Supplemental Data

Supplemental Table 1. Sources of 30 human E2 siGENOME SMARTpool siRNA library screen

Dharmacon siGENOME® SMARTpool® siRNA Library- Human Ubiquitin Conjugating Enzymes						
G-015562 Lot 15221						
Order Number	**Plate**	**Well**	**Gene Symbol**	**GENEID**	**Gene Accession**	**Sequence**
CTM-463745	Plate 1	A02	UBE2A	7319	NM_001282161	GAACAAAGCUGGCGUGAUU
CTM-463746	Plate 1	A02	UBE2A	7319	NM_001282161	GAACAAACGGGAAUAUGAA
CTM-463747	Plate 1	A02	UBE2A	7319	NM_001282161	CAGGAGAACAAACGGGAAU
CTM-463748	Plate 1	A02	UBE2A	7319	NM_001282161	CUAUGCAGAUGGUAGUAUA
CTM-463759	Plate 1	A03	UBE2B	7320	NM_003337	GAACAAAGCUGGAAUGAUU
CTM-463760	Plate 1	A03	UBE2B	7320	NM_003337	CAAACGAGAAUAUGAGAAA
CTM-463761	Plate 1	A03	UBE2B	7320	NM_003337	GGAAAACAAACGAGAAUAU
CTM-463762	Plate 1	A03	UBE2B	7320	NM_003337	AGUUAUAUUUGGACCAGAA
CTM-463763	Plate 1	A04	UBE2C	11065	NM_001281742	CAACAUUGAUAGUCCCUUG
CTM-463764	Plate 1	A04	UBE2C	11065	NM_001281742	AACCCAACAUUGAUAGUCC
CTM-463765	Plate 1	A04	UBE2C	11065	NM_001281742	CCCAACAUUGAUAGUCCCU
CTM-463766	Plate 1	A05	UBE2D1	7321	NM_003338	GAGAAUGGACUCAGAAAUA
CTM-463767	Plate 1	A05	UBE2D1	7321	NM_003338	CAACAGACAUGCAAGAGAA
CTM-463768	Plate 1	A05	UBE2D1	7321	NM_003338	GGAAGUAUUUGUCUCGAUA
CTM-463769	Plate 1	A05	UBE2D1	7321	NM_003338	CAUAAACAGUAAUGGAAGU
CTM-463770	Plate 1	A06	UBE2D2	7322	NM_003339	GGGAAUGGACUCAGAAGUA
CTM-463771	Plate 1	A06	UBE2D2	7322	NM_003339	GAGAAAAGUACAACAGAAU
CTM-463772	Plate 1	A06	UBE2D2	7322	NM_003339	CUAUCAGGGUGGAGUAUUU
CTM-463773	Plate 1	A06	UBE2D2	7322	NM_003339	CAACAGAAUAGCUCGGGAA
CTM-463774	Plate 1	A07	UBE2E1	7324	NM_001202476	GCUUGGACAUAUUGAAAGA
CTM-463775	Plate 1	A07	UBE2E1	7324	NM_001202476	GGACAAGAAUCUAUCAUUG
CTM-463776	Plate 1	A07	UBE2E1	7324	NM_001202476	CCAAAGGCGAUAACAUCUA
CTM-463777	Plate 1	A07	UBE2E1	7324	NM_001202476	GCGAUAACAUCUAUGAAUG
CTM-463778	Plate 1	A08	UBE2E2	7325	NM_152653	GCAAGAACCAGAAAGAGAA
CTM-463779	Plate 1	A08	UBE2E2	7325	NM_152653	AGAAGGAACUUGCAGAAAU
CTM-463780	Plate 1	A08	UBE2E2	7325	NM_152653	ACAAAGAGUUGAUGACAGU
CTM-463781	Plate 1	A08	UBE2E2	7325	NM_152653	CGAUGGAGAUCAACGUGAA
CTM-463782	Plate 1	A09	UBE2F	140739	NM_001278306	GGAAUAAAGUGGAUGACUA
CTM-463783	Plate 1	A09	UBE2F	140739	NM_001278306	GGGAAAUAUGUCUGAGUUU
CTM-463784	Plate 1	A09	UBE2F	140739	NM_001278306	GGAAAUAUGUCUGAGUUUA
CTM-463785	Plate 1	A09	UBE2F	140739	NM_001278306	CAUCAAACGUUAUGCCAGA
CTM-463786	Plate 1	A10	UBE2G1	7326	NM_003342	GGGAAGAUAAGUAUGGUUA
CTM-463787	Plate 1	A10	UBE2G1	7326	NM_003342	GCGAAAGAAUGGAGGGAAG
CTM-463788	Plate 1	A10	UBE2G1	7326	NM_003342	GCACCCAAAUGUUGAUAAA
CTM-463789	Plate 1	A10	UBE2G1	7326	NM_003342	GGAAGAUAGAAAUGGAGAA
CTM-463792	Plate 1	A11	UBE2G2	7327	NM_001202489	UGACGAAAGUGGAGCUAAC
CTM-463793	Plate 1	A11	UBE2G2	7327	NM_001202489	GAGAUUUACCUGUGAGAUG
CTM-463794	Plate 1	A11	UBE2G2	7327	NM_001202489	GCGAUGACCCCAUGGGCUA
CTM-463795	Plate 1	A11	UBE2G2	7327	NM_001202489	GGGAGCAGUUCUAUAAGAU
CTM-463797	Plate 1	B02	UBE2H	7328	NM_001202498	AAGAGUACAUCCAGAAAUA
CTM-463798	Plate 1	B02	UBE2H	7328	NM_001202498	CAGAAGAAUACAAGCAGAA
CTM-463799	Plate 1	B02	UBE2H	7328	NM_001202498	CGGAGGAGGCGCUGAAAGA
CTM-463800	Plate 1	B02	UBE2H	7328	NM_001202498	AAGAUGAGGCCCAGGAUAU

CTM-463802	Plate 1	B03	UBE2I	7329	NM_194261	GAGGAAAGCAUGGAGGAAA
CTM-463803	Plate 1	B03	UBE2I	7329	NM_194261	GGGAAGGAGGCUUGUUUAA
CTM-463804	Plate 1	B03	UBE2I	7329	NM_194261	CCAUCUUAGAGGAGGACAA
CTM-463805	Plate 1	B03	UBE2I	7329	NM_194261	AGGAAAGCAUGGAGGAAAG
CTM-463806	Plate 1	B04	UBE2J1	51465	NM_016021	GAGUAUAAGGACAGCAUUA
CTM-463807	Plate 1	B04	UBE2J1	51465	NM_181893	UGAAAGAAGCGGCAGAAUU
CTM-463808	Plate 1	B04	UBE2J1	51465	NM_181893	CAGCCUUCGUGGAGUAUAA
CTM-463809	Plate 1	B04	UBE2J1	51465	NM_181893	CCAAAGAACUGGCUAGGCA
CTM-464269	Plate 1	B05	UBE2K	3093	NM_001312646	GGAUGUAGAGACUGCAACA
CTM-464270	Plate 1	B05	UBE2K	3093	NM_001312646	UGUAGAGACUGCAACAGAA
CTM-464271	Plate 1	B05	UBE2K	3093	NM_001312646	GUAGAGACUGCAACAGAAU
CTM-464272	Plate 1	B05	UBE2K	3093	NM_001312646	AUGCAGUAAUAGUGGCCUU
CTM-463810	Plate 1	B06	UBE2L3	7332	NM_001256356	CCUUCAGAAUCGAAAUCAA
CTM-463811	Plate 1	B06	UBE2L3	7332	NM_001256356	CCACCGAAGAUCACAUUUA
CTM-463812	Plate 1	B06	UBE2L3	7332	NM_001256356	ACCCAAACAUCGACGAAAA
CTM-463813	Plate 1	B06	UBE2L3	7332	NM_001256356	GCCAGUAAUUAGUGCCGAA
CTM-463814	Plate 1	B07	UBE2L6	9246	NM_004223	GGACGAGAACGGACAGAUU
CTM-464093	Plate 1	B07	UBE2L6	9246	NM_004223	GUGAAUAGACCGAAUAUCA
CTM-464094	Plate 1	B07	UBE2L6	9246	NM_004223	GAAAGAAUGCCGAAGAGUU
CTM-464095	Plate 1	B07	UBE2L6	9246	NM_004223	AGUGAGAACUGGAAGCCUU
CTM-464101	Plate 1	B08	UBE2M	9040	NM_003969	CAGAGGUCCUGCAGAACAA
CTM-464102	Plate 1	B08	UBE2M	9040	NM_003969	GGAAGUUUGUGUUCAGUUU
CTM-464103	Plate 1	B08	UBE2M	9040	NM_003969	CCGAGGACCCACUGAACAA
CTM-464104	Plate 1	B08	UBE2M	9040	NM_003969	AGGUGAAGUGUGAGACAAU
CTM-464105	Plate 1	B09	UBE2N	7334	NM_003348	GGCUAUAUGCCAUGAAUAA
CTM-464106	Plate 1	B09	UBE2N	7334	NM_003348	AGACAAGUUGGGAAGAAUA
CTM-464107	Plate 1	B09	UBE2N	7334	NM_003348	CCGAACCAGAUGAGAGCAA
CTM-464108	Plate 1	B09	UBE2N	7334	NM_003348	GCAUCAAAGCCGAACCAGA
CTM-464109	Plate 1	B10	UBE2O	63893	NM_022066	CCAAAGAAGCGGAGAAAGA
CTM-464110	Plate 1	B10	UBE2O	63893	NM_022066	UCAAGAAGCUACAGGAAAA
CTM-464111	Plate 1	B10	UBE2O	63893	NM_022066	CAACAUAGAGUCUGAGAUU
CTM-464112	Plate 1	B10	UBE2O	63893	NM_022066	CACAAGAGGAAGAAGAAUA
CTM-464118	Plate 1	B11	UBE2Q1	55585	NM_017582	GGACAUAAAGAAAGGGAAU
CTM-464119	Plate 1	B11	UBE2Q1	55585	NM_017582	CAGUCGAACUCGUGAAUGA
CTM-464120	Plate 1	B11	UBE2Q1	55585	NM_017582	CAGAAGACUUAGAUCACUA
CTM-464121	Plate 1	B11	UBE2Q1	55585	NM_017582	CCAUAGAGUCAGUGAUCAU
CTM-464123	Plate 1	C02	UBE2Q2	92912	NM_001145335	AGAGAUGGCUGAAGAUAUA
CTM-464124	Plate 1	C02	UBE2Q2	92912	NM_001145335	CAGAAGAAGAGGAAGAAGA
CTM-464125	Plate 1	C02	UBE2Q2	92912	NM_001145335	AGUCAGAGGAUGAAGGAAU
CTM-464126	Plate 1	C02	UBE2Q2	92912	NM_001145335	AGAAGAAGAGGAAGAAGAA
CTM-464243	Plate 1	C03	UBE2R1	997	NM_004359	GGAAGUGGAAAGAGAGCAA
CTM-464244	Plate 1	C03	UBE2R1	997	NM_004359	GGAAAGAGAGCAAGGGGAA
CTM-464245	Plate 1	C03	UBE2R1	997	NM_004359	GCGUGACACUGGUGGACGA
CTM-464246	Plate 1	C03	UBE2R1	997	NM_004359	ACGCAGAACGUCAGGACCA
CTM-464247	Plate 1	C04	UBE2R2	54926	NM_017811	CCACAACCCUGGCGGAAUA
CTM-464248	Plate 1	C04	UBE2R2	54926	NM_017811	CGACAUUGAUGAUGAAGAU
CTM-464249	Plate 1	C04	UBE2R2	54926	NM_017811	CCACUAAGGCCGAAGCAGA
CTM-464250	Plate 1	C04	UBE2R2	54926	NM_017811	AAGAUGAGGAGGAGGAAGA
CTM-464251	Plate 1	C05	UBE2S	27338	NM_014501	GCAUCAAGGUCUUUCCCAA
CTM-464252	Plate 1	C05	UBE2S	27338	NM_014501	UCAACGUGCUCAAGAGGGA
CTM-464253	Plate 1	C05	UBE2S	27338	NM_014501	AGGGCUACUUCCUGACCAA
CTM-464254	Plate 1	C05	UBE2S	27338	NM_014501	ACAAGGAGGUGACGACACU
CTM-464255	Plate 1	C06	UBE2T	29089	NM_014176	CAACACACCUUAUGAGAAA
CTM-464256	Plate 1	C06	UBE2T	29089	NM_014176	AGGAAGAGAUGCUUGAUAA
CTM-464257	Plate 1	C06	UBE2T	29089	NM_014176	UGACAUAUCCUCAGAAUUU
CTM-464258	Plate 1	C06	UBE2T	29089	NM_014176	ACAAAAGGCUGAUGAGGAA

