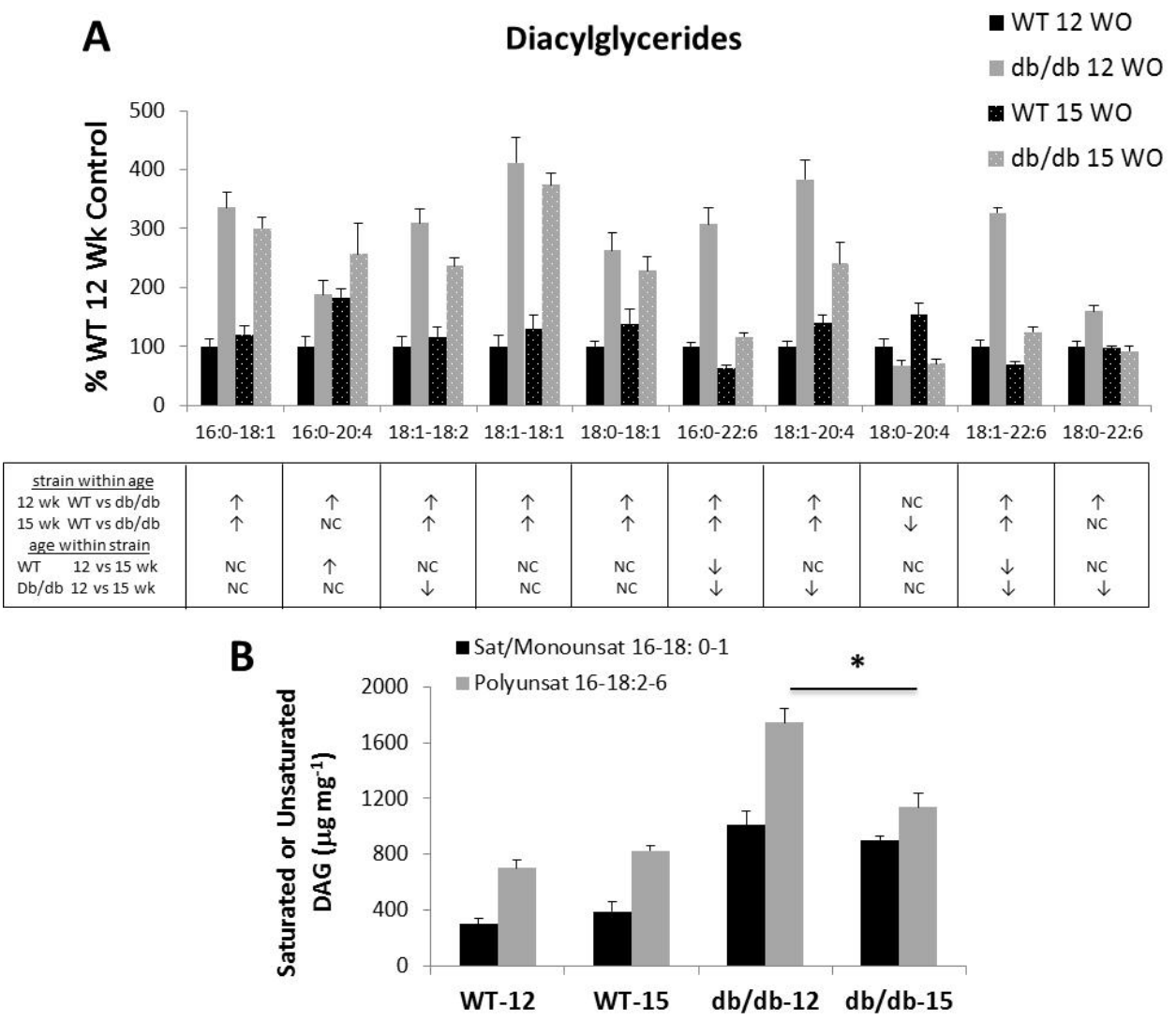
Supplemental Material

Supplemental Table 1. I*n vivo* cardiac functions in twelve and fifteen wk old wild type (WT) and db/db mice evaluated by cine-MRI.

