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Modular fluorescence complementation sensors for live cell detection of epigenetic signals at endogenous genomic loci

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Investigation of the fundamental role of epigenetic processes depends on the development of methods, which enable live-cell detection of epigenetic modifications with locus-specific resolution. Here, we address this urgent technological demand by developing four modular fluorescence complementation-based epigenetic biosensors for live cell microscopy applications. In these tools, we combine the high DNA sequence specificity of engineered anchor proteins, with the great versatility of chromatin reading domains as natural detector modules for the recognition of target epigenetic marks. Simultaneous readout of DNA sequence and epigenetic mark is detected as reconstituted fluorescent signals that arise upon binding of the anchor and detectors modules in close spatial proximity, within the nuclei of living cells. With this approach, we could directly detect DNA methylation and histone 3 lysine 9 trimethylation at defined, endogenous genomic sites, in several mouse and human cell lines. Furthermore, we could follow dynamic changes in these marks with locus-specific resolution upon drug treatment or induction of epigenetic enzymes. We anticipate that this versatile technology will play an important role in improving our understanding of how specific epigenetic signatures are set, erased and maintained during embryonic development or the onset of diseases.

Biography

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

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