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Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares

Conferencia:

DNA Bases beyond Watson and Crick

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3/04/17

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Aula de Seminarios do CIQUS

12:15h

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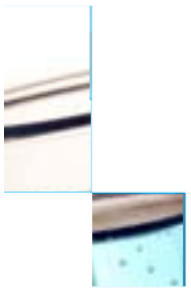

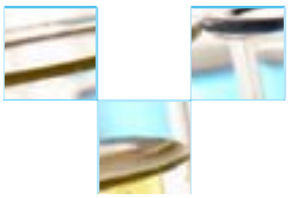

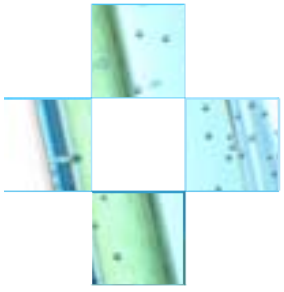

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Title: DNA Bases beyond Watson and Crick

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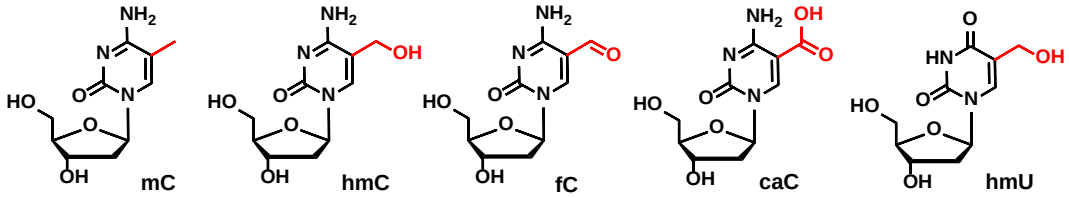
Keywords: Epigenetics, oxidized pyrimidine bases, mass spectrometry, proteomics.

Abstract: 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 results related to the function and distribution of the new epigenetic bases 5-hydroxymethylcytosine (hmC), 5-formylcytosine (fC), 5-carboxycytosine (caC) and 5-hydroxymethyluracil (Scheme 1).[1] These nucleobases seem to control epigenetic programming of cells and establish genetic programmability. Synthetic routes to these new bases will be discussed that enable the preparation of oligonucleotides. The second part of the lecture will cover mass spectroscopic approaches to decipher the biological functions of the new bases.[2] In particular, results from quantitative mass spectrometry, new covalent-capture proteomics mass spectrometry and isotope tracing techniques will be reported.[3] Finally I am dicussing potential präbiotic origins of modified bases[4].



Scheme 1: Depiction of the new epigenetic bases.

[1] M. Wagner, J. Steinbacher, T. F. Kraus, S. Michalakis, B. Hackner, T. Pfaffeneder, A. Perera, M. Müller, A. Giese, H. A. Kretzschmar, T. Carell *Angew. Chem. Int. Ed.* **2015**, *54 (42)*, 12511-12514. 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.

Thomas Carell (Ph. D) was raised in Bad-Salzuflen (Germany). He studied chemistry at the Universities of Münster and Heidelberg. In 1993 he obtained his doctorate with Prof. H. A. Staab at the Max Planck Institute of Medical Research in Heidelberg. After postdoctoral training with Prof. J. Rebek at MIT (Cambridge, USA) in 1993-1995, Thomas Carell moved to the ETH Zürich (Switzerland) as an ass. professor to start independent research. He obtained his habilitation (tenure) in 2000. He subsequently accepted a full professor position for Organic Chemistry at the Philipps-Universität in Marburg (Germany). In 2004 Thomas Carell moved to the Ludwig-Maximilians-Universität (LMU) in Munich (Germany), where he is heading a research group in chemical biology focused to analyze the chemistry of epigenetic programming in DNA and RNA. Thomas Carell is a member of the National German Academy Leopoldina and of the Berlin-Brandenburgische Academy of Arts and Sciences. He is a recipient of the Cross of Merit from the Federal Republic of Germany. Thomas Carell obtained the German Leibniz award in 2014 (comparable to a HHMI investigator in the USA).