Deficiency and pharmacological stabilization of mast cells reduce diet-induced obesity and diabetes in mice

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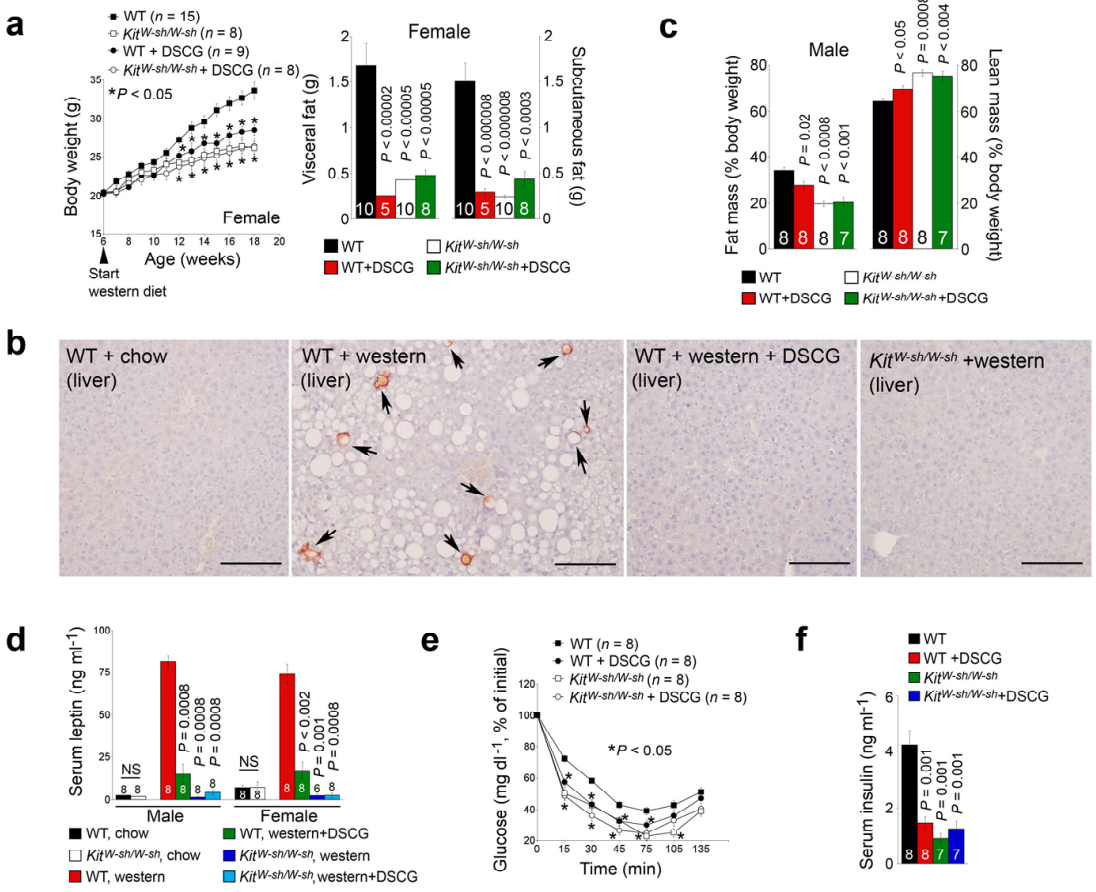

Supplementary Figure 1. Mast cell deficiency and stabilization reduced diet-induced obesity and diabetes in mice. **a.** Body weight gain (left) and visceral and subcutaneous fat weight (right) of female WT and *Kit W-sh/W-sh* mice and those receiving DSCG (all in C57BL/6 background). **b.** CD117 immunostaining for mast cells in liver paraffin sections from different mice as indicated. Arrows indicate CD117+ mast cells. Scale bar: 100 μm. Only Western diet-fed WT mice developed steatotic livers with abundant mast cell accumulation. Western diet-fed *Kit W-sh/W-sh* mice or WT mice receiving DSCG had normal liver histology similar to that in chow diet-fed WT mice. **c.** Fat and lean mass (% of body weight) in male WT and *Kit W-sh/W-sh* mice treated with or without DSCG. **d.** Serum leptin levels in male and female mice with indicated treatments. Insulin tolerance test (**e**) and serum insulin levels (**f**) in male WT and *Kit W-sh/W-sh* mice that consumed a Western diet for 12 weeks with and without DSCG treatments. $P < 0.05$ was considered statistically significant; non-parametric Mann-Whitney test. NS: no significant difference.

