

Preface

In the spring of 1998 my co-editor, colleague and friend, Randy Jirtle, approached me at a scientific meeting in San Diego, CA to discuss something that clearly had him excited. Initiating our discussion, Randy displayed the unbridled enthusiasm that is so characteristic of him. He advised me that he had spoken with my boss about organizing an international scientific meeting that would merge an evolving field with toxicology. That field was genomic imprinting and on that afternoon as we sat, he was effusive in his description of monoallelic expression. While this was not my first time hearing about genomic imprinting or the field of epigenetics that imprinting is a component of, I realized I was becoming fascinated with the opportunity to work with Randy and make an impact on merging aspects of toxicology and epigenetics.

In 1998, we had no way of knowing where that initial conversation would lead us, but we began crafting a vision to merge toxicology with epigenetics, as it was clear that the environment plays a pivotal role with epigenetic processes. It is now reasonable to argue that this vision is being shared globally, after organizing three extremely well attended international scientific meetings focusing on the interactions between environmental agents, epigenetics, and disease susceptibility.

What has in fact transpired with regard to developing the interface between epigenetics and environmental exposures over the last 15 years has been nothing short of remarkable. The advent of high throughput technologies such as genome-wide bisulfite sequencing, along with ChIP-Seq, RNA-Seq and technologies to map chromatin accessibility resulted in the generation of terabytes of data. Novel computational tools have been and are continually being developed to both store data and analyze it, as well. Investments in large multi-institutional consortia such as the NIH Roadmap Epigenome Mapping Consortium (REMC), the NHGRI supported ENCODE program, and the International Human Epigenome Consortium (IHEC) have spurred the development of these technologies and analytic tools.

There are compelling human epidemiological and animal experimental data that indicate the risk of developing adult-onset complex diseases and neurological disorders is influenced by persistent epigenetic adaptations in response to prenatal and early postnatal exposures to environmental factors. The epigenetic programs

are established as stem cells differentiate during embryogenesis, and are faithfully reproduced during mitosis. Moreover, they can also be maintained during meiosis. The plasticity of the epigenome allows the genome to express specific gene programs in a cell specific pattern that is spatially and temporally regulated, resulting in phenotypes. The capacity of the epigenome to interpret both internal and external stimuli and alter expression programs is a critical component in normal development, aging, and disease pathogenesis. In the past decade, our field has witnessed an explosion of unprecedented research on and support for epigenetics, epigenomics, and their interface with human health and disease. This research is in large measure an effort to generate a more precise understanding of how DNA and gene expression are regulated by DNA sequence, functional DNA elements, chromatin states, epigenomic signatures, and epigenetic processes.

It is becoming increasingly apparent that exposure to environmental toxicants can be associated with epigenetic changes, such as altered patterns of DNA methylation. These changes can affect gene expression patterns, and likely contribute to disease or other phenotypes associated with exposure. DNA methylation is thought to be one of the last steps of epigenetic gene regulation – a read-out of chromatin states established by other proteins. In order to understand the mechanism by which toxicants impact gene expression, we must examine how exposures perturb the proteins and processes upstream of DNA methylation and other epigenetic marks.

Epigenetic modifications, such as DNA methylation or post-translational modifications to histone tails, modifies the DNA and/or the way it is packaged into chromatin, making certain genes either more or less accessible to trans-acting elements, such as transcription factors. These epigenetic marks, however, represent limited facets in this complex process. Other proteins or protein complexes act as ‘readers’, ‘writers’ and ‘erasers’ of the epigenetic code, depositing or removing epigenetic marks or binding to them and recruiting other proteins. In addition, other factors such as non-coding RNAs, chromatin remodeling complexes, inter- and intra-chromosomal interactions and functional genomic elements play important roles in this process. Thus, to understand the mechanisms involved in the environmental control of gene regulation and the central role of epigenetics in the process, it is critical to understand all of the interacting pathways.

Exposure to environmental toxicants has been associated with changes in gene expression and DNA methylation profiles, which together likely contribute to disease or other phenotypes associated with exposure. The chapters in these volumes address a wide range of environmental exposures, such as airborne particulates, cocaine, radiation, tobacco smoke, and xenoestrogens. The health outcomes associated with these exposures include autoimmune disorders, neurodevelopmental disorders, and cancer. Importantly, dietary supplements and drugs can modify the epigenetic effects induced by these agents, thereby reducing their toxicological impact.

In the two volumes of this book, a number of leading investigators in the field of epigenetics discuss patterns of epigenomic modifications in normal cells, and how environmentally-induced changes in them are associated with disease pathogenesis.

The authors comprehensively review epigenetic processes that occur in human embryonic stem cells, as well as in differentiating cells and organs such as the brain, discussing autism, schizophrenia, and even sexual dimorphism in the developing brains of males and females. Particular emphasis is placed on the consequences of environmental exposures during development on epigenetic reprogramming that influences adult disease pathogenesis.

The overall purpose of this book is to give readers an overview of how environmental exposures can influence the development of disease by disrupting epigenetic processes and reprogramming. When Randy approached me in 1998 at the scientific meeting in San Diego, I had no idea what we would accomplish together in moving this field forward. He has been able to produce many significant contributions to the field directly from his laboratory research. Moreover, he has trained a cadre of young investigators who will continue to make an impact in enhancing our understanding of how the environment can alter epigenetic processes and influence the development of human disease. I, on the other hand, have been privileged to be among the extramural scientists at the National Institutes of Health (NIH) who develop research programs that support cutting edge science in moving this field forward.

Since that initial conversation, Randy and I have collaborated on a number of epigenetic projects. This book represents our latest collaboration to bring this field of environmental epigenomics to a growing audience. It is my desire that the readers learn as much, and have as much fun reading the chapters that constitute both volumes of this book as I did.

Frederick L. Tyson, Ph.D.

Environmental Epigenomics in Health and Disease

Epigenetics and Disease Origins

Jirtle, R.L.; Tyson, F.L. (Eds.)

2013, XV, 302 p., Hardcover

ISBN: 978-3-642-23379-1