



**Meeting Report of the *16th International Congress of Radiation Research and the 12th International Symposium on Chromosomal Aberrations.***

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The Association for Radiation Research (ARR), on behalf of the International Association for Radiation Research (IARR), hosted the 16th International Congress of Radiation Research in Manchester, UK from 25th – 29th August 2019. A total of 1008 delegates joined us for this 4-yearly premier radiation research event to share new research around the thematic areas of *Basic Mechanisms, Translational Research, Radiotherapy and, Health Effects and Ecology*. The meeting was a great success with quality presentations, in-depth workshops on defined topics and fun social events throughout. A key goal of the ARR and IARR is to promote careers of future radiation biologists and so it is of note that around a quarter of our attendees were ‘scholars-in-training’, all of whom contributed to the overall success of the programme as Session Chairs and with high quality presentations. The meeting venue ‘Manchester Central’ provided excellent facilities creating a relaxed environment for science-in-action; collaborative discussion with friends old and new. Outside, historic Manchester shone in the brilliant sunshine of an August heatwave proudly displaying itself as a modern, fun and vibrant city for all. In this Report, we focus on Theme 4 *Health Effects and Ecology* and, the satellite workshop *International Symposium on Chromosomal Aberrations (ISCA)*.

Theme 4 covered research of direct relevance to human health and our environment; structured into 11 parallel sessions comprising two keynote and two short-talk speakers. Our Plenary speaker was Nori Nakamura who explored the concept that radiation might not increase the risk of cancer through the induction of oncogenic mutations. Instead, he argued that radiation affects stromal microenvironments which leads to conditions that promote the growth of spontaneously arising cancer cells, essentially reducing the age at which cancers arise.

The Theme began with a session on radiation-induced carcinogenesis. Christophe Badie described two new murine models for studying leukaemogenesis. The first enables the tracking of pre-leukaemic cells within living animals while the second carries a single DNA modification leading to extreme sensitivity to ionising radiation (IR) induced leukaemia. Yoshiya Shimada then emphasized the role of age at exposure. Age significantly influences the risk of radiogenic cancers with children believed to be more susceptible to radiation than adults. The next session focussed on epidemiology. Amy Berrington presented a pooled analysis showing a dose response for cancer risk from paediatric computed tomography (CT) scans below 100mGy and, that repeated medical exposures increased cancer risk, although the absolute risks were small. John Boice then updated us on the U.S. Million Person Study, which is exploring health risks from chronic low dose exposures. He showed summary findings on radiation associations for leukaemia, lung cancer and other organs. In session 3 we moved to biomarkers and disease where the first speaker, Roel Quintens, outlined the potential of gene expression (exon) signatures as radiation biomarkers at low doses. Susan Bailey then described how telomere length could be a relevant biomarker of aging and health risk, presenting data showing telomere length variations before, during and after space flight.

The next session brought our attention to psycho-societal issues. Deborah Oughton talked about the invaluable lessons learnt from the Chernobyl and Fukushima accidents. She outlined the EC-funded SHAMISEN project recommendations and the aims of SHAMISEN-SINGs which seeks to engage stakeholders through citizen science. Yulia Malova described her studies investigating higher cortical functions and psychosocial well-being in Chernobyl liquidators undergoing different psychotherapeutic interventions. She showed the importance of prompt psychological treatment in supporting neuropsychological syndromes. We then moved to cover immune response to low-moderate doses with Serge

Candéias showing how radiation accelerates ageing of the T lymphocyte cell pool. He raised the question of how irradiated cells communicate with immune cells and how this may modulate the status and functionality of immune cells. Katalin Lumnitzky discussed the often-contradictory findings of low dose irradiation effects on the immune system. She argued that low dose irradiation induces subtle changes in immune responses that affect the immune fitness of an individual and, in the presence of other environmental and/or predisposing genetic factors, may increase the risk of radiation-induced cancer and non-cancer diseases.

Session 6 exploring radioecology from laboratory to field was opened by Mike Wood who outlined how the Chernobyl contaminated landscape provides a unique opportunity to study radiation effects in free-ranging wildlife. He raised important challenges when interpreting results and effective mechanisms for communicating findings to diverse publics. The second speaker was Kathryn Higley who gave an interesting insight into the art of negotiating bureaucracies for effective research, providing practical illustrations of potential obstacles and mitigations.

