FEATURED ARTICLES

BAFfle the critics*Neuroscience Gateway* (October 2007) | doi:10.1038/aba1789**Neuron-specific chromatin remodeling regulates dendritic outgrowth and morphology during development.**

In some houses, pulling up an old carpet reveals a handsome hardwood floor. As in home improvement, chromatin remodeling uncovers hidden elements, permitting transcription factors to access DNA. What is the function of chromatin remodeling in the brain? Wu *et al.* report that ATP-dependent chromatin remodeling regulates dendritic growth in a recent article in *Neuron*.

In mammals, the Brahma-related gene (BRG)/Brahma (BRM)-associated factor (BAF) complex mediates ATP-dependent chromatin remodeling. The BAF complex contains 10 proteins, several of which have multiple gene isoforms. Therefore, depending on the combination of isoforms, the BAF complex can exercise a high degree of specificity in the transcripts that it regulates. BAF45a and the actin-related protein [BAF53a](#) are necessary for the proliferation of neural progenitor cells. These isoforms are replaced by BAF45b and [BAF53b](#) during neuron differentiation. The authors generated mice lacking *BAF53b*, which is exclusively expressed in neurons. Despite normal embryo development, most *BAF53b* knockout mice died within 2 days of birth, suggesting an important role for this molecule in development.

BAF53b-deficient neurons show dendritic defects. When cultured at low density for a long period of time (16 days), hippocampal neurons from *BAF53b* knockout embryos showed reduced dendritic branching and a 50% reduction in dendritic length relative to hippocampal neurons from wild-type mice. Dendritic growth occurs in activity-independent and activity-dependent phases. After 5 days *in vitro*, *BAF53b* knockout and wild-type cultures of hippocampal, cerebellar and cortical neurons were similar. However, following depolarization induced by potassium chloride, neurons from *BAF53b* knockout mice showed reduced dendritic length and complexity relative to neurons from wild-type mice, suggesting that *BAF53b* is important in activity-dependent dendritic growth.

Researchers previously showed that the Ca^{2+} -responsive transcriptional coactivator [CREST](#) is important in activity-dependent dendritic remodeling. CREST induces transcription but does not bind DNA directly. CREST coimmunoprecipitated with both *BAF53b* and *Brg*, suggesting that the BAF complex may regulate dendritic growth by recruiting CREST to DNA.

Which genes are regulated by the BAF complex? *BAF53b* knockout mice showed reduced expression of several genes involved in neurite growth, including [GAP43](#), [Rap1a](#), [Gprin1](#) and [Ephexin1](#). Ephexin1 is a Rho guanine exchange factor that is important in

axon and growth cone extension. Previous studies showed reduced *Ephexin1* expression in *CREST* knockout relative to wild-type neurons. *Ephexin1* expression rescued normal activity-dependent dendritic extension and branching in *BAF53b* knockout mice, suggesting that *Ephexin1* deficiency may mediate the dendritic defects in *CREST* and *BAF53b* knockout mice. Chromatin immunoprecipitation showed reduced binding of Brg/Brm and CREST to *Ephexin1* and *GAP43* promoters in *BAF53b* knockout relative to wild-type neurons.

BAF53a did not rescue lethality or dendritic growth in *BAF53b* knockout mice. The BAF53 isoforms differ most in actin fold subdomain 2, which is involved in protein-protein interactions. BAF53a engineered to contain subdomain 2 from BAF53b but not BAF53b containing subdomain 2 of BAF53a did rescue normal dendritic growth in *BAF53b* knockout mice. Therefore, a protein interaction domain confers specific roles for BAF53 isoforms in neuronal differentiation and synaptogenesis.

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1. Wu, J. I. *et al.* Regulation of dendritic development by neuron-specific chromatin remodeling complexes. *Neuron* **56**, 94–108 (2007). | [Article](#) | [PubMed](#) |