

Supplementary Information for

Microglial IRF5-IRF4 Regulatory Axis Regulates Neuroinflammation

After Cerebral Ischemia and Impacts Stroke Outcomes

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Supplementary Information Text

Behavioral Assessment

All behavioral tests were performed by a blinded investigator.

Neurological Deficit Scores

3d after reperfusion, neurological deficit scores were assessed by a 4-point scale (1, 2): 0-no deficit; 1-forelimb weakness, torso turning to the ipsilateral side when held by the tail; 2-circling to the affected side; 3-unable to bear weight on affected side and 4-no spontaneous activity or barrel rolling.

Corner Test

The mouse entered a corner that was made by moving two card board pieces at an angle of 30 degrees in front of the nose. Contact with the vibrissae led to a rear and the direction in which the mouse turned was recorded. Normal mice do not exhibit a turning preference, but after ischemia, mice have a turning preference to the non-impaired side (right side by our MCAO model). The percentage of right turns was calculated for twenty trials in each sitting. The corner test has been used to detect both sensory and motor abnormalities in the stroke model in young animals (3, 4).

Hanging Wire Test

A slight modification was made to the previously used Wire Hand test (5). A wire cage (top dimensions, 18 inch × 9 inch) with its edges taped off was used for this experiment. The mouse was placed on the center of the wire lid and the lid was

slowly inverted and placed on top of the cage. The wire lid was 9 inch above the cage bedding. Latency to fall from the wire was recorded and scored. The time out period was 90 seconds.

Supplementary Figures:



Supplementary figure 1:

Flow sorted IRF5 or IRF4 CKO microglia had "near null" mRNA level of IRF5 (**A**) or IRF4 (**B**) respectively compared to their flox controls (fl/fl). N=5/group; *P<0.01 vs. flox control.

Supplementary figure 2:



Gating strategy to sequentially separate single cells, live cells, and leukocytes (including microglia).

Supplementary figure 3:



No significant difference was seen in CD68/CD206 expression on infiltrating monocytes between CKO vs. floxed mice for either IRF5 CKO (**A&B**) or IRF4 CKO (**C&D**) strain. N=5 for Lenti-GFP control and 6 for lenti-IRF4 or -IRF5 group.

Supplementary figure 4:



Representative flow plots of gating strategy for immune cell infiltration in IRF5 CKO mice brains after stroke: **(A)** Microglia, pMyeloid cells, and lymphocytes; **(B)** Monocytes and neutrophils. No significant difference was seen in absolute counts of infiltrating pMyeloid cells **(C)**, monocytes **(D)**, neutrophils **(E)** and lymphocytes **(F)** in stroke brains of IRF5 CKO vs. floxed mice. N=5 for Lenti-GFP control and 6 for lenti-IRF4 or -IRF5 group.

Supplementary figure 5:



Validation of lentivirus effects on target protein expression. **(A)** IHC staining showed lenti-GFP induced GFP expression in WT microglia 28 days after GFP-lentivirus injection. 40x; scale bar=100 μ m. Lenti-IRF4 (**B**) and lenti-IRF5 (**C**) injection induced overexpression of IRF4 and IRF5 in flow sorted microglia, evaluated by mRNA level with RT-PCR. Arrows indicate microglia. N=5/group; **P*<0.01 vs. lenti-GFP.

References

- 1. Al Mamun A, *et al.* (2018) Interferon regulatory factor 4/5 signaling impacts on microglial activation after ischemic stroke in mice. *Eur J Neurosci* 47(2):140-149.
- 2. Liu F, Benashski SE, Xu Y, Siegel M, & McCullough LD (2012) Effects of chronic and acute oestrogen replacement therapy in aged animals after experimental stroke. *J Neuroendocrinol* 24(2):319-330.
- 3. Li X, *et al.* (2004) Chronic behavioral testing after focal ischemia in the mouse: functional recovery and the effects of gender. *Exp Neurol* 187(1):94-104.
- 4. Manwani B, *et al.* (2011) Functional recovery in aging mice after experimental stroke. *Brain Behav Immun* 25(8):1689-1700.
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Table S1. Statistics reporting

FIGURE	n	DATA STRUCTURE	TEST USED	STATISTICS	P VALUE
1B	21 microglia images (Control, OGD ⁻ LPS ⁻ IL-4 ⁻) 24 microglia images (OGD ⁺ LPS ⁺ IL-4 ⁻) 32 microglia images (OGD ⁺ LPS ⁻ IL-4 ⁺) Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,74) =10.61	ANOVA p<0.0001 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0001 OGD ⁺ LPS ⁻ IL-4 ⁺) ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0001
1C	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =11.98	ANOVA p<0.0001 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0064 OGD ⁺ LPS ⁻ IL-4 ⁺) ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0092
1D	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =1.39	ANOVA p<0.0003 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0007 OGD ⁺ LPS ⁻ IL-4 ⁺) ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0005
1E	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =19.28	ANOVA p<0.0009 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁻ IL-4 ⁺ , p=0.0152 OGD ⁺ LPS ⁻ IL-4 ⁺) ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0161
1F	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =26.69	ANOVA p<0.0003 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0009 OGD ⁺ LPS ⁻ IL-4 ⁺) ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0016
1G	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =0.9046	ANOVA p<0.0002 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0064 OGD ⁺ LPS ⁺ IL-4 ⁻) ⁻ vs OGD ⁺ LPS ⁻ IL-4 ⁺ , p<0.0003
1H	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =3.156	ANOVA p<0.0020 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0051 OGD ⁺ LPS ⁺ IL-4 ⁻) ⁻ vs OGD ⁺ LPS ⁻ IL-4 ⁺ , p<0.0032
11	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test); Tukey post hoc	F _(2,8) =11.79	ANOVA p<0.0041 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p=0.0047 OGD ⁺ LPS ⁺ IL-4 ⁻) ⁻ vs OGD ⁺ LPS ⁻ IL-4 ⁺ , p<0.0028
1J	Randomly sampled from 3 independent cultures	Non-normal distribution	One-way ANOVA on ranks (Brown- Forsythe test);	F(2,8)=0.7144	ANOVA p<0.0001 OGD ⁻ LPS ⁻ IL-4 ⁻ vs OGD ⁺ LPS ⁺ IL-4 ⁻ , p<0.0183

