

Supplementary Figures

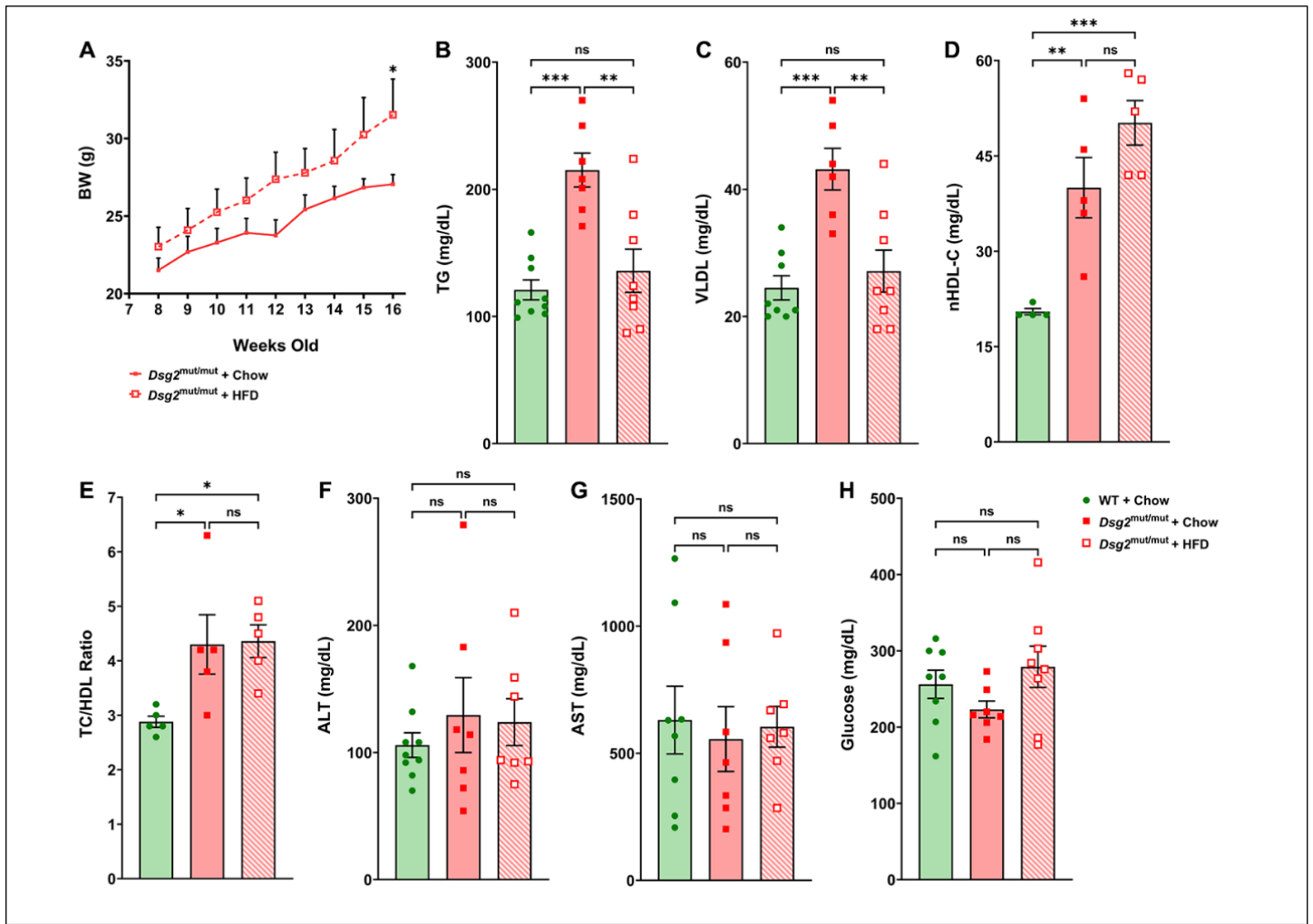


Figure S1. Weight gain and lipid perturbations in HFD-fed *Dsg2^{mut/mut}* mice. (A) Body weight (BW) of mice was recorded weekly for the duration of the 8-week study between *Dsg2^{mut/mut}* mice fed chow (*Dsg2^{mut/mut}* + Chow) or HFD (*Dsg2^{mut/mut}* + HFD). * $p \leq 0.05$ for *Dsg2^{mut/mut}* + HFD vs *Dsg2^{mut/mut}* + Chow at 16 weeks of age via two-way ANOVA with Tukey's posthoc analysis. Plasma markers were analyzed via Piccolo discs from 16-week-old mice for (B) triglycerides (TG); (C) very low-density lipoprotein (VLDL); (D) non-HDL cholesterol (nHDL-c); (E) the ratio of total cholesterol/high density lipoprotein (TC/HDL Ratio); (F) alanine aminotransferase (ALT); (G) aspartate aminotransferase (AST); and (H) glucose. Data presented as mean \pm SEM; $n \geq 7$ mice/cohort/parameter; ns, not significant; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$ via one-way ANOVA with Tukey's posthoc.

