Introducing a mouse (VeDTR system) that allows you to specify two marker genes and remove only cells expressing both.

Accurate research by deleting “cells” rather than deleting “genes” that have wide-ranging effects

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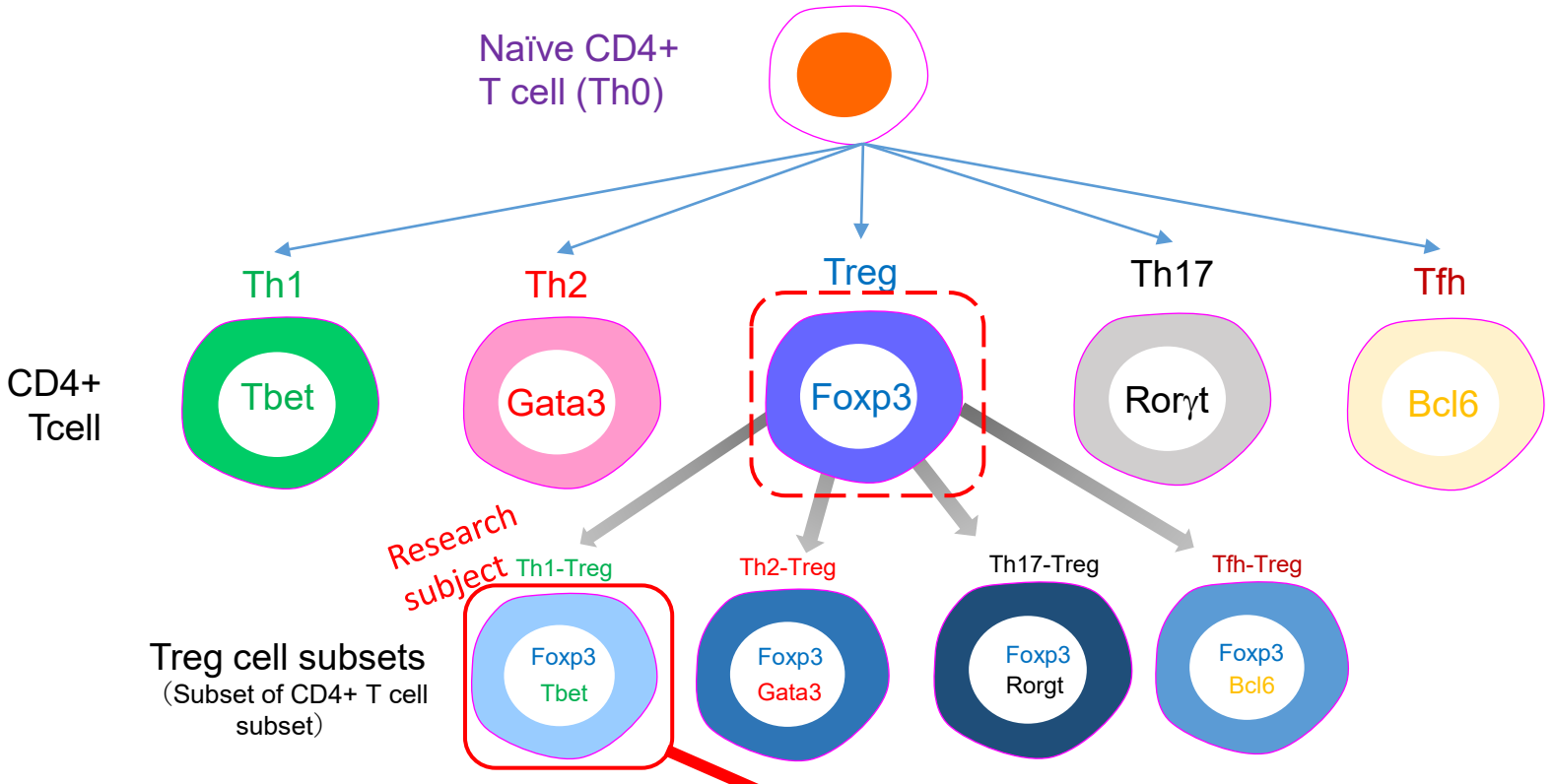
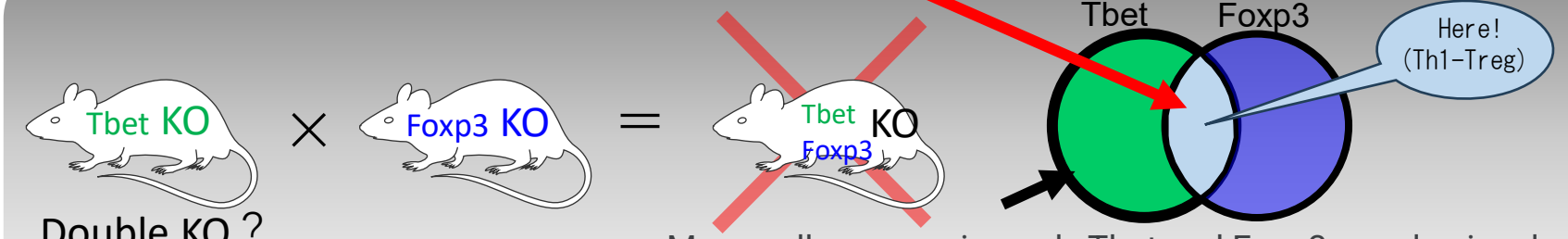
CD4 T cells have recently been differentiated into many more subsets. How can we delete and analyze "only" subdivided cells (e.g. Th1-Treg)?