			Tukey post hoc		OGD ⁻ LPS ⁻ IL-4 ⁻ vs
					OGD+LPS+IL-4 ⁻ , p=0.0083
					OGD ⁺ LPS IL-4 ⁺) ⁻ VS OGD ⁺ LPS ⁺ II -4 ⁻ n<0.0001
					Normoxia:Scramble siRNA vs.
	36 microalia imagas			Interaction:	Normoxia:IRF5 siRNA,
	(Scrambled siRNA)			$F_{(1,8)}=8.266, p<0.001$	p=0.0011
	42 microglia images		Ordinary	Dow (Saramblad va	Normoxia:Scramble siRNA vs.
	(IRF5 SiRNA)		TWO-way	siRNA) factor:	p < 0.0001
2C	48 microglia images	Non-normal distribution	ANOVA;	$F_{(1,8)}=151.7, p=0.2740$	Normoxia:Scramble siRNA vs.
	(INI4 SINNA)	distribution	Tukey multiple		OGD:IRF5 siRNA, p<0.0001
	Sample		post hoc	Column (Normoxia vs OGD) Factor:	Normoxia:IRF5 siRNA vs.
	from 3 independent			$F_{(1,8)}=39.91$, p=0.0006	0.0169
	cultures				Normoxia:IRF5 siRNA vs.
					OGD:IRF5 siRNA, p=0.0009
					Normoxia: Scramble siRNA vs. Normoxia: IRE5 siRNA
				Interaction:	p=0.0098
	36 microglia images			F(1,8)=150.8, p<0.0001	Normoxia:Scramble siRNA vs.
	(Scrambled siRNA)		Ordinary	Dow (Somethind wa	OGD:Scramble siRNA,
	42 microglia images		TWO-way	siRNA) factor:	Normoxia:Scramble siRNA vs.
2D	(IRF5 SiRNA)	Non-normal distribution	ANOVA;	F(1,8)=164.4, p=0.0010	OGD:IRF5 siRNA, p=0.0004
	Compled for a 2	distribution	Tukey multiple	Calumn (Namuania an	Normoxia:IRF5 siRNA vs.
	independent		post noc	OGD) Factor:	DGD:Scramble siRINA, p=0.9978
	cultures			$F_{(1,8)}=164.4, p=0.0005$	Normoxia:IRF5 siRNA vs.
				-	OGD:IRF5 siRNA, p<0.0001
					OGD:Scramble siRNA vs.
					Normoxia:Scramble siRNA vs.
					Normoxia:IRF4 siRNA,
	26 mianalia imagaa			Interaction: $E_{1} = 164.4 \text{ m} < 0.001$	p=0.0047
	(Scrambled siRNA)			r(1,8)=104.4, p<0.001	OGD:Scramble siRNA
	(Ordinary	Row (Scrambled vs	p=0.0002
	48 microglia images	Non-normal	TWO-way	siRNA) factor:	Normoxia:Scramble siRNA vs.
2E	(IRF4 S1RNA)	distribution	ANOVA; Tukey multiple	$F_{(1,8)}=1.379$, p=0.2740	OGD:IRF4 s1RNA, p=0.0096
	Sampled from 3		post hoc	Column (Normoxia vs	OGD:Scramble siRNA,
	independent			OGD) Factor:	p=0.0974
	cultures			F _(1,8) =29.43, p=0.0006	Normoxia:IRF4 siRNA vs.
					OGD:IKF4 SIKINA, p<0.0001 OGD:Scramble siRNA vs.
					OGD:IRF4 siRNA, p<0.0001
					Normoxia:Scramble siRNA vs.
				Interaction:	Normoxia:IRF4 siKNA, $p=0.0076$
	36 microglia images			$F_{(1,8)}=2.226$, p=0.1741	Normoxia:Scramble siRNA vs.
	(Scrambled siRNA)				OGD:Scramble siRNA,
	19 mianalia inter-		Ordinary	Row (Scrambled vs	p=0.2070
2F	40 microgna images (IRF4 SiRNA)	Non-normal	ANOVA:	$F_{(1,8)}=4.081$, p=0.0780	OGD:IRF4 siRNA n=0.0048
	()	distribution	Tukey multiple	(-,0), p 0.0700	Normoxia:IRF4 siRNA vs.
	Sampled from 3		post hoc	Column (Normoxia vs	OGD:Scramble siRNA,
	independent			OGD) Factor: $F_{(1,8)}=28.79 \text{ p}=0.0007$	p=0.2441 Normoxia IRF4 siRNA vs
	culturos			- (1,0)-20.77, p=0.0007	OGD:IRF4 siRNA, 0.9995
					OGD:Scramble siRNA vs.
					OGD:IRF4 siRNA, p=0.1435

2G	Sampled from 3 independent cultures	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(2,17)}=54.87$, p<0.0001 Row (Scrambled vs IRF5-siRNA/IRF4- siRNA) factor: $F_{(1,17)}=34.03$, p<0.0001 Column (Normoxia vs OGD) Factor: $F_{(2,17)}=73.21$, p<0.0001	Normoxia:Scramble siRNA vs. Normoxia:IRF4 siRNA, p=0.4768 Normoxia:Scramble siRNA vs. OGD:Scramble siRNA, p=0.9047 Normoxia:Scramble siRNA vs. OGD:IRF5 siRNA, $p<0.0001$ Normoxia:Scramble siRNA vs. OGD:IRF4 siRNA, $p=0.2024$ Normoxia:IRF5 siRNA vs. OGD:IRF4 siRNA, $p=0.2024$ Normoxia:IRF5 siRNA vs. Normoxia:IRF5 siRNA vs. OGD:Scramble siRNA, p=0.5055 Normoxia:IRF5 siRNA vs. OGD:Scramble siRNA, p=0.9397 Normoxia:IRF5 siRNA vs. OGD:IRF5 siRNA, $p<0.0001$ Normoxia:IRF5 siRNA, $p=0.2030$ Normoxia:IRF5 siRNA, $p=0.2030$ Normoxia:IRF4 siRNA, $p=0.2030$ Normoxia:IRF4 siRNA, $p=0.2030$ Normoxia:IRF4 siRNA, $p=0.9489$ Normoxia:IRF4 siRNA, $p=0.9489$ Normoxia:IRF4 siRNA, $p=0.9854$ OGD:IRF5 siRNA, $p<0.0001$ Normoxia:IRF4 siRNA, $p=0.9854$ OGD:Scramble siRNA vs. OGD:IRF5 siRNA, $p<0.0001$ OGD:Scramble siRNA vs. OGD:IRF5 siRNA, $p<0.0001$ OGD:Scramble siRNA vs. OGD:IRF4 siRNA, $p=0.6592$ OGD:IRF4 siRNA, $p<0.0001$
2Н	Sampled from 3 independent cultures	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(2,17)}=34.02$, p<0.0001 Row (Scrambled vs IRF5-siRNA/IRF4- siRNA) factor: $F_{(1,17)}=204.7$, p<0.0001 Column (Normoxia vs OGD) Factor: $F_{(2,17)}=33.33$, p<0.0001	Normoxia:Scramble siRNA vs. Normoxia:IRF5 siRNA, p>0.9999 Normoxia:Scramble siRNA vs. Normoxia:IRF4 siRNA, p=0.9944 Normoxia:Scramble siRNA vs. OGD:Scramble siRNA, p=0.0026 Normoxia:Scramble siRNA vs. OGD:IRF5 siRNA, p=0.0007 Normoxia:Scramble siRNA vs. OGD:IRF5 siRNA, p=0.0001 Normoxia:IRF5 siRNA, vs. OGD:IRF4 siRNA, p<0.0001 Normoxia:IRF5 siRNA vs. OGD:Scramble siRNA, p=0.9993 Normoxia:IRF5 siRNA vs. OGD:Scramble siRNA, p=0.0039 Normoxia:IRF5 siRNA vs. OGD:IRF5 siRNA, p=0.0010 Normoxia:IRF5 siRNA vs. OGD:IRF4 siRNA, p<0.0001 Normoxia:IRF4 siRNA, p<0.0001 Normoxia:IRF4 siRNA, p<0.0001 Normoxia:IRF4 siRNA, p=0.0010 Normoxia:IRF4 siRNA, p=0.0010 Normoxia:IRF4 siRNA, p=0.0001

