Published in final edited form as:
Nat Neurosci. 2013 March ; 16(3): 281–289. doi:10.1038/nn.3319.

Epigenetic Control of Female Puberty

Alejandro Lomniczi[1], **Alberto Loche**[1], **Juan Manuel Castellano**[1], **Oline K. Ronnekleiv**[1,2], **Martha Bosch**[2], **Gabi Kaidar**[1], **J. Gabriel Knoll**[1], **Hollis Wright**[1], **Gerd. P. Pfeifer**[3], and **Sergio R. Ojeda**[1]

The timing of puberty is controlled by many genes. The elements coordinating this process have not, however, been identified. Here we show that an epigenetic mechanism of transcriptional repression times the initiation of female puberty in rats. We identify silencers of the Polycomb group (PcG) as major contributors to this mechanism, and show that PcG proteins repress *Kiss1*, a puberty-activating gene. Hypothalamic expression of two key PcG genes, *Eed* and *Cbx7*, decreases and methylation of their promoters increases preceding puberty. Inhibiting DNA methylation blocks both events and results in pubertal failure. The pubertal increase in *Kiss1* is accompanied by EED loss from the *Kiss1* promoter and enrichment of histone H3 modifications associated with gene activation. Preventing the eviction of EED from the *Kiss1* promoter disrupts pulsatile GnRH release, delays puberty, and compromises fecundity. Our results identify epigenetic silencing as a novel mechanism underlying the neuroendocrine control of female puberty.