NATIONAL CANCER INSTITUTE
Technology Transfer Center

# SMAD3 Reporter Mouse for Assessing TGF-ß/Activin Pathway Activation


## Summary

Researchers at the National Cancer Institute (NCI) developed a novel mouse for the detection of TGF-ß signaling. This mouse provides the opportunity to study TGF-ß signaling in vivo and may be a useful model for preclinical pharmacology studies. The NCI seeks licensees for the TGF-ß reporter mouse.


## NIH Reference Number

E-136-2019

## Product Type

- Research Tools


## Keywords

- Transforming Growth Factor Beta; TGF-ß; mothers against decapentaplegic homolog 3; SMAD3; Animal Model; Reporter Mouse; eGFP; Oncology; Cancer; Fibrosis, Wakefield


## Collaboration Opportunity

This invention is available for licensing.

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## Description of Technology

The Transforming Growth Factor Beta (TGF-ß) ligands (i.e., TGF-ß1, -ß2, -ß3) are key regulatory proteins in animal physiology. Disruption of normal TGF-ß signaling is associated with many diseases from cancer to fibrosis. In mice and humans, TGF-ß activates TGF-ß receptors (e.g., TGFBR1), which activates SMAD proteins that alter gene expression and contribute to tumorigenesis.  Reliable animal models are essential for the study of TGF-ß signaling. A previously developed animal model for TGF-ß signaling utilizes a luciferase expression system under the control of SMAD protein responsive promoter elements (Lin et al., 2005, J. Immunol). The luciferase-based reporter mouse requires administering luciferin for bioluminescence detection. Another previously developed model is a SMAD protein-responsive, green fluorescent protein (GFP)-based reporter mouse (Neptune et al., 2003, Nat. Genet.); however, the model is no longer available.

Thus, there remains a need for novel reporter animal models to study TGF-ß signaling.

NCI investigators designed an enhanced GFP (eGFP)-based reporter construct that is more sensitive to SMAD3 activation than other existing reporter constructs. Expression of eGFP is driven by an artificial enhancer element consisting of six repeats of a strong SMAD3 binding element. This reporter was greater than ten times more sensitive in vitro than the CAGA12-based reporter, another commonly used construct to detect TGF-ß signaling. Using CRISPR/Cas9 technology, the inventors knocked this reporter construct into the Rosa26 locus, a ubiquitously expressed gene in most cells of the mouse. This strategy allows identification of tissues and cells in which signaling of TGF-βs are endogenously active during normal development, tissue homeostasis, and disease.

The mouse model is currently undergoing further validation using genetic and pharmacological approaches. It is available for licensing.

**Potential Commercial Applications**

- Development of oncology therapeutics
- Developing of fibrosis therapeutics
- Pre-clinical *in vivo* model to study TGF-β signaling and pathway antagonists
- Pre-clinical model for TGF-β/SMAD3 disease states

**Competitive Advantages**

- No requirement for luciferin injections
- Higher sensitivity for SMAD3 activation than other reporters

**Inventor(s)**

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**Development Stage**

- Pre-clinical (in vivo)

**Publications**

Yang Y, et al. A new TGF-ß pathway reporter mouse for analysis of TGF-β signaling in normal homeostasis and cancer. [(DOI 10.1158/1538-7445.AM2020-1645)]

**Patent Status**

- **Research Material:** NIH will not pursue patent prosecution for this technology

**Therapeutic Area**

- Cancer/Neoplasm
- Immune System and Inflammation
- Cardiovascular Systems
- Metabolic Disease
- Central Nervous System

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