

Preface

With a long-term interest in basic research on the biological functions of **DNA methylation**, I have been organizing International Symposia on this and related topics over a period of more than 30 years, both in Köln and in Weissenburg, Germany. The 1981 Cologne Spring Meeting at the Institute of Genetics, University of Cologne, on *DNA Methylation and Genome Organization* may well have been the first international conference on this topic.

Cologne Spring Meeting 1981

DNA Methylation and Genome Organization. March 04–07, 1981.

Weissenburg Symposium 2001

Medicine and Molecular Biology. May 03–06, 2001.

Weissenburg Symposium 2004

DNA Methylation: An Important Genetic Signal: Significance in Biology and Pathogenesis. May 12–15, 2004.

Weissenburg Symposium 2007

Medicine at the Interface between Science and Ethics. May 30–June 01, 2007.

Weissenburg Symposium 2011

Epigenetics and the Regulation of Gene Expression. June 20–22, 2011.

Weissenburg Symposium 2014

Epigenetics—A Different Way of Looking at Genetics. September 14–17, 2014.

The Venue: Weissenburg in Bayern (its official name) is an old town dating back to Roman origins (about 90 A.D.) with a well-preserved medieval center. The town is located 60 km to the South of Nuremberg and 130 km to the North of Munich. Weissenburg is a Frankonian town of some 18,000 inhabitants with diversified

industrial enterprises. The town is situated close to the *Naturpark Altmühltal* and the *Fränkisches Seenland*. The *Kulturzentrum* (dedicated as such in 1983), the venue of our symposia, was founded in 1325 as a Monastery of the Carmelites by the Emperor *Ludwig der Bayer*. Participants of former Symposia in Weissenburg have emphasized the friendly atmosphere and the opportunity for informal scientific and personal interactions inside and outside the lecture hall.

For the **2014 Symposium**, we have been fortunate in assembling an international group of leaders in their fields some of whom had attended earlier Weissenburg Symposia. As an appendix to this volume, I have attached the program for the 2014 Fifth Weissenburg Symposium on *Epigenetics—A Different Way of Looking at Genetics*.

Why *Epigenetics—A Different Way of Looking at Genetics* as the title for the symposium and the book? The designation epigenetics—a misnomer, I submit—is widely used in the literature when referring to genetic phenomena, which are not due to mutations in one of the approximately 20,000–25,000 human genes. In most such instances in human genetics, alterations in regulatory functions have been identified to cause gene silencing and its functional consequences. In all organisms, the control of gene expression is based on the defined interaction of regulatory proteins with distinct nucleotide sequences. When these regulatory pathways are disturbed or incapacitated, by mutations, promoter methylation, histone modifications, or deletions of regulatory nucleotide sequences, they then become responsible for these epigenetic alterations. Hence, from a biochemical perspective, it is difficult to envisage fundamental differences in mutations in a nucleotide sequence encompassing a gene or a regulatory element. In the human genome, many such elements, which are not part of a gene, have now been mapped in locations in between genes, e.g., by the ENCODE project (The ENCODE Project Consortium 2012). For these reasons, the term *Epigenetics* appears rather artificial; hence, the title of the Weissenburg Symposium 2014 has been deliberately chosen to allude to, and at the same time, challenge the use of this still “popular” phrase.

In contrast to prokaryotic organisms, the more complex eukaryotic genomes exhibit much larger nucleotide sequences with repetitive elements and retrotransposon insertions. A considerable portion of these repetitive sequences is actively transcribed into noncoding RNAs of largely unknown function. Many of these sequences carry important regulatory elements. The discovery of the repetitive sequences has in the “distant past” led to the unscientific claim that this “excess DNA” might be devoid of function. For years, the term “junk DNA” has been floated and vehemently discussed among adherents of the pros and cons of this, as is obvious now, completely unjustified term. Even then, one has often reasoned that evolution and conservation of energy in biology would not have allowed this enormous waste of energy during the replication and transcription of allegedly superfluous DNA sequences. Today, it is hard to comprehend how this erroneous concept could have found credence at all.

