Young Scientist Toxicology Merck Award 2013 für Aswin Mangerich

Molecular mechanisms of genotoxicology during inflammation, carcinogenesis, and aging

A plethora of DNA lesions are induced by exogenous and endogenous sources in a mammalian cell every day. Most of them are generally efficiently repaired to ensure genomic stability, but if persistent, these lesions can cause mutations, genomic instability, and cell death. The focus of Aswin Mangerich's research during the last years has been to study DNA damage and repair mechanisms on a molecular and organismic level in order to examine how these mechanisms contribute to health and disease conditions, such as inflammation, carcinogenesis and aging. Specifically, his studies focused on the following topics:

Biological chemistry of inflammation as a cause of cancer.

> E. G. Prestwich, A. Mangerich, B. Pang, J. L. McFaline, P. Lonkar, M. Sullivan, L. Trudel, K. Taghizadeh, and P.C. Dedon; Increased Levels of Inosine in a Mouse Model of Inflammation; Chemical Research in Toxicology, in press
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> A. Mangerich, C. G. Knutson, N. M. Parry, S. Muthupalani, W. Ye, E. G. Prestwich, L. Cui, J. L. McFaline, M. W. Mobley, Z. Ge, K. Taghizedeh, J. S. Wishnok, G. N. Wogan, J. G. Fox, S. R. Tannenbaum, and P. C. Dedon; Infection-induced Colitis in Mice Causes Dynamic and Tissue-specific Changes in Stress Response and DNA Damage Leading to Colon Cancer; PNAS (2012) Jul 3;109(27):E1820-9.

Functional regulation of the Werner syndrome protein (WRN) by post-translational poly(ADP-ribosyl)ation.

> O. Popp, S. Veith, J. Fahrer, V. A. Bohr, A. Bürkle and A. Mangerich; Site-specific Non-covalent Interaction of the Biopolymer Poly(ADP-ribose) with the Werner Syndrome Protein Regulates Protein Functions; ACS Chemical Biology (2013) Jan 18;8(1):179-88.
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> A. Mangerich, S. Veith, O. Popp, J. Fahrer, R. Martello, V. A. Bohr and A. Bürkle; Quantitative Analysis of WRN Exonuclease Activity by Isotope Dilution Mass Spectrometry; Mechanisms of Ageing and Development (2012) Aug;133(8):575-9.

The role of the DNA damage signalling enzyme PARP1 and its enzymatic product poly(ADP-ribose) in inflammation, aging, and carcinogenesis.

> A. Mangerich and A. Bürkle; Pleiotropic Cellular Functions of PARP1 in Longevity and Aging: Genome Maintenance Meets Inflammation; Oxidative Medicine and Cellular Longevity (2012) 2012:321653. Review
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> A. Mangerich and A. Bürkle; How to Kill Tumor Cells with Inhibitors of Poly(ADP-ribosyl)ation; International Journal of Cancer (2011) Jan 15;128(2):251-65. Review
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> A. Mangerich, N. Herbach, B. Hanf, A. Fischbach, O. Popp, M. Moreno-Villanueva, O. T. Bruns, and A. Bürkle; Inflammatory and Age-related Pathologies in Mice with Ectopic Expression of Human PARP-1; Mechanisms of Ageing and Development (2010) Jun;131(6):389-404
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> A. Mangerich, H. Scherthan, J. Diefenbach, U. Kloz, F. van der Hoeven, S. Beneke, and A. Bürkle; A Caveat in Mouse Genetic Engineering: Ectopic Gene Targeting in ES Cells by Bidirectional Extension of the Homology Arms of a Gene Replacement Vector Carrying Human PARP-1; Transgenic Research (2009) Apr;18(2):261-79
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> A. Mangerich and A. Bürkle; Inhibitoren der Poly-ADP-Ribose Polymerasen: Wirkungsweise und mögliche Indikationen für die Therapie von Tumoren (in German); Onkologie (ecomed Verlagsgesellschaft) (2012) 33. Erg. Lfg. 4/12, chapter IV-10.6. Book chapter