

Vetenskaplig redogörelse från International Conference Radiation Research (ICRR) i Warszawa 28 augusti – 2 september 2011

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Huvudsyftet med deltagandet i ICRR konferensen var att presentera "**Radiation Modulated Immune-Response and Abscopal Effect in Rats with Contra-lateral tumours**", Detta passade väl in i sessionen om Bystander effekten som var ett av de ledande huvudtemana vid konferensen.

Joniserande strålning har i *in vitro* experiment visat sig påverka inte bara direkt bestrålade celler utan påverkar även icke exponerade celler vid sidan av de bestrålade cellerna. Detta fenomen kallas "Bystander"-effekten och förmedlas dels genom direktkontakt via "gap-junctions och dels genom signalsubstanser i mediet. Biologiska effekter som mutationer, kromosombrott osv kan på detta sätt förmedlas till obestrålade celler. Vid ICRR var Bystander effekten ett hett ämnesområde med ett stort antal bidrag. Bystander effekten har bl. a. stort inflytande på hur man skall skydda rymdresenärer som exponeras kraftigt av den kosmiska strålningen. Den har också stor betydelse vid uppskattning av effekter vid låga stråldoser som vi exponeras för i vår dagliga vardag såsom radon i bostäder, radioaktiva ämnen i födan och diagnostisk inom sjukvården. Det har hittills varit tunnsått med studier av bystander effekten *in vivo*. Vårt bidrag "**Radiation Modulated Immune-Response and Abscopal Effect in Rats with Contra-lateral tumours**" väckte därför stort intresse, Vi presenterade en experimentell modell med kontralateralt implanterade tumörer på flanken hos råttor. Efter bestrålning av endast den högra tumören studerades effekten även på de icke bestrålade vänstra tumören. Vi kunde konstatera att efter bestrålning av den högra tumören tillväxt hatigheten i den icke bestrålade tumören minskade med 30 %. Vi studerade också effekten av kombination med vaccinations terapi men fick ingen ytterligare effekt vilket indikerar att inte enbart immunologiska faktorer är verksamma.

Vid konferensen presenterades ett mycket brett program som täckte de flesta ämnes områden inom Strålningsvetenskapen och pågick från tidig morgon till sen eftermiddag: Följande lista över speciella symposier speglar de olika ämnesområdena. Förutom dessa symposier pågick en enorm poster utställning och ett antal special symposier om bl. a. Neutron-infångnings-terapi (BNCT) av hjärntumörer som jag deltog aktivt i eftersom vi genomfört sådan terapi vid R2 reaktorn i Studsvik. Det kan även bli intressant för den framtida forskningsverksamheten vid ESS.

Sammanfattning av Symposier vid International Conference Radiation Research (ICCR) i Warszawa 28 augusti – 2 september 2011

I det bifogade programmet på CD i pdf format med sökfunktion finns sammanfattningar av symposierna samt en mängd andra presentationer och alla poster presentationerna.

S1. Normal tissue effects of radiation

Stem Cells, Oxidative Stress, and Normal Tissue Injury.

Use of anti-inflammatory therapies to modulate radiation-induced late effects.

Inflammation and fibrosis

Hypoxia and inflammation in radiation induced normal tissue injury.

S2. Chromatin modifications and DNA damage response

Histone methylation and heterochromatin protein 1 in DNA damage response.

Chromatin modifications and DNA damage response.

Regulation of post translational modifications in the double-strand break response.

Induction, repair and mis repair of DNA double-strand breaks (DSBs) in the context of higher-order chromatin structure.

S3. Space research

Different responses between G0 and exponentially growing cells exposed to ionizing radiation.

DNA damage and repair after low doses of charged particles.

Radiation quality dependent effects on phosphorylation kinetics of proteins involved in early DNA damage response.

Hippocampal neurogenesis and contextual fear response in C57BL/6 mice exposed to 2 Gy whole body protons.

S4. Radiation and immune response modifiers

Defining a role for body temperature in cytokine regulation and neutrophil homeostasis following total body irradiation.

Cancer cells stressed by radiotherapy become targets for CD8 T cells activated by anti-CTLA-4 treatment.

The tipping point for combination therapy: cancer vaccines with radiation.

Distinct *in vivo* responses of tumor-associated macrophages to irradiation.

S5. RRS President's symposium – biological significance of complex DNA damage: physics, chemistry and biology of complex damage

Modelling of DNA damage dependence on radiation quality.

The pros and cons of processing clustered DNA damage sites.

Formation and consequences of complex DNA lesions using radiation with different LET.

New insights into the processing of oxidatively induced clustered DNA lesions. Clinical applications?

S6. Radiation damage to biomolecules (I): peptides, proteins, membrane lipids

Radiation damage in macromolecular crystallography: current challenges.

Formation and repair of protein radicals. Role of thiyl radicals.

A new biomimetic model of free radical reactivity in lipids.

Fatty acid composition of muscle tissue measured in amphibians living in radiologically contaminated and non-contaminated environments.

