NEUROEPIGENETICS: A DISCIPLINE WITH NEW PERSPECTIVES FOR BRAIN RESEARCH

Isabelle Mansuy
Laboratory of Neuroepigenetics University and ETH Zürich Brain Research Institute, Switzerland

In recent years, the field of epigenetics has emerged as one of the most exciting and promising fields of biology envisioned to have an immense impact on medical research. At the crossroads between epigenetics and neuroscience, neuroepigenetics is a new research area that explores how epigenetic factors and mechanisms contribute to brain functions in health and disease, not only across the lifespan, but also across generations and across evolution. Recent discoveries in neuroepigenetics have established that epigenetic factors are key regulators of gene activity in the developing nervous system and the adult brain, and have provided important new knowledge for the comprehension of the brain genome. They revealed that brain functions are modulated by a combination of genetic and environmental factors and that several epigenetic factors are recruited. Further importantly, the discipline is also initiating a paradigm shift on the question of the heredity of brain functions and behaviors. It provided initial evidence that acquired traits, in particular behaviors gained by experience or exposure to particular environments, whether positive or negative, can be transmitted across generations just like innate traits. The question of the inheritance of acquired traits has long been debated and experimental evidence in environmental toxicology, nutritional science and metabolic research has accumulated in the past years. A wide range of environmental factors including trauma, stress, diet, endocrine disruptors but also enriched living conditions are now known to directly alter epigenetic programming during development and influence physiology and disease susceptibility later in life. While epigenetic marks in the brain are modified by these factors, marks in gametes (oocyte or sperm cells) can also be affected. When this happens and the alterations are stable, transgenerational epigenetic inheritance is possible and can ultimately lead to phenotypic variation and disease susceptibility in individuals across generations. New research in the past 2-3 years has started to identify some of the mechanisms involved. They implicate DNA methylation, non-coding RNAs and/or post-translational modifications of histone proteins in germ cells. These marks can be affected transiently or permanently depending on the severity, time window and duration of the environmental exposure. Such form of environmentally-induced inheritance can impact biological processes from disease etiology to the course of evolution.

The mission of future researchers in the field will be to identify the ensemble of these modifications, and determine their functional relevance for behaviors and brain diseases, and their transmission across generations. It shall help identify biomarkers relevant to early life or ancestral exposures and associated later-life diseases. The use of such biomarkers should allow early stage diagnostics prior to disease development, such that preventive medicine could become a reality. Ultimately, research in neuroepigenetics in the future is expected to have a triple conceptual, medical and societal impact. It promises to revolutionize medicine and public health, and nourish personalized medicine. This research shall also bring new prospects for the theories of evolution.