**iScience, Volume *25***

## Supplemental information

# KLF15 controls brown adipose tissue transcriptional flexibility and metabolism in response to various energetic demands

**Liyan Fan, Alexander F. Lesser, David R. Sweet, Komal S. Keerthy, Yuan Lu, Ernest R. Chan, Vinesh Vinayachandran, Olga Ilkayeva, Tapatee Das, Christopher B. Newgard, and Mukesh K. Jain**

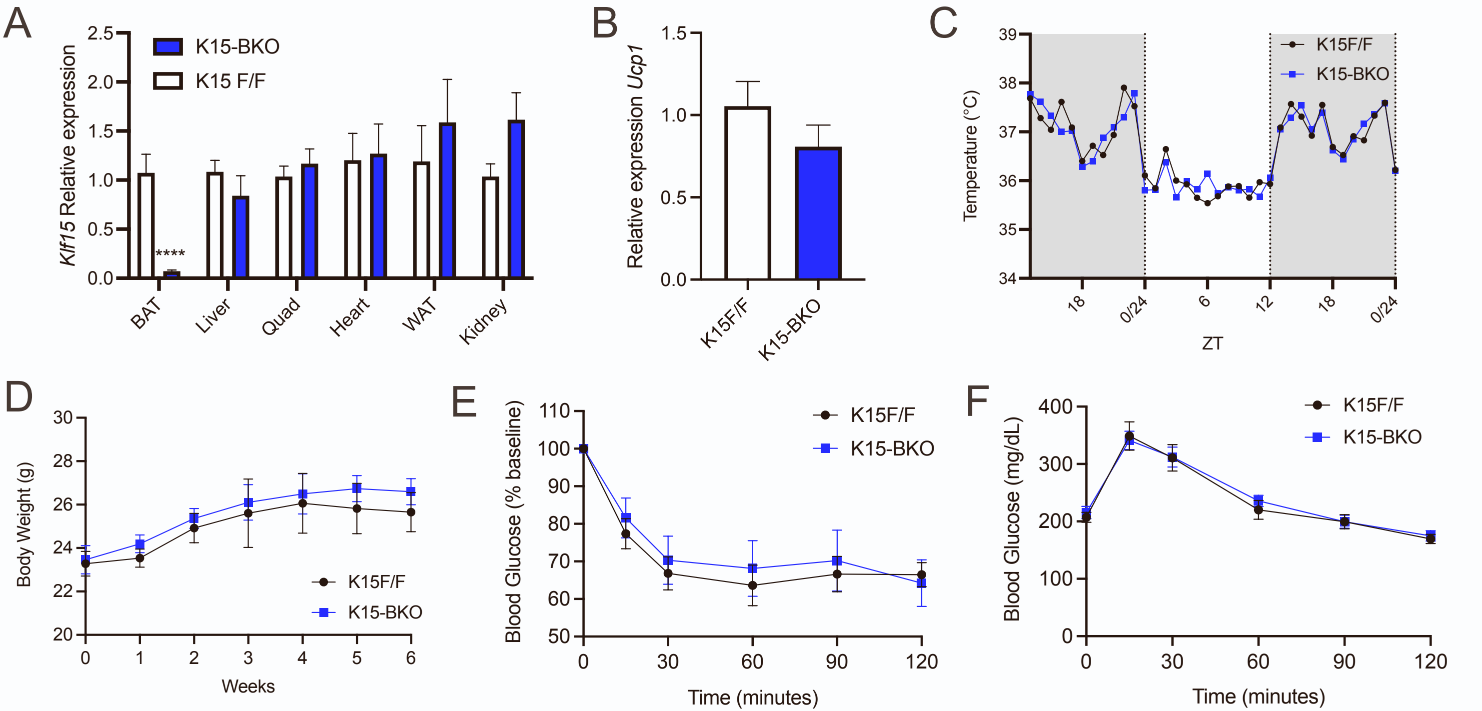


**Figure S1. Baseline metabolic characterization of K15-BKO mouse, Related to Figure 1. (A)** *Klf15* expression across multiple organs demonstrating specificity of BAT *Klf15* KO in K15-BKO animals (n=4-6). **(B)** Relative *Ucp1* expression in BAT of K15F/F vs K15-BKO (n=5-6). **(C)** Continuous core body temperature measurement using implantable temperature