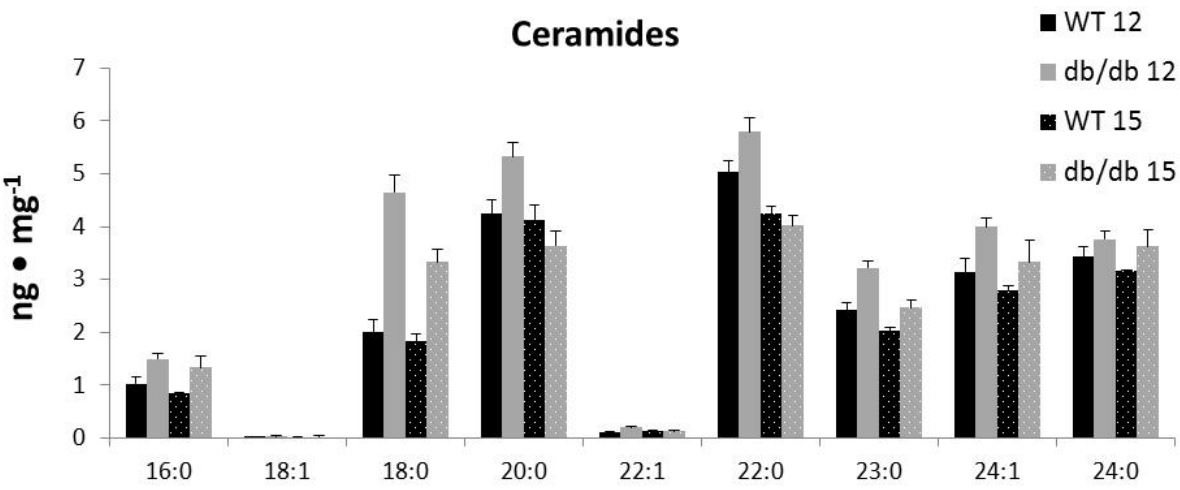
Parameter	Main Effects	P value	Wt (7)	db/db (7)	Wt (8)	db/db (12)
			12 wk of age		15 wk of age	
Body Mass (g)	Strain	0.001				
	Age	0.002	25.8 ± 0.53*	44.0 ± 1.7§	29.2 ± 0.6†	49.6 ± 1.4
	Interaction	0.395				
Heart Rate (bpm)	Strain	0.010				
	Age	0.553	469 ± 14*	381 ± 20	461 ± 29	418 ± 23
	Interaction	0.369				
Volumes						
End Diastolic Volume (µl)	Strain	0.069				
	Age	0.849	49.1 ± 3.4	49.1 ± 1.7	53.7 ± 1.8†	43.4 ± 2.8
	Interaction	0.071				
End Systolic Volume (µl)	Strain	0.015				
	Age	0.130	17.2 ± 1.6‡	16.1 ± 1.9	22.7 ± 1.5†	15.6 ± 1.3
	Interaction	0.066				
Stroke Volume (µL)	Strain	0.569				
	Age	0.114	31.9 ± 2.0	32.9 ± 1.4	31.0 ± 1.5	27.9 ± 1.9
	Interaction	0.270				
Systolic Indices						
Cardiac Output ($ml \bullet min^{-1}$)	Strain	0.010				
	Age	0.432	14.9 ± 0.9	12.4 ± 0.4	14.3 ± 1.2†	11.5 ± 0.9
	Interaction	0.868				
Cardiac Index ($ml \bullet min^{-1} \bullet g^{-1}$)	Strain	0.001				
	Age	0.010	0.58 ± 0.03‡*	0.28 ± 0.01	0.49 ± 0.3†	0.23 ± 0.02
	Interaction	0.456				
Ejection Fraction (%)	Strain	0.050				
	Age	0.019	65.3 ± 1.4‡	67.4 ± 2.9	57.8 ± 2.5†	64.3 ± 1.6
	Interaction	0.318				
Peak Ejection Rate ($\mu L \bullet ms^{-1}$)	Strain	0.017				
	Age	0.637	0.96 ± 0.04	0.80 ± 0.04	0.94 ± 0.11†	0.74 ± 0.06
	Interaction	0.776				
Diastolic Indices						
Initial Filling Rate ($\mu L \bullet ms^{-1}$)	Strain	0.049				
	Age	0.001	0.61 ± 0.10‡	0.50 ± 0.06§	0.34 ± 0.06$^{\alpha}$	0.19 ± 0.03
	Interaction	0.715				
Peak Filling Rate ($\mu L \bullet ms^{-1}$)	Strain	0.009				
	Age	0.846	1.01 ± 0.08	0.87 ± 0.06	1.07 ± 0.06†	0.78 ± 0.07
	Interaction	0.315				
Diastolic Relaxation Time	Strain	0.009	27.2 ± 3.1	32.3 ± 2.0§	29.7 ± 2.3†	40.5 ± 3.7
	Age	0.058				

(ms)	Interaction	0.254

*P<0.05 strain within 12 wk; † P<0.05 strain within 15 wk; ‡ P<0.05 Age within WT; § P<0.05 Age within db/db. $^{\alpha}$ P=0.07.



Supplemental Figure 1. (A) Diacylglyceride (DAG) accumulation in the hearts of 12 and 15 wk old db/db mice compared to age-matched WT mice. (B) Changes in DAG subspecies composition between the 12 and 15 wk db/db hearts. Black bars represent the sum of saturated and monounsatured diacylglycerides (DAG) species and gray bars represent the sum of polyunsaturated DAG species in the hearts of 12 and 15 wk old db/db and WT mice. Each bar represents the mean ± SE for 5-6 WT or db/db mice. Differences ($P<0.05$), i.e., increase, no change or decrease, are indicated by ↑, NC, and ↓, respectively in the table below the graph in panel A. Asterisk indicates $P<0.05$.



	16:0	18:1	18:0	20:0	22:1	22:0	23:0	24:1	24:0
strain within age									
12 wk WT vs db/db	↑	↑	↑	↑	↑	NC	↑	↑	NC
15 wk WT vs db/db	↑	↑	↑	NC	NC	NC	↑	NC	NC
age within strain									
WT 12 vs 15 wk	NC	NC	NC	NC	NC	↓	↓	NC	NC
Db/db 12 vs 15 wk	NC	NC	↓	↓	↓	↓	↓	NC	NC

Supplemental Figure 2. Ceramides accumulate in the hearts of 12, but not 15 wk old db/db mice compared to age-matched WT mice. Electrospray ionization-mass spectrometry was used to quantify individual lipid species. Each bar represents the mean ± SE for five to six WT or db/db mice. Statistical analysis was by Student's *t* test for each lipid subspecies and differences ($P<0.05$), i.e., increase, no change or decrease, are indicated by ↑, NC, and ↓, respectively in the table below the graph.