3F	4 mice (Sham IRF4 fl/fl) 4 mice (Sham IRF4 CKO) 6-7 mice (Stroke IRF4 fl/fl) 6-7 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Row (Sham vs Stroke) factor: $F_{(1,17)}=64.78$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,17)}=26.36$, p<0.0001	Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl, p=0.0397 Sham:IRF4 fl/fl vs. Stroke:IRF4 CKO, p<0.0001 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.2157 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p<0.0001 Stroke:IRF4 fl/fl vs.
 3E	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6-7 mice (Stroke IRF5 fl/fl) 6-7 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,17)}=33.63$, p<0.0001 Row (Sham vs Stroke) factor: $F_{(1,17)}=34.97$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,17)}=18.5$, p=0.0005 Interaction: $F_{(1,17)}=14.45$, p=0.0014	Shoke.IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.7701 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.6801 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p<0.0001 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p=0.9998 Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.8309
3C	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 7 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,17)}=25.53$, p<0.0001 Row (Sham vs Stroke) factor: $F_{(1,17)}=92.58$, p<0.0001 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,17)}=23.46$, p=0.0002	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9910 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.1530 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO, p=0.0208 Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs.
3B	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 7 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,17)}=22.86$, p=0.0002 Row (Sham vs Stroke) factor: $F_{(1,17)}=148.9$, p<0.0001 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,17)}=31.96$, p<0.0001	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9440 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0014 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p<0.0001 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001
					Normoxia:IRF4 siRNA vs. OGD:IRF4 siRNA,p=<0.0001 OGD:Scramble siRNA vs. OGD:IRF5 siRNA, p=0.9827 OGD:Scramble siRNA vs. OGD:IRF4 siRNA, p<0.0001 OGD:IRF5 siRNA vs. OGD:IRF5 siRNA vs.

	8-9 mice (Stroke IRF5 CKO)			Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,24)}$ =8.828, p=0.0066	Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0020 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0052
4C	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 11 mice (Stroke IRF5 fl/fl) 8-9 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=1.341$, p=0.2583 Row (Sham vs Stroke) factor: $F_{(1,24)}=11.53$, p=0.0024 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,24)}=10.56$, p=0.0034	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.0681 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.9996 Sham:IRF5 CKO, p=0.9996 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0004 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0199 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.2348
4E	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 11 mice (Stroke IRF5 fl/fl) 8-9 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=2.746$, p=0.1105 Row (Sham vs Stroke) factor: $F_{(1,24)}=3.973$, p=0.0577 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,24)}=0.9833$, p=0.3313	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9787 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.1880 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.8887 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0781 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0909
4F	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 8 mice (Stroke IRF5 fl/fl) 8 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,20)}=18.76$, p=0.0003 Row (Sham vs Stroke) factor: $F_{(1,20)}=16.07$, p=0.0007 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,20)}=8.929$, p=0.0073	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.8432 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0004 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.8871 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p<0.0001 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001
4H	4 mice (Sham IRF4 fl/fl) 4 mice (Sham IRF4 CKO) 10 mice (Stroke IRF4 fl/fl) 8-9 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=1.360$, p=0.2560 Row (Sham vs Stroke) factor: $F_{(1,24)}=10.47$, p=0.0038 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,24)}=7.839$, p=0.0104	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.0471 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0010 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.9908 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p=0.0352 Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0045
4I	4 mice (Sham IRF4 fl/fl) 3 mice (Sham IRF4 CKO) 10 mice (Stroke IRF4 fl/fl)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=0.0224$, p=0.8821 Row (Sham vs Stroke) factor: $F_{(1,24)}=2.432$, p=0.1320	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.036 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl, p=0.6274 Sham:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0115

