

Table S1. TNC engineered mouse models amenable for cancer research

Mouse	Reference
TNCKO mouse	
Insertion of LacZ gene into exon 2 ^(a)	Saga et al., 1992 ⁽¹⁾
Deletion of exon 2 ^(a)	Forsberg et al., 1996 ⁽²⁾
Deletion of exon 2 ^(a)	Evers et al., 2002 ⁽³⁾
CRISPR/Cas9 deletion of exon 3-5 ^(b)	Li et al., 2021 ⁽⁴⁾
MMTV-NeuNT mammary gland tumors and lung metastasis in TNCKO mouse ^(2, c)	Murdamoothoo et al., 2021 ⁽²⁾ Sun et al., 2019 ⁽²⁾
4NQO tongue OSCC and lymph node metastasis in TNCKO mouse ^(2, b)	Spenle et al., 2020 ⁽²⁾
Stochastic rat insulin promoter-driven SV40-induced PNET in TNCKO mouse ^(b)	Langlois et al., 2014 ⁽²⁾ Saupe et al., 2013 ⁽²⁾
<i>m4T1</i> (mammary gland) ^(d) and <i>mCT26</i> cells (colorectal carcinoma cells injected into the spleen) ^(b) grafted tumors in TNCKO mouse ⁽²⁾	O'Connell et al., 2011 ⁽²⁾
Stochastic PyMT mammary gland tumors and lung metastasis in TNCKO mouse ^(2, a)	Talts et al., 1998 ⁽²⁾
TNCKD cells (shTNC) / immune competent host	
<i>m4T1</i> (mammary gland) ^(d) and <i>mEO771</i> (mammary gland) ^(b) grafted tumors and lung metastasis in WT mouse	Hongu et al., 2022
<i>m4T1</i> cell grafted mammary gland tumors in WT mouse ^(d)	Li et al., 2021
<i>mNT193</i> cell grafted mammary gland tumors and lung metastasis in TNCKO mouse ^(c)	Murdamoothoo et al., 2021 ⁽²⁾ Deligne et al., 2020 ⁽²⁾ Sun et al., 2019 ⁽²⁾
<i>mAGR53</i> (Hras (Harvey Rat sarcoma virus)/shp53 transformed) primary astrocytes grafted brain tumors in WT mouse ^(b)	Angel et al., 2020
<i>mTPIN-SC</i> cell grafted prostate/subcutaneous tumors in WT mouse ^(b)	Jachetti et al., 2015
TNCKD cells (shTNC) / immune compromised host (see Table 1)	
<i>hMDA MB231-LM2</i> cell grafted mammary gland tumors and lung metastasis in nude mouse ^(e)	Hongu et al., 2022
<i>hMDA MB231</i> cell grafted mammary gland tumors in nude mouse ^(e)	Li et al., 2021
<i>hU87MG</i> cells grafted subcutaneous tumors in nude mouse ^(e)	Rupp et al., 2016
<i>hSW480</i> cells (WT) engrafted into RAG2KO or RAG2/TNCKO mouse ^(f, 2)	Spenlé et al., 2015
TNC overexpressing mouse	
Nkx2.5 promoter driven <i>mTNC</i> overexpression in cardiomyocytes ^(b)	Yonebayashi et al., 2021
CRISPR/Cas9 <i>mTNC</i> overexpression in <i>mKP</i> (KrasG12D/Trp53 null) lung carcinoma cells subcutaneous grafted tumors/lung metastasis in WT mouse ^(b)	Gocheva et al., 2017
Rat insulin promoter-driven <i>hTNC</i> over expression in Rip1Tag2 PNET ^(b)	Saupe et al., 2013 ⁽²⁾
TNC indicator mouse	
<i>mTNC</i> promoter-driven Cre-recombinase expression to induce floxed eGFP ^(c)	Lüönd et al., 2021

Mouse models with engineered TNC levels have been generated either with a KO or an overexpression of TNC. The TNCKO mouse was generated four times independently targeting exon 2 (Saga et al., 1992; Forsberg et al., 1996; Evers et al. 2002) or exon 3-5 (Li et al., 2021). Mostly the “Forsberg” mouse was used for tumor studies listed. TNCKD tumor cells (accomplished by shRNA technology) were engrafted into WT or immune compromised mice. A gain of function mouse was accomplished by overexpression of the human TNC coding sequence (lacking AD1, AD2) under control of the rat insulin promoter (Saupe et al., 2013) or by generating a compound mouse expressing the complete murine TNC coding sequence with floxed stop sequences that got removed by the Nkx2.5 promoter driven Cre-recombinase in myocytes (Yonebayashi et al., 2021). The inducible conditional TNC overexpression mouse is suitable for tissue or cell type specific TNC overexpression upon crossing with an appropriate Cre-recombinase expressing mouse. The TNC-promoter driven Cre-recombinase expressing mouse (TNC-reporter mouse) is suitable to monitor TNC expression during tumorigenesis. The floxed stop sequence of eGFP gets removed in cells expressing TNC (Lüönd et al., 2021). *hTNC*, human TNC, *mTNC*, murine TNC. (a) 129/sv, (b) C57Bl6, (c) FVB, (d) BalbC, (e) nude, (f) RAG2KO mouse. Saga et al., 1992 (1), Forsberg et al., 1996 (2), Evers et al., 2002 (3), Li et al., 2021 (4).

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