CTM-464259	Plate 1	C07	UBE2U	148581	NM_001366234	CAUCAGAAAGAAUGGAAUU
CTM-464260	Plate 1	C07	UBE2U	148581	NM_001366234	CAGUAUUACAAAUGGAAGA
CTM-464261	Plate 1	C07	UBE2U	148581	NM_001366234	GCUCAAAGUUCCAAAUUUC
CTM-464262	Plate 1	C07	UBE2U	148581	NM_001366234	GGAUCUACAGCAUCAGAAA
CTM-464265	Plate 1	C08	UBE2V2	7336	NM_003350	GGACAAACAUACAACAAUU
CTM-464266	Plate 1	C08	UBE2V2	7336	NM_003350	CUAAUGAUGUCCAAAGAAA
CTM-464267	Plate 1	C08	UBE2V2	7336	NM_003350	GGAAGAACUUGAAGAAGGA
CTM-464268	Plate 1	C08	UBE2V2	7336	NM_003350	CAGAAUAUAUAGCCUGAAA
CTM-464270	Plate 1	C09	UBE2W	55284	NM_001271015	GGAAUGACCUUAAAUGAGA
CTM-464271	Plate 1	C09	UBE2W	55284	NM_001271015	GGUCAUGUUUACUGGUGAA
CTM-464272	Plate 1	C09	UBE2W	55284	NM_001271015	CCUUAAAUGAGAAGAGUGU
CTM-464273	Plate 1	C09	UBE2W	55284	NM_001271015	GCGAACAUGUAACAAGAAU
CTM-464279	Plate 1	C10	UBE2Z	65264	NM_023079	GUGACAUGAUGGAAGGAAA
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CTM-464281	Plate 1	C10	UBE2Z	65264	NM_023079	GCAAUAACACAGUGAGGUU
CTM-464282	Plate 1	C10	UBE2Z	65264	NM_023079	GGGAAAGUCUGCUUGAGUA
CTM-464283	Plate 1	C11	BIRC6	57448	NM_016252	AAAUAAAGCUCCAGGAUUA
CTM-464284	Plate 1	C11	BIRC6	57448	NM_016252	CGGAAGAUGUUGAGUGAAA
CTM-464285	Plate 1	C11	BIRC6	57448	NM_016252	GUGAAAAGACAAAGGAAAA
CTM-464286	Plate 1	C11	BIRC6	57448	NM_016252	AAGUAGAGGCCUUGAAUAA

Supplemental Table 2. Sources of 30 mouse E2 siGENOME SMARTpool siRNA library screen

Dharmacon siGENOME® SMARTpool® siRNA Library- Mouse Ubiquitin Conjugating Enzymes						
G-014124 Lot 12783						
Order Number	**Plate**	**Well**	**Gene Symbol**	**GENEID**	**Gene Accession**	**Sequence**
CTM-464291	Plate 1	A02	*Ube2a*	22209	NM_001313696	GAACAAAGCUGGCGCGACU
CTM-464292	Plate 1	A02	*Ube2a*	22209	NM_001313696	CAGGAGAACAAGCGGGAAU
CTM-464293	Plate 1	A02	*Ube2a*	22209	NM_001313696	CAACAUAAUGGUUUGGAAU
CTM-464294	Plate 1	A02	*Ube2a*	22209	NM_001313696	GGUAGUAUAUGUCUGGAUA
CTM-464295	Plate 1	A03	*Ube2b*	22210	NM_001362686	GAGCAAAGCUGGAAUGAUU
CTM-464296	Plate 1	A03	*Ube2b*	22210	NM_001362686	GAGUAUGAGAAGAGAGUUU
CTM-464297	Plate 1	A03	*Ube2b*	22210	NM_001362686	GUUUAGAUAUCCUGCAGAA
CTM-464298	Plate 1	A03	*Ube2b*	22210	NM_001362686	AGUUAUAUUUGGACCAGAA
CTM-464299	Plate 1	A04	*Ube2c*	68612	NM_026785	AAGAAAUACCUGCAAGAAA
CTM-464300	Plate 1	A04	*Ube2c*	68612	NM_026785	CAUGACAUCUGGUGACAAA
CTM-464301	Plate 1	A04	*Ube2c*	68612	NM_026785	CUAUAUGAUGUCAGGACUA
CTM-464302	Plate 1	A04	*Ube2c*	68612	NM_026785	AGAAAUACCUGCAAGAAAC
CTM-464303	Plate 1	A05	*Ube2d1*	216080	NM_145420	GAGAAUGGACUCAGAAAUA
CTM-464304	Plate 1	A05	*Ube2d1*	216080	NM_145420	CCAGAAAGAAUUAAGUGAU
CTM-464305	Plate 1	A05	*Ube2d1*	216080	NM_145420	ACCCAAAUAUAAACAGCAA
CTM-464306	Plate 1	A05	*Ube2d1*	216080	NM_145420	CGCUUUGACUGUAUCGAAA
CTM-464307	Plate 1	A06	*Ube2d2*	641452	NM_001037292	GGGAAUGGACUCAGAAGUA
CTM-464308	Plate 1	A06	*Ube2d2*	641452	NM_001037292	GAGAAAAGUACAACAGAAU
CTM-464309	Plate 1	A06	*Ube2d2*	641452	NM_001037292	CUAUCAGGGUGGAGUAUUU
CTM-464310	Plate 1	A06	*Ube2d2*	641452	NM_001037292	CAACAGAAUAGCUCGGGAA
CTM-464311	Plate 1	A07	*Ube2e1*	22194	NM_009455	GAGCAGAACACGACAGAAU
CTM-464312	Plate 1	A07	*Ube2e1*	22194	NM_009455	GCUUGGACAUAUUGAAAGA
CTM-464313	Plate 1	A07	*Ube2e1*	22194	NM_009455	AUUAAUAGCCAAGGAGUUA

CTM-464314	Plate 1	A07	*Ube2e1*	22194	NM_009455	GACAGUGGACCAAGAGAUA
CTM-464315	Plate 1	A08	*Ube2e2*	218793	NM_001360327	CCAAAGGAGACAACAUUUA
CTM-464316	Plate 1	A08	*Ube2e2*	218793	NM_001360327	GAAUGGAGGUCAACUAUAU
CTM-464317	Plate 1	A08	*Ube2e2*	218793	NM_001360327	CCACACAGUACAUGACCAA
CTM-464318	Plate 1	A08	*Ube2e2*	218793	NM_001360327	CCAACAGAGCGGAGCAUGA
CTM-464319	Plate 1	A09	*Ube2f*	67921	NM_001355762	GGGACAAAGUGGAUGAAUA
CTM-464320	Plate 1	A09	*Ube2f*	67921	NM_001356595	UUGCAGAACUUGAAGCUAA
CTM-464321	Plate 1	A09	*Ube2f*	67921	NM_001356595	GUGAAAUGCUUGACUAAAA
CTM-464322	Plate 1	A09	*Ube2f*	67921	NM_001356595	GAACAUCAUUUGCGGGACA
CTM-464323	Plate 1	A10	*Ube2g1*	67128	NM_025985	AGACAGAAACGGAGAAUUU
CTM-464324	Plate 1	A10	*Ube2g1*	67128	NM_025985	GCGAAAGAAUGGAGGGAAG
CTM-464325	Plate 1	A10	*Ube2g1*	67128	NM_025985	GCACCCAAAUGUUGAUAAA
CTM-464326	Plate 1	A10	*Ube2g1*	67128	NM_025985	AAAUGUAGAUGCUGCGAAA
CTM-464327	Plate 1	A11	*Ube2g2*	22213	NM_019803	CCAUGAAUGAAGAGAAUUU
CTM-464328	Plate 1	A11	*Ube2g2*	22213	NM_019803	GUGAUGAUCCCAUGGGUUA
CTM-464329	Plate 1	A11	*Ube2g2*	22213	NM_019803	GGCUGAUGGCCGAGUAUAA
CTM-464330	Plate 1	A11	*Ube2g2*	22213	NM_019803	CGAUGAGAGUGGAGCAAAC
CTM-464331	Plate 1	B02	*Ube2h*	22214	NM_001169577	CAGAAGAGUACAAGCAGAA
CTM-464332	Plate 1	B02	*Ube2h*	22214	NM_001169577	CGGAAGAGGCCCUGAAGGA
CTM-464333	Plate 1	B02	*Ube2h*	22214	NM_001169577	AAGAGUACAUCCAGAAGUA
CTM-464334	Plate 1	B02	*Ube2h*	22214	NM_001169577	CCAGAAGAGUACAAGCAGA
CTM-464335	Plate 1	B03	*Ube2i*	22219	NM_001177610	GCACAAUGAACCUGAUGAA
CTM-464336	Plate 1	B03	*Ube2i*	22219	NM_001177610	CAGAGUGGAAUAUGAGAAA
CTM-464337	Plate 1	B03	*Ube2i*	22219	NM_001177610	GGGAAGGAGGCUUGUUCAA
CTM-464338	Plate 1	B03	*Ube2i*	22219	NM_001177610	GCCAAAACAGAGUGGAAUA
CTM-464339	Plate 1	B04	*Ube2j1*	56228	NM_001355494	GAAAGAAGCUGCAGAAUUG
CTM-464340	Plate 1	B04	*Ube2j1*	56228	NM_001355494	UGAAAGAAGCUGCAGAAUU
CTM-464341	Plate 1	B04	*Ube2j1*	56228	NM_001355494	GCUAACAGCUAAUGGACGA
CTM-464342	Plate 1	B04	*Ube2j1*	56228	NM_001355494	GAAUAUAUCUGGCCAAUGA
CTM-464343	Plate 1	B05	*Ube2k*	53323	NM_001310618	UGAUAGGAACGCAGUAAUA
CTM-464344	Plate 1	B05	*Ube2k*	53323	NM_001310618	GCGAAUCAGUACAAACAGA
CTM-464345	Plate 1	B05	*Ube2k*	53323	NM_001310618	AUGCAGUAGUAGCGAAUCA
CTM-464346	Plate 1	B05	*Ube2k*	53323	NM_001310618	ACGCAGUAAUAGUGGCCUU
CTM-464347	Plate 1	B06	*Ube2l3*	22195	NM_009456	UAAGAAUGCUGAAGAGUUU
CTM-464348	Plate 1	B06	*Ube2l3*	22195	NM_009456	GCUGAAGAGUUUACAAAGA
CTM-464349	Plate 1	B06	*Ube2l3*	22195	NM_009456	CUGAAGAGUUUACAAAGAA
CTM-464350	Plate 1	B06	*Ube2l3*	22195	NM_009456	ACAAAGAAAUAUGGGGAAA
CTM-464351	Plate 1	B07	*Ube2l6*	56791	NM_019949	CGAAAGAGCUGGAGAGUCU
CTM-464352	Plate 1	B07	*Ube2l6*	56791	NM_019949	UCAAUGUGCUGGUGAGUAA
CTM-464353	Plate 1	B07	*Ube2l6*	56791	NM_019949	GGAAGAAGGCAGAAGAGUU
CTM-464354	Plate 1	B07	*Ube2l6*	56791	NM_019949	CCGGAGAUGUUCAGGAAGA
CTM-464358	Plate 1	B08	*Ube2m*	22192	NM_001243968	CUGAGGUCCUGCAGAACAA
CTM-464359	Plate 1	B08	*Ube2m*	22192	NM_001243968	CUGAGGACCCACUGAACAA
CTM-464360	Plate 1	B08	*Ube2m*	22192	NM_001243968	AGCCAGUCCUUACGAUAAA
CTM-464361	Plate 1	B08	*Ube2m*	22192	NM_001243968	AAGCCAGUCCUUACGAUAA
CTM-464365	Plate 1	B09	*Ube2n*	93765	NM_080560	AGACAAGUUGGGAAGAAUA
CTM-464366	Plate 1	B09	*Ube2n*	93765	NM_080560	GGCUAUAUGCCAUGAACAA
CTM-464367	Plate 1	B09	*Ube2n*	93765	NM_080560	CUAUAUGCCAUGAACAAUA
CTM-464368	Plate 1	B09	*Ube2n*	93765	NM_080560	GCAUUAAAGCAGAACCAGA
CTM-464369	Plate 1	B10	*Ube2o*	217342	NM_173755	CCAAAGAGGAGGAGGAAGA
CTM-464370	Plate 1	B10	*Ube2o*	217342	NM_173755	UCAAGAAGCUACAGGAGAA
CTM-464371	Plate 1	B10	*Ube2o*	217342	NM_173755	CCGAAAGCACAGAGGACAA
CTM-464372	Plate 1	B10	*Ube2o*	217342	NM_173755	GGGACUUCGUGGUGGACAA
CTM-464373	Plate 1	B11	*Ube2q1*	70093	NM_027315	GGACAUAAAGAAAGGGAAU
CTM-464374	Plate 1	B11	*Ube2q1*	70093	NM_027315	GCAAGAAGUCUGAAGAUGA
CTM-464375	Plate 1	B11	*Ube2q1*	70093	NM_027315	CAGAAGACCUAGAUCACUA

