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Introduction

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Toxicoepigenomics is a rapidly developing new branch of toxicology. Currently it is a hot discipline of toxicological sciences (Trosko and Chang, 2010; Csoka and Szyf, 2009; Goldberg, Allis, and Bernstein, 2007; Watson and Goodman, 2002). Genetics is defined as heritable changes in the gene expression profiles caused by the modification of genomic DNA due to the alterations in sequence of its bases. It is long accepted that aging and various human diseases including cancer are caused by the changes in the genomic DNA sequence. This long-held 'genetic' mechanism of human diseases focuses on the genetic changes induced by the direct alterations in the genomic DNA sequence itself. Genetics, environmental factors, and xenobiotics contribute to toxicity and human disease. Recent 'omics' technologies opened the way to a systemic understanding of toxicology and pathogenesis (Waters and Fostel, 2004). Thus, they gave birth to a new branch of toxicology called *toxicogenomics*. Toxicogenomics is the integration of traditional toxicology and genomics leading to toxicity and pathogenicity induced by the heritable changes in the genomic DNA sequence itself. However, recent discoveries show that this is not always the case. It has been demonstrated that heritable gene expression, both in the disease states and induced by environmental exposures, is also altered by the DNA modifications without any direct alteration in genomic DNA sequence itself. Environmental factors such as diet, smoking, alcohol intake, environmental toxicants, and stress are capable of altering gene expression profiles that can be inherited by the future generations and such genes altered by the environmental factors without any alteration in the genomic DNA sequence can cause human diseases. This observation led to the discovery of an alternate complementary mechanism of human inheritance and disease called 'epigenetic' mechanism that does not involve any change in the genomic DNA sequence itself. Therefore, a new scientific discipline 'epigenetics' was born with the definition that it is the heritable changes in the expression of the gene without any direct alteration in the DNA sequence itself (Egger *et al*., 2004). The heritable epigenetic modifications induced by environmental factors involve DNA, histone, and chromosomes. The most common observations reported in the epigenetic

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inheritance process are DNA methylation, histone modification, and noncoding small RNAs (Bonasio, Tu, and Reinberg, 2010). These discoveries led to the increasing recognition of the importance of epigenetics in the mechanisms of toxicity. Therefore, another new branch of toxicology called *toxicoepigenomics* was born. Toxicoepigenomics is the integration of traditional toxicology and epigenetics leading to toxicity and pathogenicity induced by heritable alterations in the gene expression without any direct changes in the genomic DNA sequence itself.

An increasing body of evidence demonstrates that epigenetic patterns, altered by environmental factors, are associated with human diseases such as cancer, neurodevelopmental disorders, cardiovascular diseases, type-2 diabetes, obesity, and infertility (Meaney, 2010; Csoka and Szyf, 2009; Nicholls, 2000). Epigenetic changes have been observed in virus-associated human cancers (Li, Leu, and Chang, 2005). It is believed that early epigenetic molecular events lead to cancer development (Herceg, 2007). Epigenetic drug therapy has become an increased focus in the treatment of complex diseases including cancer (Jian, 2011). Understanding of epigenetic pathways and rapid development of sensitive detection technologies will help the development of drug therapies for these diseases, especially cancers. A systems-biology approach employing microarray analyses of epigenetic gene expression patterns have been suggested for the safety assessment of drugs (Csoka and Szyf, 2009; Trosko and Upham, 2010). More and more this approach is being used for epigenetic toxicological studies (Lefèvre and Mann, 2008; Chernov *et al*., 2010). Computational epigenomics, an emerging new discipline, will make significant contributions to toxicoepigenomics research. Chromatin immunoprecipitation (ChIP) is a useful tool for epigenetic studies. Recent technical advances such as ChIP-on-chip and ChIP-seq convert epigenetic research into a high-throughput endeavor (Bock and Lengauer, 2008). Bioinformatic methods will be useful in these efforts. Understanding the role of toxicity in pathogenesis is important. Control of the epigenetic diseases requires the identification of chemical and biological modulators of epigenetic targets. However, very little information on the potential toxicological consequence of such modulations is currently available and, therefore, requires further investigations. Better understanding of the epigenetic mechanism of human diseases, caused by environmental exposures, holds great promise for the future treatment of human diseases.

As the Editor of this monograph, *Toxicology and Epigenetics*, it gives me great pride to introduce a unique book which encompasses many aspects of toxicoepigenomics never published together before. It is only recently that epigenetic research has attracted the attention of toxicologists. The toxicoepigenomic research work, actively pursued throughout the world, will lead to major discoveries of fundamental importance and of great clinical significance. This monograph brings together the ideas and work of investigators of international reputation who have pioneered in this area of research. This book reflects the remarkable blossoming of the discipline of toxicoepigenetics in recent years. New ideas and new approaches are being brought to bear on explorations of epigenetic mechanisms in toxicology. Therefore, exciting times are ahead for the future research on toxicoepigenomics. I sincerely hope that this book will stimulate the creativity of all the investigators who are actively engaged in this rapidly developing emerging new field of research.

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