	Cytokine	$Dsg2^{mut/mut}$ (chow) vs WT (chow)		$Dsg2^{mut/mut}$ (HFD) vs WT (chow)		$Dsg2^{mut/mut}$ (HFD) vs $Dsg2^{mut/mut}$ (chow)	
		Fold Change	P-Value	Fold Change	P-Value	Fold Change	P-Value
FOLD Change	<1						
	1-2						
	2-3						
	3-4						
	>4						
	Adiponectin	1-2	0.99	1-2	0.75	1-2	0.85
	Amphiregulin	1-2	0.98	<1	0.96	<1	0.88
	Angiopoietin-1	1-2	0.98	<1	0.94	<1	0.91
	Angiopoietin-2	<1	1.00	1-2	0.94	1-2	0.93
	Angiopoietin-like 3	1-2	1.00	1-2	0.99	1-2	1.00
	BAFF/BLy5/TNFSF138	<1	0.79	<1	0.99	1-2	0.86
	Clq R1/CD93	<1	1.00	1-2	0.61	1-2	0.58
	CCL2/IE/MCP-1	<1	0.97	1-2	0.98	1-2	0.91
	CCL3/CCL4 MIP-1 a/B	<1	0.97	<1	1.00	1-2	0.97
	CCL5/RANTES	1-2	0.98	1-2	0.78	1-2	0.89
	CCL6/C10	1-2	0.98	1-2	0.97	1-2	1.00
	CCL11/Eotaxin	1-2	0.85	<1	1.00	<1	0.81
	CCL12/MCP-5	1-2	0.61	1-2	0.93	<1	0.83
	CCL17/TARC	1-2	0.91	1-2	1.00	<1	0.93
	CCL19/MIP-3B	<1	0.98	<1	0.97	<1	1.00
	CCL20/MIP-3a	<1	0.73	<1	0.95	1-2	0.89
	CCL21/6CKine	<1	0.98	2-3	0.03*	3-4	0.02*
	CCL22/MDC	<1	1.00	1-2	0.73	1-2	0.72
	CD14	1-2	0.92	1-2	0.76	1-2	0.96
	CD40/TNFRSF5	1-2	0.99	1-2	0.29	1-2	0.39
	CD160	1-2	0.94	<1	0.92	<1	0.76
	Chemerin	1-2	0.66	1-2	0.84	<1	0.94
	Chitinase 3-like 1	1-2	0.41	2-3	0.24	1-2	0.95
	Coagulation Factor III/ Tissue Factor	<1	1.00	1-2	0.86	1-2	0.86
	Complement Component C5/C5a	<1	1.00	<1	1.00	1-2	1.00
	Complement Factor D	<1	0.78	<1	0.95	1-2	0.92
	C-Reactive Protein/CRP	<1	0.97	1-2	0.80	1-2	0.67
	CX3CL1/Fractalkine	<1	0.98	2-3	0.03*	3-4	0.02*
	KC (CXCL1)	1-2	0.88	1-2	0.97	<1	0.97
	MIP-2 (CXCL2)	1-2	0.95	<1	0.98	<1	0.87
	MIG (CXCL9)	1-2	0.99	<1	0.88	<1	0.82
	IP-10 (CXCL10)	1-2	0.97	<1	0.87	<1	0.75
	I-TAC (CXCL11)	1-2	0.35	<1	0.97	<1	0.24