CTM-464376	Plate 1	B11	*Ube2q1*	70093	NM_027315	CAGUCGAACUCGUGAAUGA
CTM-464612	Plate 1	C02	*Ube2q2*	109161	NM_001346658	GGAGAUGGCUGAAGAUAUA
CTM-464613	Plate 1	C02	*Ube2q2*	109161	NM_001346658	GCUAAUAAAUGACAGCUUA
CTM-464614	Plate 1	C02	*Ube2q2*	109161	NM_001346658	CAGGAAGACUCAAAGGCAA
CTM-464615	Plate 1	C02	*Ube2q2*	109161	NM_001346658	ACUAUGAGAUGAAGGAAGA
CTM-464620	Plate 1	C03	*Ube2r1*	216150	NM_001359817	CCCAAACAUCUAUGAGACA
CTM-464621	Plate 1	C03	*Ube2r1*	216150	NM_001359817	CCAAGAUGUGGCACCCAAA
CTM-464622	Plate 1	C03	*Ube2r1*	216150	NM_001359817	ACAACUGGGAGGUGGCCAU
CTM-464623	Plate 1	C03	*Ube2r1*	216150	NM_001359817	AGACAGGGGACGUGUGCAU
CTM-464630	Plate 1	C04	*Ube2r2*	67615	NM_026275	UGAUGAAGAUGAAGAGGAA
CTM-464631	Plate 1	C04	*Ube2r2*	67615	NM_026275	GGAAAUGGAGGGACAGCAA
CTM-464632	Plate 1	C04	*Ube2r2*	67615	NM_026275	ACUCAGAACGUUAGGACUA
CTM-464633	Plate 1	C04	*Ube2r2*	67615	NM_026275	CGACAUUGAUGAUGAAGAU
CTM-464781	Plate 1	C05	*Ube2s*	77891	NM_133777	GGAGAAUUAUGAAGAGUAU
CTM-464782	Plate 1	C05	*Ube2s*	77891	NM_133777	CCAAGAAACAUGCAGGUGA
CTM-464783	Plate 1	C05	*Ube2s*	77891	NM_133777	GAAACAUGCAGGUGAGCGA
CTM-464784	Plate 1	C05	*Ube2s*	77891	NM_133777	AGGGCUACUUCCUGACUAA
CTM-464788	Plate 1	C06	*Ube2t*	67196	NM_001278115	GGAAGGAUUUGUCUAGAUA
CTM-464789	Plate 1	C06	*Ube2t*	67196	NM_001278115	AAUACUAGGUGGAGCUAAU
CTM-464790	Plate 1	C06	*Ube2t*	67196	NM_001278115	CAUGCAAGACAGAAACAAA
CTM-464791	Plate 1	C06	*Ube2t*	67196	NM_001278115	GCUAAUACACCUUAUGAGA
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CTM-464794	Plate 1	C07	*Ube2u*	381534	NM_001033773	AGAAAUGCGUCUACGUAUA
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CTM-464802	Plate 1	C09	*Ube2w*	66799	NM_001271016	AUGCAGAAACGACUACAAA
CTM-464803	Plate 1	C09	*Ube2w*	66799	NM_001271016	GAAAAGAGUGUUCAGAAUU
CTM-464804	Plate 1	C09	*Ube2w*	66799	NM_001271016	CGUCAAUGCAGAAACGACU
CTM-464805	Plate 1	C10	*Ube2z*	268470	NM_172300	CGGACUGAUUCGACAGAAA
CTM-464806	Plate 1	C10	*Ube2z*	268470	NM_172300	CGACAGAAAGUGCUGGAAA
CTM-464807	Plate 1	C10	*Ube2z*	268470	NM_172300	GCAAUAACACAGUGAGGUU
CTM-464808	Plate 1	C10	*Ube2z*	268470	NM_172300	GGGAAAGUCUGCUUGAGUA
CTM-464809	Plate 1	C11	*Birc6*	12211	NM_007566	GAACAAAGCUCCAGGCCUA
CTM-464810	Plate 1	C11	*Birc6*	12211	NM_007566	CAAAGAAUCUGAUGAGAAA
CTM-464811	Plate 1	C11	*Birc6*	12211	NM_007566	GUGAAAAGACAAAGGAAAA
CTM-464812	Plate 1	C11	*Birc6*	12211	NM_007566	GGGUAGAAGUUCAGCAAGA

Supplemental Table 3. List of RT-qPCR primers used in this study

RT-qPCR primers used in this study		
Gene	**Forward**	**Reverse**
HPRT	GCTGCAACGGCGGAA	CCTGTGGTGGACATAGCAATGATT
Hsp90	GTCCGCCGTGTGTTCATCAT	GCACTTCTTGACGATGTTCTTGC
18S RNA	GTAACCCGTTGAACCCCATT	CCATCCAATCGGTAGTAGCG
Acaca	TGGATCCGCTTACAGAGAGACT	GCCGGAGCATCTCATTCG
Acadm	AGGGTTTAGTTTTGAGTTGACGG	CCCGCTTTTGTCATATTCCG

Acadvl	CTACTGTGCTTCAGGGACAAC	CAAAGGACTTCGATTCTGCCC
Acox	GTGCAGCTCAGAGTCTGTCCAA	TACTGCTGCGTCTGAAAATCGA
Birc6	CGCGGGACCATCAAAGTCAT	GCAGTGTCTAGCAACAAGATCC
Cidea	TGACATTCATGGGATTGCAGAC	GGCCAGTTGTGATGACTAAGAC
Cox4i2	CTGCCCGGAGTCTGGTAATG	CAGTCAACGTAGGGGGTCATC
Cpt1b	CGTGCTGCTTTCTTTGTG	AGTGTTCGGTGTTGAGGC
Cycs	CCAAATCTCCACGGTCTGTTC	ATCAGGGTATCCTCTCCCCAG
Dio2	CAGTGTGGTGCACGTCTCCAATC	TGAACCAAAGTTGACCACCAG
Dgat1	TCCGTCCAGGGTGGTAGTG	TGAACAAAGAATCTTGCAGACGA
Esrra	CTCAGCTCTCTACCCAAACGC	CCGCTTGGTGATCTCACACTC
Fasn	GCTGCGGAAACTTCAGGAAAT	AGAGACGTGTCACTCCTGGACTT
Mfn1	CCTACTGCTCCTTCTAACCCA	AGGGACGCCAATCCTGTGA
Ppara	AGAGCCCCATCTGTCCTCTC	ACTGGTAGTCTGCAAAACCAAA
Ppargc1a	AAAGGATGCGCTCTCGTTCA	GGAATATGGTGATCGGGAAC
Prdm16	CAGCACGGTGAAGCCATTC	GCGTGCATCCGCTTGTG
Scl2a4	GTGACTGGAACACTGGTCCTA	CCAGCCACGTTGCATTGTAG
Srebp1c	GGAGCCATGGATTGCACATT	GGCCCGGGAAGTCACTGT
Ube2a	ATGAGGGACTTCAAGAGGTTACA	TCTGCATAGACGTTAGGATGGA
Ube2b	AAATAAACCACCAACCGTTAGGT	TCTCTTCTCATACTCCCGTTTGT
Ube2c	GCAGAGTGCGCTGCTAATC	CTGGAAGTCGGATCTCGGT
Ube2d1	CCCGTGGGGAGATGACTTGTTC	GGATAGTCTGTCGGAAAGTGGA
Ube2d2	ACAAGGAATTGAATGACCTGGC	CACCCTGATAGGGGCTGTC
Ube2e1	ATGTCGGATGACGATTCGAGG	GCTCATGCTGACTTTACTCTCC
Ube2e2	ACTGAGGCGCAGAGAGTTGA	GCTGAACTTGTTCTCGATCAGG
Ube2f	ACGCTGGCAAGCAAGTTGA	CCTCATCTGGGCTTACAGTCAG
Ube2g1	CTGGCAGAACTCAACAAAAATCC	AGATGAGCCTTAAAAACACCACC
Ube2g2	TGGCCGAGTATAAGCAATTAACC	GGCTCAAGGGGTAGTCAAGT
Ube2h	GACACGGACGTAGTCAAGCTC	GTCCACTCTCACTTTCCACAC
Ube2i	GGAGGAAGGACCACCCTTTTG	GGATAGCGCACTCCCAGTT
Ube2j1	ATGGAGACCCGCTACAACCT	GAGGCTGAGCGTGGTAATGAT
Ube2k	CAGCGAATCAAGCGGGAGTT	AGGTCCTGCTATTTCTCCTCTT
Ube2l3	GAGATCCGCAAATGTGGAATGA	ACTCTGCTGGAAAGTTGATTTCA
Ube2l6	GTGGCGAAAGAGCTGGAGAG	GGGGAAATCAATCCGCACTTG
Ube2m	AACCTGCCCAAGACGTGTG	AGCTGAATACAAACTTGCCACT
Ube2n	GCTGGCAGAACCAGTTCCT	TCCCTCAAAGGGGAATCCTG
UBE2O	AGGTCTACGACTTGAAGAACCA	ACCACTCGGAACTTGCTCTTG
Ube2o	CAATGAAGCTGGCTTTGACA	ACTGAAGTGCTGCCGAATCT
Ube2q1	CATCACGGAATCATACCCTGC	GCTGAGGGAGGTTGTAGAGTTT
Ube2q2	GACAAGAACCACGAGCGATTC	GTCATCAGAGTCCACAAACCAT
Ube2r1	GACCTCTTAGTGGATTCCGGG	CCTGCTCTCGGACTCACG
Ube2r2	AGAAAGCCCTGATGCTTGAGC	GTGTTAGGGGGTCCGAAGATG