telemetry devices at room temperature (n=6). **(D)** Body weight (g) measurements starting from 8 weeks of age. **(E)** Intraperitoneal insulin tolerance test (IPITT) and **(F)** Intraperitoneal glucose tolerance test in K15F/F and K15-BKO at 8-10 weeks of age (n=8-11). Data represent mean ± SEM. Comparisons between groups were performed using an unpaired, 2-tailed Student's t test, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

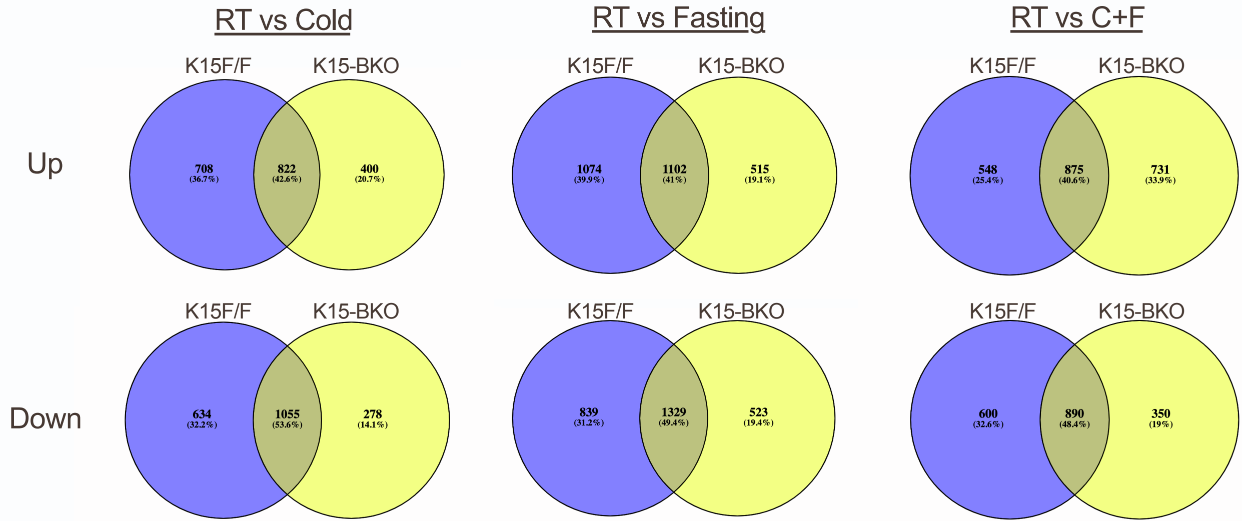


**Figure S2. K15-BKO mice demonstrate significant deviations from normal transcriptional adaptions to energy demanding states, Related to Figure 2.** Comparison of overlap of up- and down-regulated genes identified in K15F/F and K15-BKO BAT in response to cold challenge, fasting, and C+F.

