Supplementary Information

Supplementary Figure S1, and Supplementary Table S1.
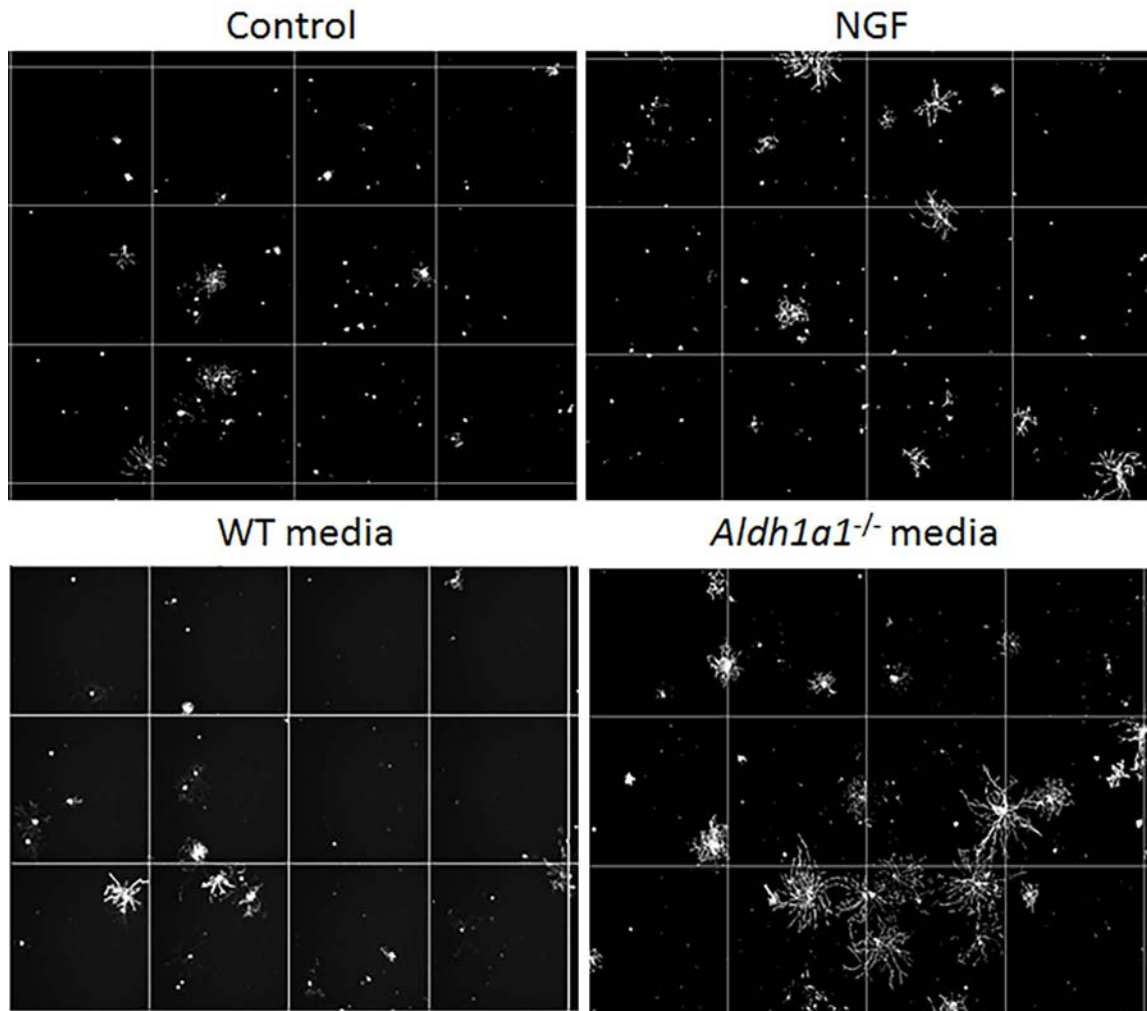