Ube2s	CAGACCCACCTGATGGCATTA	AGACCTCCAGCATAGGGAGTC
Ube2t	GTGCTGGCAGGAAAAGGATCA	ATCGGACCTGTGGAGGTTCAA
Ube2u	AGACATGGTCTCAGATAGCCAC	CCATTGCACTTGATTCTGCCG
Ube2v2	AGGTGATGGTACTGTTAGCTGG	TTGGTGGCCCAATAATCATGC
Ube2w	ATGGCGTCAATGCAGAAACGA	ATGTCTACGATCCACTGCGTG
Ube2z	GTCCACCTGACTATCCCATCC	TGGGGTTAAACCTCACTGTGT
Ucp1	CCTGCCTCTCTCGGAAACAA	TGTAGGCTGCCCAATGAACA
Ucp3	GAGATGGTGACCTACGACATCA	GCGTTCATGTATCGGGTCTTTA

Supplemental Figure Legends

Supplemental Figure S1. Assessment of energy expenditure in *Ube2o*-deficient mice on chow

(**A**) PCR genotyping of embryos from an intercross of *Ube2o*$^{+/-}$ mice (top). Lysates from *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ embryos (E13.5) were subjected to immunoblotting (bottom).

(**B**) Body weight of 8-week-old male and female *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow. *n* = 5~7 per group.

(**C**) Percentage of fat and lean mass of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow was determined by EchoMRI. *Ube2o*$^{+/+}$ *n* = 35, *Ube2o*$^{+/-}$ *n* = 10, *Ube2o*$^{-/-}$ *n* = 19.

(**D**) Oxygen consumption (VO_2) per kg of lean mass of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow was determined in metabolic chambers. *Ube2o*$^{+/+}$ *n* = 36, *Ube2o*$^{+/-}$ *n* = 10, *Ube2o*$^{-/-}$ *n* = 19.

(**E**) Energy expenditure per kg of lean mass of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow was determined in metabolic chambers. *Ube2o*$^{+/+}$ *n* = 32, *Ube2o*$^{+/-}$ *n* = 10, *Ube2o*$^{-/-}$ *n* = 19.

(**F**) Rectal temperature of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow. *Ube2o*$^{+/+}$ *n* = 18, *Ube2o*$^{+/-}$ *n* = 12, *Ube2o*$^{-/-}$ *n* = 6.

(**G**) Total RNAs from brown adipose tissue (BAT) of *Ube2o*$^{+/+}$ and *Ube2o*$^{-/-}$ mice fed an HFD for 20 weeks were subjected to RT-qPCR. *Ube2o*$^{+/+}$ *n* = 9, *Ube2o*$^{+/-}$ 12 weeks HFD *n* = 9, *Ube2o*$^{-/-}$ *n* = 4.

(**H**) Total RNAs from tibialis anterior muscles of *Ube2o*$^{+/+}$ and *Ube2o*$^{-/-}$ mice fed an HFD for 20 weeks were subjected to RT-qPCR. *Ube2o*$^{+/+}$ *n* = 5, *Ube2o*$^{+/-}$ 12 weeks HFD *n* = 5, *Ube2o*$^{-/-}$ *n* = 10.

(**I**) Immunohistochemical analysis of succinate dehydrogenase (SDH) (left) and quantification of SDH staining intensity (right) in tibialis anterior muscles of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow. Scale bars, 100 μm. *Ube2o*$^{+/+}$ *n* = 10, *Ube2o*$^{+/-}$ *n* = 5, *Ube2o*$^{-/-}$ *n* = 5.

(**J**) Citrate synthase (CS) activity in quadriceps of 8-week-old *Ube2o*$^{+/+}$, *Ube2o*$^{+/-}$ and *Ube2o*$^{-/-}$ mice on chow was determined by enzymatic assay. *Ube2o*$^{+/+}$ *n* = 8, *Ube2o*$^{+/-}$ *n* = 5, *Ube2o*$^{-/-}$ *n* = 8.

Error bars represent ± SEM. *P* value was determined by ANOVA. n.s., non-significant. **P*<0.05, ***P*<0.01, ****P*<0.001, *Ube2o*$^{+/+}$ vs. *Ube2o*$^{+/-}$; $^{\#}$*P*<0.05, $^{\#\#}$*P*<0.01, $^{\#\#\#}$*P*<0.001, *Ube2o*$^{+/-}$ vs. *Ube2o*$^{-/-}$; $^{\$}$*P*<0.05, $^{\$\$}$*P*<0.01, $^{\$\$\$}$*P*<0.001, *Ube2o*$^{+/+}$ vs. *Ube2o*$^{-/-}$.

Supplemental Figure S2. Haplo-deficiency of *Ube2o* leads to improved insulin sensitivity in diet-induced type 2 diabetes mouse model

(**A**) Body weight increase of *Ube2o*$^{+/+}$ and *Ube2o*$^{+/-}$ mice fed an HFD for 7 weeks. *Ube2o*$^{+/+}$ *n* = 6, *Ube2o*$^{+/-}$ *n* = 5.

(**B**) Blood glucose was measured in *Ube2o*$^{+/+}$ and *Ube2o*$^{+/-}$ mice on chow or HFD for 7 weeks. *Ube2o*$^{+/+}$ chow n = 14, *Ube2o*$^{+/-}$ chow n = 10, *Ube2o*$^{+/+}$ HFD n = 6, *Ube2o*$^{+/-}$ HFD n = 6.

(**C** and **D**) Glucose (C) and insulin (D) tolerance tests in *Ube2o*$^{+/+}$ and *Ube2o*$^{+/-}$ mice fed either a normal chow or an HFD for 6~7 weeks. Right graphs indicate the area under the curve (AUC) (C) and the area above the curve (AAC) (D). GTT, *Ube2o*$^{+/+}$ chow n = 14, *Ube2o*$^{+/-}$ chow n = 12, *Ube2o*$^{+/+}$ 6 weeks HFD n = 12, *Ube2o*$^{+/-}$ 6 weeks HFD n = 11; ITT, *Ube2o*$^{+/+}$ chow n = 13, *Ube2o*$^{+/-}$ chow n = 10, *Ube2o*$^{+/+}$ 7 weeks HFD n = 6, *Ube2o*$^{+/-}$ 7 weeks HFD n = 6.

Error bars represent ± SEM. *P* value was determined by Student's *t* test. n.s., non-significant. **P*<0.05, *Ube2o*$^{+/+}$ chow vs. *Ube2o*$^{+/-}$ chow; $^{\#}$*P*<0.05, $^{\#\#}$*P*<0.01, *Ube2o*$^{+/+}$ HFD vs. *Ube2o*$^{+/-}$ HFD.

Supplemental Figure S3. Generation of skeletal muscle-, adipose- or liver–specific *Ube2o* knockout mice

(**A**) Schematic presentation of targeted alleles of *Ube2o* before and after recombination. PCR primers for genotyping are indicated by arrowheads. LA, long arm; SA, short arm; *Ube2o*$^{fl\text{-}neo}$, *Ube2o* targeted allele; *Ube2o*^{fl}, *Ube2o* allele after recombination by FLP; *Ube2o*$^{\Delta}$, *Ube2o* allele after recombination by Cre.

(**B**) PCR genotyping of tail biopsies from an intercross of *Ube2o*$^{fl/+}$ mice.

(**C**) Lysates from skeletal muscle and adipose tissue of 10-week-old control (*Ube2o*$^{fl/fl}$) and *Ube2o*$^{\Delta Adip}$ mice or 12-week-old control and *Ube2o*$^{\Delta Mus}$ mice were subjected to immunoblotting.

Supplemental Figure S4. Insulin signaling in liver or visceral fat in *Ube2o*$^{\Delta Mus}$ mice on HFD is not enhanced before the onset of obesity

(**A**) Adipose depot weight of control (*Ube2o*$^{fl/fl}$) and *Ube2o*$^{\Delta Mus}$ mice on HFD for 20 weeks. SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; BAT, brown adipose tissue. *n* = 7.

(**B**) Muscle tissue weight of control and *Ube2o*$^{\Delta Mus}$ mice on chow. Gastroc., gastrocnemius muscle; Soleus, soleus muscle; TA, tibialis anterior muscle. *n* = 7.

(**C**) H&E-stained sections of tibialis anterior muscle of control and *Ube2o*$^{\Delta Mus}$ mice on chow. Scale bars, 50 μm.

(**D** and **E**) Immunoblots showing insulin (200 nM)–induced S473 phosphorylation of AKT protein and its total protein levels in the visceral adipose tissue (VAT) (D) and liver (E) from control and *Ube2o*$^{\Delta Mus}$ mice on the HFD for 7 weeks. *n* = 4.

Error bars represent ± SEM. *P* value was determined by Student's *t* test (***P*<0.01).

Supplemental Figure S5. Liver-specific *Ube2o* knockout mice do not have improved glucose and lipid metabolism on in response to HFD.

(**A**) Body weights of control (*Ube2o*$^{fl/fl}$) and *Ube2o*$^{\Delta Liv}$ mice fed an HFD for 17 weeks. *n* = 8.

(**B**) Plasmatic levels of total cholesterol (TC) (mg/dl) of control and *Ube2o*$^{\Delta Liv}$ mice on HFD for 17 weeks. *Ube2o*$^{fl/fl}$ *n* = 8, *Ube2o*$^{\Delta Liv}$ *n* = 6.

(**C**) Liver weight of control and *Ube2o*$^{\Delta Liv}$ mice on HFD for 17 weeks. *n* = 8.

(**D**) Hepatic triglyceride (TG) level per g of liver of control and *Ube2o*$^{\Delta Liv}$ mice on HFD

for 17 weeks. *n* = 8.

(**E**) Blood glucose was measured control and *Ube2o*$^{\Delta Liv}$ mice on HFD for 17 weeks. *Ube2o*$^{fl/fl}$ *n* = 7, *Ube2o*$^{\Delta Liv}$ *n* = 8.