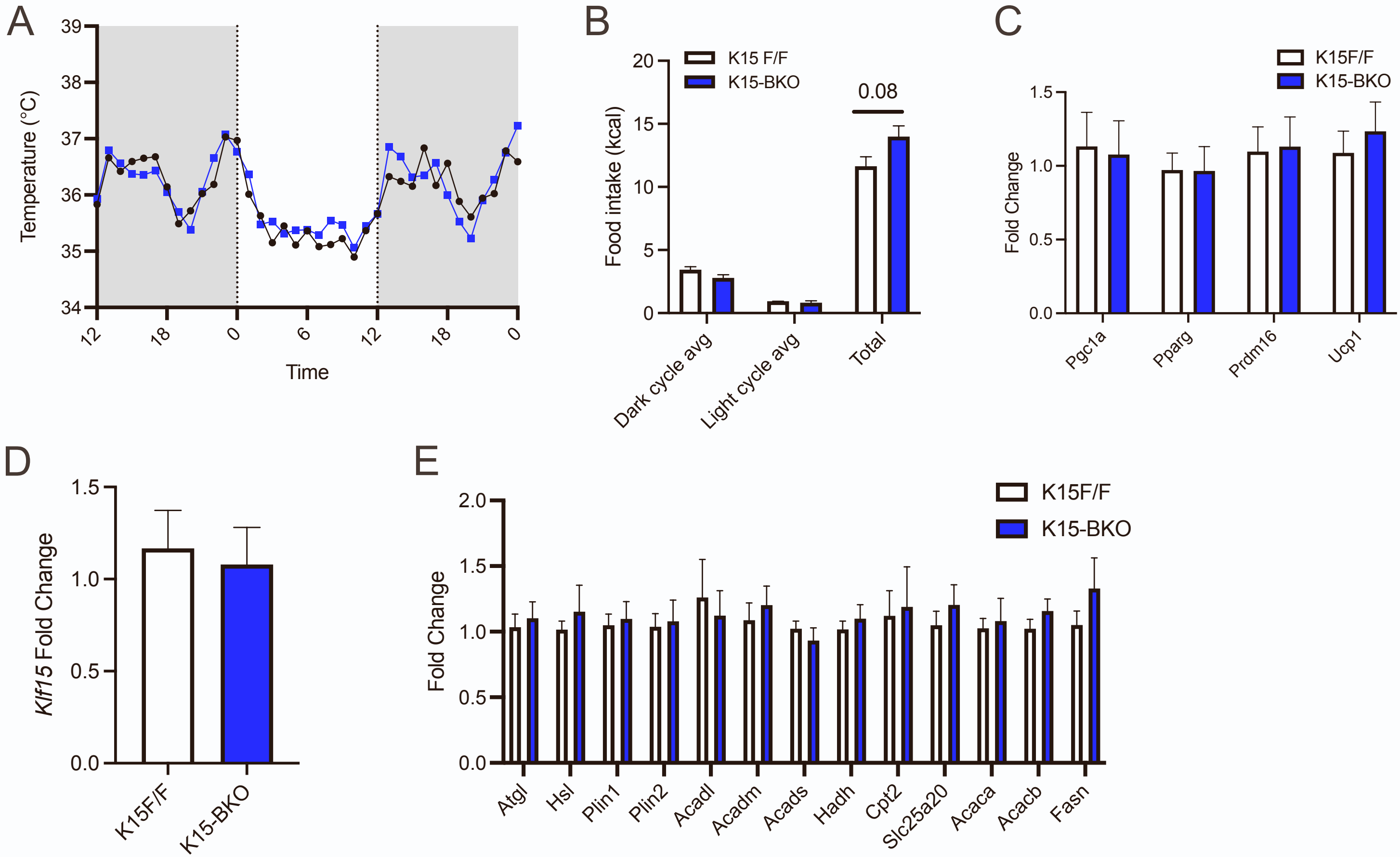


**Figure S3. K15-BKO maintain temperature in cold, Related to Figure 3. (A)** Continuous core body temperature measurement using implantable temperature telemetry devices at 4°C cold challenge (n=6). **(B)** Food intake during dark cycle, light cycle, and total across 24h cycle (n=4). **(C)** Fold change of browning genes in subcutaneous adipose tissue of K15F/F vs K15-BKO in C+F condition (n=8). **(D)** Fold change in *Klf15* expression in subcutaneous adipose tissue in C+F condition (n=8). **(E)** Fold change of select lipid metabolism genes in the subcutaneous adipose tissue of K15F/F and K15-BKO mice with C+F condition (n=8). Data represent mean ± SEM. Comparisons between groups were performed using an unpaired, 2-tailed Student's t test.