Supplementary Table 1: Energy expenditure analysis in *Kit*$^{W\text{-}sh/W\text{-}sh}$ and DSCG-treated mice.

Parameters	WT (*n* = 6) (mean ± SEM)	*Kit*$^{W\text{-}sh/W\text{-}sh}$ (*n* = 8) (mean ± SEM)	P Value*	WT + DGSC (*n* = 8) (mean ± SEM)	P Value*
Food consumption (gram per 24 hours)	3.17 ± 0.08	3.83 ± 0.26	0.03	3.25 ± 0.28	0.87
Water consumption (ml per 24 hours)	7.03 ± 0.28	6.38 ± 0.57	0.30	10.75 ± 0.62	0.02
Fecal output (gram per 24 hours)	1.53 ± 0.16	1.45 ± 0.14	0.77	1.56 ± 0.23	0.89
Urine volume (ml per 24 hours)	1.40 ± 0.10	1.65 ± 0.16	0.75	1.40 ± 0.17	0.52
O_2 consumption (ml per kg per h)	2620.31 ± 27.65	2994.16 ± 67.79	0.002	2867.29 ± 57.65	0.005
CO_2 production (ml per kg per h)	2129.04 ± 54.48	2619.41 ± 100.18	0.01	2534.96 ± 94.70	0.01

*Compared with WT mice, non-parametric Mann Whitney test. $P < 0.05$ was considered significant.

Supplementary Table 2. Serum and adipose tissue cytokine, chemokine, adipokine, and protease levels (mean ± SEM).

Serum	IL-6 (pg mL^{-1})	TNF-α (pg mL^{-1})	IFN-γ (pg mL^{-1})	MCP-1 (pg mL^{-1})	Eotaxin (pg mL^{-1})	RANTES (pg mL^{-1})	Adiponectin (ng mL^{-1})	MMP-9 (pg mL^{-1})	Cathepsin L (ng mL^{-1})
Males									
Wt +Chow	32.5±7.5	54.1±5.8	1328.4±205.2	164.5±18.4	419.0±30.9	7.2±2.6	6.7±0.7	70.5±0.3	4.6±0.6
Kit$^{W\text{-}sh/W\text{-}sh}$+Chow	30.9±3.8	51.9±6.9	1572.1±87.2	161.6±19.8	680.7±63.4***	25.1±6.1**	6.3±0.5	62.6±1.1***	5.7±0.7
Wt +Western	74.4±9.4	146.3±15.7	1714.5±123.7	459.2±24.3	477.6±26.0	8.9±1.9	8.2±0.9	71.4±0.2	5.4±0.7
Kit$^{W\text{-}sh/W\text{-}sh}$+Western	41.6±8.6	43.4±24.9**	1467.2±33.4*	115.2±14.8***	630.5±61.0	6.1±1.3	6.3±0.5	64.5±1.4***	5.6±0.9
Wt +DSCG+Western	26.7±7.7**	129.4±20.9	1403.9±180.9**	285.5±39.6**	571.7±38.2	6.1±1.6	9.0±0.6	70.8±0.2*	4.4±0.7
Females									
Wt +Chow	18.9±4.0	44.0±8.0	900.2±68.0	170.4±11.9	560.3±47.0	21.9±9.3	9.1±0.7	69.1±3.9	8.0±0.4
Kit$^{W\text{-}sh/W\text{-}sh}$+Chow	30.4±9.1	41.5±9.3	950.1±73.9	184.2±16.8	531.2±36.0	23.4±6.3	7.4±0.8	70.0±4.5	8.3±0.5
Wt +Western	28.6±8.3	91.9±16.8	1502.9±213.	648.6±73.9	549.1±33.0	16.7±6.5	9.0±0.6	71.5±0.2	9.1±0.5
Kit$^{W\text{-}sh/W\text{-}sh}$+Western	27.9±7.3	30.6±7.1***	994.3±120.7	343.7±44.4***	491.3±27.0	17.1±4.6	6.3±0.5***	65.8±4.9	8.2±0.5
Wt +DSCG+Western	31.7±4.9	91.5±16.0	1408.9±131.5	299.6±38.7***	564.5±47.0	33.3±3.4	8.5±0.7	71.0±0.2	9.5±0.6