	8-9 mice (Stroke				Sham:IRF4 CKO vs
	IRF4 CKO)			Column (IRF4 fl/fl vs	Stroke:IRF4 fl/fl, p=0.6286
				IRF4 CKO) Factor:	Sham:IRF4 CKO vs.
				F(1,24)=10.67, p=0.0030	Stroke:IRF4 CKO, p=0.7527
					Stroke:IRF4 fl/fl vs.
					Stroke:IRF4 CKO, p=0.0356
				Interaction:	Sham:IRF4 fl/fl vs. Sham:IRF4
				F(1,22)=6.887, p=0.0155	CKO, p>0.9999
	4 mice (Sham IRF4				Sham:IRF4 fl/fl vs.
	fl/fl)		Ordinary	Row (Sham vs Stroke)	Stroke:IRF4 fl/fl, p=0.0047
	4 mice (Sham IRF4		TWO-way	factor: $F_{(1,22)}=7.775$,	Sham:IRF4 fl/fl vs.
4K	CKO)	Non-normal	ANOVA:	p=0.0107	Stroke:IRF4 CKO, p=0.9999
	10 mice (Stroke IRF4	distribution	Tukey multiple		Sham:IRF4 CKO vs.
	11/11) 8.0 mice (Strole		post hoc	UDE4 CKO) Easter	Stroke:IRF4 II/II, p=0.0045
	No. 3 Prince (Stroke			$F_{4} = -7.210 \text{ p} - 0.0135$	Shall:IKF4 CKO vs. Stroke:IPE4 CKO vs.
	IKI4 CKO)			r(1,22)=7.210, p=0.0155	Stroke: IDE4 fl/fl vs
					Stroke:IRF4 CKO p=0.0005
				Interaction:	Show: IDE4 fl/fl vg Show: IDE4
				$F_{(1,22)} = 2509 \text{ n} = 0.1274$	CKO p=0.028
	4 mice (Sham IRF4			r (1,22)-2.000, p-0.127 r	Sham:IRF4 fl/fl vs.
	fl/fl)		o 11	Row (Sham vs Stroke)	Stroke:IRF4 fl/fl, $p=0.0008$
	4 mice (Sham IRF4		Ordinary	factor: $F_{(1,22)}=23.99$.	Sham:IRF4 fl/fl vs.
47	CKO)	Non-normal	TWO-way	p<0.0001	Stroke:IRF4 CKO, p=0.9977
4L	10 mice (Stroke IRF4	distribution	ANOVA;	1	Sham:IRF4 CKO vs.
	fl/fl)		Tukey multiple	Column (IRF4 fl/fl vs	Stroke:IRF4 fl/fl, p<0.0001
	8-9 mice (Stroke		post noc	IRF4 CKO) Factor:	Sham:IRF4 CKO vs.
	IRF4 CKO)			F(1,22)=21.50, p=0.0001	Stroke:IRF4 CKO, p=0.1187
					Stroke:IRF4 fl/fl vs.
					Stroke:IRF4 CKO, p<0.0001
				Interaction:	Sham:IRF4 fl/fl vs. Sham:IRF4
				$F_{(1,18)}=18.2, p=0.0005$	CKO, p>0.9999
	4 mice (Snam IRF4			\mathbf{D}_{res} (Charmon Charles)	Sham:IRF4 II/II VS.
	11/11)		Ordinary	footom Europe 45, 14	Stroke: IRF4 II/II, $p=0.2882$
	4 Inice (Shain IKF4	Non-normal	TWO-way	$r_{(1,18)} = 43.14,$	Stroke: IRE4 CKO p<0.0001
5B	6 mice (Stroke IRF4	distribution	ANOVA;	p<0.0001	Show: IRF4 CKO, p<0.0001
	fl/fl)	distribution	Tukey multiple	Column (IRF4 fl/fl vs	Stroke: IRF4 fl/fl $p=0.3899$
	6 mice (Stroke IRF4		post hoc	IRF4 CKO) Factor:	Sham:IRF4 CKO vs.
	CKO)			$F_{(1,18)}=18.45$, p=0.0004	Stroke:IRF4 CKO, p<0.0001
	,				Stroke:IRF4 fl/fl vs.
					Stroke:IRF4 CKO, p<0.0001
				Interaction:	Sham:IRF4 fl/fl vs. Sham:IRF4
				F _(1,18) =17.44, p=0.0006	CKO, p>0.9999
	4 mice (Sham IRF4				Sham:IRF4 fl/fl vs.
	fl/fl)		Ordinary	Row (Sham vs Stroke)	Stroke:IRF4 fl/fl, p=0.5624
	4 mice (Sham IRF4	NT 1	TWO-way	factor: $F_{(1,18)}=35.82$,	Sham:IRF4 fl/fl vs.
5C	CKU)	Non-normal	ANOVA;	p<0.0001	Stroke:IRF4 CKO, p<0.0001
	o IIIce (Stroke IKF4	distribution	Tukey multiple	Column (IDE4 fl/fl us	Shalli.IKF4 CKO VS. Stroko:IDE4 fl/fl p=0.6126
	6 mice (Stroke IREA		post hoc	IRE4 CKO) Factor:	Show:IRE4 CKO vs
	CKO)			$F_{(1,18)} = 17.47 \text{ n} = 0.0006$	Stroke:IRF4 CKO vs.
	cho)			1 (1,13)-17.17, p=0.0000	Stroke:IRF4 fl/fl vs
					Stroke:IRF4 CKO, p<0.0001
	4 mice (Sham IRF4			TAN	Sham:IRF4 fl/fl vs. Sham:IRF4
	fl/fl)		Ordin	Interaction:	CKO, p>0.9999
	4 mice (Sham IRF4		TWO way	г _(1,18) =39.81, p<0.0001	Sham:IRF4 fl/fl vs.
5D	CKO)	Non-normal		Row (Sham ve Strake)	Stroke:IRF4 fl/fl, p=0.9595
	6 mice (Stroke IRF4	distribution	Tukey multiple	factor: $F_{(1,10)}$ -70.71	Sham:IRF4 fl/fl vs.
	fl/fl)		post hoc	p < 0.0001	Stroke:IRF4 CKO, p<0.0001
	6 mice (Stroke IRF4		Post not	P (0.0001	Sham:IRF4 CKO vs.
	CKO)				Stroke:IRF4 fl/fl, p=0.9685

				Column (IRF4 fl/fl vs IRF4 CKO) Factor: F(1,18)=60.08, p<0.0001	Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p<0.0001 Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p<0.0001
5E	4 mice (Sham IRF4 fl/fl) 4 mice (Sham IRF4 CKO) 6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=0.5823$, p=0.4565 Row (Sham vs Stroke) factor: $F_{(1,18)}=128.3$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,18)}=1.454$, $p=0.2455$	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.9915 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl, p<0.0001 Sham:IRF4 fl/fl vs. Stroke:IRF4 CKO, p<0.0001 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p<0.0001 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p<0.0001 Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.4294
5F	5 mice (Sham IRF5 fl/fl) 5 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=13.33$, p=0.0018 Row (Sham vs Stroke) factor: $F_{(1,18)}=54.54$, p<0.0001 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,18)}=11.05$, p=0.0038	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9960 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0457 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0720 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001
5G	5 mice (Sham IRF5 fl/fl) 5 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=1.189$, p=0.2899 Row (Sham vs Stroke) factor: $F_{(1,18)}=13.73$, p<0.0001 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,18)}=1.342$, p=0.2618	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p>0.9999 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl, p=0.0008 Sham:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0252 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0008 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0228 Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs.
5Н	5 mice (Sham IRF5 fl/fl) 5 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=0.1190,$ p=0.7342 Row (Sham vs Stroke) factor: $F_{(1,18)}=77.40,$ p<0.0001 Column (IRF5 fl/fl vs IRF5 CKO) Factor: $F_{(1,18)}=0.4526,$ p=0.5097	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9960 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p<0.0001 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.8735
51	5 mice (Sham IRF5 fl/fl) 5 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: F(1,18)=34.90, p<0.0001 Row (Sham vs Stroke) factor: F(1,18)=124.5, p<0.0001	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p<0.0001 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl, p=0.0290 Sham:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.001

