Radiation Biology and DNA Repair - Löbrich Laboratory

The main focus of our current and intended research projects is on the elucidation of the mechanisms of DNA double-strand break (DSB) repair following ionising irradiation. We employ cellular and molecular approaches to identify factors and pathways involved in the sensing and processing of DSBs induced by ionising radiation and other destructive agents. The work is important for the application of radiation and chemical compounds in the clinic for treating malignant diseases as well as for estimating the risk of radiation exposure in natural settings and in the clinic. Mechanistic studies of DNA repair processes have, of course, implications which go beyond radiobiological questions and lie at the heart of cancer research. In particular the elucidation of the cellular and molecular pathways responding to DNA breaks will help to understand the process of carcinogenesis.

Studies on the biological effectivness of space radiation in low earth orbit

The mechanisms underlying the carcinogenic risk of low doses of ionising radiation are poorly understood. Moreover, the quantitative risk level associated with exposure to space radiation is insufficiently defined. The objectives of this research project involve an assessment of the effects of space radiation by analysing the induction and repair of DSBs, genetic lesions believed to represent the most critical damages generated by ionising radiation.

The repair of DSBs after high-LET exposure

The aim of this project is to investigate the repair of DSBs induced by high-LET radiation in human cells. The experiments are performed at the GSI facilities in Darmstadt. It has been known for several years that high-LET-induced DSBs are generally more slowly repaired than breaks induced by X- or □-rays. Moreover, the level of residual DSBs after prolonged repair incubation appears to correlate with the cell killing capacity of a given radiation quality over a substantial LET range. It is, therefore, important to understand the basis of the compromised DSB repair kinetics of high-LET radiations.

Mechanisms involved in the response to DSBs

We were recently able to quantify the contribution of homologous recombination and non-homologous end joining for the repair of DSBs in defined cell cycle phases, and thereby provided a quantitative evaluation of the two major repair pathways for the repair of individual breaks that are produced in mammalian cells by DNA-damaging agents. We have also recently shown that cells from individuals with the neuro-degenerative and cancer-prone disease ataxia telangiectasia (AT) have a DSB rejoining defect after low doses used to monitor survival, and we have provided evidence that this DSB repair defect underlies the radiosensitivity of AT cells and cells from other patients with chromosomal instability syndromes. The current focus of this research direction lies in the molecular characterisation of the DSB repair defect in AT cells.

Clinical applications of the knowledge gained from DSB response studies

While DSB repair studies have hitherto been restricted to human cells in culture, immuno fluorescence microscopy offers the intriguing possibility to follow the repair process in humans. We have extended the methodological approach from cell culture systems to peripheral blood lymphocytes and were able to detect DSBs in humans that were exposed to diagnostic and therapeutic X-ray doses. This approach has allowed us to assess the extent of DNA damage after various time points following radiation exposure of individuals and, therefore, to quantify DSB repair processes in vivo.

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TECHNISCHE UNIVERSITÄT DARMSTADT

Curriculum Vitae

Name: Markus Löbrich

Position: Full Professor
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Biographical:

Date of Birth	December 28, 1965, Gießen
Citizenship	German
Marital Status	Married with Katja Elena Löbrich, two daughters
Address	Bornhofener Weg 7, 35510 Butzbach/Ostheim

Education:

1990	Diplom in Physics (M.S.)
1993	Dr. rer. nat. (Ph.D.)
1996	Postdoc training in Biology
1999	Habilitation in Biophysics

Work History:

1985 – 1987	Basic study in Physics at the *Technische Hochschule Darmstadt,* Germany
1987 – 1990	Advanced study in Physics at the *Justus-Liebig-Universität (JLU) Gießen,* Germany
	May 1989 – July 1990: Master thesis at the *Strahlenzentrum der JLU Gießen* in the Department of Radiation Biophysics: “The effect of ionising radiation on the inhibition of transcription of ribosomal DNA”
	September 1990: Major exams for the degree ‘Diplom-Physiker’
1990 – 1994	Employed as Research Scientist at the *Strahlenzentrum der JLU Gießen* in the Department of Radiation Biophysics
	July 1992 – June 1993:

	Scientific stay as a fellow of the German Academic Exchange Service (DAAD) at the *Lawrence Berkeley National Laboratory* in Berkeley, CA, USA in the Department of Radiation Biology and DNA Repair
	September 1993: Ph.D. thesis at the *Strahlenzentrum der JLU Gießen* in the Department of Radiation Biophysics: "Mechanisms of DNA double-strand break repair in mammalian cells exposed to ionising radiation"
	November 1993: Major exams for the degree 'Dr. rer. nat.'
1994 – 1996	Postdoc at the *Lawrence Berkeley National Laboratory* in Berkeley, CA, USA in the Department of Radiation Biology and DNA Repair
1996 – 1999	Assistant Professor *(Hochschulassistent, C1)* at the *JLU Gießen* for Cellular and Molecular Radiation Biophysics
	March 1997 – May 1997: Scientific stay at the *Istituto Superiore di Sanità* in Rome, Italy
	March 1998 – April 1998: Scientific stay at the *Lawrence Berkeley National Laboratory* in Berkeley, CA, USA
	April 1999: Habilitation in Biophysics at the *JLU Gießen*
1999 – 2006	Associate Professor *(Universitätsprofessor, C3)* at the *Saarland University* in Homburg, Medical Faculty, Biophysics Department, Radiation Biology and DNA-Repair Group
	October 1999 – 2007 Authorized Representative for Radiation Protection of the *Saarland University*
	October 2002 – 2007 Associated Member *(kooptiertes Mitglied)* in the Faculty for Natural Sciences – Technical Faculty III of the *Saarland University* (involves the right to act as main advisor for Ph.D. dissertations)
2006 – 2007	Full Professor (W3) at the *Saarland University* in Homburg, Medical Faculty, Biophysics Department, Radiation Biology and DNA-Repair Group
since 2007	Full Professor (W3) at the *TU Darmstadt* (University of Technology Darmstadt), Radiation Biology and DNA-Repair Group

Awards and Honours:

5/1998	Hanns-Langendorff-Award for the paper "Repair of x-ray-induced DNA double-strand breaks in specific NotI restriction fragments in human fibroblasts: Joining of correct and incorrect ends" (PNAS 92, 12050-12054), award of the *Vereinigung Deutscher Strahlenschutzärzte*

7/2002	Friedrich-Dessauer-Award for “outstanding scientific contributions in the field of Radiation Research“, award of the *Gemeinschaftsausschuss Strahlenforschung GAST und der Gesellschaft der Freunde und Förderer des Röntgen-Museums*
1/2003	Appointed member of the Committee for Radiation Risk of the *National Radiation Protection Board* (Ausschuss Strahlenrisiko der Strahlenschutzkommission)
1/2005	Appointed member of the Executive Committee of the *National Radiation Protection Board* (Hauptausschuss der Strahlenschutzkommission)
9/2005	Michael-Fry-Research-Award for “extraordinary contributions to the field of radiation research”, award of the *Radiation Research Society*
5/2006	Offer of the Director Position at the *GSF-Institute for Radiation Biology*; this offer is connected with an offer of a *Professorship for Radiation Biology* at the *Technical University Munich*