Brain, Behavior, and Immunity 25 (2011) 25–39

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

Named Series: Epigenetics, Brain, Behavior, and Immunity

# Epigenetics and psychoneuroimmunology: Mechanisms and models

ARTICLE INFO

*Keywords:*
Epigenetics
Chromatin
Stress responsivity
Behavior
Hypothalamic–pituitary–adrenal axis

ABSTRACT

In this Introduction to the Named Series "Epigenetics, Brain, Behavior, and Immunity" an overview of epigenetics is provided with a consideration of the nature of epigenetic regulation including DNA methylation, histone modification and chromatin re-modeling. Illustrative examples of recent scientific developments are highlighted to demonstrate the influence of epigenetics in areas of research relevant to those who investigate phenomena within the scientific discipline of psychoneuroimmunology. These examples are presented in order to provide a perspective on how epigenetic analysis will add insight into the molecular processes that connect the brain with behavior, neuroendocrine responsivity and immune outcome.



## 1. Introduction

A remarkable growth in the understanding of epigenetics and the impact of epigenetics on contemporary biology has occurred in recent years. This growth in the field of epigenetics has transformed our conceptualization of the impact of the environment upon our genes and upon our health (Feinberg, 2008). As well, the study of epigenetics has fueled research in the behavioral sciences, as recent work demonstrates that epigenetic modifications shape behavior, modulate stress responsivity, and alter immune function. This facet of epigenetics seeks to understand the interactive linkages that connect the psychological and social environment with the epigenetic processes that modulate gene expression and influence behavior (Zhang and Meaney, 2010). In a similar manner, the integrative field of psychoneuroimmunology continues to advance the understanding of the complex networks that connect brain, behavior and immunity. In that field, attention is now focused on the analysis and understanding of the molecular processes, which underlie these complex networks. This understanding, viewed through the lens of epigenetics, provides for a new opportunity to address long-standing as well as emerging issues in psychoneuroimmunology.

The psychosocial context of the environment can substantially change behavior and alter nervous, endocrine and immune function (Eskandari and Sternberg, 2002). Recent findings within the realm of behavioral epigenetics demonstrate that stressors and/or adverse psychosocial environments can affect gene expression by altering the epigenetic pattern of DNA methylation and/or chromatin structure. The vast majority of existent evidence within the scope of behavioral epigenetics emanates from investigations of early life adversity that produce epigenetic modifications within relevant brain regions that influence behavior. As well, emerging evidence shows that, adults also respond epigenetically to environmental signals, which in turn influence behavior, physiological outcome, and disease risk (Feinberg, 2008; Foley et al., 2009; Handel et al., 2010). At this time, however, few studies have evaluated whether the epigenome of cells and tissues of the immune system is sensitive to the environmental context, and this area provides ample opportunity for further exploration. What is clear, however, is that the advances in this field add to the "seductive allure of behavioral epigenetics," which has generated intense interest within many scientific disciplines (Miller, 2010). Given the central influence of the environment on the integrative network that links brain, behavior, and immunity; this allure promises to invigorate many facets of investigation in psychoneuroimmunology that seek to unravel how environmental signals are transduced to the genome.

The overarching mission of this Journal is to understand the behavioral, neural, endocrine, and immune system interactions relevant to health and disease. With this in mind, the purpose of this Introduction to the Named Series "Epigenetics, Brain, Behavior, and Immunity" is to; provide an overview of epigenetic processes, present available examples of scientific inquiry demonstrating the influence of epigenetics relevant to psychoneuroimmunology, and finally to provide a perspective on future possibilities wherein epigenetics may significantly enrich the understanding of the associations that exist among brain, neuroendocrine, immune and behavioral processes.

## 2. Overview of epigenetic processes

### 2.1. The epigenome

Epigenetics refers to a variety of processes that affect gene expression independent of actual DNA sequence. Epigenetic information provides instruction on how, where, and when, genetic information will be used. Hence, the importance of epigenetic information is that it regulates gene expression. Epigenetics can refer to heritable effects on gene expression, or to the stable long-term alteration of the transcriptional potential of a cell, which may not necessarily be heritable. Most importantly, epigenetic information is susceptible to change, and as such, represents an

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doi:10.1016/j.bbi.2010.08.009

marks in other disease associated tissues. Epigenetic marks are tissue and cell specific, as well as dependent on stage of life and gender. Evaluation of postmortem specimens provides useful data but is also fraught with issues related to tissue preservation and retrospective design limitations. Yet, significant insight regarding environmental-signaled epigenetic modifications in human tissues and cells may be gleaned from the evaluation of surgically removed tissues/organs. Despite these challenges, integrating epigenetics into human investigations in psychoneuroimmunology offers exciting possibilities for the future. Such studies can provide key insight regarding the impact of environment–gene interaction on behavior and vulnerability to disease over the lifespan. Likewise, understanding those epigenetic processes that contribute to a resilient phenotype in human paradigms can lead to new insight about individual differences in response to environmental challenge.

In conclusion, it is likely that epigenetic patterns translate or at least contribute to the relationship between the environment and human health. This possibility opens wide a vista of potential interventions, including behavioral or dietary interventions that can take advantage of the plasticity of the epigenome (Handel et al., 2010). Interventions aimed at manipulating the epigenome are currently underway for many hematological malignancies and many more will follow. Direct manipulation of the epigenome is a real and promising possibility (Feinberg, 2008). Although there is much work to do, epigenetics and the epigenome deserve consideration for any investigation analyzing the linkages among brain, behavior, and immunity. The scope of epigenetics offers ample opportunity to chart new directions in basic, translational, and clinical research within the broad framework of psychoneuroimmunology. Important questions await investigation that can integrate multiple levels of inquiry, from molecular to behavioral. More than 25 years ago, scientists were captivated by the allure of the emerging field of psychoneuroimmunology. At this juncture, it is now clear that psychoneuroimmunology and the emerging field of epigenetics share a common vision that guides discovery, and the fusion of these two fields can only lead to remarkable scientific advancements.

## Conflicts of interest

Authors declare that there are no conflicts of interest.

## Acknowledgments

The study was supported in part by the National Cancer Institute R21-CA–117261 and R01-CA-134736. The authors gratefully acknowledge the expertise of Kelly Loster Kosik in the preparation of the manuscript.

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Herbert L. Mathews
*Department of Microbiology and Immunology, Stritch School of Medicine, Loyola University of Chicago, 2160 South First Ave., Maywood, IL 60153, USA*
*Fax: +1 708 216 9574.*
*E-mail address*: hmathew@lumc.edu

Linda Witek Janusek
*Marcella Niehoff School of Nursing, Department of Health Promotion, Loyola University of Chicago, Maywood, IL 60153, USA*