	CXCL13/BL/CBA-1	2-3	0.21	1-2	1.00	<1	0.23
	CXCL16	1-2	0.87	1-2	0.68	1-2	0.23
	Cystatin C	1-2	1.00	1-2	0.94	1-2	0.96
	DKK-1	<1	0.99	1-2	0.96	1-2	0.92
	DPP4/CD26	<1	0.87	1-2	0.92	1-2	0.64
	EGF	1-2	1.00	1-2	0.96	1-2	0.97
	Endoglin/CD105	1-2	1.00	1-2	0.44	1-2	0.49
	Endostatin	<1	0.96	1-2	0.52	2-3	0.38
	Fetuin A/AHSG	1-2	0.99	1-2	0.87	1-2	0.94
	FGF acidic	1-2	1.00	1-2	0.97	1-2	0.98
	FGF-21	1-2	0.99	<1	0.84	<1	0.80
	Flt-3 Ligand	1-2	0.81	<1	1.00	<1	0.81
	Gas 6	1-2	0.59	<1	1.00	<1	0.51
	G-CSF	1-2	0.73	<1	0.83	<1	0.39
	GDF-15	<1	0.99	<1	0.91	<1	0.96
	GM-CSF	<1	0.89	<1	0.96	1-2	0.98
	HGF	<1	0.95	1-2	0.93	1-2	0.79
	sICAM-1 (CD54)	<1	0.96	1-2	0.48	2-3	0.35
	IFN-γ	1-2	0.84	1-2	1.00	<1	0.88
	IGFBP-1	1-2	1.00	1-2	0.73	1-2	0.80
	IGFBP-2	<1	0.84	1-2	0.93	1-2	0.63
	IGFBP-3	<1	1.00	<1	0.85	<1	0.88
	IGFBP-5	1-2	0.95	<1	0.99	<1	0.90
	IGFBP-6	1-2	0.69	2-3	0.21	1-2	0.70
	IL-1a (IL-1F1)	2-3	0.22	<1	1.00	<1	0.19
	IL-1B (IL-1F2)	1-2	0.47	<1	1.00	<1	0.46
	IL-1ra (IL-1F3)	1-2	0.88	1-2	0.96	<1	0.97
	IL-2	1-2	1.00	1-2	1.00	1-2	1.00
	IL-3	1-2	0.88	1-2	1.00	<1	0.88
	IL-4	1-2	0.90	1-2	0.97	<1	0.98
	IL-5	1-2	0.41	1-2	0.92	<1	0.64
	IL-6	1-2	0.77	1-2	0.75	1-2	1.00
	IL-7	<1	0.96	1-2	0.74	1-2	0.59
	IL-10	1-2	0.90	<1	0.93	<1	0.71
	IL-11	1-2	0.79	<1	0.93	<1	0.57
	IL-12p40	2-3	0.15	1-2	1.00	<1	0.18
	IL-13	2-3	0.24	1-2	0.99	<1	0.31
	IL-15	1-2	0.54	1-2	0.91	<1	0.78
	IL-17A	2-3	0.08	1-2	0.86	<1	0.22
	IL-22	<1	0.91	1-2	0.82	1-2	0.58
	IL-23	1-2	1.00	1-2	0.90	1-2	0.94
	IL-27p28	1-2	0.90	1-2	0.74	1-2	0.96
	IL-28A/B	1-2	0.56	1-2	0.72	<1	0.96
	IL-33	<1	0.95	1-2	0.62	2-3	0.44
	LDLR	<1	0.87	1-2	0.68	2-3	0.39
	Leptin	1-2	0.75	<1	1.00	<1	0.74
	LIF	1-2	0.44	1-2	0.98	<1	0.57
