

Final Report on the 11th Biennial DGDR Meeting

September 7-10, 2010 in Jena

The 11th Biennial DGDR Meeting of the German Society of DNA Research took place from September 7-10, 2010 in Jena. The meeting had been hosted by the Leibniz Institute of Age Research (Fritz Lipmann Institute) and the Friedrich Schiller University Jena under the main supervision of Frank Grosse. To our convention we could gather an international community of excellent and outstanding DNA repair researchers; we could welcome 158 registered participants from 14 different countries, which is remarkable since the meeting was only announced nation-wide. The members of the scientific committee were: Alexander Buerkle (Konstanz), Jochen Dahm-Daphi (Hamburg), Martin Digweed (Berlin), Frank Grosse (Jena), Karl-Otto Greulich (Jena), Andrea Hartwig (Berlin), Bernd Kaina (Mainz), Tanja Schwerdtle (Münster), Jürgen Thomale (Essen), Zhao-Qi Wang (Jena), and Lisa Wiesmüller (Ulm).

DGDR conventions aim to particularly improve the mutual understanding and exchange of experience and knowledge between young scientists and senior experts in the field of DNA repair research. Besides awarding prizes for the best poster presentations (six awards with 200 € each), we selected among the received abstracts 15 scientists to present their special research topic. Except the talks of the invited speakers all oral presentations were chosen among blinded abstracts in order to guarantee a fair selection of the best. Furthermore we offered meeting fellowships of 600 € each for graduate, PhD and postdoctoral students again by choosing the best abstracts from the anonymous-made applicants. This year the travel grants were awarded to: Mary Bakhanashvili (Tel-Hashomer, Israel), Myun-Hwa Dunlop (New Haven, USA), Elise Fouquerel (Illkirch, France), Sabrina Köcher (Hamburg, Germany), Nadine Mathieu (Zürich, Switzerland), and Daniela Salles (Rio de Janeiro, Brasil).

Meanwhile, the DGDR meetings accentuate recent advances in the rapidly growing field of DNA repair and related subjects. This year our focus was on DNA replication-mediated DNA repair events that also included DNA recombination. Although the molecular machineries of the three “big R’s”, repair, replication, and recombination, are mechanistically related they are mostly treated as independent fields with separated meetings. In Jena, we tried to bridge and thus bring together researchers from the big R’s to present and discuss common and overlapping issues. To this end we had a particular focus on *Checkpoint Controls*, *Animal Models*, *Repair Enzymes*, such as helicases and poly(ADP)-polymerases, *Translesion Synthesis and Mismatch Repair* and the related aspects of *Ubiquitin Modifications* and *Fidelity* of replication and repair.

As a special highlight we could host Prof. Dr. Larry Loeb from the University of Seattle, who as early as in 1972 pointed out that inaccuracies in repair and replication might significantly contribute to the development of cancer. Eventually, this led to his “Mutator Hypothesis” as cause for the accumulation of hundreds of mutations in human cancers. In his Keynote Lecture he gave a startling overview on his techniques studying intracellular mutation rates and his brand-new approaches on overloading organisms with mutations to induce an “error catastrophe” for the benefit of human beings. In honor of his life-long outstanding contributions to the field of DNA repair, we awarded him the Honorary Membership of our society. After Phil Hanawalt, Errol Friedberg and Yosef Shiloh, Larry is now the fourth honorary member of our society.

Another good tradition of our meetings is the Public Lecture, this time given by Lisa Wiesmüller from the University of Ulm. Lisa’s field of interest is on novel approaches for detection of breast cancer risk and for treatment modalities that use “synthetic lethality” for the benefit of the affected patients. This lecture was open for the general public and well received by Jena’s citizens. In this context the local newspaper made an interview with Prof. Wiesmüller and published a report on her contribution.

Among the invited speakers, there were some short-term cancellations happening 1-3 days before the beginning of the convention, mostly due to accidents that required surgical treatments and did not allow travelling anymore. Therefore, the talk of Marco Foiani (Milan) was taken over by Stephen Meyn (Toronto), the lecture of John Diffley was held by his coworker Boris Pfander (Clare Hall), and the talk of Zvi Livneh (Rehovot) was replaced by the talk of Christian Speck (London). Christian and Stephen were recruited from the list of the proffered papers. Both of them did an excellent job with their full-length contributions.

Among the invited talks as well as the proffered papers there were some highlights that deserve particular mentioning. The invited speaker Lorena Beese (Durham, USA) gave an impressive and lucid comparison of structural and functional aspects of error-prone and error-free DNA polymerases. Jochen Kuper (invited) from the Kisker lab in Würzburg contributed an enlightening lecture on the recently solved structure of the Xeroderma pigmentosum D protein, a DNA helicase with various branching points to human diseases. Christian Schiller (selected) from the Hopfner lab in Munich presented structural data of the Mrn-Nbs1 complex, a mediator of homologous recombination again with high relevance for human diseases. The talks by the young German researchers revealed that structural biology in Germany meanwhile is on the same high level as in the US.

