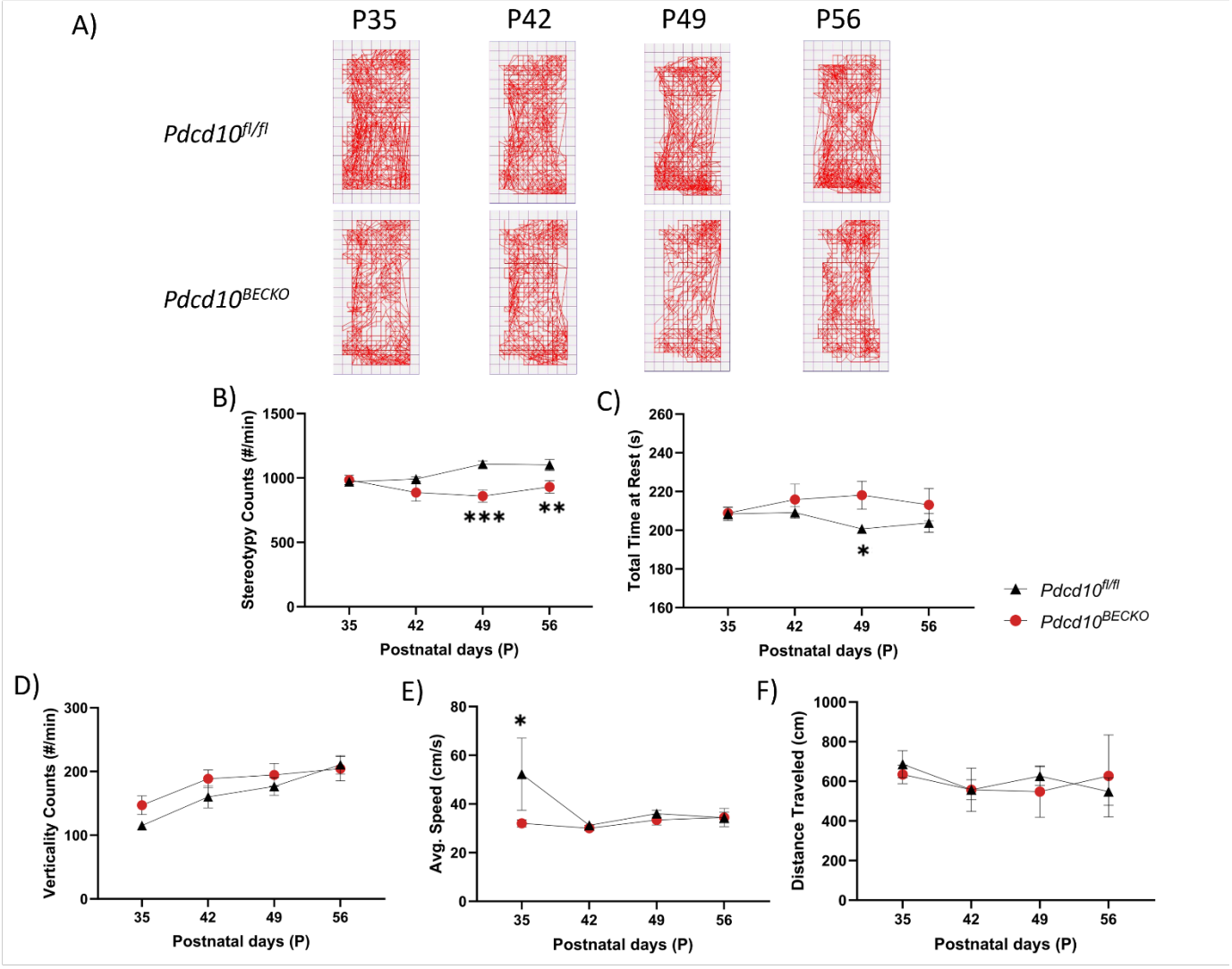
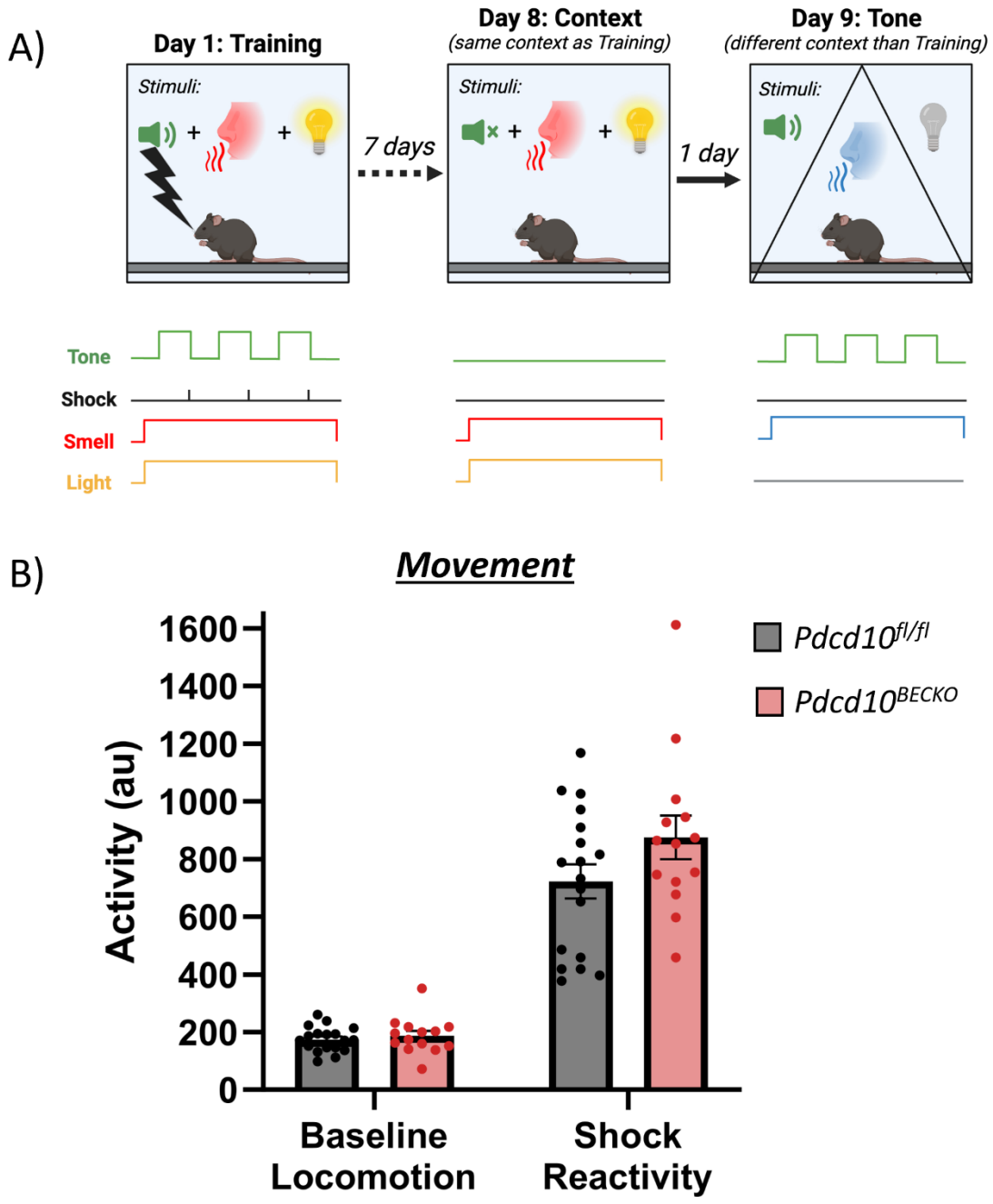
Supplemental figures