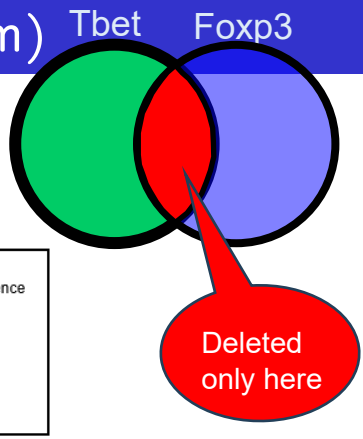
Double KO ?

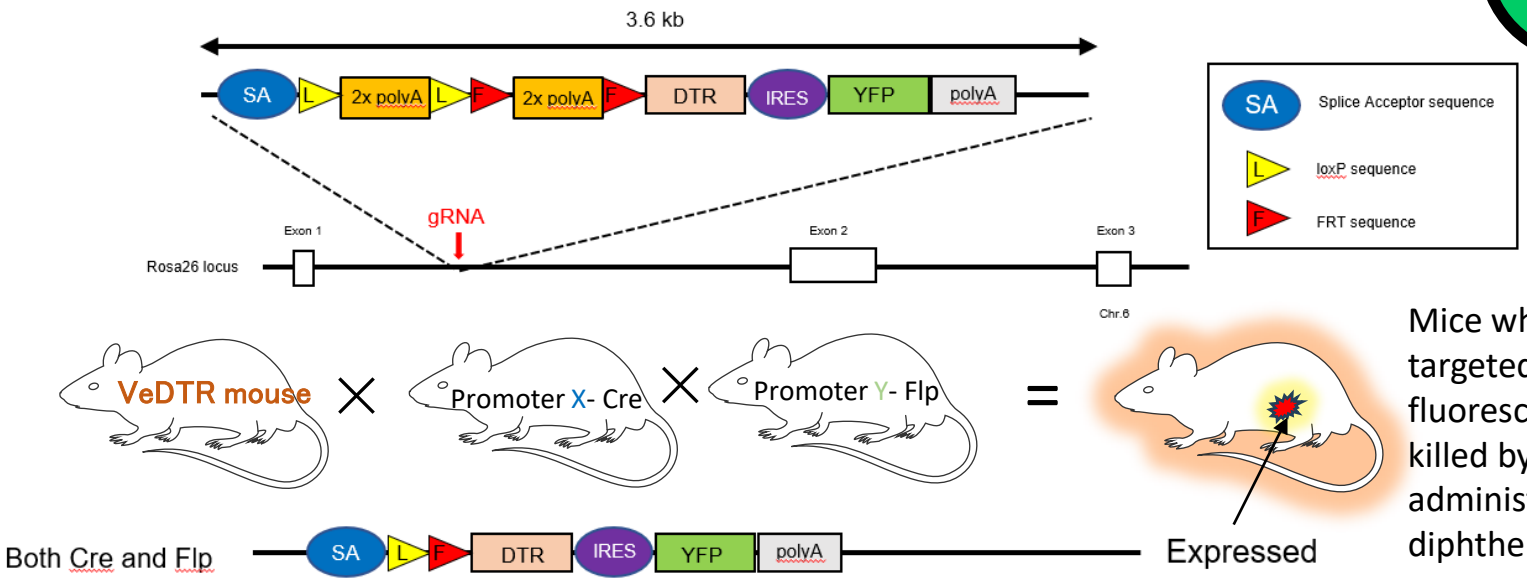
→Many cells are collaterally deleted

Many cells expressing only Tbet and Foxp3 are also involved

Interest is only cells that express both Foxp3 and Tbet

Using Cre-loxP and Flp-FRT, only cells expressing both emit fluorescence or can be removed with drugs (VeDTR system)



