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, this data provide insights into time-sensitive consequences of CREBBP mutations and corresponding associations with human diseases [1].

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