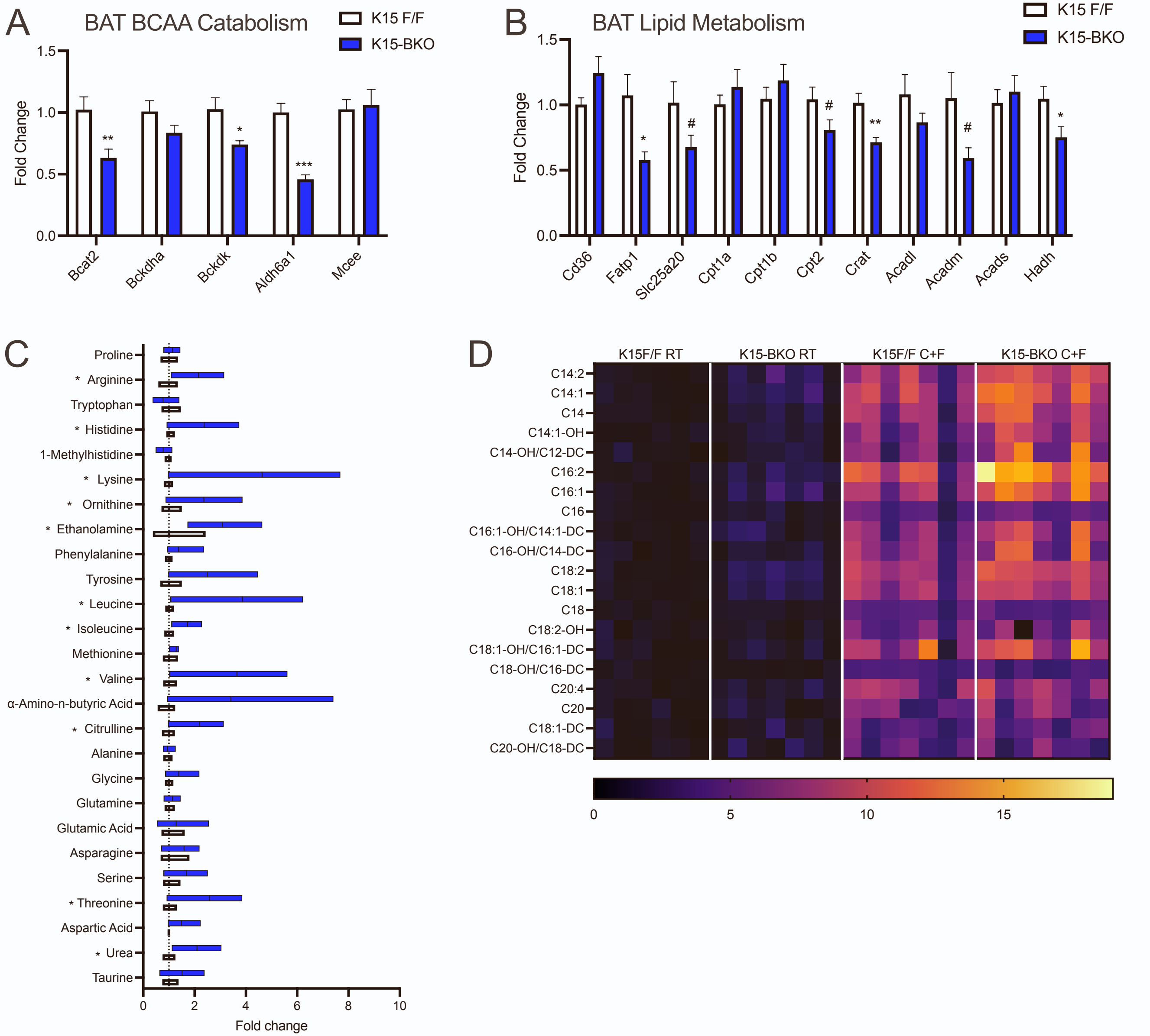


**Figure S4. K15-BKO experience altered BCAA and FA metabolism in C+F conditions, Related to Figure 4. (A)** qPCR of BCAA catabolism genes in BAT of K15 F/F vs K15-BKO mice (n=6-8). **(B)** qPCR of BCAA catabolism genes in BAT of K15 F/F vs K15-BKO mice (n=6-8). **(C)** Circulating amino acid levels at C+F, normalized to K15F/F (n=5). **(D)** Heatmap depicting circulating acylcarnitine levels K15F/F and K15-BKO at RT and after C+F, normalized to K15F/F RT (n=7). Data represent mean ± SEM. Comparisons between groups were performed using an unpaired, 2-tailed Student's t test, #p <0.1, *p<0.05, **p<0.01, ***p<0.001.

**Table S1. PCR primers, Related to STAR Methods.**

| Gene name | Forward | Reverse |
|---|---|---|
| Klf15 | ACAGGCGAGAAGCCCTTT | CATCTGAGCGGGAAAACCT |
| Cyclophilin B | TTCTTCATAACCACAGTCAAGACC | ACCTTCCGTACCACATCCAT |
| Fatp1 | GACAAGCTGGATCAGGCAAG | GAGGCCACAGAGGCTGTTC |
| Cd36 | TTGTACCTATACTGTGGCTAAATGAGA | CTTGTGTTTTGAACATTTCTGCTT |
| Cpt1a | GACGAATCGGAACAGGGATA | TGGCATAGCTGTCAATAGATGC |
| Cpt1b | GAGTGACTGGTGGGAAGAATATG | GCTGCTTGCACATTTGTGTT |
| Slc25a20 | TGAAGGCCCTGTTACACTCA | CCTCCAGAGAGTCAGCCATC |
| Cpt2 | CCAAAGAAGCAGCGATGG | TAGAGCTCAGGCAGGGTGA |
| Alt1 | CCTTCAAGCAGTTTCAAGCA | GCTCCGTGAGTTTAGCCTTG |
| Alt2 | GGAGCTAGCGACGGTATTTCT | GATACTGGGGGATGGGAATC |
| Bcat2.1 | GCTGCAGCCACACTAGGAC | TCTTTTGGACCCACATAGAAGC |
| Bcat2 | TGCTCTGGTCTGCACTACTCTC | GTAGCATCCTGTCCATGTTGAG |
| Bckdk | TGCTCAAGAATGCCATGAGA | TGAGATCCTGATGATGAGATCAAT |
| Bckdha | TTCGGGGCTTGGCTAGAT | GAACTGGGGCTTGTCGTC |
| Bckdhb | ATTAGCCAAAGACCCCACTG | CGTAAACCAACAGTGCATCG |
| Ucp1 | GGCAATCCTTCTGTTTTTGC | CCAAAGTCCGCCTTCAGA |