S7. Advances in combined therapies: ionizing radiation, hyperthermia and chemotherapy

Combined radio-xyz-therapy. A clinical perspective.

Combined therapies in treatment of bladder cancer.

Can targeting normal, homeostatic vasomotor function by mild hyperthermia result in improved responses to radiation or chemotherapy?

S8. Environmental radiobiology

Adaptive responses and bystander effects in a multiple stressor context.

Lessons Learned....Lessons Lost....Observations in Radioecology 25 Years after Chernobyl.

Chernobyl birds.

Radiation effects on earthworms.

S9. Doses received from modern medical procedures

Diagnostic radiology and interventional procedures.

Nuclear medicine for diagnostics and therapy.

Doses from radiotherapy.

S10. Autophagy: a double-edged sword in cellular radiation response

The unfolded protein response enables high rates of autophagy and protection against metabolic stress in tumors.

Induction of autophagic cell death in renal cell carcinoma.

Radiation dose protection and mitigation by Carbamazepine (CBZ) is autophagy independent.

S11. Radiation damage to biomolecules (II): nucleic acids and their constituents

Charge transfer in DNA.

Formation of radiation-induced DNA sugarphosphate backbone radicals via ionization and excitation pathways.

How can we exploit the properties of low energy and hydrated electrons to improve radiotherapy?

S12. Ethics of radiation protection

Ethical aspects and culture of radiological protection in medicine and research.
The ethical foundation of the radiation protection system.
Ethics of radiological protection for nuclear power production and waste management.

S13. New modalities for cancer treatment

Manipulating the tumour microenvironment in combined modality therapy.
Nanoparticle targeting and radiosensitization.
Targeting tumour metabolism to improve the outcome of radiotherapy.
Combining PARP inhibitors with radiation therapy: rationale, strategy and potential biomarkers.

S14. Non-targeted effect-its mechanism and significance

Introduction to non-targeted effects.
Is radiation-induced non-targeted response relevant to human health.
The origin of radiation carcinogenesis is not DNA damage.
Modular systems biology and low dose radiation responses.
Circulatory disease from exposure to low-level ionizing radiation and estimates of potential population risks: a meta-analysis of epidemiological studies.
Highlights of the NOTE (Non Target Effects Program) program 2006-2010.

S15. The use of archiving data and biological material – examples and strategies

The STORE data warehouse; an international infrastructure for data sharing in radiobiology.
Mining the lifespan studies of beagles exposed to radiation *in utero* or as juveniles.
The Chernobyl Tissue Bank – a model for integrating “omics” research on single blocks of tissue.
The use of unique archived data and biological samples by the Radiation Effects Research Foundation.
Qualitative and quantitative proteomic analysis using formalin-fixed paraffin-embedded (FFPE) tissue.

S16. Induction of secondary cancers by ionizing radiation

Understanding and potentially reducing second cancers after radiotherapy.
The delayed genetic effects of radiotherapy – what we know and what we do not.
Relation between DNA repair defects and development of secondary cancers.
Modelling the induction of secondary cancers from radiotherapy.

S17. Multiple stressors (covers humans and environmental studies)

Multiple stressors – issues to ponder.
Developmental co-exposure to low doses of ionizing radiation and environmental toxicants during a critical period of brain development exacerbate cognitive defects in adult mice.
Portable Langendorff system for determination of effects of nanoparticles after radiation.
Epidemiology of uranium workers in France. Radiological and not-radiological exposure and its effects.
Sublethal effects in juvenile atlantic salmon (*Salmosalar*) induced by multiple stressors (gamma radiation and metals).

S18. Radiation-produced intermediates – basic problems

DNA damage induced by fast-flowing metastable species in a cold plasma.
A comparison of X-ray, proton and alpha beam track structures using Monte Carlo simulations.
Reaction of carotenoids with free radicals and singlet oxygen.
Scavengers as a mitigating strategy against radiation damage in macromolecular crystallography.

S19. Vascular endothelial cell response to radiation - a new dimension

Irradiated endothelium and mechano transduction signaling.
Vascular-mediated normal tissue injury - where are we and where are we going?
Adhesiveness of aortic endothelium is increased in response to high LET radiation.
Targeting vascular endothelium for radio sensitization and tumor cure.

S20. What, if anything have 'omics technologies taught us about radiation effects/risks?

Influence of omics research on radiation paradigms and risk: past and future.
Insight into the bystander effect from functional genomics.
What ‘OMICS’ can and cannot tell us about DNA damage response and DNA repair in embryonic stem cells?
What have ‘omics studies taught us about health risks?

S21. Theragnostic radiotherapy

The perspectives of TPMCC (Therapeutic Personalized Multimodality cancer Care) in combined treatment for cancer of the head and neck.
Feasibility and Safety of reducing the irradiation dose in regions of active neurogenesis for prophylactic cranial irradiation in patients with small-cell lung cancer.
Radiotherapy of painful vertebral hemangiomas.
Is there a role for neoadjuvant therapy in gastric cancer?