	6 mice (Stroke IRF5 CKO)			Column (IRF5 fl/fl vs IRF5 CKO) Factor: F(1,18)=045.99, p<0.0001	Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0079 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001
5J	5 mice (Sham IRF4 fl/fl) 5 mice (Sham IRF4 CKO) 6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=2.614$, p=0.1233 Row (Sham vs Stroke) factor: $F_{(1,18)}=122.7$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,18)}=21.43$, p=0.0002	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.2106 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p<0.0001 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.0013 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p<0.0001 Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0011
5K	5 mice (Sham IRF4 fl/fl) 5 mice (Sham IRF4 CKO) 6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=0.0737$, p=0.7890 Row (Sham vs Stroke) factor: $F_{(1,18)}=1.333$, p=0.2633 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,18)}=0.0547$, p=0.8176	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p>0.9999 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl, p=0.9229 Sham:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.7613 Sham:IRF4 CKO, p=0.7613 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.9138 Sham:IRF4 CKO, p=0.7465 Stroke:IRF4 CKO, p=0.7465
5L	5 mice (Sham IRF4 fl/fl) 5 mice (Sham IRF4 CKO) 6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=8.6660,$ p=0.0087 Row (Sham vs Stroke) factor: $F_{(1,18)}=22.85,$ p=0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,18)}=9.3310,$ p=0.0068	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.9998 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl, p=0.5757 Sham:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0002 Sham:IRF4 CKO, p=0.0002 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.6227 Sham:IRF4 CKO, p=0.0002 Stroke:IRF4 CKO, p=0.0002 Stroke:IRF4 CKO, p=0.0016
5M	5 mice (Sham IRF4 fl/fl) 5 mice (Sham IRF4 CKO) 6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,18)}=5.83$, p=0.0266 Row (Sham vs Stroke) factor: $F_{(1,18)}=26.73$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,18)}=3.515$, p=0.0771	Sham:IRF4 fl/fl vs. Sham:IRF4 CKO, p=0.9828 Sham:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0005 Sham:IRF4 CKO vs. Stroke:IRF4 fl/fl, p=0.1218 Sham:IRF4 CKO vs. Stroke:IRF4 CKO, p=0.0002 Stroke:IRF4 fl/fl vs. Stroke:IRF4 CKO, p=0.0243
6A	7 mice (Stroke IRF5 fl/fl)	Non-normal distribution	t test (two- tailed)	$t_{(11)}$ =4.203 (Cortex) $t_{(11)}$ =3.800 (Striatum)	fl/fl vs CKO, p=0.0018 (Cortex)

	6 mice (Stroke IRF5			$t_{(11)}=5.279$	fl/fl vs CKO, p=0.0035
	CKO)			(Hemisphere)	(Striatum)
					fl/fl vs CKO, p=0.0004
					(Hemisphere)
	6 mice (Stroke IRF5				fl/fl vs CKO p=0 1765 (30
6B	fl/fl)	Non-normal	t test (two-	$t_{(10)}=1.545$ (30 days)	davs)
0D	6 mice (Stroke IRF5	distribution	tailed)		duysy
-	CKO)				
	6 mice (Stroke IRF5				fl/fl vs CKO, p=0.0010 (3
6C	fl/fl)	Non-normal	t test (two-	$t_{(10)}=4.595$ (3 days)	days)
	6 mice (Stroke IRF5	distribution	tailed)	$t_{(10)}=0.5044 (30 \text{ days})$	fl/fl vs CKO, $p=0.6249$ (30
-	CKO)				days)
	6 mice (Stroke IRF5	Non normal	t toot (true	-5.571 (2 days)	fl/fl vs CKO, p=0.0002 (3)
6D	11/11) 6 mice (Strole IDE5	Non-normal	t lest (two-	$l_{(10)}=3.371$ (5 days)	f(f) = 0.2150 (20)
	CKO)	distribution	talleu)	l(10) = 1.515 (50 days)	dave)
	6 mice (Stroke IRE5				$fl/fl_{VS} CKO_{p=0.2560}$ (3
	fl/fl)	Non-normal	t test (two-	$t_{(10)} = 1.2050 (3 \text{ days})$	days)
6E	6 mice (Stroke IRF5	distribution	tailed)	$t_{(10)}=2.8600 (30 \text{ days})$	f[/f] vs CKO, p=0.0169 (30
	CKO)			·(10)(20	davs)
	6 mice (Stroke IRF5				fl/fl vs CKO, p=0.1182 (3
Œ	fl/fl)	Non-normal	t test (two-	$t_{(10)}=1.7090$ (3 days)	days)
OF	6 mice (Stroke IRF5	distribution	tailed)	$t_{(10)}=2.431$ (30 days)	fl/fl vs CKO, p=0.0354 (30
	CKO)				days)
	6 mice (Stroke IRF5				fl/fl vs CKO p=0.0779 (30)
6G	fl/fl)	Non-normal	t test (two-	$t_{(10)} = 1.946 (30 \text{ days})$	davs)
00	6 mice (Stroke IRF5	distribution	tailed)	<i>i</i> (10)-1.940 (30 ddys)	uays)
	CKO)				
	6 mice (Stroke IRF5				fl/fl vs CKO, p=0.1855 (30
6H	fl/fl)	Non-normal	t test (two-	$t_{(10)}=1.4220$ (30 days)	days)
	6 mice (Stroke IRF5	distribution	tailed)		5 /
	CKU)				$fl/fl v \in CVO$ $p=0.2219$
	6 7 mice (Stroke			$t_{\rm ev} = 1.015$ (Cortex)	(Cortex)
	IRF5 fl/fl)	Non-normal	t test (two	$t_{(11)} = 1.013$ (Contex) $t_{(11)} = 3.338$ (Striatum)	fl/fl vs CKO p=0.0066
6I	6 mice (Stroke IRF5	distribution	tailed)	$t_{(11)}=1.507$	(Striatum)
	CKO)			(Hemisphere)	fl/fl vs CKO, p=0.1660
	,				(Hemisphere)
	6 mice (Stroke IRF4				
61	fl/fl)	Non-normal	t test (two-	$t_{\rm max} = 2.762$ (20 days)	fl/fl vs CKO, p=0.0037 (30
05	6 mice (Stroke IRF4	distribution	tailed)	l(10) = 5.705 (50 days)	days)
	CKO)				
	6-7 mice (Stroke				fl/fl vs CKO, p=0.0143 (3
6K	IRF4 fl/fl)	Non-normal	t test (two-	$t_{(10)}=2.863$ (3 days)	days)
	6 mice (Stroke IRF4	distribution	tailed)	$t_{(10)}=0.542$ (30 days)	fl/fl vs CKO, p=0.5995 (30)
	CKU)				$\frac{days}{days}$
	10-7 mice (Stroke	Non normal	t tast (two	$t_{(10)} = 3.087 (2.4 \text{ avg})$	11/11 VS CKO, p=0.0103 (3)
6L	6 mice (Stroke IRF4	distribution	tailed)	$t_{(10)} = -4.065 (30 \text{ days})$	f[/f] vs CKO p=0.0019 (30
	CKO)	distribution	(anea)	<i>i</i> (10)-4.005 (50 ddys)	davs)
	6-7 mice (Stroke				fl/fl vs CKO, p=0.0393 (3
	IRF4 fl/fl)	Non-normal	t test (two-	$t_{(10)}=2.370$ (3 days)	davs)
6M	6 mice (Stroke IRF4	distribution	tailed)	$t_{(10)}=4.065 (30 \text{ days})$	fl/fl vs CKO, p=0.0005 (30
	CKO)		· ·		days)
	6-7 mice (Stroke				fl/fl vs CKO, p=0.0307 (3
6N	IRF4 fl/fl)	Non-normal	t test (two-	t(10)=2.477 (3 days)	days)
UIN	6 mice (Stroke IRF4	distribution	tailed)	<i>t</i> (10)=8.437 (30 days)	fl/fl vs CKO, p<0.0001 (30
	CKO)				days)
60	6 mice (Stroke IRF4	Non-normal	t test (two-	$t_{(10)} = 0.238 (30 \text{ days})$	fl/fl vs CKO, p=0.8161 (30
	fl/fl)	distribution	tailed)	1(10)-0.230 (30 days)	days)

