Major Resources Table

In order to allow validation and replication of experiments, all essential research materials listed in the Methods should be included in the Major Resources Table below. Authors are encouraged to use public repositories for protocols, data, code, and other materials and provide persistent identifiers and/or links to repositories when available. Authors may add or delete rows as needed.

Animals (in vivo studies)

Species	Vendor or Source	Background Strain	Sex
Mus musculus	Jackson Laboratory	C57BL/6J	F/M
Mus musculus	Gift from Markus Schwaninger, University of Lübeck	Slco1c1-CreERT2	F/M
Mus musculus	Gift from Wang Min, Yale University	Pdcd10$^{fl/fl}$	F/M
Mus musculus	Gift from Michael Karin, UCSD	Ikkb$^{fl/fl}$	F/M
Mus musculus	Jackson Laboratory	Aldh1l1-EGFP/Rpl10a	F/M

Genetically Modified Animals

	Species	Background Strain
Parent - Male	Mus musculus	Slco1c1-CreERT2;Pdcd10$^{fl/fl}$
Parent - Female	Mus musculus	Pdcd10$^{fl/fl}$
Parent - Male	Mus musculus	Slco1c1-CreERT2;Ikkb$^{fl/fl}$
Parent - Female	Mus musculus	Ikkb$^{fl/fl}$
Parent - Male	Mus musculus	Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Aldh1l1-EGFP/Rpl10a
Parent - Female	Mus musculus	Pdcd10$^{fl/fl}$;Aldh1l1-EGFP/Rpl10a

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration
GFAP	ThermoFisher Scientific	13-0300	1:200
GFAP	Agilent Dako	GA524	1:300
Iba1	FUJIFILM Wako	019-19741	1:100
Isolectin B4	Sigma-Aldrich	L2895	1:80
Isolectin B4-Biotin	Sigma-Aldrich	L2140	1:80
Anti-mouse CD41 (Clone: MWReg30)	Biolegend	133907	1:50
Anti-mouse CD41 (Clone: MWReg30)	Biolegend	133935	1:50
Anti-mouse CD45 (Clone: S18009D)	Biolegend	160308	1:50
CX3CR1 (Clone: SA011F11)	Biolegend	149022	1:50
Ly6G (Clone: 1A8)	Biolegend	127626	1:50
CD16/32 (Clone: S17011E)	Biolegend	156615	1:50
CD206 (Clone: C068C2)	Biolegend	141710	1:50

DOI [to be added]

VCAM1 (Clone 429 MVCAM.A)	Biolegend	105712	1:500
Anti-mouse CD45 (Clone: 30-F11)	Biolegend	103129	1:200
Anti-mouse Cd11b (Clone: M1/70)	Biolegend	101207	1:200
Anti-mouse TCRβ (Clone: H57-597)	Biolegend	109207	1:200
Anti-mouse CD4 (Clone: GK 1.5)	Invitrogen	14-0041-82	1:200
Anti-mouse CD8 (Clone: 53-6.7)	Biolegend	100721	1:200
Anti-mouse CD19 (Clone: 6D5)	Biolegend	115530	1:200
Anti-mouse Ly6G (Clone: 1A8)	BD Biosciences	561105	1:200
Anti-mouse F4/80 (Clone: BM8)	Biolegend	123147	1:200
Anti-mouse CD206 (Clone: C068C2)	Biolegend	141723	1:200
Anti-mouse Ly6C (Clone: HK1.4)	Biolegend	128007	1:200
Anti-mouse CD64 (Clone: X54-5/7.1)	Biolegend	139305	1:200
Anti-mouse CD11c (Clone: N418)	Biolegend	117307	1:200
Anti-mouse CX3CR1 (Clone: SA011F11)	Biolegend	149025	1:200
Anti-Rabbit IgG, Alexa Fluor 488	Jackson ImmunoResearch Laboratory	711-546-152	1:300
Anti-Rabbit IgG, Alexa Fluor 594	Jackson ImmunoResearch Laboratory	711-585-152	1:300
Anti-Rat IgG, Alexa Fluor 594	Jackson ImmunoResearch Laboratory	112-586-052	1:300
NDUFA4L2	Proteintech	16480-1-AP	1:50
THBD	R&D systems	AF3894	1:100
CD74	Biolegend	151002	1:100
IL1b	R&D Systems	AF-401-NA	1:500
Phospho p65	Cell signaling	3031S	1:500

Data & Code Availability

Description	Source / Repository	Persistent ID / URL
RNAseq data	Gene Expression Omnibus	GSE204979

Other

Description	Source / Repository
FAM-FLICA Caspase-1 probe	Immunochemistry technologies #97
LD FVS700 Fixable dye	BD Biosciences #564997
MCC950 Sodium	Selleckchem #S7809
O.C.T. Compound	Fisher Scientific #4585
(Z)-4-Hydroxytamoxifen	Tocris #3412
Fluoromount-G mounting medium	Southern Biotec #0100-20
MojoSortTM Mouse CD45 Nanobeads	Biolegend #480028

DOI [to be added]

ARRIVE GUIDELINES

The ARRIVE guidelines (https://arriveguidelines.org/) are a checklist of recommendations to improve the reporting of research involving animals. Key elements of the study design should be included below to better enable readers to scrutinize the research adequately, evaluate its methodological rigor, and reproduce the methods or findings.

Study Design

Groups	Sex	Age	Littermates (Yes/No)
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$ Pdcd10$^{fl/fl}$	F/M	P15	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$ Pdcd10$^{fl/fl}$	F/M	P50	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$ Pdcd10$^{fl/fl}$	F/M	P80	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Aldh1l1-EGFP/Rpl10a Pdcd10$^{fl/fl}$;Aldh1l1-EGFP/Rpl10a	F/M	P80	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/fl}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/wt}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{wt/wt}$	F/M	P15	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/fl}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/wt}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{wt/wt}$	F/M	P50	Yes
Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/fl}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{fl/wt}$ Slco1c1-CreERT2;Pdcd10$^{fl/fl}$;Ikkb$^{wt/wt}$	F/M	P80	Yes

Sample Size: Please explain how the sample size was decided Please provide details of any *prior* sample size calculation if done.

Sample sizes were calculated by assuming a two-sided alpha=0.05, 80% power, and homogeneous variances for two samples using estimates of means and standard deviation from previous studies[4,13,15,16]. At least three biologically independent experiments and multiple sections were analyzed to ensure reproducibility.

Inclusion Criteria

Animals were genotyped between 2 and 3 weeks of age to confirm the genotypes. Genotypes were also performed at the end of the experiments when animals were euthanized.

Exclusion Criteria

N/A

Randomization

Animals were randomly assigned to treatment groups and for their genotype and gender. *Slco1c1-CreERT2;Pdcd10fl/fl* and *Pdcd10fl/fl* littermate controls were all injected with tamoxifen. In those cases where we used non-injected animals, these were randomized.

Blinding

The experiments are blinded by researchers carrying out all experiments until all data is collected and analyzed.