	Lipocalin-2/NGAL	2-3	0.07	2-3	0.01*	1-2	0.88
	LIX	2-3	0.22	1-2	0.76	<1	0.59
	M-CSF	1-2	0.90	1-2	0.69	1-2	0.94
	MMP-2	1-2	0.97	2-3	0.02*	2-3	0.06
	MMP-3	<1	1.00	3-4	<0.0001*	3-4	<0.0001*
	MMP-9	<1	0.79	3-4	0.003*	3-4	0.0003*
	Myeloperoxidase/MPO	1-2	1.00	2-3	0.02*	2-3	0.03*
	Osteopontin (OPN)/Spp1	1-2	0.99	2-3	0.05*	2-3	0.09
	Osteoprotegerin/TNFRSF11B	<1	0.88	1-2	0.85	2-3	0.57
	PD-EGF/ Thymidine phosphorylase	<1	0.76	1-2	0.99	2-3	0.69
	PDGF-BB	1-2	1.00	1-2	0.92	1-2	0.96
	Pentraxin 2/SAP	3-4	0.005*	2-3	0.02*	<1	0.89
	Pentraxin 3/TSG-14	2-3	0.03*	1-2	0.47	<1	0.32
	Periostin/OSF-2	2-3	0.03*	2-3	0.14	<1	0.74
	Prof-1/DLK-1/FA1	1-2	0.51	1-2	0.83	<1	0.84
	Proliferin	1-2	0.99	1-2	0.53	1-2	0.64
	Proteinase 9/PCSK9	1-2	0.67	2-3	0.13	1-2	0.55
	RAGE	1-2	0.68	1-2	0.29	1-2	0.82
	RBP4	1-2	1.00	1-2	0.84	1-2	0.90
	Reg3G	1-2	0.84	1-2	0.99	<1	0.89
	Resistin/Retn	1-2	1.00	2-3	0.04*	2-3	0.06
	E-Selectin/CD62E	1-2	0.77	1-2	0.75	1-2	1.00
	P-Selectin/CD62P	2-3	0.26	2-3	0.17	1-2	0.99
	Serpine 1/PAI-1	2-3	0.27	3-4	0.0002*	1-2	0.06
	Serpin F1/PEDF	2-3	0.16	1-2	0.27	<1	0.94
	Thrombospondin	1-2	0.39	1-2	0.93	<1	0.60
	TIM-1/KIM-1/HAVCR	2-3	0.13	1-2	0.68	<1	0.50
	TNF-alpha	3-4	0.004*	1-2	0.54	<1	0.07
	VCAM-1/CD106	1-2	0.68	1-2	0.39	1-2	0.91
	VEGF	1-2	0.52	1-2	0.97	<1	0.67
	WISP-1/CCN4	1-2	0.53	1-2	0.57	<1	0.99

Figure S2. Increased myocardial inflammatory cytokines from $Dsg2^{mut/mut}$ mice fed a HFD. Fold-change and p -values, assessed via one-way ANOVA with Tukey's posthoc analysis from 16-week-old $Dsg2^{mut/mut}$ mice fed chow or HFD ($Dsg2^{mut/mut}$ + Chow and $Dsg2^{mut/mut}$ + HFD; respectively) and WT mice fed chow (WT + Chow).