The contributions of speakers from Illkirch, France, Konstanz, and Jena were placed around the poly(ADP)-ribose polymerase and poly(ADP)ribosylation during single-strand break repair. Valerie Schreiber (Illkirch, invited) spoke about PARP-9, a novel member of the poly(ADP)-ribose polymerases that is overproduced in human lymphomas. Francoise Danzer (Illkirch, selected) discussed mouse models of PARP-3 and the influence of this enzyme on mitotic segregation and genome stability. Elise Fouquerel (selected) presented her data on the recruitment of the poly(ADP)-ribose degrading enzyme PARG (G stands for glycosylase) to sites of DNA-damage via the proliferating cell nuclear antigen PCNA. Zhao-Qi Wang (Jena, invited) presented his recent findings on interactions between PARP1/PARG and the checkpoint kinases ATR/Chk1, again based on whole animal studies. Last but not least Sasha Beneke (selected) from the Buerkle lab in Konstanz presented exciting correlations of the capacity of PAR-formation and the life-span of mammals, a novel aspect of this important class of repair enzyme that has not yet been dealt with appropriately.

The roles of ubiquitylation and SUMOylation in post-replicative repair and the structural maintenance of chromosomes were subject of the contributions of Helle Ulrich (Clare Hall) and Oscar Fernandez-Capetillo (Madrid). Helle (invited) presented illustrative evidence that ubiquitylation of PCNA at stalled replication forks is necessary for a switch from replicative to translesion DNA synthesis, the latter allowing a reading through damaged nucleobases. A novel aspect of this type of DNA repair became apparent by her recent findings that polymerase switching must not necessarily accompany DNA replication. Rather, the replication fork starts anew after a damaged site and the resulting gap is filled in later by translesion synthesis in the G2 phase of the cell cycle. Oscar (invited and supported by an EMBO young scientists travel award) looked at a battery of different mouse strains to reveal the role of the SUMO ligase Mms21 for the suppression of mitotic recombination and cancer formation. His data gave strong evidence that Mms21 is a haplo-insufficient tumor suppressor that might seriously exacerbate a p53 heterozygosity during cancer development. Structural maintenance of chromatin was also the issue of Tina Bauerschmidt (selected) from the Helleday laboratory in Oxford, UK. She detected that following ionizing radiation the cohesin proteins Smc1 and 3 become phosphorylated and attracted to sites of DNA double strand breaks, showing for the first time that cohesins are involved in double-strand break repair.

Another highlight of the meeting was the lectures on fidelity of replication and repair. Tom Kunkel (invited, but paid by the NIEH, Durham) presented his newest data on error accumulation in yeast using whole-chromosome sequencing. He not only showed that leading and lagging strand of the replication fork are synthesized with different mutation signatures which in turn allow an assignment of DNA polymerases ϵ to δ to the leading and lagging strand, respectively, but also presented evidence that there exist specific initiation

sites for Okazaki-fragment priming by DNA polymerase α . Using this approach he showed that errors made by the latter polymerase are most likely repaired by the exonuclease of the lagging strand DNA polymerase δ . A novel role for the exonuclease of the tumor suppressor protein p53 was suggested by Mary Bakhanashvili from Israel (selected). Mary presented evidence that p53 contributes to the excision of oxidized bases from mitochondrial DNA. The invited speaker Uli Hübscher (Zürich) showed that each of the replicative polymerases α , δ , and ϵ is able to incorporate adenines opposite oxidized guanosines that, if not repaired, give rise to transversion mutations. This is counteracted by a repair pathway consisting of the MutY glycosylase and DNA polymerase λ , which accurately inserts cytosines opposite 8-oxo-Gs. Tanja Schwerdtle (Münster, invited) looked at the impact of meta(oid) species on excision repair pathways, how these effects lead to carcinogenicity and neurotoxicity. Since contaminations with metals and metalloids are a burden of modern times her talk perfectly combined environmental and medical aspects of DNA repair.

In the breaks of the lecture sessions, there were as many as 108 poster presentations. The posters were visited by the members of the scientific committee and evaluated according to their scientific quality, the mode of presentation and the quality of the oral defense. According to these criteria, six poster prizes were awarded to young scientists from Galway, Darmstadt, Jena (2x), Berlin, and Novosibirsk.

The meeting was held in friendly atmosphere where most of the invited speakers stayed from the first to the last day, discussing with colleagues and particularly with the younger participants the various aspects of DNA repair. After the meeting we got a lot of positive responses and wishes to repeat such a meeting in not a too long little while.

Frank Große
Jena, January 25th 2011