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Setting of DNA methylation – biological and technical approaches

DNA methylation is an important epigenetic modification that in concert with histone tail modifications is essential for gene regulation. In mammals, the DNA methylation patterns are set during embryogenesis and development but aberrantly altered during the onset and progression of diseases like cancer. The DNMT3A and 3B DNA methyltransferases play central roles in these processes, but it is still largely unknown, how DNA methylation patterns are generated and maintained in cells. I will present novel concepts of the regulation of DNMT3A based on allosteric mechanisms and interacting proteins. Technologically novel DNA methylation patterns can be generated by targeted methylation using DNA methyltransferases fused to designed DNA recognition domains (zinc finger, TAL effector, or modified CRISPR/Cas9 complex). Targeted DNA methylation is a promising approach for durable gene regulation, with many applications in basic research and clinics. I will present the progress in this field, mainly the application of CRISPR/dCas9 for targeted DNA methylation and discuss question like stability, methods to achieve an allele specific targeting and methylation.

Recent Publications

1. Jeltsch A and Jurkowska R Z (2016) Allosteric control of mammalian DNA methyltransferases-a new regulatory paradigm. *Nucleic Acids Research* 44(18):8556-8575.
2. Jeltsch A and Jurkowska R Z (eds.) (2016) DNA Methyltransferases-Role and Function. In: *Advances in Experimental Medicine and Biology*, ISBN: 978-3-319-43622-7, Springer International Publishing.
3. Emperle M, Rajavelu A, Reinhardt R, Jurkowska R Z and Jeltsch A (2014) Cooperative DNA binding and protein/DNA fiber formation increases the activity of the DNMT3A DNA methyltransferase. *Journal of Biological Chemistry* 289:29602-29613.
4. Jeltsch A and Jurkowska R Z (2014) New concepts in DNA methylation. *Trends in Biochemical Sciences* 39(7):310-8.
5. Deplus R, Jeltsch A, Fuks F, et al. (2014) Regulation of DNA methylation patterns by CK2-mediated phosphorylation of DNMT3A. *Cell Reports* 8:743-53.

Biography

Albert Jeltsch completed his PhD working on the mechanism of restriction endonucleases at University Hannover in 1994. Afterwards, he started to study DNA methyltransferases at Justus-Liebig University Giessen and at Jacobs University Bremen. Since 2011, he is a Professor of Biochemistry at the University Stuttgart. He received the Gerhard-Hess award (DFG) and BioFuture award (BMBF). He has long standing expertise in "Biochemical study of DNA and protein methyltransferases, methyl lysine reading domains and in rational and evolutionary protein design". His work has been published in more than 200 publications in peer reviewed journals and he is in the editorial boards of several journals.

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