Meeting Report, Third EU-US Workshop on "Nucleotide excision repair and crosslink repair – from molecules to mankind", Smolenice Castle, Slovak Republic, May 7th-11th 2017

Peter J. McHugh[1], Caroline Kisker[2], Miroslav Chovanec[3], and Bennett Van Houten[4]

[1] Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom; [2] Rudolf Virchow Center for Experimental Biomedicine, University of Wuerzburg, Wuerzburg, Germany; [3] Cancer Research Institute, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovakia; [4] Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA

Abstract:

The purpose of this workshop was to bring together scientists from the EU and US to discuss our current understanding of how protein machines assemble and sort through genomic DNA to identify specific damaged sites which are repaired through the two critical repair pathways: nucleotide excision repair or interstrand crosslink repair. Several of the enzymes perform dual functions in both pathways, thus combining these two topics in one meeting provided tremendous synergy and was a unique feature of this workshop. Many endogenous agents, environmental toxicants and chemotherapeutic agents cause a spectrum of DNA lesions that are repaired through these two mechanisms. The importance of the repair pathways acting on these forms of DNA damage is underscored by the fact that their loss or dysregulation is associated with a variety of devastating heritable human conditions including cancer, neurodegeneration, premature aging and severe developmental abnormalities. The workshop covered research conducted on molecules to mankind, and included discussions of disease syndromes associated with poor repair of these forms of damage. The meeting also provided an unparalleled opportunity to interact with scientists from the EU, US, and throughout the world, who are driving the field.

1. Introduction:

It has been estimated that the average human cell suffers about 10,000 spontaneous DNA lesions *per* day [1]. Environmental factors (both natural and man-made) can increase this amount of DNA damages by 1-2 orders of magnitude [2, 3]. These DNA lesions are removed by specialized DNA repair pathways, which help to maintain genome integrity. Defects in these pathways can cause DNA mutations and/or cell death, and at the organismal level manifest as premature aging, neurodegeneration and cancer-prone syndromes [4]. In humans, nucleotide excision repair (NER), through the action of some 30 different proteins, removes lesions that significantly distort the structure of the DNA including ultraviolet (UV)-induced photoproducts, carcinogenic polycyclic aromatic hydrocarbon adducts, and even certain forms of oxidative damage [4, 5]. Deficiencies in this pathway can cause several human diseases including Xeroderma Pigmentosum (XP), which is characterized by mutations in one of eight genes [6] and is associated with an increased predisposition to skin cancer. Lesions involving both DNA strands, interstrand crosslinks (ICL), can be formed by environmental agents such as psoralens, aldehydes, lipid oxidation products (pro-inflammatory toxic responses), and chemotherapeutic agents such as cisplatin, mitomycin C and the nitrogen mustards [2, 7]. Repair of this class of DNA lesions involves the action of a large number of proteins including nucleases, polymerases, and protein modification enzymes, some of which have only been recently characterized. NER and ICL repair share several common steps and many proteins, for example, the XPF^{FANCQ}-ERCC1 nuclease [8]. Another important set of proteins involved in ICL repair belong to the Fanconi Anemia (FA) pathway [7]. FA is a genetic disorder that is characterized by congenital abnormalities, bone marrow failure and a highly elevated risk of hematological and squamous cell cancers. Cells from FA patients are extremely sensitive to killing by crosslinking agents. Genetic analyses suggest 22 complementation groups, with seven gene products forming a core complex. How these proteins function to repair ICL is far from being completely understood, see www.rockefeller.edu/fanconi/ [7, 9]. Thus, a small focused meeting in which experts who actively pursue research on these two DNA repair pathways were able to exchange new data and ideas helped to stimulate growth in the field. The goals of this 3rd joint EU-US workshop were three-fold: 1) to highlight the state of the science and current technologies being used to study these pathways; 2) to exchange ideas between scientists in the EU and US; and 3) to provide a forum for scientists in the local region to meet and engage with scientists from the EU and US who are driving the field.