There has been renewed interest in non-cancer effects particularly from radiation protection viewpoints. In this longer session we heard updated data on non-cancer effects in various exposed cohorts. Nobuyuki Hamada discussed the scientific basis of the International Commission on Radiological Protection (ICRP)'s 2011 recommendation to reduce the dose threshold for vision impairing cataracts and for reducing the equivalent dose limit for the lens. Elizabeth Ainsbury expanded on this by outlining the work of EU CONCERT 'LDLensRad' in exploring the biological basis for low-dose cataract formation. Dr Ainsbury showed that age, genetic background and dose are key determinants of cataract risk in mouse models. Kotaro Ozasa then presented an update of the non-cancer outcomes in the Life Span Study cohort

and its sub-cohort, the Adult Health Study. The key headlines were that mortality from heart disease and stroke increased with dose but the associations varied by disease subtype and this differed between the two cohorts.

A second radioecology session covered factors enabling a more holistic ecosystem-based approach to environmental radiation protection. Larry Kaputka defined a 'wicked problem' involved in the ecosystem approach. He discussed the 'adverse outcome pathway' which investigates low dose radiation effects across species and scales of organisation pointing out that while effects are measurable at the level of individual species, investigation at an ecosystem level is currently 'magical thinking'. Paul Schofield then discussed epigenetic effects and their role in bridging between hierarchical levels from genes to organisms. He focussed on the importance of epigenetics in transmitting information and in modulating the expression of gene products to respond to environmental conditions, primarily focussing on methylation and acetylation changes. Mizuki Ohno then described, in the trans-generational session, an experimental system to study DNA damage and repair processes in germline cells. Yuri Dubrova then showed data suggesting the manifestation of transgenerational instability is triggered by a threshold dose of acute paternal irradiation and that this effect in humans may be more common among the children of cancer survivors treated by mutagenic anticancer drugs than those exposed to therapeutic ionizing radiation.

The session on low dose/dose rate (LD/R) effects began with Gayle Woloschak describing animal models used to study radiation effects, emphasizing studies with sufficiently large data sets to evaluate LD/R effects. She discussed the complications of stress-associated increases in the background incidence of cancer and highlighted the archival biospecimens available for use by other researchers. Simon Bouffler then discussed the

limited power of human studies to assess risk at LD/R, and the use of the linear non-threshold (LNT) model. He described work underway by the ICRP, the US National Council on Radiation Protection and Measurements, and the United Nations Scientific Committee on the Effects of Atomic Radiation to evaluate the LNT model and develop approaches to integrate understanding of biological mechanisms underlying cancer and non-cancer causation by radiation into risk assessment. The health effects of internal exposures was explored by Jean-Marc Bertho who highlighted that exposure in real life is more complex than simple exposure to ionizing radiation arguing that chemical pollution and stress should be taken into account. He presented data demonstrating enhanced effects due to interactions between radiation and chemicals and discussed how this may impact on (non)-linearity of effects. Eric Blanchardon then described an inter-comparison exercise undertaken to determine uncertainties of lifetime dose estimation after occupational exposure to Uranium. He showed there to be a large discrepancy in the dose estimates (EURADOS Report 2017-3), likely due to differences in the protocols applied to estimate the dose, concluding a need for the harmonization of protocols to estimate doses for epidemiological studies.

The satellite workshop *International Symposium on Chromosomal Aberrations (ISCA)* was organised for the 12<sup>th</sup> time during the ICRR meeting and took place on Tuesday the 27<sup>th</sup> of August 2019. The first ISCA was organised in 1989 and ISCA12 was organised by Dr Christophe Badie and Ms Roisin McCarron from PHE to celebrate the 30<sup>th</sup> anniversary of ISCA's. To be noted is that a logo was specifically created on the occasion by Mr Érik Guarisco. The workshop ran all day and was organised as four different themes; Chromosome aberrations based biodosimetry, High linear energy transfer (LET) radiation and chromosome responses, Molecular mechanisms and finally, Molecular and cellular radiation cytogenetics.