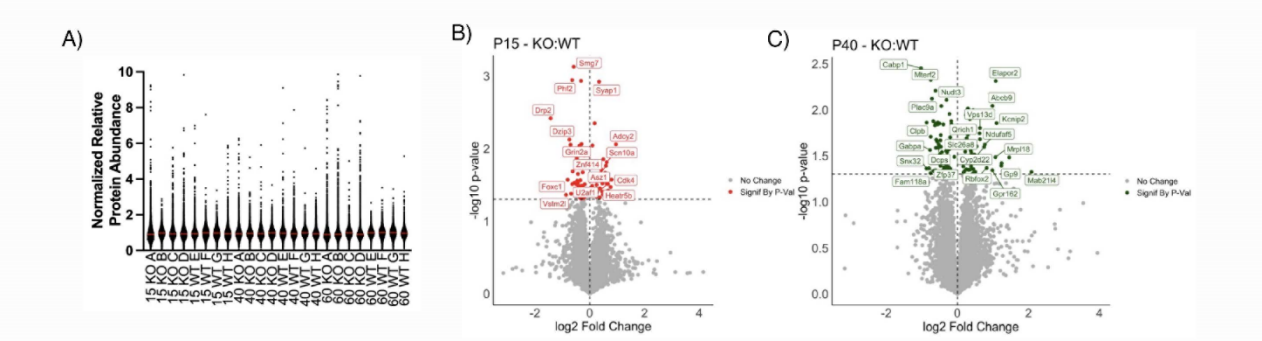
Supplemental Figure 1. *Pdcd10*^{BECKO} mice Open Field Test. A) Representative track plot reports recorded during the 30 min test sessions (Med Associates Inc.). B) *Pdcd10*^{BECKO} male and female mice show decrease in stereotypy after P42 (n = 8 *Pdcd10*$^{fl/fl}$ and 6 *Pdcd10*^{BECKO}). C) *Pdcd10*^{BECKO} male and female mice show increased resting time at P49. D) No significant differences were found in verticality between groups. E) *Pdcd10*^{BECKO} male and female mice show a decrease in average movement speed at P35. F) No significant differences were found between