2. Meeting Venue:

This was the third in its series (http://www.exon.sk/smolenice2017/) aiming to bring together scientists working on NER and ICL repair. There have been no major international meetings since

our 2013 workshop that selectively address these dynamic fields, and it is very clear from the feedback that we have received that this FEBS Workshop is now established globally as the pre-eminent meeting in these research areas. Seventy scientists from around the world presented their latest work, emphasising a wide range of approaches, from single-molecule biochemical experiments to studies in whole animals and patients. The meeting was held in Smolenice castle, Smolenice, Slovakia (Fig. 1A), that is a purpose-adapted conference centre of the Slovak Academy of Sciences, featuring lecture facilities, poster viewing areas and accommodation. This intimate setting in the Little Carpathians was particularly conducive to scientific interactions outside of the formal sessions, and feedback indicates that the delegates generally found this an important factor in the Workshop's tremendous success.

3. Scientific Program Highlights:

The Workshop commenced with introductory remarks by the organisers. **Peter McHugh**, **Ben Van Houten** and **Caroline Kisker** spoke briefly to welcome the delegates and outline the aims of the meeting. Peter McHugh introduced FEBS and thanked them, and the NIEHS, NIH for their great support. **Miroslav Chovanec** introduced the venue and key housekeeping points that helped the Workshop run very smoothly.

The scientific programme commenced with the Keynote lecture by **Jesper Svejstrup** (Crick Institute, UK). Jesper presented a lecture that introduced the state-of-the-art in transcription-coupled nucleotide excision repair (TC-NER) followed by a game-changing study that shows how short and long transcripts from the *ASCC3* gene act antagonistically to control recovery from UV-induced damage [10]. **Juan Garaycoechea** (MRC, LMB, UK) described a study on how the ethanol metabolite, acetaldehyde, induces damage in haematopoietic stem cells, which activate p53 and cause genome rearrangement [11]. **Jadwiga Nieminszczy** (University of Oxford, UK and ICR, London) described how the recently discovered EXD2 exonuclease can be detected at stalled replication forks where it is involved in activation of the ATR-dependent checkpoint [12]. **Julian Stingele** (Crick Institute, UK) described elegant recent work on the human SPRTN protein, a metal-protease required for the degradation of DNA-protein crosslinks during replication-coupled repair [13]. The first day was rounded off with a series of 3-minute flash talks given by poster presenters, allowing them to summarise and preview their poster. This was a huge success, promoting extremely interactive poster viewing sessions on the second and third evenings of the Workshop (Fig. 1B).

Monday morning commenced with a session on NER. **Orlando Schärer** (UNIST, South Korea) described how ICL can be processed by both translesion polymerases, and in some cases surprisingly also by replicative polymerases following unhooked of the ICL by either a replication-coupled process or NER [14]. **Ben Van Houten** (University of Pittsburgh, USA) presented single molecule analysis of the NER protein, Rad4, and how it uses anomalous diffusion around cyclobutane pyrimidine dimers to facilitate repair [15, 16]. **Wei Yang** (NIH, USA), our ASBMB supported speaker, presented data on the XPB and XPD TFIIH-associated helicases and their role in NER, focusing on their unwinding and ATPase activities during lesion recognition [17]. **Wim Vermeulen** (Erasmus Medical Centre, Netherlands) explained that CSA and the cullin-containing CRL^{CSA} complex are critical for TC-NER, and described two new interacting regulatory factors including the TRiC chaperonin. Three short talks from selected poster presenters followed. **Hannes Lans** (Erasmus Medical Centre, Netherlands) described how the SWI/SNF ATPases BRM and BRG1 stabilise the TFIIH NER factor. **Yasemin Turkyilmaz** (Erasmus Medical Centre, Netherlands) described a novel protein that might play a role in enhancing NER. **Hajnalka Majoros** (University of Szeged, Hungary) presented evidence that a SERPIN protein might play a role in the repair of UV-induced damage by NER.

