The last decade witnessed the confluence of two rapidly evolving Biomedical disciplines: Epigenetics and Neurobiology. Although key seminal articles investigating the interplay between epigenetic mechanisms and neuronal plasticity and behavior were published decades earlier, the number of such studies has dramatically increased in recent years. These studies have demonstrated that the epigenetic regulation of chromatin, via conformational and chemical modifications of its components, primarily DNA methylation and the post-translational modification of histones, is not restricted to dividing cells but also plays a critical role in neurons. Neuronal activity can alter the epigenetic state of neuronal genes and, in turn, these epigenetic changes can influence the future responses of the neuron and thereby have important consequences in brain function and dysfunction. From development to experience-driven remodeling of neuronal circuits, from drug addiction to schizophrenia, the investigation of epigenetic mechanisms in neuronal function is having a major impact in the Neurosciences.

This Special Issue of Neuropharmacology on Neuroepigenetic disorders brings together leading experts in the emerging area of Neuroepigenetics to review the impressive and rapid progress that took place during the last few years and to define the challenges ahead. A wide variety of topics are examined that range from basic molecular mechanisms underlying cognitive processes in the normal brain to the etiology of different neuropsychiatric disorders. Thus, the first half of this Special Issue is primarily dedicated to review the mechanisms involved in the regulation and function of epigenetic processes in the normal brain. It starts with an authoritative review by J. David Sweatt and colleagues, who have played a seminal role in the development of this area of research, discussing the role of the main epigenetic modifications of the chromatin in two forms of plasticity that critically contribute to higher brain function: intrinsic and synaptic plasticity (Guzman-Karlsson et al., 2014). Then follow articles that cover the whole panel of epigenetic mechanisms that are being investigated in neurons and that are likely to contribute to neuroplasticity processes, including the regulation of higher-order (Vogel-Ciernia and Wood, 2014) and 3D (Wilczynski, 2014) chromatin organization, the regulation of histone modifications by activity-dependent kinases (Ciccarelli and Giustetto, 2014), and the specific contribution of transcriptional repressor complexes (Adachi and Monteggia, 2014, Schoch and Abel, 2014) and microRNAs (Saab and Mansuy, 2014) to epigenetic regulation. Although some of these articles already introduce the important contribution of epigenetic dysregulation to brain pathology, this topic is discussed in greater detail in the second half of the Special Issue, which is more clinically oriented. The introductory and comprehensive article by Tsai’s group discussing the role of histone acetylation and DNA methylation in brain disorders (Rudenko and Tsai, 2014) is followed by timely and up to date reviews dedicated to specific brain conditions, such as congenital intellectual disability disorders (Kleefstra et al., 2014), Alzheimer’s disease (Fischer, 2014), Huntington’s disease (Valor and Guiretti, 2014), stress-related brain disorders (Klengel et al., 2014) and schizophrenia and bipolar disorder (Kato and Iwamoto, 2014).
Together, these review articles reflect a complex and exciting mosaic of novel findings and theories that offers a fresh perspective on unsolved problems in Neurosciences.

The rapid progress presented here was driven by the fascinating implications of considering chromatin as a novel and suitable substrate for memory storage and by the identification of epigenetic dysregulation as an essential component in the etiology of many brain disorders. As often occurs with rapidly developing areas of research, the new findings led to even more questions. As discussed in several articles in this Special Issue, the ongoing development and refinement of genome-wide techniques to explore the epigenome, in combination with physiological experiments, announces a second phase of discoveries that have the potential to radically change our view on the role of epigenetic mechanisms in behavior and brain function. In the near future, these techniques will allow the analysis of the profiles and dynamics of specific epigenetic marks in restricted neuronal populations, for example, the cells responding to a given stimuli or specifically affected by a given pathology. This Special Issue aims to serve as a turning point for both evaluating the exciting developments that occurred in past years and the broad research horizon ahead.