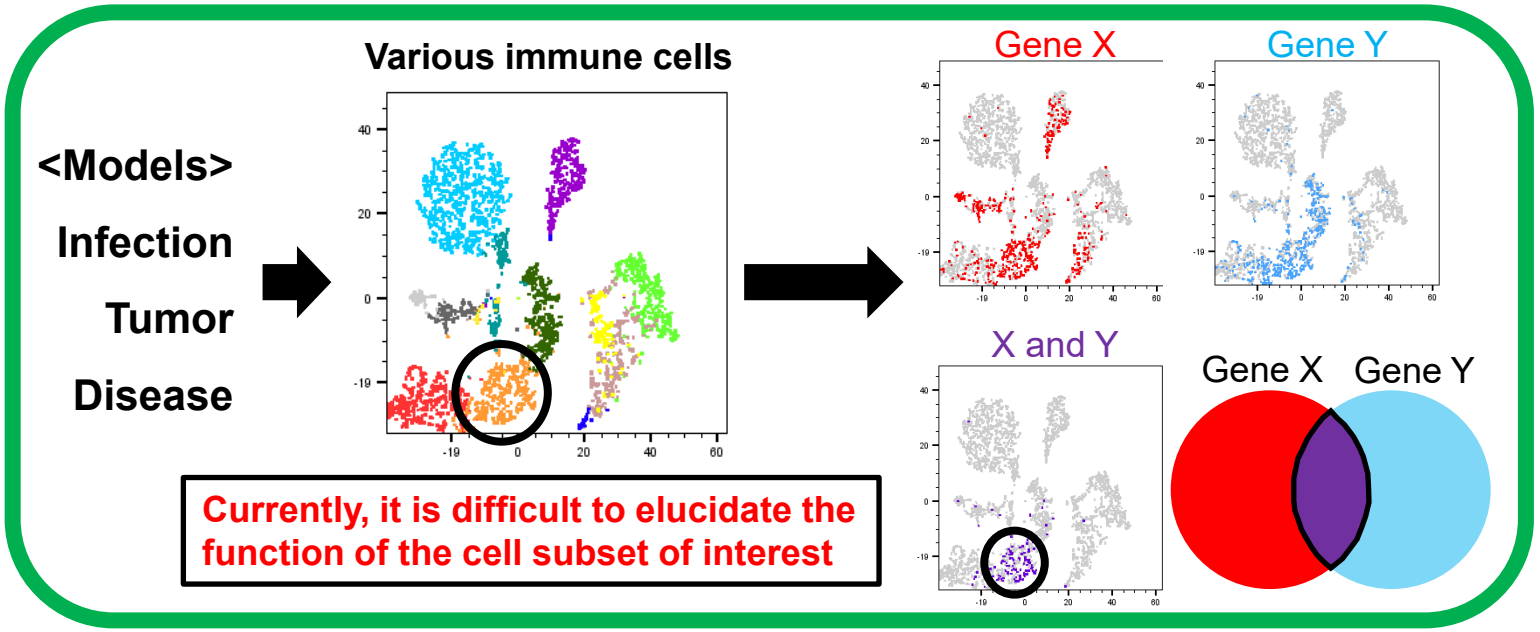


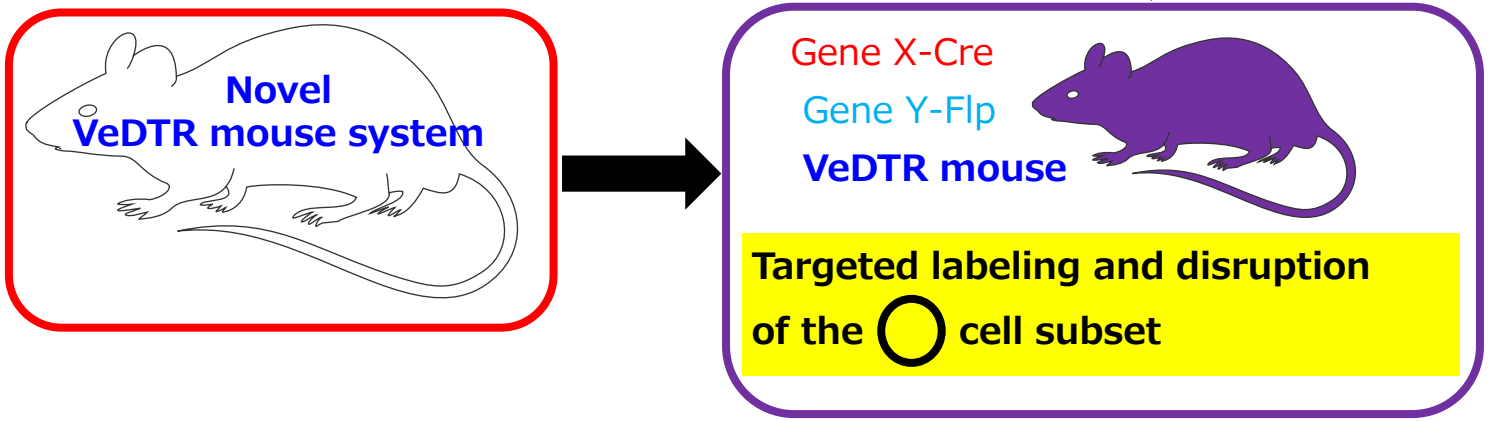
Mice where only the targeted cells emit fluorescence and are killed by administration of diphtheria toxin

Development and growth are the same as normal mice, target cells can be analyzed using fluorescence, and only target cells can be removed by administering diphtheria toxin.

Patent Pending（PCT/JP2023/025274）

Cell-specific KO is possible in any cell fraction if two sets of characteristic genes that define that cell are found.





More detailed analysis of target cells is possible using fluorescence as an indicator.

