Biochimica et Biophysica Acta 1839 (2014) 621–622

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

journal homepage: www.elsevier.com/locate/bbagrm

Editorial

Molecular mechanisms of histone modification function

The many functions that a eukaryotic cell carries out require that its genetic material is maintained, read and translated in a highly organized manner. Besides rapid reaction to external stimuli long-term differentiation and developmental programs need to be faithfully executed. The blueprint for these processes resides within DNA as inheritable material. However, the many differences in the biology of diverse organisms and individual cells cannot be explained solely on the basis of different gene sequences and content. Epigenetic processes direct organized and specific use of a given genome in a time and space resolved manner.

The molecular target of epigenetic signaling is chromatin, the packaging form of the genetic material in eukaryotic cells. Here, DNA is complexed with histone proteins (linker histones of H1-type and core histones H2A, H2B, H3 and H4) in repeating units called nucleosomes. While the molecular architecture of all nucleosomes is essentially the same throughout the genome, chemical modifications of DNA (e.g. by methylation) and in particular of the different histone proteins mark locally and globally distinct areas of chromatin.

Since the initial description of general histone acetylation as well as other modifications by Vincent Allfrey in the 1960s a waste number of different types and sites of posttranslational modifications on the core and linker histones have been recognized. Combining data from different experimental model systems and using varying technical approaches more than 150 marks on the histone proteins have been mapped until now. In agreement with a role in directing the functional state of associated DNA these modifications appear to function in all kinds of biological processes that eukaryotic genomes undergo such as for example transcription, replication, recombination and repair. Not surprisingly, varying patterns of histone modifications are implicated in normal as well as disease developmental processes.

Immediate regulatory roles of histone modifications in cellular signaling as well as their causal function in directing usage of the genetic material were questioned for a long time. The major breakthrough in this field came by the identification and characterization of enzymes and enzyme systems controlling histone modification state almost two decades ago. The findings that previously studied transcriptional regulators act in modifying and demodifying histones spurred huge interest into histone marks promising molecular insights into complex epigenetic phenomena. Much progress has been made during the last 20 years not only to link individual and combinations of histone modifications to defined biological states of genomes but also in our understanding of the ways these marks work on a biochemical level.

These days, large-scale efforts are not only devoted to globally map discrete patterns of histone modifications in different cellular states but also to deduce the complex logic governing this intricate signaling system. Besides these approaches molecular analysis of the readout and translation of histone modifications is required to comprehend the interplay of histone modifications and structural and functional changes of chromatin. This special issue of BBA Gene Regulatory Mechanisms is devoted to these "molecular mechanisms of histone modification function".

In the first section entitled *concepts and ideas* Bryan Turner provides a general overview of signaling to and from chromatin by histone modifications (pp 623-626). Rothbart and Strahl pick up on these basic concepts and in their contribution elute to the complexities of chromatin regulation by chemical modifications and the challenges we are facing in trying to comprehend this signaling system (pp 627-643).

The second section *technologies and experimental approaches* features a review article by Beat Fierz and colleagues on chemical and synthetic biology approaches (pp 644-656). It is accompanied by an update on novel mass spectrometry based assays developed to determine local patterns of histone modifications and their readout by Tiziana Bonaldi and colleagues (pp 657-668). While the field of analyzing binding factors of histone modifications was initially mostly driven by educated guesses and analogy findings, Wilkinson and Gozani summarize general strategies now used to identify and characterize histone modification binding domains (pp 669-675).

The large section *readout of different histone modifications* is devoted to the major types of histone marks: modification of different histone lysine residues by acetylation (pp 676-685), methylation (pp 686-693), or ubiquitination (pp 694-701), methylation of arginines (pp 702-710) as well as phosphorylation of threonine and serine residues (pp 711-718). The laboratories of Ming-Ming Zhou, Catherine Musselman, Moshe Oren, Mark Bedford, and Christian Seiser summarize in detail what is known about the readout and translation of these types of histone modification marks on a biochemical and cell biology level.

In the final section *interplay and crosstalk* Du and Patel provide detailed insight into combinatorial readout of histone modifications and its functional consequences (pp 719-727). In this general context Peterson and colleagues focus on the interplay of histone modifications with complex molecular machines for remodeling chromatin (pp 728-736). Lastly, Hiragami-Hamada and Fischle summarize emerging evidence that connects the readout and translation of histone modifications to non-coding RNA (pp 737-742).

I hope that you will enjoy browsing through this special issue of BBA Gene Regulatory Mechanisms on the "molecular mechanisms of histone modification function". In putting the themes and articles of this volume together I aimed not only to cover the ground for specialists but also to introduce newcomers to this exciting field. Hopefully, you will not only

http://dx.doi.org/10.1016/j.bbagrm.2014.06.003

find answers to common questions but are also provoked to come up with exciting new thoughts.

Since 2006 Wolfgang Fischle is Max Planck Research Group Leader of the Laboratory of Chromatin Biochemistry at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany. He did his undergraduate studies in Biochemistry at the University of Tübingen, Germany finishing with a Diploma (eq. to MSc) in 1996. For his PhD work, which was funded by the Boehringer Ingelheim Fonds, he joined the laboratory of Eric Verdin at The J. David Gladstone Institutes at the University of California in San Francisco, USA. There he identified a new class of histone deacetylases and worked out regulatory mechanisms of chromatin modifying complexes containing these enzymes. After graduation in 2002 he did postdoctoral work in the laboratory of C. David Allis first at the University of Virginia in Charlottesville, USA and later at The Rockefeller University in New York, USA. Funded by a postdoctoral fellowship of the Damon Runyon Cancer Research Foundation he identified and characterized different proteins binding distinct histone lysine methylation marks. In particular, he formulated the theory of binary switches that describes how adjacent histone modifications regulate each other's readout. His laboratory continues to explore how chromatin marks exert their functions on a molecular level using multidisciplinary approaches combining biochemistry, biophysics with systems and molecular biology.

Wolfgang Fischle
Laboratory of Chromatin Biochemistry, Max Planck Institute for Biophysical Chemistry, Am Fassberg 11, 37077 Göttingen, Germany
Tel.: +49 5512011340.
E-mail address: wfischl@gwdg.de.