

LIFE SCIENCES

seminar series

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Ebola Virus Disease in West Africa – Outbreak Response & Operational Research

April 27, 2016

Thursday, 16:00

Seminar room 132, pavilion A11
University campus Bohunice

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Epigenetic information is stored in the form of modified bases in the genome. The positions and the kind of the base modifications determines the identity of the corresponding cell. Setting and erasing of epigenetic imprints controls the complete development process starting from an omnipotent stem cells and ending with an adult specialized cell. I am going to discuss the latest results related to the function and distribution of the epigenetic marker bases 5-hydroxymethylcytosine (hmC), 5-formylcytosine (fC), 5-carboxycytosine (caC) and 5-hydroxymethyluracil (Scheme 1).^[1] These nucleobases control epigenetic programming of stem cells and some of these bases are also detected at relatively high levels in brain tissues. Synthetic routes to these new bases will be discussed that enable today preparation of oligonucleotides containing the new bases. The second part of the lecture will cover mass spectroscopic approaches to decipher the biological functions of the new epigenetic bases of which some were described in the past as pure DNA lesions.^[2] In particular, results from quantitative mass spectrometry, new covalent-capture proteomics mass spectrometry and isotope tracing techniques will be reported. The data allow us to unravel the chemistry in stem cells and the protein networks that are controlled by the epigenetic base modifications.^[3] Finally I am discussing potential prebiotic origins of these modified bases^[4]

[1] M. Wagner, J. Steinbacher, T. F. Kraus, S. Michalakis, B. Hackner, T. Pfaffeneder, A. Perera, M. Müller, A. Giese, H. A. Kretschmar, T. Carell *Angew. Chem. Int. Ed.* **2015**, doi: 10.1002/anie.201502722. Age-Dependent Levels of 5-Methyl-, 5-Hydroxymethyl-, and 5-Formylcytosine in Human and Mouse Brain Tissues.

[2] Perera, D. Eisen, M. Wagner, S. K. Laube, A. F. Künzel, S. Koch, J. Steinbacher, E. Schulze, V. Splith, N. Mittermeier, M. Müller, M. Biel, T. Carell, S. Michalakis *Cell Rep.* **2015**, *11*, 1-12. TET3 Is Recruited by REST for Context-Specific Hydroxymethylation and Induction of Gene Expression

[3] C.G. Spruijt, F. Gnerlich, A.H. Smits, T. Pfaffeneder, P.W.T.C. Jansen, C. Bauer, M. Münzel, M. Wagner, M. Müller, F. Khan, H.C. Eberl, A. Mensinga, A.B. Brinkman, K. Lephikov, U. Müller, J. Walter, R. Boelens, H. van Ingen, H. Leonhardt, T. Carell, M. Vermeulen *Cell.* **2013**, *152*, 1146-59. Dynamic readers for 5-(hydroxy)methylcytosine and its oxidized derivatives

[4] S. Becker, I. Thoma, A. Deutsch, T. Gehrke, P. Mayer, H. Zipse, T. Carell, *Science*, **2016**, *352* (6287), 833-836.

A high-yielding, strictly regioselective prebiotic purine nucleoside formation pathway.