Foxp3-Cre / Tbx21-Flp
VeDTR mice

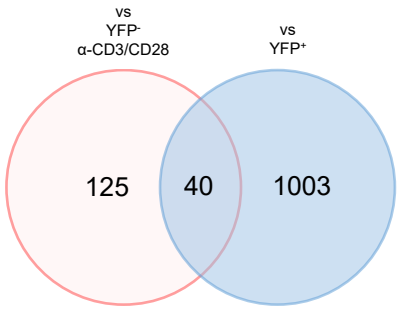
spleen

Sorting of
CD4+ CD25+
T cells

Isolation of
YFP+ or YFP-
Treg

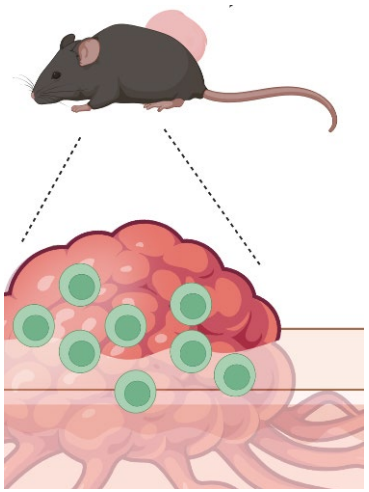
α-CD3/α-CD28
刺激

Bulk RNAseq

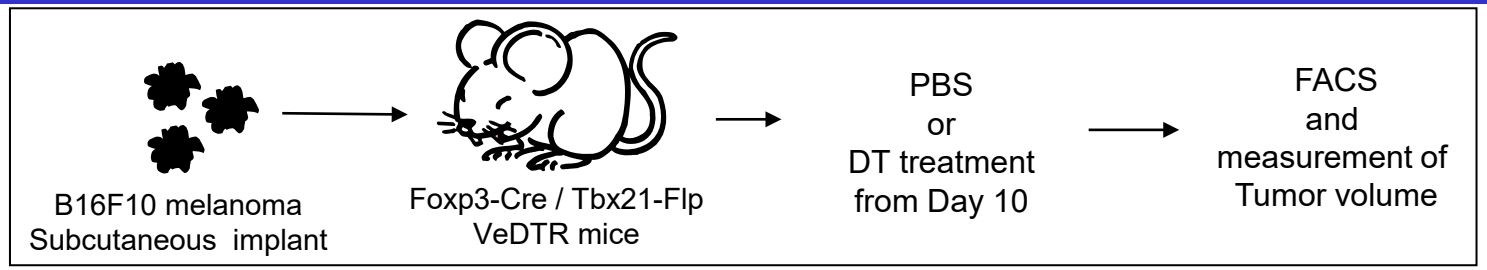


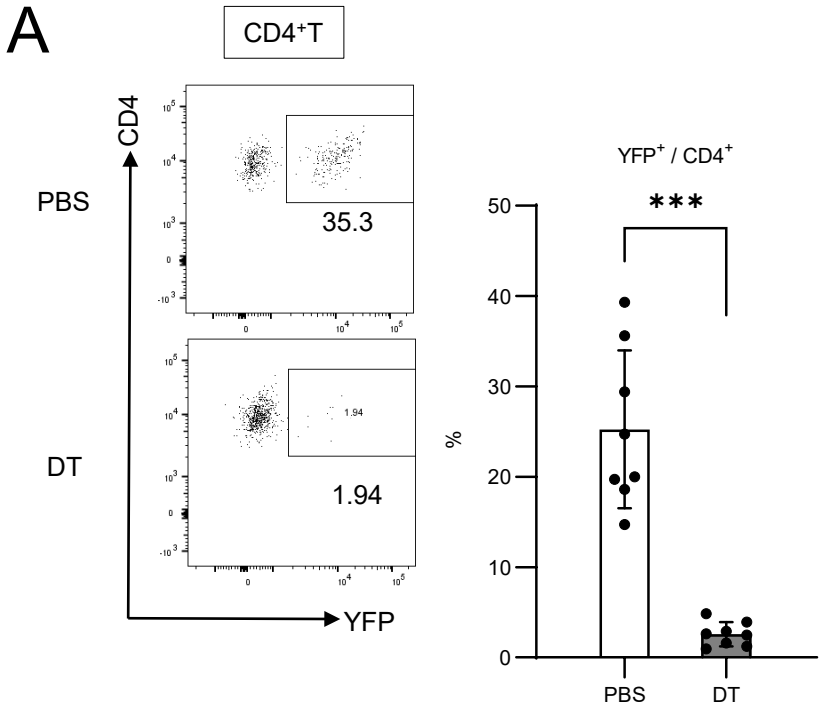
Prf1	perforin 1 (pore forming protein)
Mt3	metallothionein 3
Ctla2b	cytotoxic T lymphocyte-associated protein 2 beta
Cd68	CD68 antigen
Lat2	"linker for activation of T cells family, member 2"
Spp1	secreted phosphoprotein 1 （Osteopontin）
Ifng	interferon gamma
Srxn1	sulfiredoxin 1 homolog (S. cerevisiae)
Havcr2	hepatitis A virus cellular receptor 2
Prdm1	"PR domain containing 1, with ZNF domain"
Ccl3	chemokine (C-C motif) ligand 3
Il10	interleukin 10
Adam8	a disintegrin and metallopeptidase domain 8
Ccr5	chemokine (C-C motif) receptor 5
Ccl4	chemokine (C-C motif) ligand 4
Ttc39c	tetratricopeptide repeat domain 39C
Tnfrsf8	"tumor necrosis factor receptor superfamily, member 8"
Gzmb	granzyme B
Mt2	metallothionein 2
Nfil3	"nuclear factor, interleukin 3, regulated"
Tigit	T cell immunoreceptor with Ig and ITIM domains
Pcyt1a	"phosphate cytidylyltransferase 1, choline, alpha isoform"
Mt1	metallothionein 1
Tubb6	"tubulin, beta 6 class V"
Il1r2	"interleukin 1 receptor, type II"
Adap1	ArfGAP with dual PH domains 1
Nkg7	natural killer cell group 7 sequence
Dgat1	diacylglycerol O-acyltransferase 1
Ptpn5	"protein tyrosine phosphatase, non-receptor type 5"

