sequencer and clinical exome sequencing. It is one of the largest genetic centres in Hungary, performing 6,000 genetic tests annually including prenatal analysis. This close connection with the clinical units also ensures access to clinical samples.

Next generation sequencing - Illumina platform

Photo: UD/Sandor Nagy

ID Card:

Analytical platform type:
Genomics

Main techniques proposed:
Next Generation Sequencing (RNA-seq, DNA-seq, ChIP-seq) microarray (gene expression, SNP, CNV), clinical sample collection and processing (biobanking)

Delay to start:
None

Duration of experiment:
Technique-dependent

Training proposed:
See details on website

Address:
University of Debrecen, Medical and Health Science Center
Debrecen Clinical Genomic Center
4032 Debrecen, Hungary, Nagyerdei krt. 98. Pf. 6.

Access:
Genomics and biobanking core facility

Internet link:
http://genomics.med.unideb.hu

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Related to:
MELODI, ALLIANCE, CARPEM

PRMT1 AND PRMT8 REGULATE RETINOIC ACID-DEPENDENT NEURONAL DIFFERENTIATION WITH IMPLICATIONS TO NEUROPATHOLOGY. Z. Simandi Z et al., Stem Cells. 2015 Mar;33(3):726-41.
THE ACTIVE ENHANCER NETWORK OPERATED BY LIGANDED RXR SUPPORTS ANGIOGENIC ACTIVITY IN MACROPHAGES. B. Daniel, et al. Genes Dev. 2014 Jul 15;28(14):1562-77.

AIR²

Access to INFRASTRUCTURES for Radiation protection Research

Issue	Exposure platforms	Databases, Sample banks, Cohorts	Analytical platforms, Models, Tools
Published to date:			
Oct 2015, #1	FIGARO	FREDERICA	RENEB
Nov 2015, #2	B3, Animal Contamination Facility	The Wismut Cohort and Biobank	The Genomic Medicine and Bioinformatics CF
Coming soon:			
Dec 2015, #3	Cosmic Silence	STORE	Metabohub

Future events:

9-11 Nov 2015: 7th MELODI Workshop, Munich, Germany
Registration: over

12 Nov 2015: deadline for Next Call for Interdisciplinary Research at GANIL (France)

17-18 March 2016: 18th International Conference on Medical Physics, Radiation Protection and Radiobiology, ICMPRPR 2016, London, UK
Registration: until 17 Nov 2015 (for author)

24-25 March 2016: 18th International Conference on Radioactivity and Radiation Protection, ICRRP 2016, Madrid, Spain
Registration: until 24 Nov 2015 (for author)

10-15 April 2016: 1st International Conference on Radioanalytical and Nuclear Chemistry, RANC-2016, Budapest, Hungary
Registration: open

9-13 May 2016: 14th Congress of the International Radiation Protection Association, IRPA14, Cape Town, South Africa
Registration: until 1st May 2016

4-8 Sept 2016: 42nd Annual Meeting of the European Radiation Research Society, ERR2016, Amsterdam, Netherlands
Registration open

19-23 Sept 2016: Radiation Protection Week RPW2016, Oxford, Uk.

3-5 Oct 2016: International Conference on Research Infrastructures, ICRI2016, Cape Town, South Africa

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