Monday afternoon saw the first session dedicated to ICL repair and FA. **Pierre Henri Gaillard** (INSERM, Marseille, France) presented new data showing that the helicase RTEL1, associated with the SLX4 nuclease platform (mutated in some forms of FA) which might be important for both telomere stability and ICL repair [18]. **Neil McDonald** (Crick Institute, UK) presented the first structures of the complete XPF^{FANCQ}-ERCC1 dimer, a structure which has eluded researchers for many years and has important implications for both NER and ICL repair. **Minoru Takata** (Kyoto University, Japan) gave the first of two talks describing a new FA protein, RFWD3. Minoru focused on a key role for this factor in stripping DNA of RPA and RAD51 during the homologous recombination-dependent step of ICL repair [19]. **Puck Knipscheer** (Hubrecht Institute, Netherlands) explained how the *Xenopus leavis in vitro* cell-free replication system has been used to define the repair pathways acting upon acetaldehyde-induced ICL, a physiologically relevant form of DNA damage. Both the FA pathway and a novel pathway are implicated [20, 21]. **Helen Walden** (Dundee University, UK) presented elegant structural and biochemical studies that have allowed her group to pin down the mechanism of FANCD2 ubiquitination (a key step in FA pathway activation) by the FANCL and FANCT proteins [22]. Finally, **Lei Li** (MD Anderson Cancer Center, USA) described work that indicates a cancer cell-essential role for the FANCD2 protein, which counteracts the endogenous replicative stress that cancer cells experience.

The morning of May 9th was free, allowing delegates to take one of two organised trips. One option was an extended hike through the beautiful lower Carpathian Mountains, another a shorter walk that included a visit to the spectacular Driny Cave complex. Both proved popular and allowed much further informal discussions amongst delegates. Scientific sessions resumed in the afternoon, with a session dedicated to NER with a biochemical and structural flavour. **Björn Schumacher** (University of Cologne, Germany) discussed the link between NER and stress, cell survival and aging within the germline and soma of *Caenorhabditis elegans* [23]. **Nigel Savery** (Bristol University, UK) described biochemical and single molecule studies that continue to lead to breakthrough advances in bacterial TC-NER [24, 25]. **Malcolm White** (St. Andrews University, UK) spoke on the evolutionary relationship between NER factors with a focus on archaea, a model which has facilitated ground-breaking advances in understanding lesion recognition [26]. Finally, **Li Fan** (University of California Riverside, USA) discussed new data on the interactions of archaeal XPB helicases with the nucleases that execute NER [27]. Three short talks rounded off the day, **Pawel Zawadzki** (Adam Mickiewicz University, Poland) demonstrated how single molecule imaging coupled to live cell microscopy was helping to unravel the dynamics of bacterial NER factors. **Chiara Balbo Pogliano** (Zurich University, Switzerland) presented studies implicating the ASH1L histone methyltransferase in global genome NER, while **Charlotte Hodson** (St. Vincent's Institute, Australia) described a role for the FANCM protein in unwinding R-loops, RNA-DNA hybrid structures that are genotoxic.

The final day started with a second session on ICL repair. **Johannes Walter** (Harvard University, USA) presented elegant new data describing how ICL-arrested replication forks can be reversed by the FANCM protein, providing intermediates for nucleolytic incision [28]. **John Rouse** (Dundee University, UK) presented the second talk on the role of RFWD3 in maintaining genome stability, highlighting the importance of the interactions between RFDW3 and RPA for ICL repair [29]. **Sharon Cantor** (UMASS Medical School, USA) described new work on the role of FANCJ [30] and BRCA1 in protecting replication forks from degradation. **Michael Seidman** (NIA/NIH, USA) showed work that extends his group's ground-breaking analysis on the role of replication fork traverse in the replicative repair of ICL in mammalian cells [31, 32]. Four short talks followed. **Lonnie Swift** (University of Oxford, UK) described a novel role for the SNM1A ICL repair exonuclease in the repair of DNA double-strand breaks. **Karina Movsesian** (Masaryk University, Czech Republic) described her work on characterising the abnormalities in RAD51 filament formation that underlies some forms of FA. **Karun Mutreja** (University of Zurich, Switzerland) demonstrated how forks are remodelled in response to ICL, using innovative technologies, while **Eduard Goffa** (Biomedical Research Centre of the Slovak Academy of Sciences, Slovakia) spoke about an FA-like ICL repair

operating in budding yeast [33], which may provide a powerful model tool to study replication-coupled ICL repair.

On the final afternoon we returned to NER. **Neil Kad** (Kent University, UK) demonstrated how the early stages of damage recognition during bacterial NER can be visualised in single molecule studies using DNA tightropes [34-36]. **Marcin Nowotny** (Warsaw, Poland) discussed new structural information on RuvC, XPG and components of the SLX4 complex [37]. **Patty Opresko** (University of Pittsburgh, USA) described how, in contrast to several previous studies, efficient NER operates at telomeres, and also presented elegant new approaches to studying both NER and base excision repair at telomeres [38-41]. **Simon Reed** (Cardiff University, UK) demonstrated the power of genomic methods to reveal links between NER and chromatin remodelling throughout the genome [42, 43].