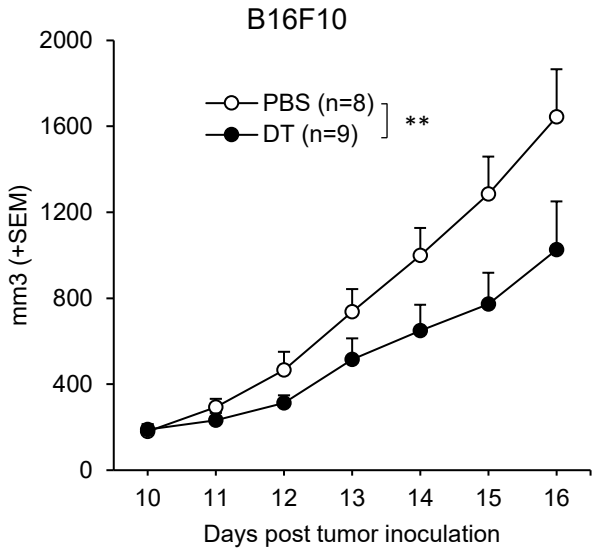
It is also possible to search for characteristic markers of cells gathered in diseased areas.



It is also possible to remove the target cells by administering DT and observe the effects.

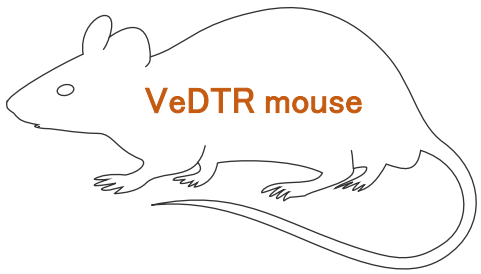






Removal of Th1-Treg leads to tumor (B12melanoma) growth

looking for technology license and new joint research.



- Analysis of specific subsets of subdivided immune cells is possible with fluorescence and cell deletion
- Can be removed at any time without affecting growth and development
- Target cells are not limited to the immune system
- Can also be used to create new disease model mice

Please tell us your wishes

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A genetic method specifically delineates Th1-type Treg cells andtheir roles in tumor immunity