Epigenomics of Rare Disease

Some rare diseases have an epigenetic component or involve epigenetically regulated genes [[5](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#5)]. While genetic mutations are very rare, epigenetic changes are common and occur through our lifetimes. Therefore, when discussing the etiologic factors in some rare diseases, the interplay between genetics and epigenetics should be considered. The current definition of epigenetics is “the study of heritable changes in gene expression that occur independent of changes in the primary [DNA sequence](https://www.omicsgroup.org/journals/variant-maps-to-identify-coding-and-noncoding-dna-sequences-of-genomes-selected-from-multiple-species-2329-6577-1000153.php?aid=70955)” [[6](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#6)]. At the molecular level: DNA methylation, histone modification, and RNA-associated silencing are currently defined as the three main inter-related mechanism of epigenetic inheritance [[6](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#6)]. Disruption of one or other of these interacting systems caused by genetic, environmental factors as well as stress, diet, lifestyle, and aging can lead to inappropriate expression or silencing of genes, resulting in “epigenetic diseases” [[6](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#6)]. In particular, the nervous system represents an immensely complex structure and makes it especially sensitive to these epigenetic changes, and consequently, many mental disorders are caused by mutations in the epigenetic machinery [[7](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#7)]. For examples, genetic mutations of genes related to DNA methylation found in [Rett syndrome](https://www.omicsonline.org/rett-syndrome.php" \t "_blank) (RTT) (due to mutations in the methyl-binding domain protein MeCP2) [[8](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#8)], and in [immunodeficiency](https://www.omicsonline.org/internal-medicine/immunodeficiency.php) centromere instability facial syndrome 1 (ICF1) (due to mutations in the DNA methyltransferase DNMT3) [[9](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#9),[10](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#10)] or to histone modifiers found in Rubinstein-Tabi syndrome (RTS) (due to mutations in the histone acetyltransferase p300/CBP) [[11](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#11)], and in Sotos syndrome (associated with mutations in the histone methyltransferase NSD1) [[12](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#12)]. As new members of the epigenetic machinery are described, the number of human syndromes associated with epigenetic alterations increases [[13](http://raredisorders.imedpub.com/epigenetics-in-rare-diseases.php?aid=19195#13)].

### Epigenomics of Common Disease

Genome-wide association studies (GWAS) have identified a multitude of genetic variants associated with complex traits including common diseases. However, their effect sizes are modest and the majority of causality remains unexplained for most common diseases. The aim of this project is to integrate GWAS with epigenome-wide association studies (EWAS) to gain a more complete picture of the aetiology of common diseases.