Supplemental Figure 1 The schematic diagram of the genomic region of human BRCA1 and NBR2 genes with different splicing isoforms. Arrows represent the direction of transcription.
Supplemental Figure 2 AMPK inactivation by compound C or AMPKα siRNA treatment. (a) MDA-MB-231 cells were treated with 20 µM Compound C in 25 or 0 mM glucose-containing medium for 24 hours, and then subjected to Western blotting analysis to measure AMPK activation. (b) MDA-MB-231 cells transfected with AMPKα or control (Ctrl) siRNA were cultured in 25 or 0 mM glucose-containing medium for 24 hours, and then subjected to Western blotting analysis to measure AMPK activation. Unprocessed original scans of blots are shown in Supplemental Fig. 8.
Supplemental Figure 3 NBR2 knockdown affects autophagy and cell proliferation in response to energy stress. (a) The effect of NBR2 deficiency on GFP-LC3 puncta formation. 786-O cells infected with either control shRNA or NBR2 shRNA were transfected with GFP-LC3 plasmid, and then cultured in 25 or 0 mM glucose-containing medium for 18 hours. GFP-LC3 punctate foci were then detected using fluorescence microscopy. (Scale bars, 20 µm) (b) The effect of NBR2 deficiency on ULK1 phosphorylation and p62 degradation in response to glucose starvation. MDA-MB-231 cells infected with either control shRNA or NBR2 shRNA were cultured in 25 or 0 mM glucose-containing medium for 12h. Cell lysates were then analyzed by Western blotting. (c, d) Cells infected with either control shRNA or NBR2 shRNA were cultured in 1mM glucose-containing medium for different days as indicated, and then subjected to cell proliferation analysis (Mean ± s.d., n=3 biologically independent extracts, two-tailed paired Student’s t-test). Source data for c, d can be found in Supplementary Table 1. Unprocessed original scans of blots are shown in Supplemental Fig. 8.
Supplemental Figure 4 Mechanistic studies of NBR2 regulation of AMPK.
(a) Protein lysates were prepared from HEK293T cells transfected with empty vector (EV), NBR2 full length (FL), T4, or T5 fragment expression vectors, and analyzed by Western blotting as indicated. (b) Protein lysates prepared from UMRC2 cells stably expressing EV or NBR2 #1 expression vectors were immunoprecipitated by IgG, LKB1 or Folliculin antibodies, and then were analyzed by Western blotting as indicated. Aliquots of the protein lysates (input) were also analyzed directly. (c) 786-O cells infected with either control shRNA or NBR2 shRNA were cultured in medium containing 0 or 25 mM glucose for 12 hours. Protein lysates were prepared and immunoprecipitated by IgG or LKB1 antibodies, and then were analyzed by Western blotting as indicated. Aliquots of the protein lysates (input) were also analyzed directly. (d) Empty vector (EV) or LKB1-infected Hela cells were transfected with EV or NBR2 #1 expression vectors. Protein lysates were prepared and analyzed by Western blotting as indicated. Unprocessed original scans of blots are shown in Supplemental Fig. 8.
Supplemental Figure 5  The working model of the reciprocal regulation between NBR2 and AMPK under energy stress, and its relevance to cancer development. See discussion for detailed description.
Supplemental Figure 6  

NBR2 deficiency affects AMPK activation under long periods of energy stress. (a) MDA-MB-231 cells infected with either control shRNA or NBR2 shRNA were cultured in 0 mM glucose-containing medium for different hours, and protein lysates were prepared and analyzed by Western blotting. (b) MDA-MB-231 cells were cultured in 0 mM glucose-containing medium for different hours, and then subjected to real-time PCR analysis to measure NBR2 expression (Mean ± s.d., n=3 biologically independent extracts, two-tailed paired Student’s t-test). Source data for b can be found in Supplementary Table 1. Unprocessed original scans of blots are shown in Supplemental Fig. 8.
**Supplemental Figure 7** *NBR2* deficiency does not affect *BRCA1* expression. (a) MDA-MB-231 cells infected with either control shRNA or *NBR2* shRNA were cultured in 25 or 0 mM glucose-containing medium for 24 hours, and then subjected to real-time PCR analysis to measure *BRCA1* expression (Mean ± s.d., n=3 biologically independent extracts, two-tailed paired Student’s t-test). (b) Cell lysates were also analyzed by Western blotting as indicated. Source data for a can be found in Supplementary Table 1. Unprocessed original scans of blots are shown in Supplemental Fig. 8.
Fig. 1d

Supplemental Figure 8 Unprocessed scans of full blots.
**Fig. 2b**

**Fig. 2c**

Supplemental Figure 8 continued
Supplemental Figure 8 continued

Fig. 3f

Fig. 4d
Fig. 5

Supplemental Figure 8 continued
Supplemental Figure 8 continued
Supplemental Figure 8 continued
Supplemental Figure 8 continued
Supplemental Figure 8 continued
Supplementary Table 1  Statistics source data.
Raw numbers (cell number) or normalized values of the indicated figure panels are provided.