

Supplementary Table S1. Aging, genotype, melatonin effect on clock gene expression in WT and NLRP3^{-/-} mice. Significant differences determined by *Tukey multiple comparison of mean* post-hoc test after Multifactorial-ANOVA.

Table S1.1. TRANSCRIPT: <i>Clock</i> . Post-hoc test: Tukey multiple comparison of mean											
<u>Aging effect on WT</u>			<u>Genotype effect</u>			<u>Melatonin effect on WT</u>			<u>Melatonin effect on NLRP3^{-/-}</u>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
0	Y vs OA	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	0	Y vs OA + aMT	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
	EA vs OA	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05	6	Y vs OA + aMT	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
6	Y vs EA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		EA vs EA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
	Y vs OA	<0.05		WT EA vs NLRP3 ^{-/-} EA	<0.05	12	Y vs OA + aMT	<0.05		WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
	EA vs OA	<0.05		WT OA vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05	6	WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
12	EA vs OA	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05	18	Y vs EA + aMT	<0.05	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
18	Y vs OA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		Y vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
	EA vs OA	<0.05		WT EA vs NLRP3 ^{-/-} EA	<0.05		EA vs EA + aMT	<0.05		WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
			12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05		OA vs OA + aMT	<0.05			
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05						
			18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05						
				NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05						
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05						

Table S1.2. TRANSCRIPT: *Bmall*. Post-hoc test: Tukey multiple comparison of mean

<u><i>Aging effect on WT</i></u>			<u><i>Genotype effect</i></u>			<u><i>Melatonin effect on WT</i></u>			<u><i>Melatonin effect on NLRP3^{-/-}</i></u>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
0	Y vs EA	<0.001	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.001	0	Y vs EA + aMT	<0.001	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.001
	Y vs OA	<0.001		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.001		Y vs OA + aMT	<0.001		WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.001
6	Y vs EA	<0.001	6	WT Y vs NLRP3 ^{-/-} Y	<0.01	6	Y vs EA + aMT	<0.05	12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.001
	EA vs OA	<0.05	12	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		Y vs OA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.001
18	Y vs EA	<0.001	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.001	18	Y vs EA + aMT	<0.001	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	Y vs OA	<0.001		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.001		Y vs OA + aMT	<0.001		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.001
				WT Y vs NLRP3 ^{-/-} Y	<0.001		EA vs EA+aMT	<0.001		WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.001
							EA + aMT vs OA	<0.001			
							EA + aMT vs OA + aMT	<0.001			

Table S1.3. TRANSCRIPT: *Per2*. Post-hoc test: Tukey multiple comparison of mean

<i>Aging effect on WT</i>			<i>Genotype effect</i>			<i>Melatonin effect on WT</i>			<i>Melatonin effect on NLRP3^{-/-}</i>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
0	Y vs EA	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05	6	Y vs EA + aMT	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	EA vs OA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
6	Y vs OA	<0.05		WT EA vs NLRP3 ^{-/-} EA	<0.05	12	Y vs EA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
	EA vs OA	<0.05		WT OA vs NLRP3 ^{-/-} OA	<0.05		EA vs EA + aMT	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
18	Y vs EA	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	18	Y vs EA + aMT	<0.05		WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
	Y vs OA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		Y vs OA + aMT	<0.05	12	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
	EA vs OA	<0.05		WT EA vs NLRP3 ^{-/-} EA	<0.05		EA vs EA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
			12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05		OA vs OA + aMT	<0.05		WT Y vs NLRP3 ^{-/-} Y	<0.05
				NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05					WT EA vs NLRP3 ^{-/-} EA	<0.05
			18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05					WT OA vs NLRP3 ^{-/-} OA	<0.05
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05					WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
				WT Y vs NLRP3 ^{-/-} Y	<0.05					WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
				WT EA vs NLRP3 ^{-/-} EA	<0.05				18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
				WT OA vs NLRP3 ^{-/-} OA	<0.05					NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
										WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
										WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05

Table S1.4. TRANSCRIPT: *Chrono*. Post-hoc test: Tukey multiple comparison of mean