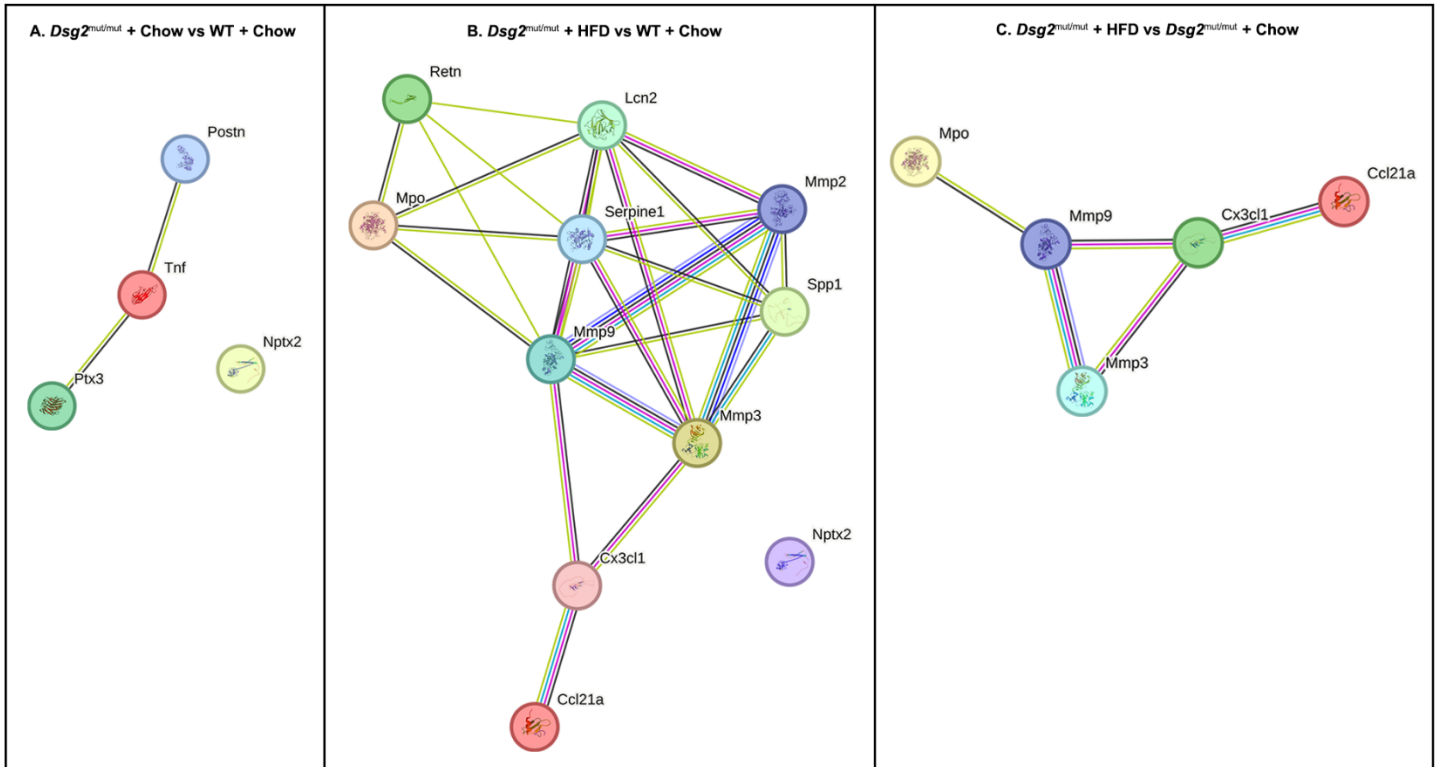


Figure S3. Associations between cardiac inflammatory markers in *Dsg2^{mut/mut}* mice via STRING analysis. (A-C) Predicted protein-protein interactions from 16-week-old mice via STRING analyses from cytokines that were significantly upregulated in (A) *Dsg2^{mut/mut}* mice fed chow (*Dsg2^{mut/mut}* + Chow) vs WT mice fed chow (WT + Chow); (B) *Dsg2^{mut/mut}* mice fed HFD (*Dsg2^{mut/mut}* + HFD) vs WT + Chow; and (C) *Dsg2^{mut/mut}* + HFD vs *Dsg2^{mut/mut}* + Chow. Periostin, Postn; tumor necrosis factor alpha, Tnf α ; pentraxin-3, Ptx3; pentraxin-2, Nptx2; matrix metalloproteinase-2, -3, and -9, Mmp-2, Mmp-3, and Mmp-9, respectively; osteopontin, Spp1; lipocalin-2, Lcn2; myeloperoxidase, MPO; Resistin, Retn; C-X3-C motif chemokine ligand-1, Cx3cl1; and C-C motif chemokine ligand-21, Ccl21a.