WAT	IL-6 (pg mg^{-1})	TNF-α (pg mg^{-1})	IFN-γ (pg mg^{-1})	MCP-1 (pg mg^{-1})	Eotaxin (pg mg^{-1})	RANTES (pg mg^{-1})	Adiponectin (ng mg^{-1})	MMP-9 (pg mg^{-1})	Cathepsin L (ng mg^{-1})
Males									
Wt +Chow	21.0±2.7	198.6±12.1	196.0±32.7	22.0±6.8	9.0±4.0	22.1±2.7	379.2±37.0	42.4±4.1	9.0±0.5
Kit$^{W\text{-}sh/W\text{-}sh}$+Chow	22.5±1.5	225.1±18.8	204.5±25.3	32.4±6.1	10.4±3.5	8.6±3.1**	357.7±31.0	40.1±2.9	9.7±0.7
Wt +Western	28.7±2.8	187.6±12.5	212.5±29.7	115.4±18.2	5.8±2.2	15.7±4.9	373.1±23.0	35.4±2.2	8.8±0.4
Kit$^{W\text{-}sh/W\text{-}sh}$+Western	20.9±1.8*	124.5±14.4**	192.5±18.2	41.7±12.2**	6.0±3.4	20.2±3.7	426.5±46.0	41.4±5.1	9.1±0.5
Wt +DSCG+Western	30.8±5.2	231.2±13.3	245.0±9.5	57.4±7.7**	16.4±3.2**	26.4±3.2	266.1±27.0*	41.4±3.4	8.8±0.5

*P < 0.04; **P < 0.02; ***P < 0.005. Non-parametric Mann-Whitney test to compare the corresponding WT groups. P < 0.05 was considered significant.

Supplementary Table 3. Clinical and biological parameters of patients used for serum tryptase ELISA.

Parameter	**Obese subject** (average [range])	**Lean subject** (average [range])	***P* value**[†]
Patient number	80	32	N/A
Age (year)	37.3 [20.0~66.0]	41.4 [20.0~62.0]	0.11
Body mass index (BMI, kg per mm^2)	48.5 [32.0~85.3]	22.9 [19.9~25.6]	<0.01
Sex (female to male)	69/11	22/10	0.45
Fasting glucose (mM)	5.1 [3.7~7.4]	4.5 [3.4~5.3]	<0.01
Fasting insulin (μU mL^{-1})	15.4 [3.9~68.3]	3.6 [0.4~7.9]	<0.01
Homeostasis Model Assessment (HOMA)	3.5 [0.8~15.3]	0.7 [0.1~0.8]	<0.01
Quantitative insulin-sensitivity check index (QUICKI)	0.3 [0.3~0.4]	0.4 [0.4~0.7]	<0.01
Total cholesterol (mmol)	4.8 [2.8~7.1]	4.9 [3.1~7.8]	0.67
High density lipoprotein (mmol)	1.4 [0.6~2.2]	1.6 [0.8~2.6]	0.03
Triglyceride (mmol)	1.2 [0.4~3.7	1.0 [0.5~2.2]	0.06
Tryptase (ng mL^{-1})	13.1 [1.0~73.0]	7.7 [0.0~23.3]	0.01

[†]Comparison between obese and lean subjects. *Chi* square test was used for qualitative traits and unpaired *t*-test for quantitative traits. $P < 0.05$ was considered statistically significant.

Supplementary Table 4. Clinical and biological parameters for patients used for immunohistology analysis.

Parameter	**Obese subject** (average [range])	**Lean subject** (average [range])	***P* value**[†]
General measurement			
Patient number	12	10	N/A
Sex (female to male)	6/6	10/0	0.002
Age (year)	47.8 [20~63]	35.2 [30~42]	0.004
Body mass index (BMI, kg per mm^2)	49.9 [36.0~62.1]	23.7 [21.9~26.2]	<0.0001
Glucose homeostasis			
Glucose (mmol L^{-1})	6.4 [4.2~10.3]	4.8 [3.7~6.3]	0.11
Insulin (μU mL^{-1})	22.0 [4.7~84.2]	7.2 [4.0~13.0]	<0.03
Homeostasis Model Assessment (HOMA)	7.3 [1.3~29.3]	1.7 [0.7~3.6]	0.38
Quantitative insulin-sensitivity check index (QUICKI)	0.3 [0.2~0.4]	0.4 [0.3~0.4]	<0.03
Type 2 diabetes			
Glycemia (>7 mmol L^{-1} or treatment)	*n* = 5	*n* = 0	0.007

[†]Comparison between obese and lean subjects. *Chi* square test was used for qualitative traits and Mann-Whitney *U* test for quantitative traits. $P < 0.05$ was considered statistically significant.