groups in distance traveled. Data are presented as a mean ± SEM. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.



Supplemental Figure 2. *Pdcd10*^{BECKO} mice Fear Conditioning Assessment.
A) Experimental setup for Pavlovian fear conditioning in mice. On Day 1 (Training), mice were placed in a conditioning box scented with isopropyl alcohol, with the lights turned on. The mice experienced a 2-minute acclimation period, followed by three consecutive trials of a 30-second auditory tone co-terminating with a mild footshock, with intervals of 30 seconds between trials.

Post-trial, mice remained in the box for an additional 5 minutes to assess short-term memory recall. On Day 8 (Context), mice were reintroduced to the identical box environment from the training phase (minus the tone and shock) to evaluate recognition of the context and long-term context memory associated with fear. Finally, on Day 9 (Tone), mice were placed in a novel environment with distinct walls, floors, and scent, without lighting. The altered environment was coupled with three repetitions of the 30-second tone (with no footshock) to examine long-term memory recall of the tone. The experiment measures the mice's memory and fear responses to the conditioning stimuli over time. B) Baseline locomotion and shock reactivity during the 2min training baseline period and 2s footshock. While group differences were observed in short- and long-term fear memory, no differences were observed in baseline locomotion (n = 18 *Pdcd10*$^{fl/fl}$ and 14 *Pdcd10*^{BECKO}) or reactivity to the footshock.



D)

Term	Count	%	PValue	Fold Enrichment	Bonferroni	Benjamini
mmu04810:Regulation of actin cytoskeleton	40	2.80	3.34E-07	2.42	1.03E-04	1.03E-04
mmu03010:Ribosome	32	2.24	2.45E-06	2.53	7.57E-04	3.79E-04
mmu05014:Amyotrophic lateral sclerosis	51	3.57	7.03E-06	1.93	2.17E-03	7.24E-04
mmu05022:Pathways of neurodegeneration - multiple diseases	60	4.20	1.27E-05	1.78	3.92E-03	9.82E-04
mmu04510:Focal adhesion	33	2.31	1.66E-05	2.27	5.11E-03	1.03E-03
mmu04723:Retrograde endocannabinoid signaling	26	1.82	4.31E-05	2.46	1.32E-02	1.90E-03
mmu04530:Tight junction	28	1.96	5.33E-05	2.33	1.63E-02	2.06E-03
mmu03040:Spliceosome	29	2.03	7.06E-05	2.25	2.16E-02	2.23E-03
mmu05100:Bacterial invasion of epithelial cells	17	1.19	7.22E-05	3.13	2.21E-02	2.23E-03
mmu05205:Proteoglycans in cancer	31	2.17	1.24E-04	2.12	3.76E-02	3.49E-03
mmu04360:Axon guidance	28	1.96	1.94E-04	2.16	5.82E-02	5.00E-03
mmu04520:Adherens junction	17	1.19	7.21E-04	2.58	2.00E-01	1.57E-02
mmu04144:Endocytosis	35	2.45	7.59E-04	1.82	2.09E-01	1.57E-02
mmu04012:ErbB signaling pathway	16	1.12	7.87E-04	2.66	2.16E-01	1.57E-02
mmu04666:Fc gamma R-mediated phagocytosis	17	1.19	8.14E-04	2.56	2.22E-01	1.57E-02
mmu05211:Renal cell carcinoma	14	0.98	8.97E-04	2.88	2.42E-01	1.58E-02
mmu03015:mRNA surveillance pathway	18	1.26	9.22E-04	2.44	2.48E-01	1.58E-02