S22. Nanotechnology targeting DNA damage and repair pathways: advances from the clinic

Targeting the epidermal growth factor receptor (EGFR) family to render tumor cells susceptible to poly (ADP-Ribose) polymerase (PARP) inhibition.
Re-engineering the DNA double strand break machinery for therapeutic purposes.
Use of gamma-H2AX to monitor DNA damage and repair in translational cancer research.
Application of gold nanoparticles as radiosensitising agents.

S23. New developments in radiation dosimetry

Dosimetry techniques to support long-term health risk studies.
Developments in dosimetry methods in radiotherapy.

Developments in dosimetry for exposures in the environment.

Developments and new trends for radiation accident dosimetry with biological samples and personal items.

S24. Radiation chemistry in materials science

Nano-/micro-fabrication of polymeric materials using focused ion beams.

New strategy to form by radiolytic method nanoparticles of metal and semiconductor.

Reaction of thermalized electrons in resist materials

S25. Cell adhesion/ migration in response to irradiation

Targeting the irradiation-induced proangiogenic and pro-invasive phenotype.

Mechanisms and consequences of radiation-induced phenotypes.

Should I stay or should I go? Cell migration after irradiation.

S26. Radiation research award session

Experimental radiation-induced heart disease: past, presence and future.

Genetic variation in immunity alters murine response to whole thorax irradiation.

S27. Tumor hypoxia and radioresistance

Molecular mechanism behind HIF-1-mediated radioresistance and postirradiation recurrence of tumors.

Novel oxygen sensitive signaling pathways and their potential as therapeutic targets.

Imaging of hypoxia-induced radiation resistance and treatment response.

S28. Computational approach to understanding DNA protection by protein binding

Effect of protein binding to direct and indirect radiation damage to DNA.

The action of amino acids on electron irradiated DNA films.

The development of new radio protectors – DNA binding studies with methylproamine analogues.

Structural analysis of the interaction between the Ku protein and DNA.

S29. Radiation chemical studies of bioactive compounds

Mechanistic studies on herbal drugs and their active ingredients in relation to their antioxidant and radioprotection ability.

Radioprotection by the soy isoflavone genistein.

Novel tools in the research on antioxidants - the global profiling of ROS/RNS in cell-free and cellular systems.

S30. Biological effects of low doses

Biological effects at low doses - European Low Dose Risk Research Strategy

do we know about the mechanisms of cancer induction and how might this affect the shape of the dose-response at low doses.

The risk of cancer from low level exposure to radiation – the epidemiological evidence.

What do we know about the factors underlying individual susceptibilities and how large is this variation?

Molecular epidemiology and low dose risk.

What do we know about the mechanisms of non-cancer effects at low and moderate doses?

Radiation risk of cancer and noncancer mortality in atomic bomb survivors, 1950-2003.

S31. Dynamics of repair of radiation-induced cellular DNA damage in real time

Repair mechanisms of DNA strand breaks identified by visualizing proteins in human cells.

Study of early DNA damage responses after charged particle irradiation by beamline microscopy.

Movement of DNA double-strand breaks.

Visualization of spatiotemporal Dynamics of ionizing radiation induced clustered DNA lesions.

S32. New tools in biological dosimetry

The automated micronucleus assay as a reliable biodosimetric tool for population triage in largescale radiation accidents.

MULTIBIODOSE: multi-disciplinary biodosimetric tools to manage high scale radiological casualties.

BOOSTER: BiO-dOSimetric Tools for triage to Responders.

Towards the validation of gene expression modifications as a biodosimeter.

Standardisation of biological dosimetry by cytogenetics: status, advantages and limitations.

S33. Countermeasures in case of accidental radiation exposure

Animal Models for countermeasure research.

Mesenchymal stem cell therapy for treatment of localized radiation injuries (the minipig model).

Studies on hematopoietic protection and immunity adjustment in combined radiation-thermal injury.

The somatostatin analog, SOM 230, is a highly effective mitigator of intestinal radiation injury.

S34. Stem cells and regenerative medicine for the treatment of radiotherapy side effects

Stem cell sparing radiotherapy: a novel approach to the prevention of radiation induced xerostomia.

Cognitive restoration after cytotoxic cancer treatments.

Hepatocyte transplantation for amelioration of RILD.

Mesenchymal stem cell ameliorates severe radiation pelvic complication: clinical transfer.

Bone regeneration and engineering in irradiated fields.

Regenerative medicine based on stem cell injection for radiation burn treatment.

Fat grafting after Mastectomy and radiotherapy.

S35. Radiation research and nuclear power

Radiation chemistry effects on nuclear solvent extraction: examples from CMPO radiolysis.

Chemistry for the nuclear energy of the future.

Radiation-induced aqueous chemistry and corrosion in nuclear reactor environments.

Modeling and simulation for controlling chemistry in advanced nuclear energy systems.