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Comparative analysis of ChIP-seq peak calling methods

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Over the past two centuries, the age at menarche has advanced from 17 years of age to 12 years of age in most western nations. This is alarming not only due to the psychological impacts for females, but also the physical effects such as a higher risk for breast and uterine cancer. Genome-wide association studies have demonstrated the existence of more than 100 polymorphisms associated with the timing of female puberty, yet these modifications in the DNA sequence together explain less than 5% of pubertal disorders. The inescapable conclusion is that information other than that provided by DNA must play a role. Hence, the Lomniczi Lab has been studying epigenetic mechanisms as a means of integrating cues and coordinating gene networks involved in the neuroendocrine control of puberty. This project aims at identifying new genomic areas controlled by this mechanism during pubertal development of the hypothalamus. We performed ChIP-Seq—Chromatin Immunoprecipitation (ChIP) assays followed by Whole Genome Sequencing (Seq)—to analyze the epigenetic landscape of the hypothalamus at different ages. The specific aim of this project is to compare two methods of ChIP-Seq data peak calling and analysis in order to: 1) generate a precise landscape of chromatin modifications of the hypothalamus during pubertal development and 2) save money and time. A comparative analysis was performed between peaks called from MACS, the current industry method using reference DNA and ritornello, a reference-free method. Ritornello was found to be more restrictive than MACS based on peak count but it may be too restrictive to be effective alone. Thus, it is recommended that ritornello be used as a double-checking method for MACS.

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