# RafTR Mouse

**Catalogue number:** 151557
**Sub-type:** Mouse
**Images:**

## Contributor

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**Images:**

## Tool details

***FOR RESEARCH USE ONLY**

**Name:** RafTR Mouse

**Alternate name:**

**Class:**
**Conjugate:**
**Description:** Peripheral nerves have the remarkable ability to regenerate following trauma, afterwhich, a coordinated period of Schwann cell demyelination and recruitment of the inflammatoryresponse form key steps in clearing the path for axonal regrowth to take place. During the course ofnerve regeneration these same processes need to be switched off and reversed in order to allow thenerve to remyelinate and regain normal function. Following Tmx treatment/withdrawal, the Schwanncell RafTR mice display striking similarities to mice in which peripheral nerves have been cut orcrushed - both in the response to, and recovery from, nerve damage. Furthermore, because of the cellspecific nature of the Raf signal and the lack of damage to axons observed in this model, the Schwanncell RafTR mice will serve as a key to further understanding the central role of Schwann cells incontrolling and coordinating the inflammatory response - thought to be essential for the rapid clearanceof myelin that precedes nerve regeneration. In many diseases that affect the peripheral nervoussystem, including inherited demyelinating disorders and peripheral neuropathies induced by pathogenssuch as Leprosy, both demyelination and inflammation form central tenants of the disease pathologiesand thus are important targets for drug therapy. Using the Schwann cell RafTR mouse model ademyelinating, inflammatory state can be induced and maintained by prolonged Tmx treatment.Furthermore, this

pseudo-disease-like phenotype can be titered by regulating the dosage of Tmx given to the animals. Thus, the Schwann cell RafTR mice may serve as a model for targeting the inflammatory symptoms that accompany and exacerbate demyelinating diseases.The Schwann cell RafTR mice may also provide an important insight into the development and treatment of Neurofibromatosis type 1, a common inherited disorder in which patients are predisposed to develop tumours of the peripheral nervous system (Neurofibromas). These tumours are initiated by Schwann cells in which the small GTPase Ras becomes basally more active. Raf is one of the key downstream effectors of Ras and it is therefore highly likely that Raf kinase activation in the Schwann cell RafTR mouse mimics some of the behavioural changes that are observed within the tumour initiating cells at the earliest stages of tumourigenesis. Within neurofibromas Schwann cells are found in an undifferentiated state with a variety of non-neoplastic cells including inflammatory cells that help to create a pro-proliferative microenvironment which closely resembles that of the injured nerve. Therefore the Schwann cell RafTR mouse model may be useful in helping to dissect the contribution of this pathway in both the initiation and maintenance of the tumour microenvironment. A gene specific promoter The transgenic construct, p0Cx32, restricts transgene expression to the myelinated Schwann cells of the peripheral nervous system. Schwann cell RafTR mice develop normally and are indistinguishable from control animals due to the silent nature of the expressed transgene. However, RafTR protein can be readily and specifically detected in the peripheral nervous system and Schwann cell Raf-kinase signalling can be rapidly induced following administration of the oestrogen analogue tamoxifen (Tmx). Activation of the RafTR protein in Schwann cells triggers a widespread programme of demyelination within the peripheral nervous system that results in severe ataxia and impaired motor function. Cellular changes within the nerves include Schwann cell dedifferentiation and proliferation together with increased permeability of the blood nerve barrier and recruitment of inflammatory cells such as macrophages. Despite this extensive tissue remodelling and loss of nerve function, axonal fibres remain structurally unaffected. Prolonged treatment with Tmx maintains the demyelinated/inflammatory state and thus the ataxic phenotype, however, the mice are able to make a full behavioural recovery following Tmx withdrawal due to remyelination of nerve fibres by Schwann cells (in which Raf is no longer activated).



**Purpose:**
**Parental cell:**
**Organism:**
**Tissue:**
**Model:**
**Gender:**
**Isotype:**
**Reactivity:**
**Selectivity:**
**Host:**
**Immunogen:**
**Immunogen UNIPROT ID:**
**Sequence:**
**Growth properties:**
**Production details:** The RafTR coding sequence was amplified by PCR from the vector pLXSN3-RAFTR using the forward; 5'-CATTCCATGGAGTACTCACAGCCG-3' and reverse primers; 5'-CGATGACGTCAGATCGTGTTGGGGAAGC-3' respectively. The resulting 2.2kb fragment was cloned directly into the AatII site of P0Cx32-Nco-Myc-Aat following removal of the Myc-Tag ATG in the NcoI site. The vector backbone of P0Cx32-RafTR was removed using EcoR1/HindIII and the 7Kb fragment containing p0Cx32-RafTR was then used for pronuclear injection. Pronuclear injection of the cDNA fragment and embryo transplantation was performed by the Cancer Research UK Transgenic Service (Clare Hall). The Schwann cell specific P0 promoter in the mp0TOTA expression vector (Feltri et al. San Raffaele Scientific Institute, Milano) will be used to drive expression of a Raf kinase/oestrogen receptor ligand-binding domain fusion protein (RafTR) that has previously been characterised (Lloyd A.C. et al., 1997. Genes Dev. 11:663-77. PMID: 9119230) .
**Formulation:**

## Target details

**Target:** Raf Kinase/Estrogen Receptor fusion protein (RafTR)

**Target alternate names:**

**Target background:**

**Molecular weight:**

**Ic50:**

## Applications

**Application:**
**Application notes:**

## Handling

**Format:**
**Concentration:**
**Passage number:**
**Growth medium:**
**Temperature:**
**Atmosphere:**
**Volume:**
**Storage medium:**
**Storage buffer:**
**Storage conditions:**
**Shipping conditions:** Embryo/Spermatoza- Dry Ice



## Related tools

**Related tools:**

## References

**References:** Nilsen et al. 2003. Oncogene. 22(35):5381-6. PMID: 12934097. ; Gene-targeted mice lacking the Ung uracil-DNA glycosylase develop B-cell lymphomas. ; Nilsen et al. 2000. Mol Cell. 5(6):1059-65. PMID: 10912000. ; Uracil-DNA glycosylase (UNG)-deficient mice reveal a primary role of the enzyme during DNA replication.