In addition to the scientific lectures, two 'breakout' sessions that addressed the challenges of; i. Career progression, and ii. Work-life balance, were very well attended and received, and an interactive productive dialogue took place (Fig. 1B). The Workshop, ended with a special talk, presented by **Miroslav Piršel**, who recently retired from the Slovak Academy of Sciences. Miro was a co-organiser of the 2103 FEBS NER-ICL Workshop and was instrumental in putting DNA repair workshops within Slovakia on an international stage since 1989. Miro spoke about the history of DNA repair meetings in Slovakia [44], in a very entertaining and informative presentation.

References:

[1] T. Lindahl, D.E. Barnes, Repair of endogenous DNA damage, Cold Spring Harbor symposia on quantitative biology, 65 (2000) 127-133.
[2] A. Ciccia, S.J. Elledge, The DNA damage response: making it safe to play with knives, Molecular cell, 40 (2010) 179-204.
[3] J.H. Hoeijmakers, Genome maintenance mechanisms for preventing cancer, Nature, 411 (2001) 366-374.
[4] J.H. Hoeijmakers, DNA damage, aging, and cancer, The New England journal of medicine, 361 (2009) 1475-1485.
[5] Y. Peng, H. Wang, L. Santana-Santos, C. Kisker, B. Van Houten, Nucleotide excision repair from bacteria to humans: structure-function studies, in: Trevor M. Penning (Ed.) Chemical Carcinogenesis, Springer Science + Business Media, New York, 2011, pp. 267-296.
[6] L.J. Niedernhofer, V.A. Bohr, M. Sander, K.H. Kraemer, Xeroderma pigmentosum and other diseases of human premature aging and DNA repair: molecules to patients, Mechanisms of ageing and development, 132 (2011) 340-347.
[7] A.J. Deans, S.C. West, DNA interstrand crosslink repair and cancer, Nature reviews. Cancer, 11 (2011) 467-480.
[8] S.Q. Gregg, A.R. Robinson, L.J. Niedernhofer, Physiological consequences of defects in ERCC1-XPF DNA repair endonuclease, DNA Repair, 10 (2011) 781-791.
[9] H.B. Dong, D.W. Nebert, E.A. Bruford, D.C. Thompson, H. Joenje, V. Vasiliou, Update of the human and mouse Fanconi anemia genes, Hum Genomics, 9 (2015).
[10] L. Williamson, M. Saponaro, S. Boeing, P. East, R. Mitter, T. Kantidakis, G.P. Kelly, A. Lobley, J. Walker, B. Spencer-Dene, M. Howell, A. Stewart, J.Q. Svejstrup, UV Irradiation Induces a Non-coding RNA that Functionally Opposes the Protein Encoded by the Same Gene, Cell, 168 (2017) 843-855 e813.
[11] L.B. Pontel, I.V. Rosado, G. Burgos-Barragan, J.I. Garaycoechea, R. Yu, M.J. Arends, G. Chandrasekaran, V. Broecker, W. Wei, L. Liu, J.A. Swenberg, G.P. Crossan, K.J. Patel, Endogenous Formaldehyde Is a Hematopoietic Stem Cell Genotoxin and Metabolic Carcinogen, Mol Cell, 60 (2015) 177-188.
[12] J. Nieminuszczy, R. Broderick, W. Niedzwiedz, EXD2 - a new player joins the DSB resection team, Cell Cycle, 15 (2016) 1519-1520.