Aging effect on WT		
Hour	Comparison	P value
6	Y vs EA	<0.05
	Y vs OA	<0.05
	EA vs OA	<0.05
12	Y vs EA	<0.05
	Y vs OA	<0.05
	EA vs OA	<0.05
18	Y vs OA	<0.05
	EA vs OA	<0.05
<u>Genotype effect</u>		
Hour	Comparison	P value
0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05
	WT Y vs NLRP3 ^{-/-} Y	<0.05
	WT EA vs NLRP3 ^{-/-} EA	<0.05
	WT OA vs NLRP3 ^{-/-} OA	<0.05
6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05
	WT EA vs NLRP3 ^{-/-} EA	<0.05
	WT OA vs NLRP3 ^{-/-} OA	<0.05
12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05
	WT Y vs NLRP3 ^{-/-} Y	<0.05
	WT EA vs NLRP3 ^{-/-} EA	<0.05
	WT OA vs NLRP3 ^{-/-} OA	<0.05
18		
<u>Melatonin effect on WT</u>		
Hour	Comparison	P value
0	Y vs EA + aMT	<0.05
	Y vs OA + aMT	<0.05
	EA vs EA + aMT	<0.05
	OA vs OA + aMT	<0.05
	Y vs EA + aMT	<0.05
	Y vs OA + aMT	<0.05
6	EA vs EA + aMT	<0.05
12	Y vs EA + aMT	<0.05
	Y vs OA + aMT	<0.05
	EA vs EA + aMT	<0.05
	OA vs OA + aMT	<0.05
18	Y vs EA + aMT	<0.05
	Y vs OA + aMT	<0.05
	EA vs EA + aMT	<0.05
<u>Melatonin effect on NLRP3^{-/-}</u>		
Hour	Comparison	P value
0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
	WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
	WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
	NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
12	WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
	WT OA +aMT vs NLRP3 ^{-/-} OA +aMT	<0.05

Table S1.4. TRANSCRIPT: *Chrono*. Post-hoc test: Tukey multiple comparison of mean (continued)

<i>Aging effect on WT</i>			<i>Genotype effect</i>			<i>Melatonin effect on WT</i>			<i>Melatonin effect on NLRP3^{-/-}</i>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
			18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05	18	OA vs OA + aMT	<0.05	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05					NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
				WT Y vs NLRP3 ^{-/-} Y	<0.05					WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
				WT EA vs NLRP3 ^{-/-} EA	<0.05					WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
				WT OA vs NLRP3 ^{-/-} OA	<0.05						

Table S1.5. TRANSCRIPT: *Rev-erba*. Post-hoc test: Tukey multiple comparison of mean

<u><i>Aging effect on WT</i></u>			<u><i>Genotype effect</i></u>			<u><i>Melatonin effect on WT</i></u>			<u><i>Melatonin effect on NLRP3^{-/-}</i></u>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
0	Y vs EA	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	6	Y vs EA + aMT	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	EA vs OA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05		Y vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
6	Y vs EA	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	12	Y vs EA + aMT	<0.05	12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
	Y vs OA	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05		Y vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
12	Y vs EA	<0.05	12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05		EA vs EA + aMT	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
	Y vs OA	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
	EA vs OA	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05	18	Y vs EA + aMT	<0.05	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
							Y vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
							EA vs EA + aMT	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05

Table S1.6. TRANSCRIPT: *Rora*. Post-hoc test: Tukey multiple comparison of mean

<u>Aging effect on WT</u>			<u>Genotype effect</u>			<u>Melatonin effect on WT</u>			<u>Melatonin effect on <i>NLRP3</i>^{-/-}</u>		
Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value	Hour	Comparison	P value
0	Y vs OA	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	0	Y vs EA + aMT	<0.05	0	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
6	Y vs OA	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
	EA vs OA	<0.05		WT Y vs NLRP3 ^{-/-} Y	<0.05	6	Y vs OA + aMT	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
18	EA vs OA	<0.05	6	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05	12	Y vs OA + aMT	<0.05		NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
				NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05		NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05	18	Y vs EA + aMT	<0.05	12	NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
				WT Y vs NLRP3 ^{-/-} Y	<0.05		Y vs OA + aMT	<0.05		NLRP3 ^{-/-} OA vs NLRP3 ^{-/-} OA + aMT	<0.05
				WT EA vs NLRP3 ^{-/-} EA	<0.05		EA vs EA + aMT	<0.05		WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
				WT OA vs NLRP3 ^{-/-} OA	<0.05		OA vs OA + aMT	<0.05	18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA + aMT	<0.05
			12	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} EA	<0.05					NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA + aMT	<0.05
				NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05					NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} EA + aMT	<0.05
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05					WT EA + aMT vs NLRP3 ^{-/-} EA + aMT	<0.05
				WT EA vs NLRP3 ^{-/-} EA	<0.05					WT OA + aMT vs NLRP3 ^{-/-} OA + aMT	<0.05
			18	NLRP3 ^{-/-} Y vs NLRP3 ^{-/-} OA	<0.05						
				NLRP3 ^{-/-} EA vs NLRP3 ^{-/-} OA	<0.05						
				WT Y vs NLRP3 ^{-/-} Y	<0.05						
				WT EA vs NLRP3 ^{-/-} EA	<0.05						