

Figure number	Test	Technic	Treatment	Genotype	Sex	Age	Number	Mean	SEM(±)	Statistical test	Stat	P value	post hoc test	Comparison	t	P value
1C	co-localization test	Immunohistochemistry	co-local area with Aβ	5XFAD	M	8-9m	10 (for each groups)	-3.188	0.3148	unpaired t-test		<0.0001				
1F	cell volume analysis	Immunohistochemistry	PyrPeg in cell unit	5XFAD	M	8-9m	10 (for each groups)	-297	30.91	unpaired t-test		<0.0001				
2E	expression density	Immunohistochemistry	p16 <sup>ink4a</sup> expression	5ZXFAD / age matched littermate control	M	8-9m	10 (for each groups)	3.614	0.8285	unpaired t-test		0.0005				
2H	cell unit analysis	Immunohistochemistry	p16 <sup>ink4a</sup> expression with Iba1 or GFAP	5ZXFAD / age matched littermate control	M	8-9m	10 (for each groups)	37.08	2.845	unpaired t-test		<0.0001				
3A	expression density	western blot	p16 <sup>ink4a</sup>	BV2 cell				-1.5667	0.2963	unpaired t-test		0.0061				
3B	expression density	qRT-PCR	p16 <sup>ink4a</sup>	BV2 cell				-0.8275	0.1126	unpaired t-test		0.0003				
3F	cell viability test	MTT assay	p16 <sup>ink4a</sup> PLGA NPs	BV2 cell						Two-way ANOVA	F(3, 15) = 2.083	0.6126	Bonferroni's test			
3J	cell unit analysis	Immunohistochemistry	AAV-GFP NPs	WT	M	7w-8w	10 (for each groups)			one-way ANOVA		0.0115	tukey test	GFAP vs Iba1 GFAP vs NeuN Iba1 vs NeuN		<0.0001 0.0046 <0.0001
4B	distance/velocity	behavior test	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	7 (for each groups)			Two-way ANOVA	F(2, 39) = 0.07171	0.9309	Bonferroni's test	trial 1 trial 2 trial 3		0.4284 0.7481 0.5151
4E	time to target	behavior test	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	8 (for each groups)			Two-way ANOVA	F(4, 56) = 13.74	<0.0001	Bonferroni's test	Trial 1 Trial 2 Trial 3 Trial 4 Trial 5		>0.9999 <0.0001 <0.0001 <0.0001 <0.0001
4G	cell area analysis	Immunohistochemistry	Abeta	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	7 (for each groups)		one-way ANOVA	F(3, 24) = 63.49	<0.0001	tukey test	Cortex hippocampus		<0.0001 <0.0001
4H	cell surface area	Immunohistochemistry	Iba1	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	10 (for each groups)	-1.78	0.1952	unpaired t-test		<0.0001			
	plaque-close cell number	Immunohistochemistry	Iba1	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	10 (for each groups)	-1.75	0.1561	unpaired t-test		<0.0001			
4I	Abeta amount	ELISA	Abeta	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	8 (for each groups)	-37.57	2.415	unpaired t-test		<0.0001			
4J	expression density	western blot	p-Rb/Rb, Cyclin D1 Cyclin B1	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	9 (for each groups) 9 (for each groups) 9 (for each groups)	1.56 0.54 0.55	0.1939 0.088 0.1286	unpaired t-test unpaired t-test unpaired t-test		<0.0001 <0.0001 <0.0001			
5B	staining density	SA-beta-gal assay	colocal correlation	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	6 (for each groups)	-0.1159	0.02198	unpaired t-test		<0.0001			
5C	colocalization	SA-beta-gal assay	colocalization	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	6 (for each groups)	-3.792	0.4752	unpaired t-test		<0.0001			
5D	expression fold		mRNA	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD	M	8-9m	6 (for each groups)			Two-way ANOVA	F(10,110)=52.39	<0.0001	Tukey test		<0.0001