The field of **epigenetic mechanisms in biology** comprises a wide scope of research interests aimed at elucidating the regulation of genetic activities under many different conditions in cells and organisms across the entire spectrum of

biology and medicine. One way of explaining the significance of this genetic discipline is to remind ourselves of the apparent paradox that the chimpanzee and even the mouse have about the same number of an almost identical or at least very similar set of genes as humans. For a logical account for the obvious disparities between these species, it is useful to recall the differences in the ways they control gene activities during development and in postnatal life under the huge gamut of environmental conditions and their variabilities. The biochemical mechanisms responsible for epigenetic functions are only partly understood. A first important contribution came from studies on DNA methylation, i.e., from modifications of the genome itself, which were in due course followed by the realization that modifications of the DNA-binding histones, and probably of many additional DNA-binding proteins, play an important role in affecting genetic activities. Additionally, small RNAs contribute to the enormous repertoire of regulatory mechanisms in many different ways.

Epigenetics in all fields of biology and medicine. Thus, it has not been surprising that an increasing number of human diseases, many of them with proven or indirectly suggested genetic causation, could be attributed to epigenetic alterations in the absence of classical mutations in any of the genes possibly related to these diseases. Today, it is general knowledge that many of the common diseases, among them the neoplasias, can be causally linked to epigenetic alterations. The field has become huge. When interrogating PubMed, e.g., for *Epigenetics and Cancer*, thousands of hits are scored. Another fascinating realm of research has been opened by asking age-old questions about the influence of the environment on the genome via epigenetic mechanisms (Szyf 2012). Nowadays, PubMed interrogations offer far more than 1000 publications dealing with this important topic. Similarly, contributions of epigenetic research to the study of the highly complex psychiatric diseases have constantly increased in number and quality (Labrie et al. 2012).

Hence, when we set out to organize this Symposium on *Epigenetics*, we had to consider inviting researchers from many different fields in biology and medicine, and one meeting could not possibly attempt to cover all these aspects in depth. As will be apparent from a look into the program, we have been fortunate to attract many of the leaders in the fields. The main **areas in epigenetics** which were among the topics at the Fifth Weissenburg Symposium and are also reflected in this book's chapters have been the following:

Epigenetic Mechanisms

Epigenetics and Development

Complex Diseases

Tumor Biology

Immunology, Virology

Regulatory Systems

Thanks and acknowledgments are due to the members of the advisory board who have helped in selecting the speakers—Dirk Eick, München, Bernhard

Fleckenstein, Erlangen, Christoph Plass, Heidelberg, Andreas Radbruch, Berlin, Jörn Walter, Saarbrücken.

It is also a pleasure to recognize financial support for the Symposium by the Fritz Thyssen Stiftung, Köln (Az. 30.14.0.033); the DKFZ Cross Program Topic “epigenetics@dkfz”; DFG in Heidelberg, Priority Program, SPP1463 “Epigenetic Regulation of Normal Hematopoiesis and its Dysregulation in Myeloid Neoplasia,” Heidelberg/Freiburg; the Institute of Clinical and Molecular Virology, University Erlangen-Nürnberg; the SFB 1064 (Chromatin Dynamics), München; Grünenthal GmbH, Aachen; Qiagen, Hilden; and last but not least Takara Bio Europe S.A.S.

Erlangen, Germany
Cologne, Germany

Walter Doerfler

References

- The ENCODE Project Consortium. *Nature* 2012;489:57–74.
Szyf M. The early-life social environment and DNA methylation. *Clin Genet.* 2012;81:341–9.
Labrie V, Pai S, Petronis A. Epigenetics of major psychosis: progress, problems and perspectives. *Trends Genet.* 2012;28:427–35.

Epigenetics - A Different Way of Looking at Genetics

Doerfler, W.; Böhm, P. (Eds.)

2016, XVI, 254 p. 41 illus., 9 illus. in color., Hardcover

ISBN: 978-3-319-27184-2