		1	1		
	6 mice (Stroke IRF4 CKO)				
6P	6 mice (Stroke IRF4 fl/fl) 6 mice (Stroke IRF4 CKO)	Non-normal distribution	t test (two- tailed)	<i>t</i> (10)=3.507 (30 days)	fl/fl vs CKO, p=0.0057 (30 days)
7B	4 mice (Sham Lenti- IRF4) 4 mice (Sham Lenti- GFP) 4 mice (Sham Lenti- IRF5) 7 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=0.025$, p=0.9725 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,24)}=6.298$, p=0.0063 Column (Sham vs Stroke) Factor: $F_{(1,24)}=20.82$, p=0.0001	Lenti-IRF4:Sham vs. Lenti- IRF4:Stroke, $p=0.1434$ Lenti-IRF4:Sham vs. Lenti- GFP:Sham, $p=0.9583$ Lenti-IRF4:Sham vs. Lenti- GFP:Stroke, $p=0.0250$ Lenti-IRF4:Sham vs. Lenti- IRF5:Sham, $p=0.3182$ Lenti-IRF4:Sham vs. Lenti- RF5:Stroke, $p=0.0004$ Lenti-IRF4:Stroke vs. Lenti- GFP:Sham, $p=0.5865$ Lenti-IRF4:Stroke vs. Lenti- GFP:Stroke, $p=0.8561$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p=0.0314$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p=0.0314$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.1556$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.0038$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.0038$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.8389$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.5572$ Lenti-IRF5:Sham vs. Lenti- IRF5:Stroke, $p=0.0903$
7C	4 mice (Sham Lenti- IRF4) 4 mice (Sham Lenti- GFP) 4 mice (Sham Lenti- IRF5) 7 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,24)}=1.939$, p=0.1649 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,24)}=8.959$, p=0.0012 Column (Sham vs Stroke) Factor: $F_{(1,24)}=40.49$, p<0.0001	Lenti-IRF4:Sham vs. Lenti- IRF4:Stroke, $p=0.0007$ Lenti-IRF4:Sham vs. Lenti- GFP:Sham, $p=0.9997$ Lenti-IRF4:Sham vs. Lenti- GFP:Stroke, $p=0.0123$ Lenti-IRF4:Sham vs. Lenti- IRF5:Sham, $p=0.7527$ Lenti-IRF4:Sham vs. Lenti- IRF5:Stroke, $p=0.9858$ Lenti-IRF4:Stroke vs. Lenti- GFP:Sham, $p=0.0003$ Lenti-IRF4:Stroke vs. Lenti- GFP:Stroke, $p=0.9341$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Sham, $p<0.0001$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p=0.0006$ Lenti-GFP:Sham vs. Lenti- GFP:Stroke, $p=0.1556$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.8917$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.9202$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.9202$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.0004$

					Lenti-GFP:Stroke vs. Lenti-
					IRF5:Stroke, p=0.0178
					Lenti-IRF5:Sham vs. Lenti-
					IRF5:Stroke, p=0.2830
7E	4 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 4 mice (Sham Lenti- IRF5) 7 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,21)}=1.347$, p=0.2815 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,21)}=2.575$, p=0.1000 Column (Sham vs Stroke) Factor: $F_{(1,21)}=9.732$, p=0.0052	Lenti-IRF4:Sham vs. Lenti- IRF4:Stroke, $p=0.9417$ Lenti-IRF4:Sham vs. Lenti- GFP:Sham, $p=0.9913$ Lenti-IRF4:Sham vs. Lenti- GFP:Stroke, $p=0.9732$ Lenti-IRF4:Sham vs. Lenti- IRF5:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti- IRF5:Stroke, $p=0.0472$ Lenti-IRF4:Stroke vs. Lenti- GFP:Sham, $p=0.6147$ Lenti-IRF4:Stroke vs. Lenti- GFP:Stroke, $p>0.9999$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Sham, $p=0.6147$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Sham, $p<0.9557$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p=0.0807$ Lenti-GFP:Sham vs. Lenti- IRF5:Sham, $p=0.9874$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.0110$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.0328$ Lenti-GFP:Stroke vs. Lenti- IRF5:Sham, $p=0.9809$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p=0.0399$ Lenti-IRF5:Sham vs. Lenti- IRF5:Stroke, $p=0.0232$
7F	3 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 3 mice (Sham Lenti- IRF5) 6 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,22)}=7.584$, p=0.0031 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,22)}=7.725$, p=0.0029 Column (Sham vs Stroke) Factor: $F_{(1,22)}=101.1$, p<0.0001	Lenti-IRF4:Sham vs. Lenti- IRF4:Stroke, $p=0.0137$ Lenti-IRF4:Sham vs. Lenti- GFP:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti- GFP:Stroke, $p=0.0005$ Lenti-IRF4:Sham vs. Lenti- IRF5:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-IRF4:Stroke vs. Lenti- GFP:Sham, $p=0.0265$ Lenti-IRF4:Stroke vs. Lenti- GFP:Stroke, $p=0.5232$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Sham, $p=0.0143$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p=0.0011$ Lenti-GFP:Sham vs. Lenti- IRF5:Sham, $p>0.9999$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p<0.0001$

					Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, p=0.0068 Lenti-IRF5:Sham vs. Lenti-
76	3 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 3 mice (Sham Lenti- IRF5) 6 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,22)}=4.349$, p=0.0230 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,22)}=4.467$, p=0.0211 Column (Sham vs Stroke) Factor: $F_{(1,22)}=50.54$, p<0.0001	IRF5:Stroke, $p<0.0001$ Lenti-IRF4:Sham vs. Lenti-IRF4:Stroke, $p=0.0124$ Lenti-IRF4:Sham vs. Lenti-GFP:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti-GFP:Stroke, $p=0.0259$ Lenti-IRF4:Sham vs. Lenti-IRF5:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti-IRF5:Stroke, $p<0.0001$ Lenti-IRF4:Stroke vs. Lenti-GFP:Stroke, $p<0.0001$ Lenti-IRF4:Stroke vs. Lenti-GFP:Sham, $p=0.1664$ Lenti-IRF4:Stroke vs. Lenti-GFP:Stroke, $p=0.9173$ Lenti-IRF4:Stroke vs. Lenti-IRF5:Sham, $p=0.1290$ Lenti-IRF4:Stroke vs. Lenti-IRF5:Stroke, $p<0.0017$ Lenti-GFP:Sham vs. Lenti-IRF5:Stroke, $p=0.0387$ Lenti-GFP:Sham vs. Lenti-IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti-IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti-IRF5:Stroke, $p=0.0271$ Lenti-GFP:Stroke vs. Lenti-IRF5:Stroke, $p=0.0498$ Lenti-IRF5:Sham vs. Lenti-IRF5:Stroke, $p<0.0001$
7H	3 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 3 mice (Sham Lenti- IRF5) 6 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,22)}=8.035$, p=0.0019 Row (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) factor: $F_{(1,22)}=7.992$, p=0.020 Column (Sham vs Stroke) Factor: $F_{(1,22)}=50.54$, p<0.0001	Lenti-IRF4:Sham vs. Lenti- IRF4:Stroke, $p=0.0005$ Lenti-IRF4:Sham vs. Lenti- GFP:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti- GFP:Stroke, $p<0.0001$ Lenti-IRF4:Sham vs. Lenti- IRF5:Sham, $p>0.9999$ Lenti-IRF4:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-IRF4:Stroke vs. Lenti- GFP:Sham, $p=0.0018$ Lenti-IRF4:Stroke vs. Lenti- GFP:Stroke, $p=0.3391$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Sham, $p=0.0008$ Lenti-IRF4:Stroke vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Sham vs. Lenti- IRF5:Sham, $p>0.9999$ Lenti-GFP:Sham vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Stroke, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Sham, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Sham, $p<0.0001$ Lenti-GFP:Stroke vs. Lenti- IRF5:Sham, $p<0.0001$

					Lenti-IRF5:Sham vs. Lenti- IRF5:Stroke, p<0.0001
8B	6 mice (Stroke Lenti- IRF4) 6 mice (Stroke Lenti- GFP) 5 mice (Stroke Lenti- IRF5)	Non-normal distribution	t test (two- tailed)	$t_{(11)}=2.234$ (Lenti-IRF4 vs Lenti-GFP, Cortex) $t_{(11)}=0.4118$ (Lenti- IRF4 vs Lenti-GFP, Striatum) $t_{(11)}=1.505$ (Lenti-IRF4 vs Lenti-GFP, Hemisphere) $t_{(11)}=4.028$ (Lenti-IRF5 vs Lenti-GFP, Cortex) $t_{(11)}=1.028$ (Lenti-IRF5 vs Lenti-GFP, Striatum) $t_{(11)}=4.427$ (Lenti-IRF5 vs Lenti-GFP, Hemisphere)	Lenti-IRF4 vs Lenti-GFP, p=0.0472 (Cortex) Lenti-IRF4 vs Lenti-GFP, p=0.6884 (Striatum) Lenti-IRF4 vs Lenti-GFP, p=0.1604 (Hemisphere) Lenti-IRF5 vs Lenti-GFP, p=0.0770 (Cortex) Lenti-IRF5 vs Lenti-GFP, p=0.0919 (Striatum) Lenti-IRF5 vs Lenti-GFP, p=0.0017 (Hemisphere)
8C	4 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 4 mice (Sham Lenti- IRF5) 7 mice (Stroke Lenti- IRF4) 6 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,23)}=2.990$, p=0.0678 Row (Sham vs Stroke) factor: $F_{(1,23)}=172.6$, p<0.0001 Column (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) Factor: $F_{(1,23)}=2.990$, p=0.0678	Sham:Lenti-GFP vs. Sham:Lenti-IRF4, $p>0.9999$ Sham:Lenti-GFP vs. Sham:Lenti-GFP vs. Stroke:Lenti-GFP, $p<0.0001$ Sham:Lenti-GFP vs. Stroke:Lenti-IRF4, $p<0.0001$ Sham:Lenti-GFP vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p>0.9999$ Sham:Lenti-IRF5, $p>0.9999$ Sham:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Stroke:Lenti-IRF5, $p<0.0001$ Stroke:Lenti-IRF5, $p<0.0001$ Stroke:Lenti-IRF5, $p=0.0225$ Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF5, $p=0.0225$ Stroke:Lenti-IRF5, $p=0.0062$
8D	4 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 3 mice (Sham Lenti- IRF5) 7 mice (Stroke Lenti- IRF4) 5 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,23)}=4.225$, p=0.0274 Row (Sham vs Stroke) factor: $F_{(1,23)}=28.88$, p<0.0001 Column (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) Factor: $F_{(1,23)}=0.944$, p=0.4036	Sham:Lenti-GFP vs. Sham:Lenti-IRF4, p>0.9999 Sham:Lenti-GFP vs. Sham:Lenti-IRF5, p=0.9425 Sham:Lenti-GFP vs. Stroke:Lenti-GFP, p=0.4741 Sham:Lenti-GFP vs. Stroke:Lenti-IRF4, p=0.3072 Sham:Lenti-GFP vs. Stroke:Lenti-IRF5, p=0.0012 Sham:Lenti-IRF5, p=0.9772

