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UNDERSTANDING THE ROLE OF PRDM12B IN ZEBRAFISH DEVELOPMENT

Function of the adult nervous system relies on the appropriate establishment of neural circuits during embryogenesis. In vertebrates, the neurons that make up motor circuits form in distinct domains along the dorsoventral (DV) axis of the neural tube. Each domain is characterized by a unique combination of transcription factors (TFs) that promote a specific fate, while repressing the fates of adjacent domains. The *prdm12* TF is required for the expression of *eng1b* and the generation of V1 interneurons in the p1 domain, but the details of its function remain unclear.

We used CRISPR/Cas9 genome editing technology to generate the first germline mutants for the *prdm12* gene and used this resource, together with classical luciferase reporter assays and co-immunoprecipitation experiments, to study *prdm12b* function in zebrafish. We also generated germline mutants for *bhlhe22* and *nkx6.1* to examine how these TFs act with *prdm12b* to control p1 formation.

We find that *prdm12b* mutants lack *eng1b* expression in the p1 domain and also possess an abnormal Mauthner cell-dependent escape response. Using cell culture-based luciferase reporter assays, we demonstrate that Prdm12b acts as transcriptional repressor, most likely by recruiting EHMT2/G9a. We also show that the Bhlhe22 TF binds to the Prdm12b zinc finger domain to form a Bhlhe22:Prdm12b complex. However, *bhlhe22* mutants display normal *eng1b* expression in the p1 domain. While *prdm12* has been proposed to promote p1 fates by repressing expression of the *nkx6.1* TF, we do not observe an expansion of the *nkx6.1* domain upon loss of *prdm12b* function, nor is *eng1b* expression restored upon simultaneous loss of *prdm12b* and *nkx6.1.*

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