Science in China Series C: Life Sciences

www.scichina.com
life.scichina.com
www.springerlink.com

Special Topic

• Editorial •

Molecular epigenetics: dawn of a new era of biomedical research

At about the same time in 1940s when Erwin Schrödinger published his famous little book *What Is Life*, which sparked the birth of molecular biology, the term *epigenetics* was coined by the English biologist Conrad Waddington. The concept of epi-inheritance can be traced back to French naturalist Jean-Baptiste Lamarck's idea of "inheritance of acquired traits". Nevertheless, epigenetics as an experimental science owes much credit to Barbara McClintock's pioneering work on transposable elements in *maize*. In early 1950s, she put forward a theory that alteration in chromatin structure is responsible for the peculiar non-Mendelian rules of inheritance – a concept nowadays widely accepted as the corner stone of modern epigenetics.

Progresses in the last couple of decades have greatly facilitated our understanding of the molecular mechanisms of epigenetic inheritance. First, DNA methylation is a key component of the epigenetic program in plants and mammals. Methylation of CpG dinucleotide repeats in mammals, and both CpG and non-CpG sequences in plants play critical roles in classical models of epigenetics such as imprinting, transposon dynamics, X chromosome inactivation, as well as in cell type specification during development. Second, post-translational modifications of histones have great impact on chromatin structure and epigenetic control of gene expression. In particular, the discovery of histone methyltransferases in 2000 has fueled a decade of epigenetic "gold rush" that is still ongoing. A large number of histone methyltransferases have been identified, and remarkably, these enzymes are highly specific for the position of lysine residues on histones H3 and H4. The lysine residues can also be methylated to different extents, with one to three methyl groups added, by different enzymes or the same enzyme but in a highly regulated manner. Transcribed or repressed genomic loci are marked by a combination of different histone methylation sites and number of methyl groups attached. Third, the latest addition of important players in epigenetics is micro RNA. At about the same time when the first histone methyltransferases were discovered, small RNAs were found to down regulate gene expression by mRNA degradation or translational inhibition. In 2002, a connection between the RNAi machinery and epigenetic inheritance in the fission yeast *S. pombe* was found. Accompanied by the discovery of a diverse and vast number of endogenous micro RNAs, it has become increasingly clear that micro RNAs are an integral component of the cellular epigenetic program.

Today, many important issues concerning the molecular mechanisms of epigenetics remain unresolved. In this issue of *Science in China Series C: Life Sciences*, three important areas of epigenetic research are reviewed by leading experts in their respective fields. Drs. Lan and Shi provided a comprehensive review of the current understanding of methylation of histone and non-histone proteins, focusing on inheritance of histone methyl marks and dynamic regulation of histone methylation by demethylases. The area of micro RNA biology is presently advancing with each passing day, Dr. He's review summarizes the latest knowledge of micro RNA biogenesis and the mechanism by which micro RNA functions in post-transcriptional gene silencing. How DNA methylation is regulated has been a subject of great interest. While the function and mechanisms of active DNA demethylation are still a matter of considerable debate, in the plant *Arabidopsis* an interesting pathway of active DNA demethylation involving the participation of micro RNA has been characterized, and this important and interesting subject is insightfully reviewed by Drs. Chinnusamy and Zhu.

It is clear that the triad of DNA methylation, histone modifications and micro RNA constitutes the intricate net-

Citation: Xu R M. Molecular epigenetics: dawn of a new era of biomedical research. Sci China Ser C-Life Sci, 2009, 52(4): 309-310, doi: 10.1007/s11427-009-0057-9

work of the epigenetic program in eukaryotic life. An in-depth understanding of the epigenetic mechanism will require detailed knowledge of each of the individual processes and their inter-dependence. This is an exciting time for epigenetic research, as the induced pluripotent stem cell (iPS) technology, which is based on the manipulation of the epigenetic program of differentiated cells, is bringing about the dawn of a new era of biomedicine. There is every reason to believe that we are experiencing a revolution, although belated, but not to be dwarfed in scope or impact in comparison to the development of molecular biology during 1950s to 1990s, in biomedical research.

XU Rui-Ming

Institute of Biophysics, Chinese Academy of Sciences
15 Datun Road, Chaoyang District, Beijing 100101, China
Email: rmxu@sun5.ibp.ac.cn

Author's Biographical Sketch

XU Rui-Ming is an Investigator and CAS-Novo Nordisk Great Wall Professor at Institute of Biophysics (IBP), Chinese Academy of Sciences (CAS). His research interest includes structural studies of epigenetic control of gene expression and mRNA processing. Prior to joining IBP, he was a professor at School of Medicine of New York University and Cold Spring Harbor Laboratory in the US, respectively.

doi: 10.1007/s11427-009-0057-9