

Selected references – Isabelle Mansuy

Bohacek, J., Gapp, K., Saab, B. J., & Mansuy, I. M. (2013). Transgenerational epigenetic effects on brain functions. *Biological Psychiatry*, 73, 313-320.

Notes: Psychiatric diseases are multifaceted disorders with complex etiology, recognized to have strong heritable components. Despite intense research efforts, genetic loci that substantially account for disease heritability have not yet been identified. Over the last several years, epigenetic processes have emerged as important factors for many brain diseases, and the discovery of epigenetic processes in germ cells has raised the possibility that they may contribute to disease heritability and disease risk. This review examines epigenetic mechanisms in complex diseases and summarizes the most illustrative examples of transgenerational epigenetic inheritance in mammals and their relevance for brain function. Environmental factors that can affect molecular processes and behavior in exposed individuals and their offspring, and their potential epigenetic underpinnings, are described. Possible routes and mechanisms of transgenerational transmission are proposed, and the major questions and challenges raised by this emerging field of research are considered

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Bohacek, J. & Mansuy, I. M. (2013). Epigenetic inheritance of disease and disease risk. *Neuropsychopharmacology*, 38, 220-236.

Notes: Epigenetic marks in an organism can be altered by environmental factors throughout life. Although changes in the epigenetic code can be positive, some are associated with severe diseases, in particular, cancer and neuropsychiatric disorders. Recent evidence has indicated that certain epigenetic marks can be inherited, and reshape developmental and cellular features over generations. This review examines the challenging possibility that epigenetic changes induced by environmental factors can contribute to some of the inheritance of disease and disease risk. This concept has immense implications for the understanding of biological functions and disease etiology, and provides potential novel strategies for diagnosis and treatment. Examples of epigenetic inheritance relevant to human disease, such as the detrimental effects of traumatic stress or drug/toxic exposure on brain functions, are reviewed. Different possible routes of transmission of epigenetic information involving the germline or germline-independent transfer are discussed, and different mechanisms for the maintenance and transmission of epigenetic information like chromatin remodeling and small noncoding RNAs are considered. Future research directions and remaining major challenges in this field are also outlined. Finally, the adaptive value of epigenetic inheritance, and the cost and benefit of allowing acquired epigenetic marks to persist across generations is critically evaluated

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Franklin, T. B., Saab, B. J., & Mansuy, I. M. (2012). Neural mechanisms of stress resilience and vulnerability. *Neuron*, 75, 747-761.

Notes: Exposure to stressful events can be differently perceived by individuals and can have persistent sequelae depending on the level of stress resilience or vulnerability of each person. The neural processes that underlie such clinically and socially important

differences reside in the anatomical, functional, and molecular connectivity of the brain. Recent work has provided novel insight into some of the involved biological mechanisms that promises to help prevent and treat stress-related disorders. In this review, we focus on causal and mechanistic evidence implicating altered functions and connectivity of the neuroendocrine system, and of hippocampal, cortical, reward, and serotonergic circuits in the establishment and the maintenance of stress resilience and vulnerability. We also touch upon recent findings suggesting a role for epigenetic mechanisms and neurogenesis in these processes and briefly discuss promising avenues of future investigation
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Franklin, T. B. & Mansuy, I. M. (2011). The involvement of epigenetic defects in mental retardation. *Neurobiology of Learning and Memory*, 96, 61-67.

Notes: Mental retardation is a group of cognitive disorders with a significant worldwide prevalence rate. This high rate, together with the considerable familial and societal burden resulting from these disorders, makes it an important focus for prevention and intervention. While the diseases associated with mental retardation are diverse, a significant number are linked with disruptions in epigenetic mechanisms, mainly due to loss-of-function mutations in genes that are key components of the epigenetic machinery. Additionally, several disorders classed as imprinting syndromes are associated with mental retardation. This review will discuss the epigenetic abnormalities associated with mental retardation, and will highlight their importance for diagnosis, treatment, and prevention of these disorders

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Mansuy, I. M. & Mohanna, S. (2011). Epigenetics and the human brain: where nurture meets nature. *Cerebrum.*, 2011, 8.

Notes: While our genetic code determines a great deal of who and what we are, it does not act alone. It depends heavily on the epigenome, an elaborate marking of the DNA that controls the genome's functions. Because it is sensitive to the environment, the epigenome is a powerful link and relay between our genes and our surroundings. Epigenetic marks drive biological functions and features as diverse as memory, development, and disease susceptibility; thus, the nurture aspect of the nature/nurture interaction makes essential contributions to our body and behaviors. As scientists have learned more about how the epigenome works, they have begun to develop therapies that may lead to new approaches to treating common human conditions