(**F** and **G**) Glucose (GTT) (F) and insulin (ITT) (G) tolerance tests in control and *Ube2o*$^{\Delta Liv}$ mice on HFD for 14~15 weeks. Insets indicate the area under the curve (AUC) (F) and the area above the curve (AAC) (G). *Ube2o*$^{fl/fl}$ *n* = 10, *Ube2o*$^{\Delta Liv}$ *n* = 8.

(**H**) Immunoblots showing insulin (200 nM)–induced tyrosine phosphorylation of IRS1 immunoprecipitates and S473 phosphorylation of AKT protein and their total protein levels in liver from control and *Ube2o*$^{\Delta Liv}$ mice on HFD for 17 weeks. *n* = 4.

Error bars represent ± SEM. *P* value was determined by Student's *t* test (n.s., non-significant).

Supplemental Figure S6. UBE2O regulates metabolic adaptation to energy stress through AMPKα2.

(**A**) Fatty acid oxidation (FAO) was determined by measuring $^{14}CO_2$ and [^{14}C]ASM produced in C2C12 myotubes expressing Ube2o shRNA together with Prkaa2 shRNA treated with vehicle or etomoxir incubated with [1-^{14}C] palmitate for 3 hours. *n* = 6.

(**B**) Basal oxygen consumption rate (OCR) from (a) was measured with a Seahorse XFe96 extracellular flux analyzer. *n* = 8.

(**C**) Total RNAs from C2C12 myotubes expressing Ube2o shRNA together with Prkaa2 shRNA were subjected to RT-qPCR for *Ppargc1a* and its target genes. *n* = 3.

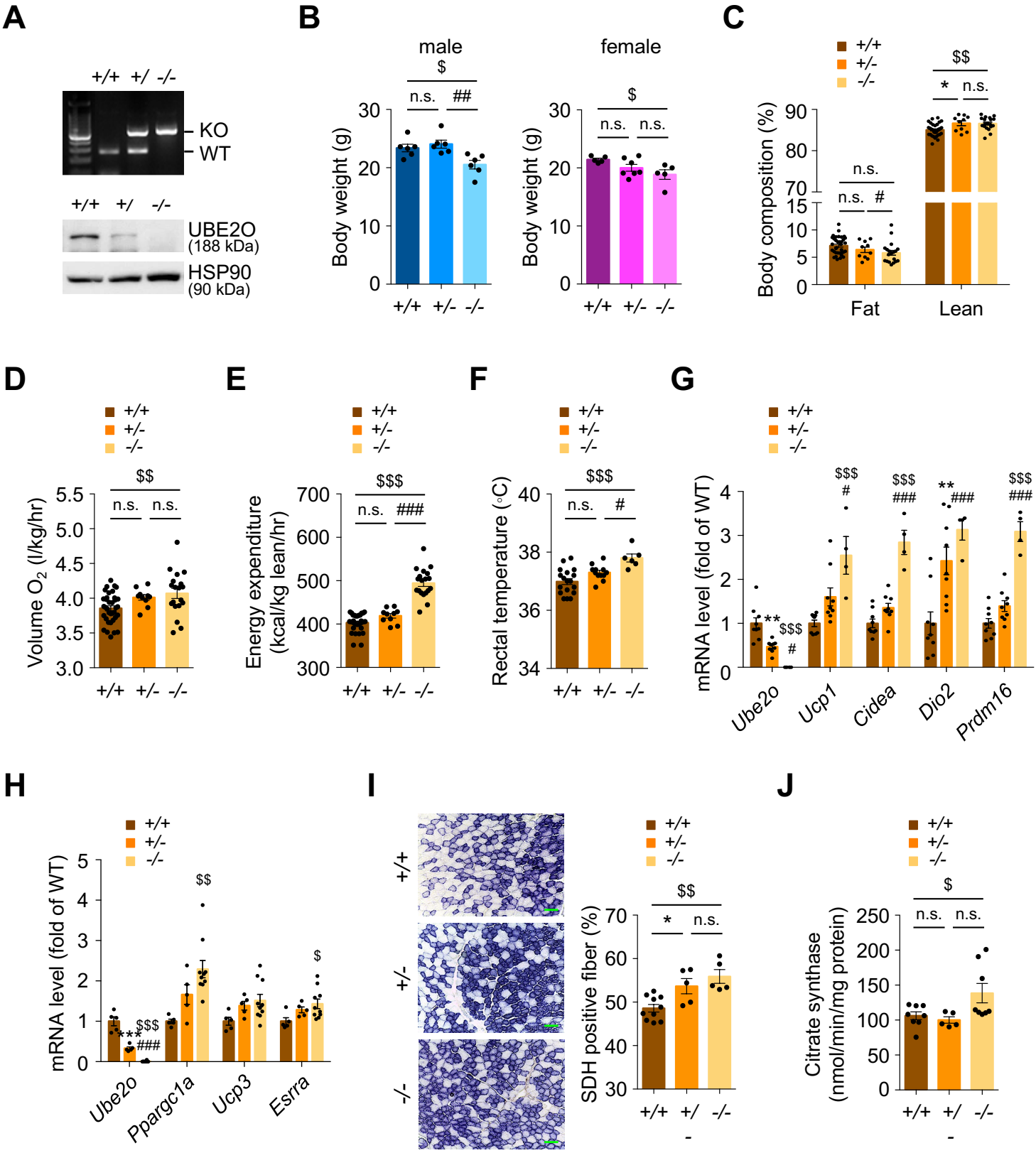
(**D**−**F**) C2C12 myotubes ectopically expressing UBE2O were incubated in glucose-free medium for 4 hours. The NADP+/NADPH ratio (D), GSSG/GSH ratio (E) and ROS level

(F) were then determined. GSSG, oxidized glutathione; GSH, reduced glutathione. $n = 4$.

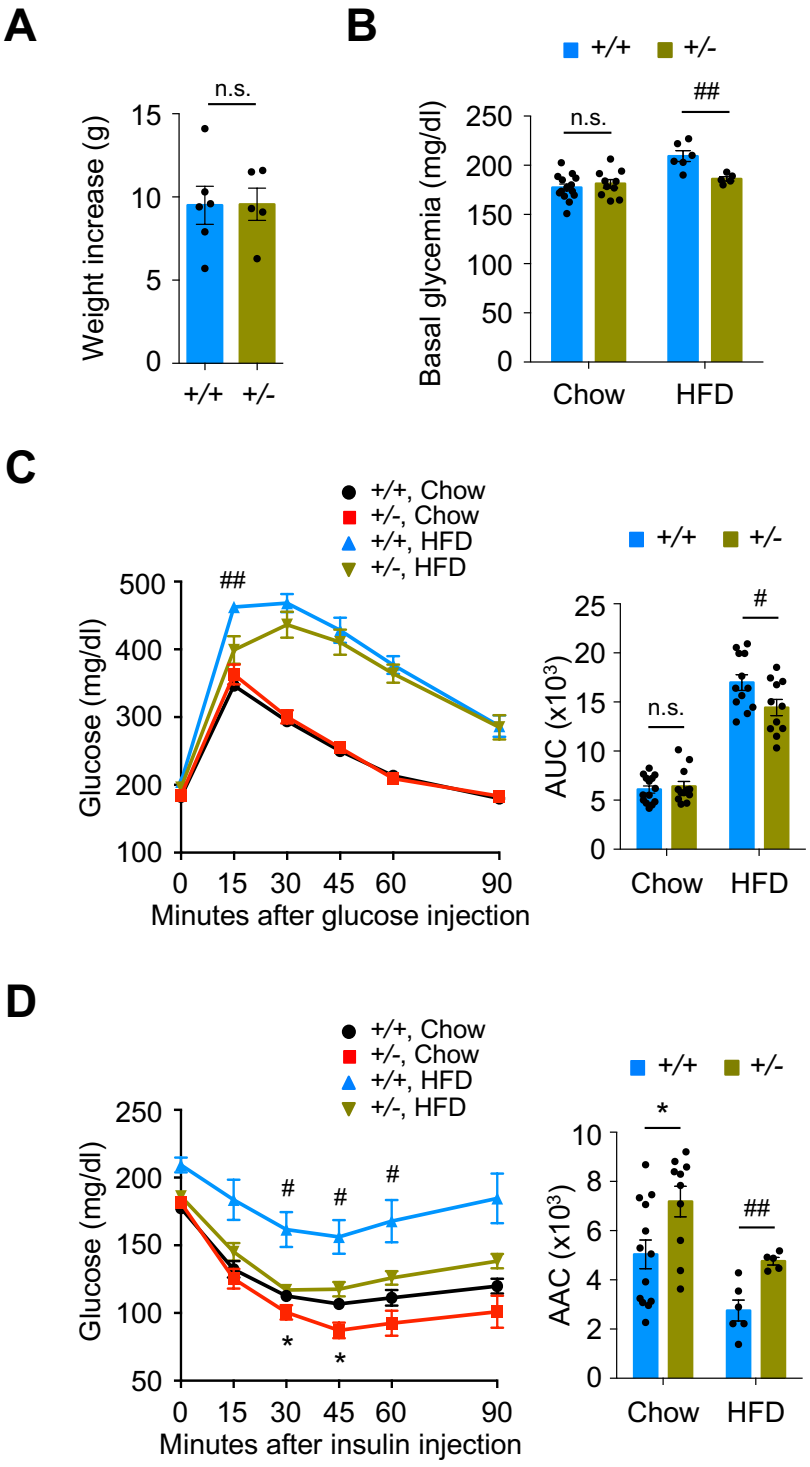
(**G**−**I**) C2C12 myotubes expressing Ube2o shRNA together with Prkaa2 shRNA were incubated in glucose-free medium for 4 hours. The NADP+/NADPH ratio (G), GSSG/GSH ratio (H) and ROS level (I) were then determined. $n = 3$.

Error bars represent ± SEM. *P* value was determined by ANOVA (n.s., non-significant; $^{*,\#}P<0.05$; $^{**,\#\#}P<0.01$; $^{***,\#\#\#}P<0.001$).

