

Essential Roles of the of SWI/SNF-like BAF Chromatin Remodeling Complexes in Thymocyte Development

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T cells develop through distinct stages directed by a series of signals. We explored the roles of SWI/SNF-like BAF chromatin remodeling complexes in this process by gradual deletion of the ATPase subunit Brg through several stages of early T cell development. Brg-deficient cells were blocked at each of the transitions examined. Bcl-xL overexpression suppressed cell death and led to cell accumulation, but could not relieve the blockades. Brg deletion completely abolished *Myc* expression, resulting in *P21CIP1/WAF1* induction and cell cycle arrest in the Bcl-xL rescued cells. Brg directly bound the Wnt-regulated *Myc* promoter at a proximal TCF site, which has important implications for the mechanisms of *Myc* activation through DNA melting. Multiple other Wnt target genes including *c-Kit* were also misregulated, revealing an essential role of Brg in Wnt signaling in T cells. In addition, a subset of pre-TCR dependent events was blocked in Brg-deficient cells. Despite the general requirement of Brg for developmental progressions, Brg is not a global gene regulator. We propose that specific signaling pathways use Brg not only to directly regulate transcription, but also to progressively pattern chromatin through successive stages of development.

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