[13] J. Stingele, R. Bellelli, F. Alte, G. Hewitt, G. Sarek, S.L. Maslen, S.E. Tsutakawa, A. Borg, S. Kjaer, J.A. Tainer, J.M. Skehel, M. Groll, S.J. Boulton, Mechanism and Regulation of DNA-Protein Crosslink Repair by the DNA-Dependent Metalloprotease SPRTN, Mol Cell, 64 (2016) 688-703.
[14] U. Roy, S. Mukherjee, A. Sharma, E.G. Frank, O.D. Scharer, The structure and duplex context of DNA interstrand crosslinks affects the activity of DNA polymerase eta, Nucleic Acids Res, 44 (2016) 7281-7291.
[15] M. Kong, L. Liu, X. Chen, K.I. Driscoll, P. Mao, S. Bohm, N.M. Kad, S.C. Watkins, K.A. Bernstein, J.J. Wyrick, J.H. Min, B. Van Houten, Single-Molecule Imaging Reveals that Rad4 Employs a Dynamic DNA Damage Recognition Process, Mol Cell, 64 (2016) 376-387.
[16] M. Kong, B. Van Houten, Rad4 recognition-at-a-distance: Physical basis of conformation-specific anomalous diffusion of DNA repair proteins, Prog Biophys Mol Biol, 127 (2017) 93-104.
[17] C.L. Li, F.M. Golebiowski, Y. Onishi, N.L. Samara, K. Sugasawa, W. Yang, Tripartite DNA Lesion Recognition and Verification by XPC, TFIIH, and XPA in Nucleotide Excision Repair, Mol Cell, 59 (2015) 1025-1034.
[18] P.M. Dehe, P.H. Gaillard, Control of structure-specific endonucleases to maintain genome stability, Nat Rev Mol Cell Biol, 18 (2017) 315-330.
[19] S. Inano, K. Sato, Y. Katsuki, W. Kobayashi, H. Tanaka, K. Nakajima, S. Nakada, H. Miyoshi, K. Knies, A. Takaori-Kondo, D. Schindler, M. Ishiai, H. Kurumizaka, M. Takata, RFWD3-Mediated Ubiquitination Promotes Timely Removal of Both RPA and RAD51 from DNA Damage Sites to Facilitate Homologous Recombination, Mol Cell, 66 (2017) 622-634 e628.
[20] W.S. Hoogenboom, D. Klein Douwel, P. Knipscheer, Xenopus egg extract: A powerful tool to study genome maintenance mechanisms, Dev Biol, 428 (2017) 300-309.
[21] D. Klein Douwel, W.S. Hoogenboom, R.A. Boonen, P. Knipscheer, Recruitment and positioning determine the specific role of the XPF-ERCC1 endonuclease in interstrand crosslink repair, EMBO J, 36 (2017) 2034-2046.
[22] F.E. Morreale, A. Bortoluzzi, V.K. Chaugule, C. Arkinson, H. Walden, A. Ciulli, Allosteric Targeting of the Fanconi Anemia Ubiquitin-Conjugating Enzyme Ube2T by Fragment Screening, J Med Chem, 60 (2017) 4093-4098.
[23] M. Rieckher, A. Bujarrabal, M.A. Doll, N. Soltanmohammadi, B. Schumacher, A simple answer to complex questions: Caenorhabditis elegans as an experimental model for examining the DNA damage response and disease genes, J Cell Physiol, (2017) doi: 10.1002/jcp.25979.
[24] J. Fan, M. Leroux-Coyau, N.J. Savery, T.R. Strick, Reconstruction of bacterial transcription-coupled repair at single-molecule resolution, Nature, 536 (2016) 234-237.
[25] K. Sanders, C.L. Lin, A.J. Smith, N. Cronin, G. Fisher, V. Eftychidis, P. McGlynn, N.J. Savery, D.B. Wigley, M.S. Dillingham, The structure and function of an RNA polymerase interaction domain in the PcrA/UvrD helicase, Nucleic Acids Res, 45 (2017) 3875-3887.
[26] D. Constantinescu-Aruxandei, B. Petrovic-Stojanovska, J.C. Penedo, M.F. White, J.H. Naismith, Mechanism of DNA loading by the DNA repair helicase XPD, Nucleic Acids Res, 44 (2016) 2806-2815.
[27] L. Fan, K.T. DuPrez, XPB: An unconventional SF2 DNA helicase, Prog Biophys Mol Biol, 117 (2015) 174-181.
[28] D.R. Semlow, J. Zhang, M. Budzowska, A.C. Drohat, J.C. Walter, Replication-Dependent Unhooking of DNA Interstrand Cross-Links by the NEIL3 Glycosylase, Cell, 167 (2016) 498-511 e414.
[29] L. Feeney, I.M. Munoz, C. Lachaud, R. Toth, P.L. Appleton, D. Schindler, J. Rouse, RPA-Mediated Recruitment of the E3 Ligase RFWD3 Is Vital for Interstrand Crosslink Repair and Human Health, Mol Cell, 66 (2017) 610-621 e614.
[30] S.B. Cantor, S. Nayak, FANCJ at the FORK, Mutat Res, 788 (2016) 7-11.
[31] F. Rohleder, J. Huang, Y. Xue, J. Kuper, A. Round, M. Seidman, W. Wang, C. Kisker, FANCM interacts with PCNA to promote replication traverse of DNA interstrand crosslinks, Nucleic Acids Res, 44 (2016) 3219-3232.
[32] M.A. Trakselis, M.M. Seidman, R.M. Brosh, Jr., Mechanistic insights into how CMG helicase facilitates replication past DNA roadblocks, DNA Repair (Amst), 55 (2017) 76-82.
[33] P.J. McHugh, T.A. Ward, M. Chovanec, A prototypical Fanconi anemia pathway in lower eukaryotes?, Cell Cycle, 11 (2012) 3739-3744.