| Mut | TGCAGTGCGGACAATGTTAT | GCACACTGCCAGACATCG |
| Fah | CCTGCAGACTCTTAGACATGGA | GATTGGCTCTCCGAATCTGT |
| Glud1 | GGTCATCGAAGGTACCG | TCAGTGCTGTAACGGATACCTC |
| Sds | CTACTCCTCTCGCTCGCTCT | CTTCACATGGAGGGACTCCT |
| Hmgcl | GTGAAGATGGCGTCAGTGAG | AGTGCCCATGGAGGAGGT |
| Acaa2 | AAATGTGCGCTTCGGAAC | CGGTTAATCCTGCCCACAAAG |
| Mcee | CACTGGGGAGTCATAGTCCAA | TGCACTGATGTTGTCCACCT |
| Got1 | GCTGTGCTTCTCGCCTAGTT | AAGACTGCACCCCTCCAAC |
| Got2 | ATGGCTGCTGCCTTTCAC | GATCTGGAGGTCCCATTTCA |
| Acaa1 | GGTCTTATGACATTGGCATGG | CTCTGGCTTTCTCACTCTCCA |
| Aldh6a1 | CTGGGCAGAGTCGGTGAG | GGCATTTACCTTAGAAGAAACCTG |
| Fh1 | GCACCCCAATGATCATGTTA | ATTGCTGTGGGAAAGGTGTC |
| Sdhd | CCTGCTCTGTGGTGGACTACT | CCCATGAACGTAGTCGGTAAC |
| Aco2 | GTTGGGGGTGAGAAAGACCT | GAAGCCCACACCATACTTGG |
| Idh3a | GAGGTTTTGCTGGTGGTGTT | TGAAATTTCTGGGCCAATTC |
| Idh3b | ATGCTGCGGCATCTCAAT | CCATGTCTCGAGTCCGTACC |
| Idh3g | CATCCTCATTGTACGGGAAAA | ACCACTCCTGCTACGCTCTC |
| Ogdh | TCTCATCCACAGACAAACTTGG | AGGAAGTGCTGGCTCCTGT |
| Suclg1 | CACATTCACAAGAAGGGAAGAAT | GGTTGTTTGGTGAACTGCTTC |
| Suclg2 | GAAAATCTGGGCTTCCTTGG | GAAAATCTGGGCTTCCTTGG |
| Sdha | TGTTCAGTTCCACCCCACA | TCTCCACGACACCCTTCTG |
| Cs | GGAAGGCTAAGAACCCTTTGG | TCATCTCCGTCATGCCATAGT |
| Mdh2 | TTGTGATGTGGTGGTCATCC | ACAGGTCATCCCGTGTCATT |
| Sdhc | GAAGAAGAACACGAGTTCAAACC | GTGCCATAGGAAGAGACCATTT |
| Sdhb | CTGGTGGAACGGAGACAAGT | GCGTTCCTCTGTGAAGTCGT |
| Fbp1 | ACTTTGACCCTGCCATCAAT | ACCATAGGGGGCTGAACC |
| Pcx | TCCGTGTCCGAGGTGTAAA | CAGGAACTGCTGGTTGTTGA |
| G6pc | TCTGTCCCGGATCTACCTTG | GAAAGTTTCAGCCACAGCAA |
| Crat | GCCATTGCTATGCACTTCAAC | GGTCCGAAGAACATGACACA |
| Ldha | GGCACTGACGCAGACAAG | TGATCACCTCGTAGGCACTG |