Figure

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5E	cell number counting	Immunohistochemistry	ki67	p16ink4a PLGA	5XFAD	M	8-9m	9 (for	1.911	0.1495	unpaired t-test		<0.0001				
5F	cell number counting	Immunohistochemistry	Lamp1	p16ink4a PLGA	5XFAD	M	8-9m	9 (for	1.956	0.136	unpaired t-test		<0.0001				
5I	cell number counting	Immunohistochemistry	TREM2	p16ink4a PLGA	5XFAD	M	8-9m	9 (for	1.978	0.1223	unpaired t-test		<0.0001				
5J	cell number counting	Immunohistochemistry	clec7a	p16ink4a PLGA	5XFAD	M	8-9m	9 (for	1.733	0.1577	unpaired t-test		<0.0001				
6B	phagocytosis analysis	Immunohistochemistry	phagosome number	p16ink4a siRNA/scramble siRNA	BV2 cell						Two-way ANOVA	F(2, 18) = 53.24	<0.0001	tukey test	<5		<0.0001
6E	Density	FACS	phagosome density	p16ink4a siRNA/scramble siRNA	BV2 cell						Two-way ANOVA	F(4, 20) = 37.36	<0.0001	tukey test	2 hours		<0.0001
															1 day		<0.0001
6J	cell unnumber (%)	FACS	G2/M, S, G0/G1	p16ink4a siRNA/scramble siRNA	BV2 cell						Two-way ANOVA	F(2, 18) = 6.256	0.0087	Bonferroni's test	G0/G1		0.0432
6L	expression density	western blot	p-Rb/Rb, Cyclin D1, Cyclin B1	p16ink4a siRNA/scramble siRNA	BV2 cell				1.92	0.2074	unpaired t-test		<0.0001				
									-0.728	-0.1338			0.0006				
									-0.672	0.1255			0.0007				

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Supple	1E	expression density	western blot	GFAP	5XFAD_WT	M	8-9m	6	0.6625	0.2239	unpaired t-test		0.0253						
				Ab	5XFAD_WT	M	8-9m	6	1.033	0.3061	unpaired t-test		0.0331						
				NeuN	5XFAD_WT	M	8-9m	6	-0.4725	0.02869	unpaired t-test		0.0022						
				Iba1	5XFAD_WT	M	8-9m	6	0.94	0.2767	unpaired t-test		0.0146						
	3	log2(CDKN2A TPM+1)	GTEx (genotype-tissue expression)	Amygdala					152			Kruska-wallis test			Dunn's multiple comparisons test	20-29 vs all		n.s.	
				Anterior cingulate cortex				176			20-29 vs 30-39			0.05					
				caudate basal ganglia				246			20-29 vs all			n.s.					
				cerebellum				241			20-29 vs all			n.s.					
				cortex				255			20-29 vs 60-69			0.0028					
				frontal cortex BA9				209			20-29 vs 70-79			0.0075					
				hippocampus				197			20-29 vs 60-69			0.034					
				hypothalamus				202			20-29 vs 60-69			0.0148					
				nucleus aaumbens basal ganglia				246			20-29 vs 70-79			0.0157					
				putamen basal ganglia				205			20-29 vs all			n.s.					
				spinal cord cervical C1				159			20-29 vs all			n.s.					
				substantial nigra				139			20-29 vs all			n.s.					
				4D	expression density	western blot	p16 <sup>ink4a</sup>	AD patient/healthy control	F/M		5		1.376	0.3067		unpaired t-test		0.002	
	Ab	AD patient/healthy control	F/M					5	1.336	0.3595	unpaired t-test		0.0059						
	Iba1	AD patient/healthy control	F/M					5	0.322	0.0823	unpaired t-test		0.0045						
	5A	expression	qRT-PCT	p16 <sup>ink4a</sup>	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD TG	M	8-9m	6	-0.5667	0.09006	unpaired t-test						<0.0001	
	5C	expression density	western blot	p16 <sup>ink4a</sup>	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD TG	M	8-9m	6	-3	0.2908	unpaired t-test						<0.0001	
	5E	expression density	Immunohistochemistry	p16 <sup>ink4a</sup>	p16 <sup>ink4a</sup> PLGA NPs/scramble siRNA PLGA NPs	5XFAD TG	M	8-9m	10	-0.88	0.08943	unpaired t-test						<0.0001	