[34] C.D. Hughes, H. Wang, H. Ghodke, M. Simons, A. Towheed, Y. Peng, B. Van Houten, N.M. Kad, Real-time single-molecule imaging reveals a direct interaction between UvrC and UvrB on DNA tightropes, Nucleic Acids Res, 41 (2013) 4901-4912.
[35] M. Simons, M.R. Pollard, C.D. Hughes, A.D. Ward, B. Van Houten, M. Towrie, S.W. Botchway, A.W. Parker, N.M. Kad, Directly interrogating single quantum dot labelled UvrA2 molecules on DNA tightropes using an optically trapped nanoprobe, Sci Rep, 5 (2015) 18486.
[36] J. Wang, J.T. Barnett, M.R. Pollard, N.M. Kad, Integrating Optical Tweezers, DNA Tightropes, and Single-Molecule Fluorescence Imaging: Pitfalls and Traps, Methods Enzymol, 582 (2017) 171-192.
[37] M. Nowotny, V. Gaur, Structure and mechanism of nucleases regulated by SLX4, Curr Opin Struct Biol, 36 (2016) 97-105.
[38] E. Fouquerel, J. Lormand, A. Bose, H.T. Lee, G.S. Kim, J. Li, R.W. Sobol, B.D. Freudenthal, S. Myong, P.L. Opresko, Oxidative guanine base damage regulates human telomerase activity, Nat Struct Mol Biol, 23 (2016) 1092-1100.
[39] L. Garcia-Exposito, E. Bournique, V. Bergoglio, A. Bose, J. Barroso-Gonzalez, S. Zhang, J.L. Roncaioli, M. Lee, C.T. Wallace, S.C. Watkins, P.L. Opresko, J.S. Hoffmann, R.J. O'Sullivan, Proteomic Profiling Reveals a Specific Role for Translesion DNA Polymerase eta in the Alternative Lengthening of Telomeres, Cell Rep, 17 (2016) 1858-1871.
[40] D. Parikh, E. Fouquerel, C.T. Murphy, H. Wang, P.L. Opresko, Telomeres are partly shielded from ultraviolet-induced damage and proficient for nucleotide excision repair of photoproducts, Nat Commun, 6 (2015) 8214.
[41] R. Tippana, H. Hwang, P.L. Opresko, V.A. Bohr, S. Myong, Single-molecule imaging reveals a common mechanism shared by G-quadruplex-resolving helicases, Proc Natl Acad Sci U S A, 113 (2016) 8448-8453.
[42] R. Waters, P. van Eijk, S. Reed, Histone modification and chromatin remodeling during NER, DNA Repair (Amst), 36 (2015) 105-113.
[43] S. Yu, K. Evans, P. van Eijk, M. Bennett, R.M. Webster, M. Leadbitter, Y. Teng, R. Waters, S.P. Jackson, S.H. Reed, Global genome nucleotide excision repair is organized into domains that promote efficient DNA repair in chromatin, Genome Res, 26 (2016) 1376-1387.
[44] M. Piršel, M. Chovanec, A. Dudáš, K. Kleibl, B. Van Houten, Fourth DNA repair workshop on DNA damage and repair: mechanisms and biological consequences Smolenice Castle, 2-5 May 2004, DNA Repair (Amst), 3 (2004) 1639-1659.

Figure legends

Figure 1. A. Smolenice Castle and B. Attendees during the meeting.