Chromatin-related Intellectual disability syndromes: Molecular etiology and therapy, (ChromISyn)

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Intellectual development disorders represent one of the biggest medical challenges in our society. Their cause includes the mutation of genes encoding proteins involved in the regulation of gene expression through changes in the chromatin. Our proposal focuses on one of such disorders, the Rubinstein-Taybi syndrome (RSTS). This rare genetic disorder is caused by mutation in the genes that encode the proteins CBP and p300. These two proteins mediate the acetylation of the chromatin, a chemical reaction that is thought to favor transcription. Here, we propose to investigate the role of these two proteins in development of the nervous system, neuronal plasticity in the adult brain, and pathophysiology of cells derived from patients. Next, we will take advantage of recent technological advances that allow a comprehensive and fully unbiased analysis of changes in the chromatin, to identify the molecular mechanisms underlying the defects observed in the cells from patients and animal models of the disease. Finally, we will also use novel techniques that allow a precise manipulation of the chromatin to correct the detected alterations and assess whether this correction ameliorates or eliminates the observed defects. Of note, the impact of our project goes well beyond RSTS because other intellectual development disorders are likely to affect the same processes.