

## 5 w



7 w

| WT     | ob/ob | _     |
|--------|-------|-------|
| -64228 |       | ACLY  |
|        | 11    | ACC   |
|        |       | FASN  |
|        |       | Actin |





Liver



**Supplementary Figure 1:** Shown are the immunoblots used for quantification by densitometry and shown in Figure 1B. Depicted are immunoblots to detect ACLY, FASN and ACC protein levels in iWAT fat (A) or liver tissues (B) from WT control or ob/ob mice at 5, 7 and 11 weeks of age. N = 4 - 5 mice per group.

## Liver

<u>p-AKT</u>



**Supplementary Figure 2:** Representative protein immunoblot of AKT phosphorylation in liver tissue, in response to a bolus insulin injection (1 U/kg). Bottom panels depict densitometry analysis of the data from the Westerns described for top panel (N = 6 or 7). Graphs show the mean -/+ SEM. N = 5 to 7 per group, compared with WT controls, by Student's t test. \* P < 0.05; \*\* P < 0.01; \*\*\* P < 0.001.



**Supplementary Figure 3:** Food intakes were measured at 3 and 13 weeks post-TAM treatment. Though attenuation of glucose intolerance (**Figure 4G**) was observed, no significant changes in food intake were noted in iAdFASNKO mice. N=4 to 6 mice per group.



Supplementary Figure 4: (A) Liver, pancreas and skeletal muscle tissue lysates from control and UCP1-FASNKO mice were immunoblotted for FASN or tubulin protein as indicated.
(B) Body weight gain in control and UCP1-FASNKO mice were fed with chow or HFD for 12 weeks. N = 3-6 mice per group.



**Supplementary Figure 5:** FASN deletion and β3-adrenoreceptor stimulation in adipocytes of mature mice increases tyrosine hydroxylase (TH) and neuropeptide Y (NPY) content and activates the PKA signaling pathway in iWAT. Depicted are representative immunoblots to detect FASN, TH, NPY and tubulin (A), phospho-HSL, phospho-perilipin and perilipin (B) levels in iWAT from control, CL316,243-treated mice or iAdFASNKO mice.

| Gene           | Forward                 | Reverse                   |
|----------------|-------------------------|---------------------------|
| PPARγ1         | GACTACCCTTTACTGAAATTACC | GTGGTCTTCCATCACGGAGA      |
| PPARγ2         | ATGGGTGAAACTCTGGGAG     | GTGGTCTTCCATCACGGAGA      |
| SREBP1c        | GGCCCGGGAAGTCACTGT      | GGAGCCATGGATTGCACATT      |
| SREBP2         | GCAGCAACGGGACCATTCT     | CCCCATGACTAAGTCCTTCAACT   |
| $ChREBP\alpha$ | CGACACTCACCCACCTCTTC    | TTGTTCAGCCGGATCTTGTC      |
| ChREBPβ        | TCTGCAGATCGCGTGGAG      | CTTGTCCCGGCATAGCAAC       |
| FASN           | GGAGGTGGTGATAGCCGGTAT   | TGGGTAATCCATAGAGCCCAG     |
| ELOVL6         | TCAGCAAAGCACCCGAAC      | AGCGACCATGTCTTTGTAGGAG    |
| ACLY           | ACCCTTTCACTGGGGATCACA   | GACAGGGATCAGGTATTCCTTG    |
| SCD1           | TTCTTGCGATACACTCTGGTGC  | CGGGATTGAATGTTCTTGTCG     |
| GLUT4          | GTGACTGGAACACTGGTCCTA   | CCAGCCACGTTGCATTGTAG      |
| PEPCK          | CTGCATAACGGTCTGGACTTC   | CAGCAACTGCCCGTACTCC       |
| DGAT2          | GCGCTACTTCCGAGACTACTT   | GGGCCTTATGCCAGGAAACT      |
| PDK4           | AGGGAGGTCGAGCTGTTCTC    | GGAGTGTTCACTAAGCGGTCA     |
| ACC1           | TGTACAAGCAGTGTGGGCTGGCT | CCACATGGCCTGGCTTGGAGGG    |
| ACC2           | GGAGGCTGCATTGAACACAAGT  | TGCCTCCAAAGCGAGTGACAAA    |
| ME1            | ATCACTTTGGATGTGGGAACAG  | CAGGAAGGCGTCATACTCAGG     |
| MDH1           | AAGGCATGGAGAGGAAGGAC    | AGTTCGTATTGGCTGGGTTTC     |
| UCP1           | ACTGCCACACCTCCAGTCATT   | CTTTGCCTCACTCAGGATTGG     |
| CIDEA          | ATCACAACTGGCCTGGTTACG   | TACTACCCGGTGTCCATTTCT     |
| PGC1 $\alpha$  | AGCCGTGACCACTGACAACGAG  | GCTGCATGGTTCTGAGTGCTAAG   |
| PRDM16         | CAGCACGGTGAAGCCATTC     | GCGTGCA TCCGCTTGTG        |
| $PPAR\alpha$   | TATGGAGTGACATAGAGTGTGCT | CCACTTCAATCCACCCAGAAAG    |
| ELOVL3         | TTCTCACGCGGGTTAAAAATGG  | GAGCAACAGATAGACGACCAC     |
| ТН             | GTCTCAGAGCAGGATACCAAGC  | CTCTCCTCGAATACCACAGCC     |
| 36B4           | TCCAGGCTTTGGGCATCA      | CTTTATCAGCTGCACATCACTCAGA |
| HPRT           | TCAGTCAACGGGGGACATAAA   | TCAGTCAACGGGGGACATAAA     |
| GAPDH          | AGGTCGGTGTGAACGGATTTG   | TGTAGACCATGTAGTTGAGGTCA   |

## Supplementary Table 1: Primer sequences used in qRT-PCR analysis