

Cellular differentiation is, by definition, epigenetic. Genome-wide profiling of pluripotent cells and differentiated cells suggests global chromatin remodelling during differentiation, which results in a progressive transition from a fairly open chromatin configuration to a more compact state. Genetic studies in mouse models show major roles for a variety of histone modifiers and chromatin remodellers in key developmental transitions, such as the segregation of embryonic and extra-embryonic lineages in blastocyst stage embryos, the formation of the three germ layers during gastrulation and the differentiation of adult stem cells. Furthermore, rather than merely stabilizing the gene expression changes that are driven by developmental transcription factors, there is emerging evidence that chromatin regulators have multifaceted roles in cell fate decisions.

Recurrent mutations in [chromatin modifiers](#) are specifically prevalent in [adolescence](#) or [adult](#) patients with [Sonic hedgehog medulloblastoma](#) (SHH MB). Merk et al. report that mutations in the acetyltransferase [CREBBP](#) have opposing effects during the development of the cerebellum, the primary site of origin of SHH MB. Our data reveal that loss of Crebbp in cerebellar granule neuron progenitors (GNPs) during embryonic development of mice compromises GNP development, in part by downregulation of brain-derived neurotrophic factor (Bdnf). Interestingly, concomitant cerebellar hypoplasia was also observed in patients with Rubinstein-Taybi syndrome, a congenital disorder caused by germline mutations of CREBBP. By contrast, loss of Crebbp in GNPs during postnatal development synergizes with oncogenic activation of SHH signaling to drive MB growth, thereby explaining the enrichment of somatic CREBBP mutations in SHH MB of adult patients. Together, our data provide insights into time-sensitive consequences of CREBBP mutations and corresponding associations with human diseases ¹⁾.

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Merk DJ, Ohli J, Merk ND, Thatikonda V, Morrissy S, Schoof M, Schmid SN, Harrison L, Filser S, Ahlfeld J, Erkek S, Raithatha K, Andreska T, Weißhaar M, Launspach M, Neumann JE, Shakarami M, Plenker D, Marra MA, Li Y, Mungall AJ, Moore RA, Ma Y, Jones SJM, Lutz B, Ertl-Wagner B, Rossi A, Wagener R, Siebert R, Jung A, Eberhart CG, Lach B, Sendtner M, Pfister SM, Taylor MD, Chavez L, Kool M, Schüller U. Opposing Effects of CREBBP Mutations Govern the Phenotype of Rubinstein-Taybi Syndrome and Adult SHH Medulloblastoma. *Dev Cell*. 2018 Mar 9. pii: S1534-5807(18)30107-2. doi: 10.1016/j.devcel.2018.02.012. [Epub ahead of print] PubMed PMID: 29551561.

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