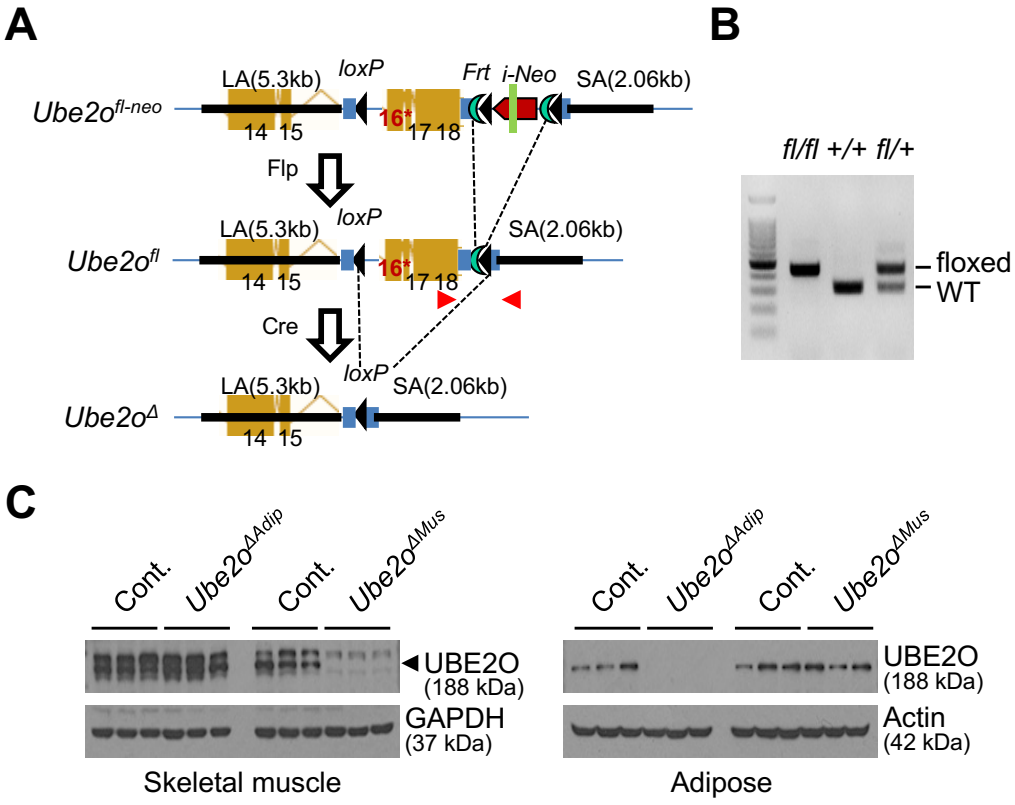
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



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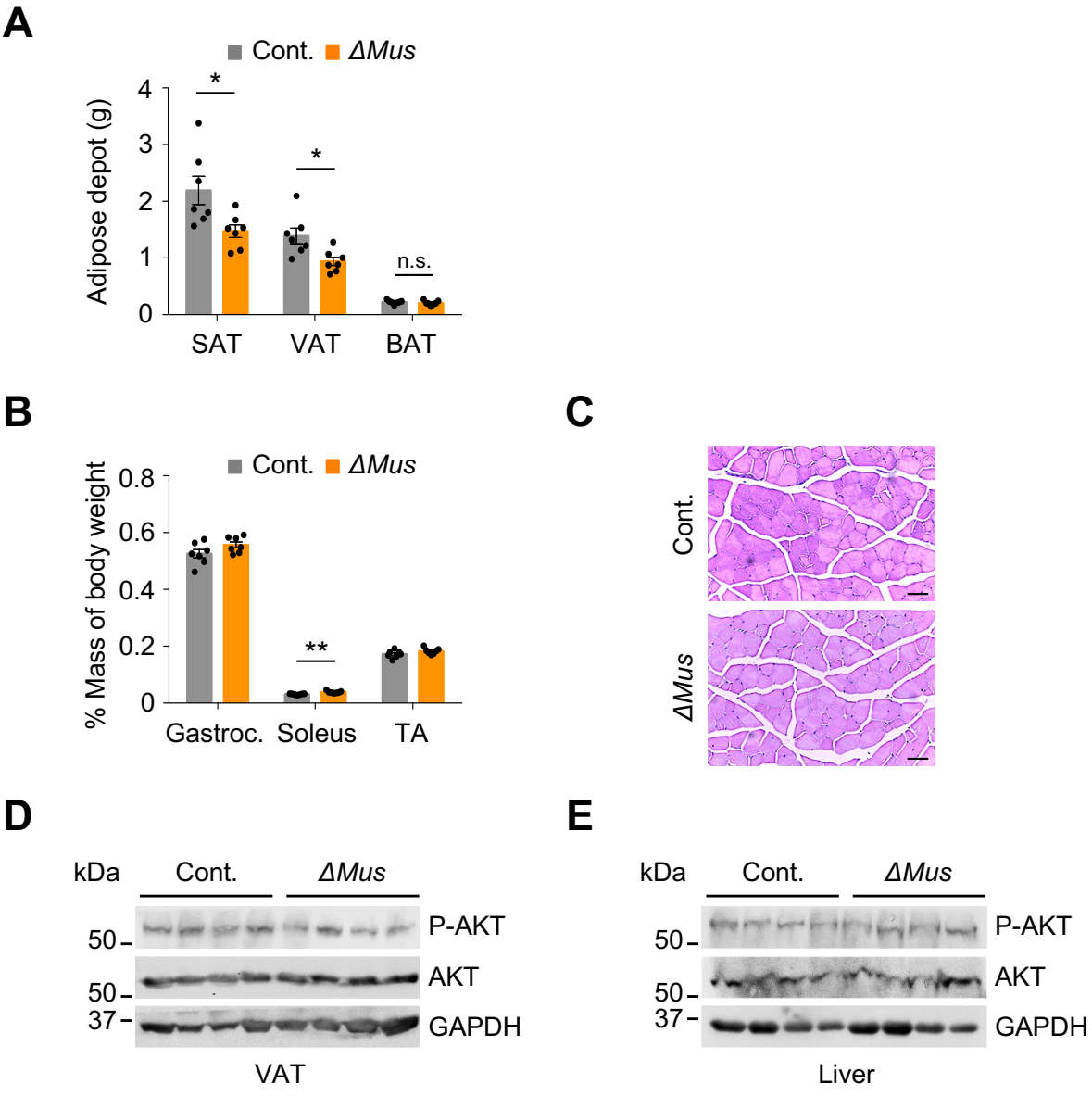

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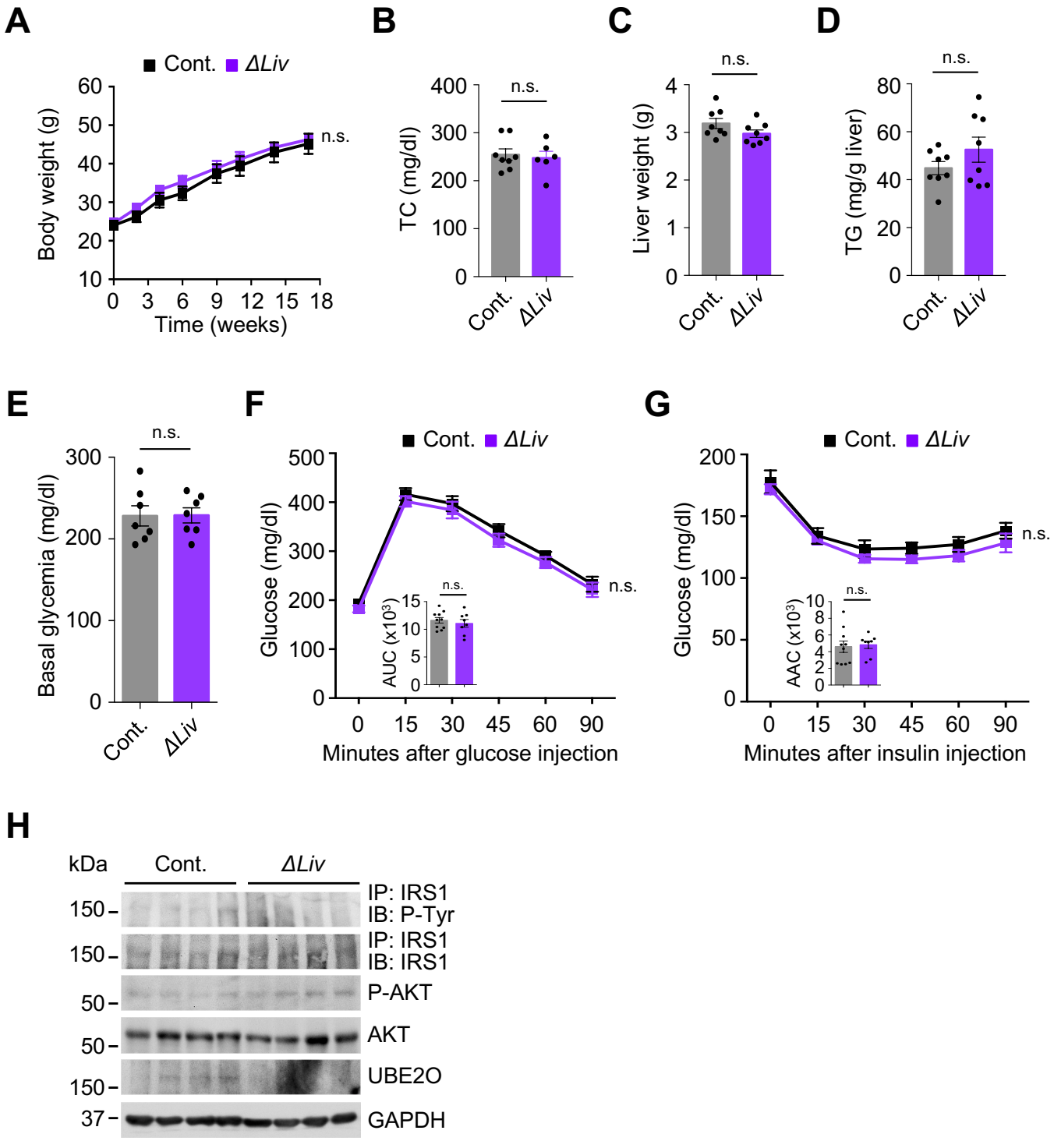

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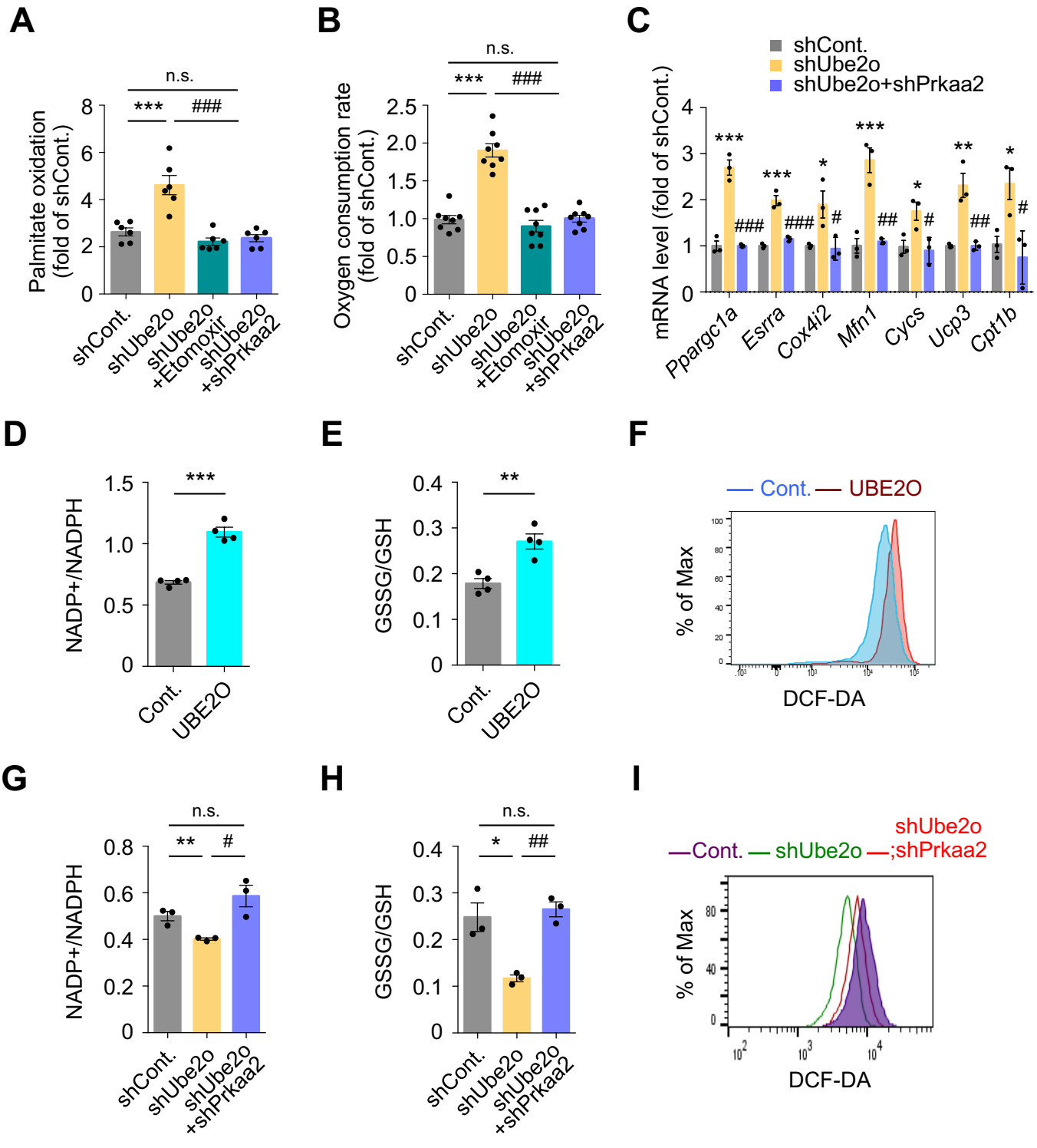