Figure S1

Medium of *Aldh1a1*$^{-/-}$ thermocytes induces innervation

DRG neurons (500 neurons per well) were cultured in DRG culture medium only or in DRG culture medium with NT-3 (1 ng/mL), with NGF (10ng/mL), with WT secretome (1/1, v/v), or with *Aldh1a1*$^{-/-}$ secretome (1/1, v/v) for 24 hours. WT and *Aldh1a1*$^{-/-}$ adipocytes differentiated for 5 days. 'Secretome' refers to media collected from these cells for 24h. Representative images show ~25% of area used for the automatic quantification of neuronal parameters in Figure 2 per one condition using a Thermo

Scientific™ ArrayScan™ XTI Live High Content microscope. Nine independent experiments were performed using DRG from three mice. Each DRG batch was analyzed in triplicate. Data are shown as mean ± SD obtained with one DRG batch. Asterisks indicate P<0.05 between different groups; Mann-Whitney U test. An image in Figure 2A shows an enlarged single square image that was randomly selected as a representative image from n=9.

Table S1. Body weight and adipose tissue weights in mice from animal studies 1-3

Study 1. WT and *Aldh1a1⁻/⁻* (A1KO) mice on a high-fat (HF) diet

Study group (N=19)	Body Wt. (g)		Sub Fat (g)		iAb Fat (g)		Brown Fat (g)	
	M	F	M	F	M	F	M	F
WT (*n*=5m,5f)	52.76±3.68	40.43±3.51$^{\#}$	2.85±0.58	3.22±0.85	1.75±0.12	2.84±0.91	0.35±0.07	0.15±0.04$^{\#}$
A1KO (*n*=5m, 4f)	28.75±1.88*	22.92±2.04$^{\#}$*	0.92±0.35*	0.55±0.13*	1.23±0.33*	0.65±0.20$^{\#}$*	0.11±0.04*	0.09±0.02*

$^{\#}$ *p*<0.05, Male (m) vs. female (f); * *p*<0.05, WT vs. A1KO, Mann-Whitney U.

Study 2. Comparison of WT and *Aldh1a1⁻/⁻* (A1KO) mice on a regular chow diet

Study group (N=39)	Body Wt. (g)		Sub Fat (g)		iAb Fat (g)		Brown Fat (g)	
	M	F	M	F	M	F	M	F
WT (*n*=12m,9f)	26.22± 3.23	21.08±3.03$^{\#}$	0.28±0.10	0.33±0.2	0.48±0.15	0.38±0.2	0.07±0.03	0.07±0.03
A1KO (*n*=10m,8f)	21.93±2.10*	19.18±1.84$^{\#}$*	0.24±0.06	0.29±0.1	0.23±0.07*	0.27±0.1	0.17±0.26	0.07±0.03

$^{\#}$ *p*<0.05, Male vs. Female; * *p*<0.05, WT vs. A1KO, Mann-Whitney U test

Proof-of-concept Study 3. WT mice on a high-fat (HF) diet treated with encapsulated WT and Aldh1a1⁻/⁻ (A1KO) cells

Study group Host:(*N*=18^{ſ}, f) Injected with:	Body Wt. (g)			Sub Fat (g)			iAb Fat (g)		
	WT (*n*=5) Veh	WT (*n*=5) encWT	WT(*n*=5) encAIKO	WT (*n*=5) Veh	WT (*n*=5) encWT	WT(*n*=5) encAIKO	WT (*n*=5) Veh	WT (*n*=5) encWT	WT(*n*=5) encAIKO
WT	41.0±4.8	38.5±7.8	37.0±6.3	2.7±0.9	2.0±0.8	2.3±0.6	4.1±1.0	4.6±1.7	4.1±1.2

n.s. within groups (Veh, encWT, and encA1KO).ſ, *n*=18 includes Veh,encWT, encAIKO groups (*n*=5/group) and mice injected with empty capsules (*n*=3).