| | | |
|---|---|---|
| Pgc1a | AATTTTTCAAGTCTAACTATGCAGACC | CAAAATCCAGAGAGTCATCTTGC |
| Pparg | GAAAGACAACGGACAAATCACC | GGGGGTGATATGTTTGAACTTG |
| Prdm16 | TCTCGGATCCCATCCTCA | GGAAGATCTTGCCACAGTA |
| Cidea | TTCAAGGCCGTGTTAAGGA | CCTTTGGTGCTAGGCTTGG |
| Atgl | GAGCTTCGCGTCACCAC | CACATCTCTCGGAGGACCA |
| Hsl | GCGCTGGAGGAGTGTTTTT | CGCTCTCCAGTTGAACCAA |
| Plin1 | AACGTGGTAGACACTGTGGTACA | TCTCGGAATTCGCTCTCG |
| Plin2 | CTCCACTCCACTGTCCACCT | GCTTATCCTGAGCACCCTGA |
| Acadl | GCTTATGAATGTGTGCAACTCC | CCGAGCATCCACGTAAGC |
| Acadm | TCTTCCCCACAGCTCAGGT | GTAATCCAAGCCTGCACCA |
| Hadh | TGGATACTACAAAGTTCATCTTGGA | AAGGACTGGGCTGAAATAAGG |
| Acaca | GCGTCGGGTAGATCCAGTT | CTCAGTGGGGCTTAGCTCTG |
| Acacb | TGAATCTCACGCGCCTACTA | GCCTCTCTTCACCAGATGGA |
| Fasn | CAACATGGGACACCCTGAG | GTTGTGGAAGTGCAGGTTAGG |