Figure 1C

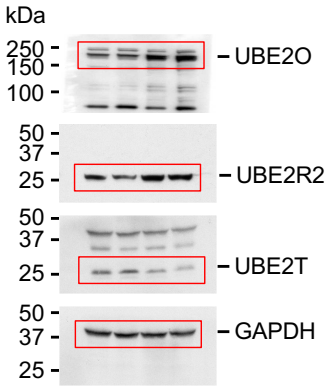


Figure 1D

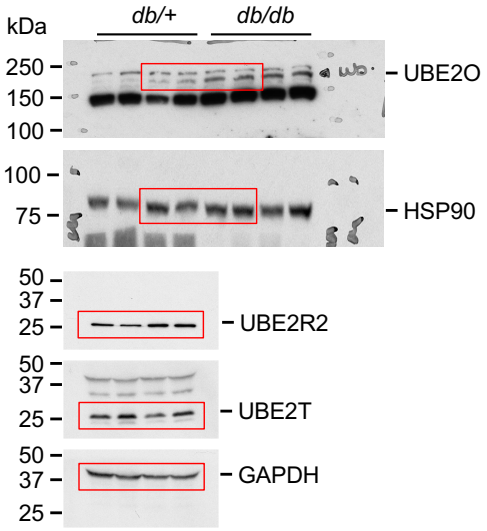
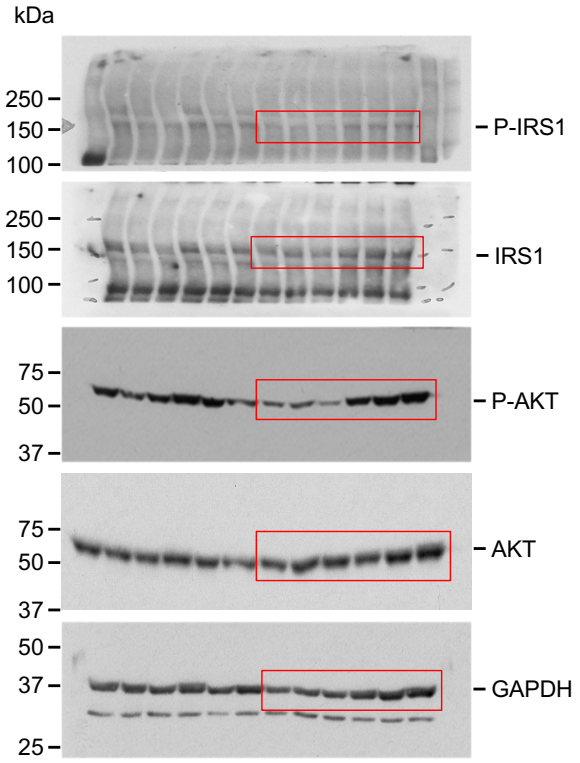


Figure 3H



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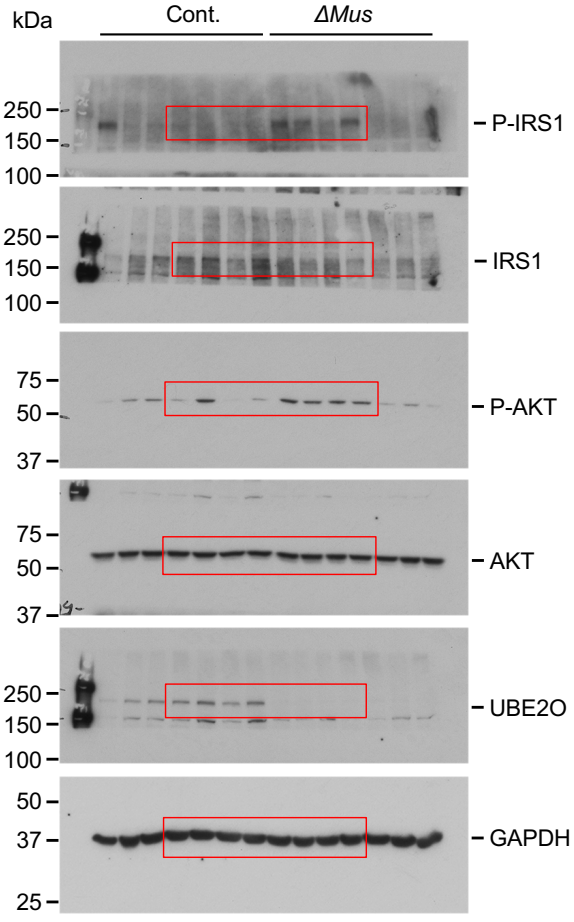