E)

Term	Count	%	PValue	Fold Enrichment	Bonferroni	Benjamini
mmu05012:Parkinson disease	58	3.95	1.07E-12	2.79	3.46E-10	1.78E-10
mmu05016:Huntington disease	63	4.29	1.10E-12	2.64	3.56E-10	1.78E-10
mmu05014:Amyotrophic lateral sclerosis	71	4.84	1.96E-12	2.44	6.33E-10	2.11E-10
mmu05020:Prion disease	53	3.61	6.01E-10	2.52	1.94E-07	4.85E-08
mmu05010:Alzheimer disease	65	4.43	4.40E-09	2.15	1.42E-06	2.84E-07
mmu05022:Pathways of neurodegeneration - multiple diseases	74	5.04	9.87E-09	1.99	3.19E-06	4.78E-07
mmu00190:Oxidative phosphorylation	33	2.25	1.04E-08	3.10	3.35E-06	4.78E-07
mmu04721:Synaptic vesicle cycle	22	1.50	2.92E-07	3.62	9.45E-05	1.18E-05
mmu04130:SNARE interactions in vesicular transport	14	0.95	5.28E-07	5.38	1.70E-04	1.89E-05
mmu04142:Lysosome	29	1.98	1.62E-06	2.72	5.22E-04	5.22E-05
mmu04144:Endocytosis	44	3.00	5.45E-06	2.07	1.76E-03	1.60E-04
mmu03050:Proteasome	15	1.02	9.20E-06	4.05	2.97E-03	2.42E-04
mmu04714:Thermogenesis	39	2.66	9.76E-06	2.14	3.15E-03	2.42E-04
mmu01100:Metabolic pathways	171	11.66	2.07E-05	1.34	6.67E-03	4.42E-04
mmu04724:Glutamatergic synapse	24	1.64	2.19E-05	2.67	7.05E-03	4.42E-04
mmu04723:Retrograde endocannabinoid signaling	26	1.77	2.09E-04	2.23	6.53E-02	3.37E-03
mmu01232:Nucleotide metabolism	18	1.23	2.43E-04	2.72	7.56E-02	3.74E-03
mmu03013:Nucleocytoplasmic transport	22	1.50	2.82E-04	2.38	8.69E-02	4.13E-03
mmu04141:Protein processing in endoplasmic reticulum	28	1.91	3.69E-04	2.08	1.12E-01	5.18E-03
mmu05208:Chemical carcinogenesis - reactive oxygen species	33	2.25	5.90E-04	1.88	1.74E-01	7.94E-03
mmu04514:Cell adhesion molecules	28	1.91	9.13E-04	1.96	2.55E-01	1.18E-02

Supplemental Figure 3. *Pdcd10*^{BECKO} whole-brain proteome profiling. A) The graph depicts the distribution of peptide abundance in *Pdcd10*$^{fl/fl}$ and *Pdcd10*^{BECKO} murine brain tissue at various developmental stages (P15, P40, and P60) as indicated. B-C) Volcano plot of peptides quantified from *Pdcd10*$^{fl/fl}$ and *Pdcd10*^{BECKO} murine brain tissue at P15 (*B*) and P40 (*C*). The –log10-transformed *p* values associated with individual peptides are plotted against the log2-transformed fold change in abundance between *Pdcd10*$^{fl/fl}$ and *Pdcd10*^{BECKO} brains. Color intensities depict peptides with significantly higher (right) or lower (left) levels in *Pdcd10*^{BECKO} compared to *Pdcd10*$^{fl/fl}$. D) Mass spectrometry analysis of whole-brain samples was used to analyze protein levels in the brains of P15 *Pdcd10*$^{fl/fl}$ mice. E) D) Mass spectrometry analysis of whole-brain samples was used to analyze protein levels in the brains of P40 *Pdcd10*$^{fl/fl}$ mice.