Sox10-GFP/DTA transgenic mice

Category

Biological Materials/Genetically Modified Organisms

This line, Sox10-lox-eGFP-polyA-lox-DTA (referred to as Sox10-GFP/DTA) was designed for studies of oligodendrocyte (OL) lineage cells but, with an appropriate Cre driver, could be used for any Sox10-expressing cell population (e.g. Schwann cells). In the absence of Cre, GFP labels the entire OL lineage (as well as other cells outside the CNS that express Sox10). In the presence of Cre, DTA expression results in death of all Cre/Sox10-expressing cells.

To generate the Sox10-lox-eGFPpolyA-lox-DTA transgene, we used a 120Kb NotI fragment from a Sox10 genomic PAC isolated from library RCPI-21 from the UK HGMP Resource Centre. The library contains genomic DNA from a female mouse strain 129S6/SvEvTac (Osoegawa 2000). The 120kb region included all Sox10 coding exons, as well as ~60kb upstream and ~50kb downstream.

We replaced the entire Sox10 open reading frame with a floxed eGFP-SV40polyA4 cassette, followed by an attenuated G383A version of DTA (from Ian Maxwell, University of Colorado, Denver). In the developing and adult mouse, eGFP expression can be detected in Sox10-expressing cells, including oligodendrocyte-lineage cells in the CNS (Fig.1). In the presence of Cre recombinase, the eGFP-polyA4 cassette is removed, activating the DTA cassette and killing the expressing cells. Founder transgenics were generated by pronuclear injection and one line selected for propagation (“Sox10-GFP/DTA”). Generation of the mice is described in Kessaris et al. 2006 and Iannarelli 2017 and a further example of their use in Xing et al. 2023.

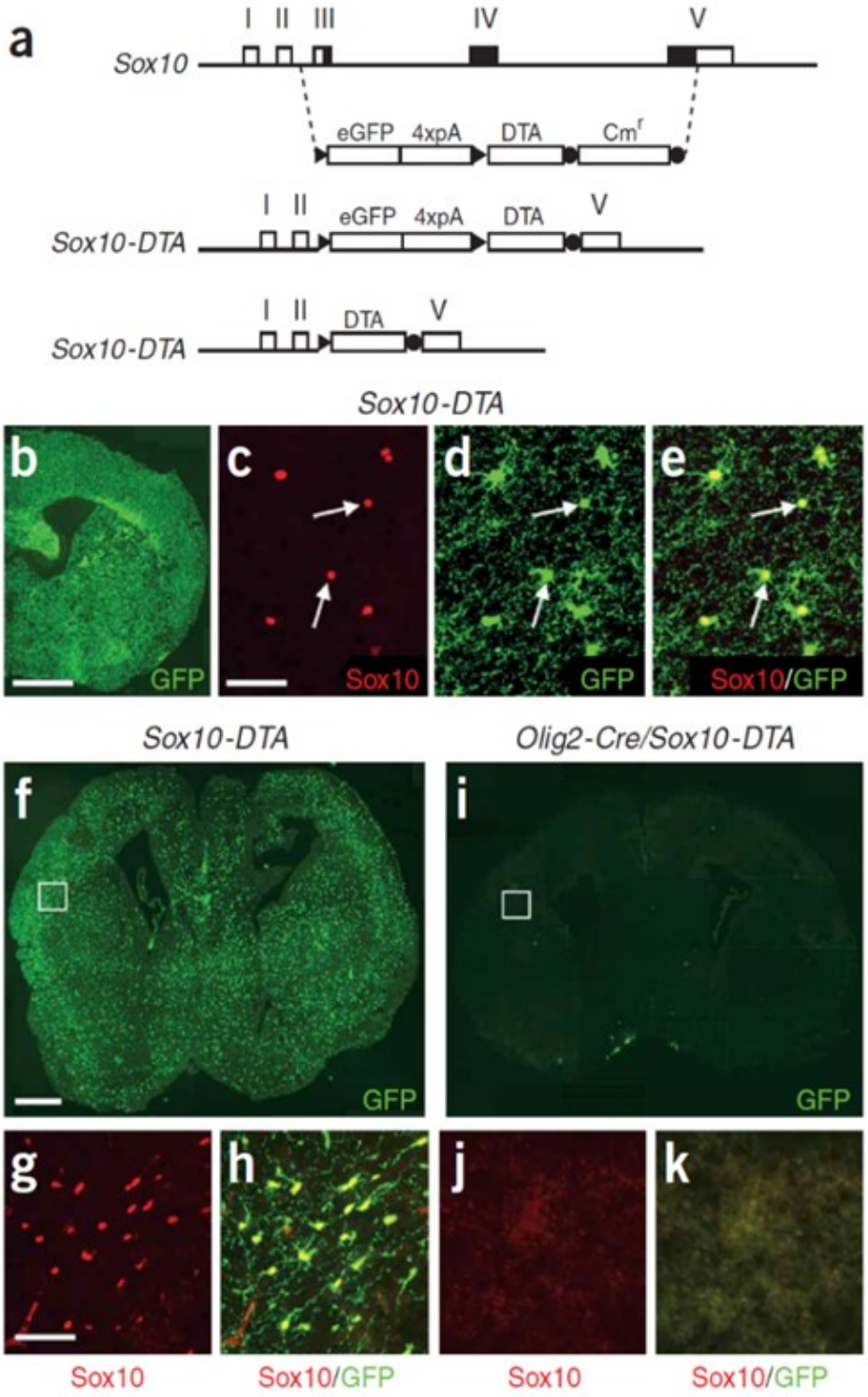

Fig. 1. (a) intron/exon structure of the Sox10 locus (top). The genomic region spanning exons III – V was replaced with the cassette lox-eGFP-polyA4-lox-DTA-frt-Cmr-frt by homologous recombination in bacteria. The Cmr cassette was then removed by transient activation of Flp recombinase in bacteria, producing a latent DTA transgene that expresses GFP under Sox10 transcriptional control. In the presence of Cre recombinase the GFP-polyA cassette is removed, thus activating the DTA cassette and killing the expressing cells. (b-e) Coronal section through the telencephalon of a Sox10-DTA transgenic mouse at P3 and high-mag images of the cortex from the same section. All Sox10+ lineage cells in the Sox10-GFP/DTA mouse co express GFP, demonstrating the veracity of transgene expression. (f-k) The DTA transgene was activated by crossing Sox10- GFP/DTA to an Olig2-Cre mouse, excising the GFP cassette in all Olig2-expressing precursors and their descendants, hence activating expression of DTA and highly specific killing of all Sox10+ OL lineage cells, as demonstrated by the loss of all (Sox10+, GFP+) cells in the double-transgenics (compare f-h with i-k).

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