Figure 5J

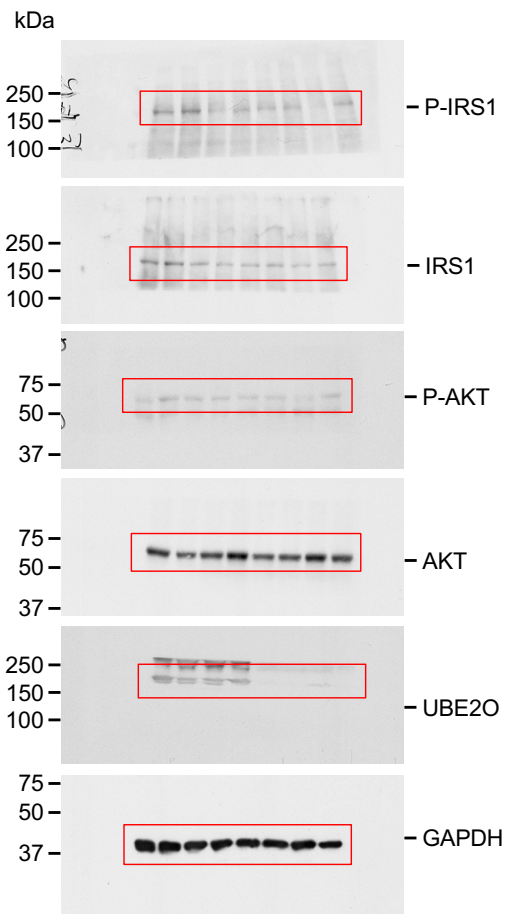


Figure 6A

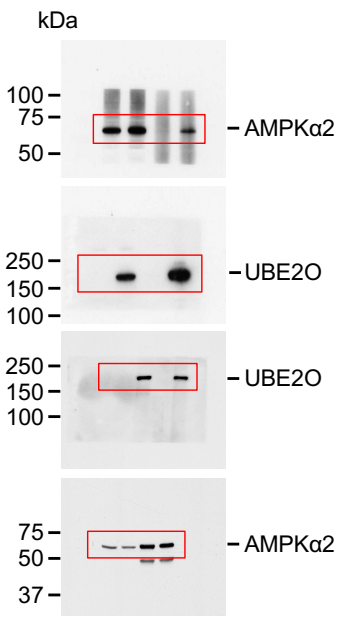


Figure 6B

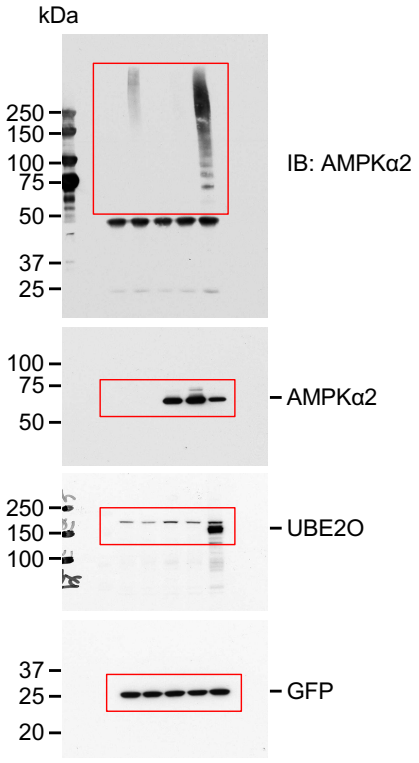


Figure 6C

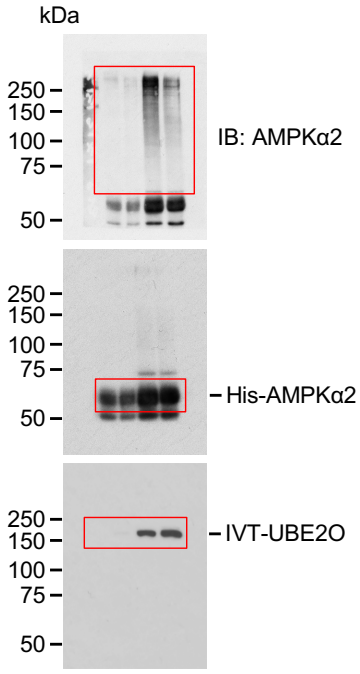


Figure 6D

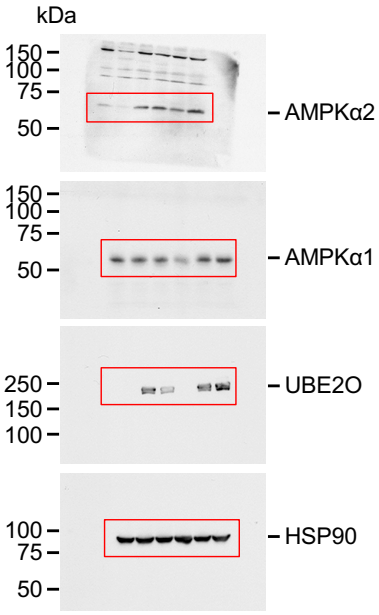


Figure 6E

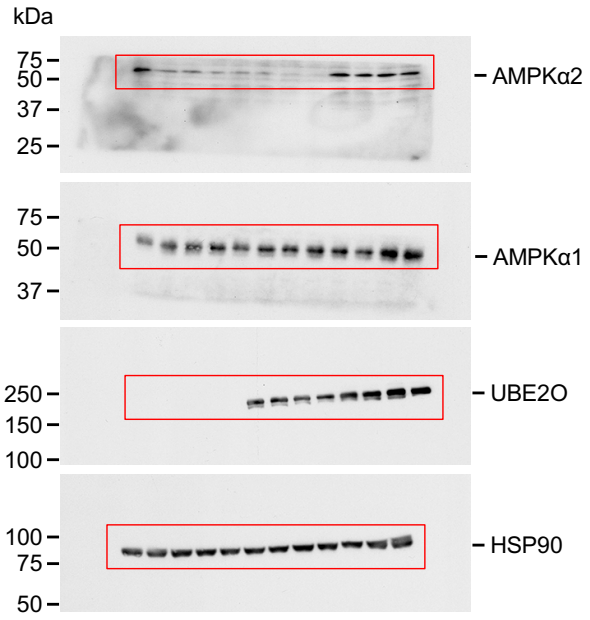


Figure 6F

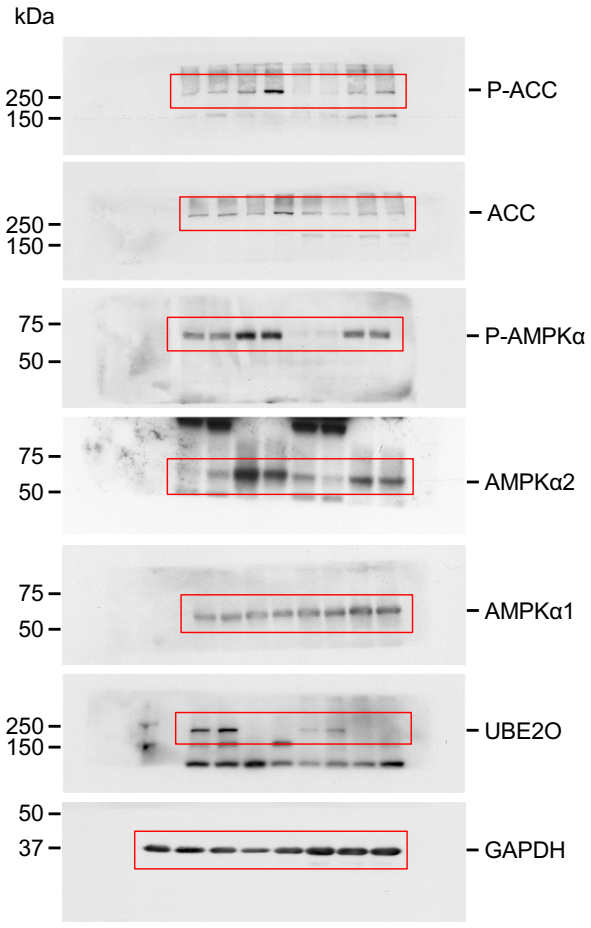


Figure 6G

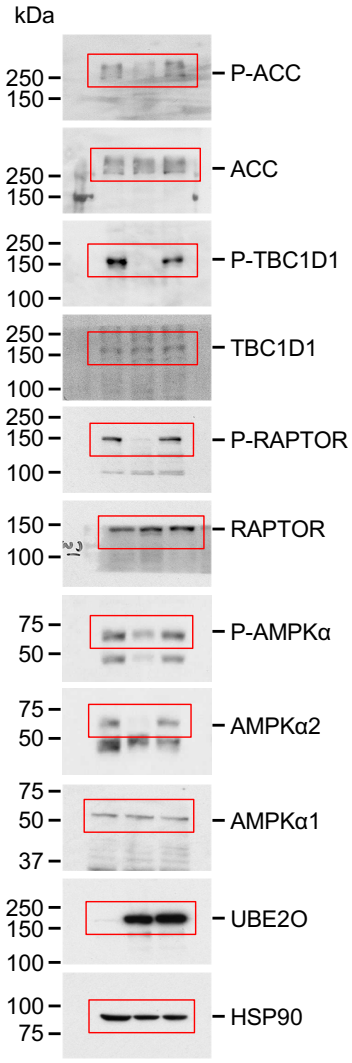


Figure 6I

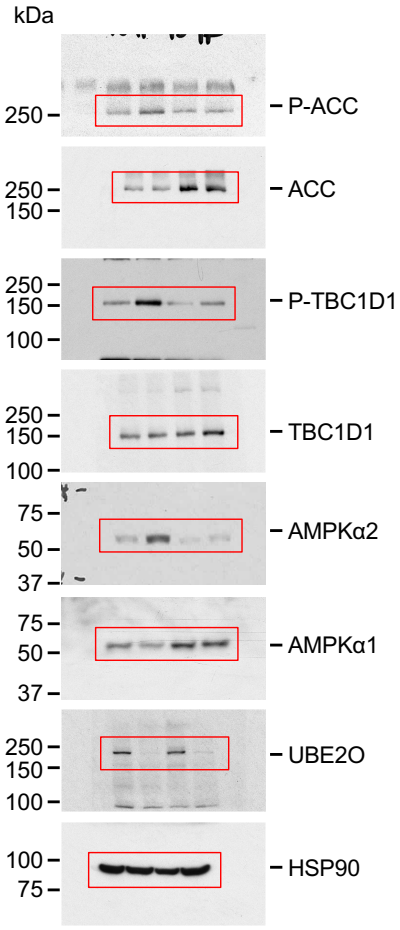
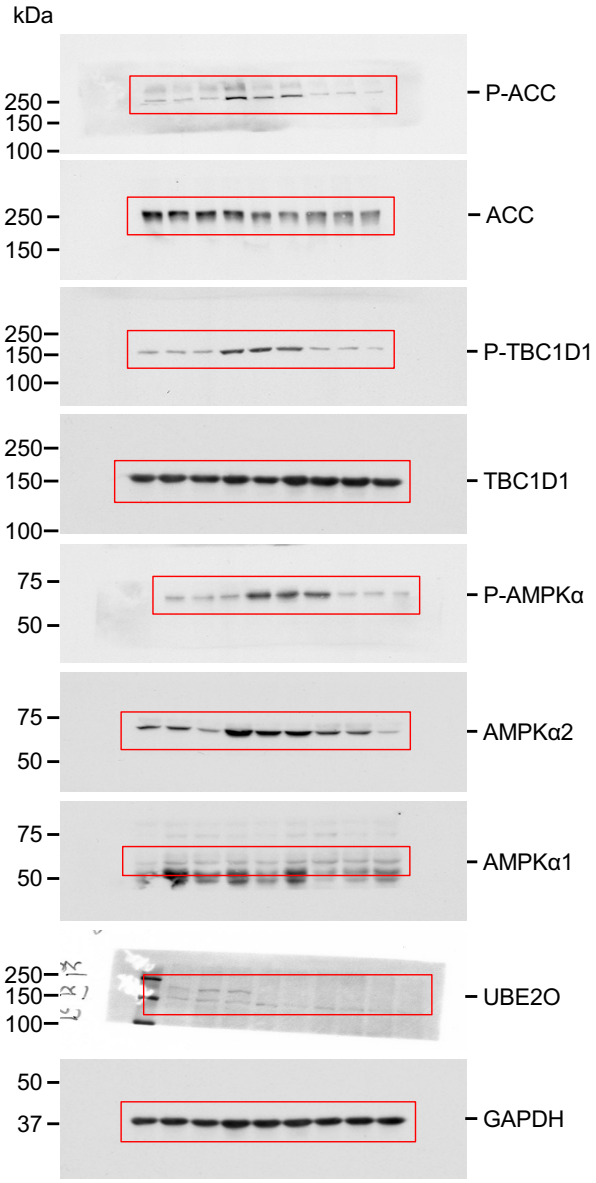
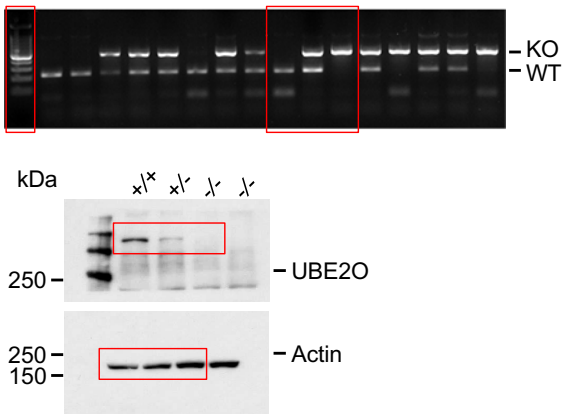


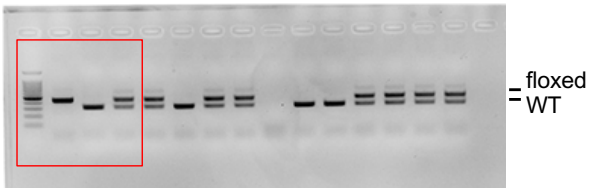
Figure 7I



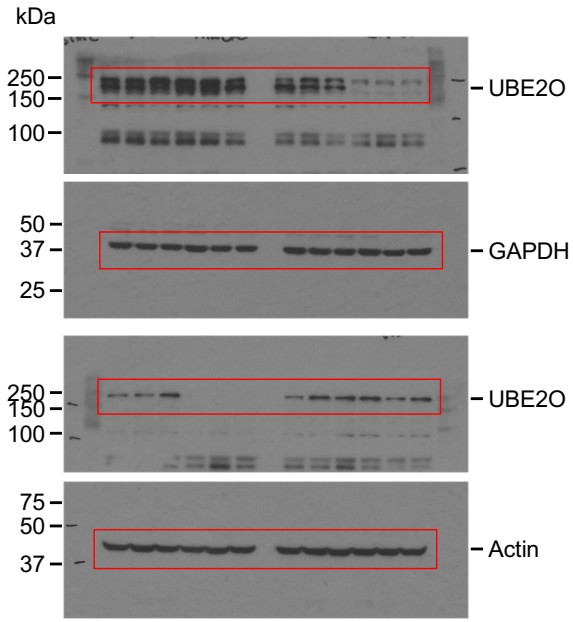
Supplemental Figure 1A



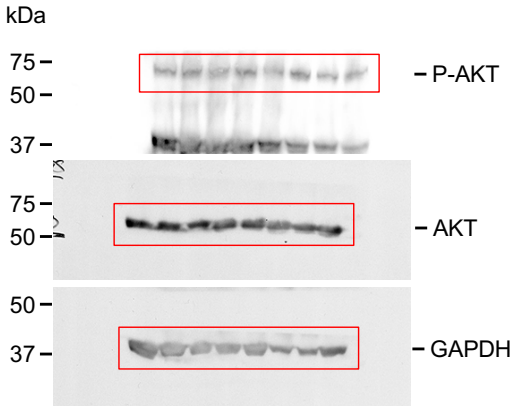
Supplemental Figure 3B



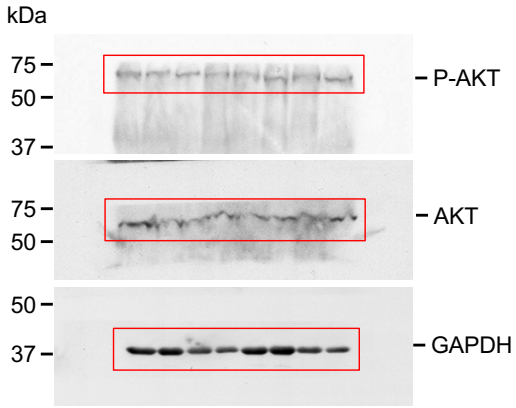
Supplemental Figure 3C



Supplemental Figure 4D



Supplemental Figure 4E



Supplemental Figure 5J