One poster session took place during the lunch break. The symposium was successful with approximately 200 registered participants.

After a short introduction and welcome by Christophe Badie, the symposium started with Christian Johannes who provided a summary of the highlights reported at ISCA meetings over the years. Next, Yumiko Suto gave an overview of the current state and perspectives of radiation cytogenetics in Japan. She emphasized the challenge of scoring large numbers of metaphases for low dose exposure studies, the need for collaboration between laboratories and, automation of analysis to support medical triage in radiation accidents with mass casualties. Adayabalam Balajee spoke about cytogenetic follow-up human studies describing the dependency of the long-term persistence of chromosomal aberrations on radiation quality and the exposure mode.

The second session was started by Yun Rose Li, who presented sequencing data to provide a global genomic landscape of radiation-induced tumours in mice using Trp53 deficiency models and also, discussed the identification of ionising radiation signatures. George Iliakis spoke about the complex chromosomal aberrations generated by endonuclease-defined clusters of DSBs mimicking DNA lesions induced by high LET radiation. Next, Rhona Anderson spoke about the challenges and potential of using complex chromosome aberrations as biomarkers of internal alpha emitters in human blood lymphocytes. Finally, Michael Cornforth shared his view on single and multi-parameter descriptors of chromosomal response to ionising radiation including the effects of total absorbed dose, dose rate, and radiation quality. Alternative approaches such as the use of the mean inactivation dose and other approaches to provide LET-dependent “cytogenetic signatures” were discussed.

The first afternoon session started with Stephen West who provided insights into the role of specific endonucleases involved in the removal of recombination intermediates generated by homologous recombination (HR)-mediated DNA repair; he demonstrated that their loss of function leads to chromosome segregation failure, resulting in DNA damage and ultimately genome instability. Next, Penny Jeggo focused on the fidelity of DNA DSB repair, detailing the role of canonical non-homologous end joining (c-NHEJ) and HR which represent the major DNA DSB pathways as well as the role of ataxia-telangiectasia mutated (ATM) signalling and phase of the cell cycle in translocation formation. The next invited speaker was Serge Candéias who also focused on chromosomal translocations but in the context of developing T lymphocyte cell receptor gene rearrangement by V(D)J recombination in mice. He concluded that radiation does not impair genetic stability during T-cell receptor gene rearrangement.

Susan Bailey focused on chromosomal inversions demonstrating that a novel approach called directional genomic hybridization (dGH), a cytogenomics-based strand-specific methodology, allows high-resolution inversion detection, hence representing a valuable biodosimeter following a variety of human radiation exposure scenarios such as those of atomic veterans and astronauts. Laure Sabatier spoke about immuno-FISH approaches allowing gamma-H2AX, chromosome painting and, telomere and centromere staining on premature condensed chromosomes to be quantified in the same cells. This approach will enable the assessment of chromosomal rearrangements within the first hours post-irradiation. Marco Durante presented recent work on radiation-induced micronuclei (MN) which can release DNA to the cytosol, triggering the cGAS-STING pathway leading to the production of IFN-Alpha and an immune response, a pathway which may be exploited in cancer treatment. His recent findings lead to the conclusion that ionising radiation can induce



cytosolic DNA independently of the induction of MN. He was followed by Gene Koh who talked about whole genome sequencing experiments in human cell line models explaining that they allow identification of specific mutational signatures in human cancer genomes.

In summary, the organisers of ICRR2019 and the international programme committee would like to thank all presenters for their enthusiasm and high quality presentations and, to all Session Chairs and satellite workshop organisers. Their contributions stimulated a great deal of critical discussion and new research development for improving our understanding of the impact of radiation on human health and our environment, particularly in the low dose region. Unfortunately we are unable to provide information on all speakers and so apologise to those we have not covered however abstracts remain available on the meeting website (<http://icrr2019manchester.com/>) and the meeting proceedings will be available on the ARR (<https://www.le.ac.uk/cm/arr/home.html>) and IARR (<https://www.radres.org/page/IARR>) websites. A special issue of British Journal of Radiology will include articles covering award lectures and, a further Meeting Report covering Themes 1-3 will be published in the International Journal of Radiation Biology.

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