					Sham:Lenti-IRF4 vs. Stroke:Lenti-GFP, p=0.4913 Sham:Lenti-IRF4 vs. Stroke:Lenti-IRF4, p=0.3297 Sham:Lenti-IRF4, p=0.0023 Sham:Lenti-IRF5, p=0.0023 Sham:Lenti-IRF5 vs. Stroke:Lenti-GFP, p=0.1266 Sham:Lenti-IRF5 vs. Stroke:Lenti-IRF4, p=0.0737 Sham:Lenti-IRF5, p=0.0003 Stroke:Lenti-IRF5, p=0.0003 Stroke:Lenti-IRF5, p=0.0003 Stroke:Lenti-GFP vs. Stroke:Lenti-IRF4, p=0.9979 Stroke:Lenti-IRF5, p=0.0244 Stroke:Lenti-IRF4 vs.
8E	4 mice (Sham Lenti- IRF4) 3 mice (Sham Lenti- GFP) 4 mice (Sham Lenti- IRF5) 6 mice (Stroke Lenti- IRF4) 6 mice (Stroke Lenti- GFP) 6 mice (Stroke Lenti- IRF5)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,23)}=1.276$, p=0.2982 Row (Sham vs Stroke) factor: $F_{(1,23)}=400.6$, p<0.0001 Column (Lenti-GFP vs Lenti-IRF5 vs Lenti- IRF4) Factor: $F_{(1,23)}=2.906$, p=0.0750	Stroke:Lenti-IRF5, $p=0.0776$ Sham:Lenti-GFP vs. Sham:Lenti-IRF4, $p=0.9999$ Sham:Lenti-GFP vs. Sham:Lenti-GFP vs. Stroke:Lenti-GFP, $p<0.0001$ Sham:Lenti-GFP vs. Stroke:Lenti-IRF4, $p<0.0001$ Sham:Lenti-GFP vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p>0.9999$ Sham:Lenti-IRF5, $p>0.9999$ Sham:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF4 vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5 vs. Stroke:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Sham:Lenti-IRF5, $p<0.0001$ Stroke:Lenti-IRF5, $p<0.0001$ Stroke:Lenti-IRF5, $p=0.0850$ Stroke:Lenti-IRF4, $p=0.0871$
S1A	5 mice (IRF5 fl/fl) 5 mice (IRF5 CKO)	Non-normal distribution	t test (two- tailed)	t ₍₇₎ =2.557	fl/fl vs CKO, p=0.0377
S1B	4 mice (IRF4 fl/fl) 5 mice (IRF4 CKO)	Non-normal distribution	t test (two- tailed)	<i>t</i> (7)=3.466	fl/fl vs CKO, p=0.0105
S3A	6 mice (IRF5 fl/fl) 6 mice (IRF5 CKO)	Non-normal distribution	t test (two- tailed)	t(10)=0.341	fl/fl vs CKO, p=0.7402
S3B	6 mice (IRF5 fl/fl) 6 mice (IRF5 CKO)	Non-normal distribution	t test (two- tailed)	t(10)=0.514	fl/fl vs CKO, p=0.6180
S3C	6 mice (IRF4 fl/fl) 6 mice (IRF4 CKO)	Non-normal distribution	t test (two- tailed)	t(10)=0.619	fl/fl vs CKO, p=0.5496
S3D	6 mice (IRF4 fl/fl) 6 mice (IRF4 CKO)	Non-normal distribution	t test (two- tailed)	t(10)=1.296	fl/fl vs CKO, p=0.2360
S4C	4 mice (Sham IRF5 fl/fl)	Non-normal distribution	Ordinary TWO-way	Interaction: F _(1,16) =0.118, p=0.7357	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p>0.9999

	4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)		ANOVA; Tukey multiple post hoc	Row (Sham vs Stroke) factor: $F_{(1,16)}=22.37$, p=0.0002 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,16)}=0.1252$, p=0.7281	Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl, p=0.0311 Sham:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0117 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0318 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0119 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.9449
S4D	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,16)}=1.257$, p=0.2787 Row (Sham vs Stroke) factor: $F_{(1,16)}=60.94$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,16)}=1.342$, p=0.2637	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p>0.9999 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0012 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p<0.0001 Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.3081
S4E	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,16)}=0.8161$, p=0.3797 Row (Sham vs Stroke) factor: $F_{(1,16)}=21.73$, p=0.0003 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,16)}=0.8421$, p=0.3724	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p>0.9999 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.0057 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p=0.0749 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p=0.0058 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.4943
S4F	4 mice (Sham IRF5 fl/fl) 4 mice (Sham IRF5 CKO) 6 mice (Stroke IRF5 fl/fl) 6 mice (Stroke IRF5 CKO)	Non-normal distribution	Ordinary TWO-way ANOVA; Tukey multiple post hoc	Interaction: $F_{(1,16)}=0.3946$, p=0.5388 Row (Sham vs Stroke) factor: $F_{(1,16)}=85.81$, p<0.0001 Column (IRF4 fl/fl vs IRF4 CKO) Factor: $F_{(1,16)}=0.215$, $p=0.6491$	Sham:IRF5 fl/fl vs. Sham:IRF5 CKO, p=0.9996 Sham:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 fl/fl, p<0.0001 Sham:IRF5 CKO vs. Stroke:IRF5 CKO, p<0.0001 Stroke:IRF5 fl/fl vs. Stroke:IRF5 CKO, p=0.8235
S5B	5 mice (Lenti-GFP) 5 mice (Lenti-IRF4)	Non-normal distribution	t test (two- tailed)	t ₍₈₎ =5.209	Lenti-GFP vs Lenti-IRF4, p=0.0008
S5C	5 mice (Lenti-GFP) 5 mice (Lenti-IRF4)	Non-normal distribution	t test (two- tailed)	t ₍₈₎ =5.558	Lenti-GFP vs Lenti-IRF5, p=0.0004