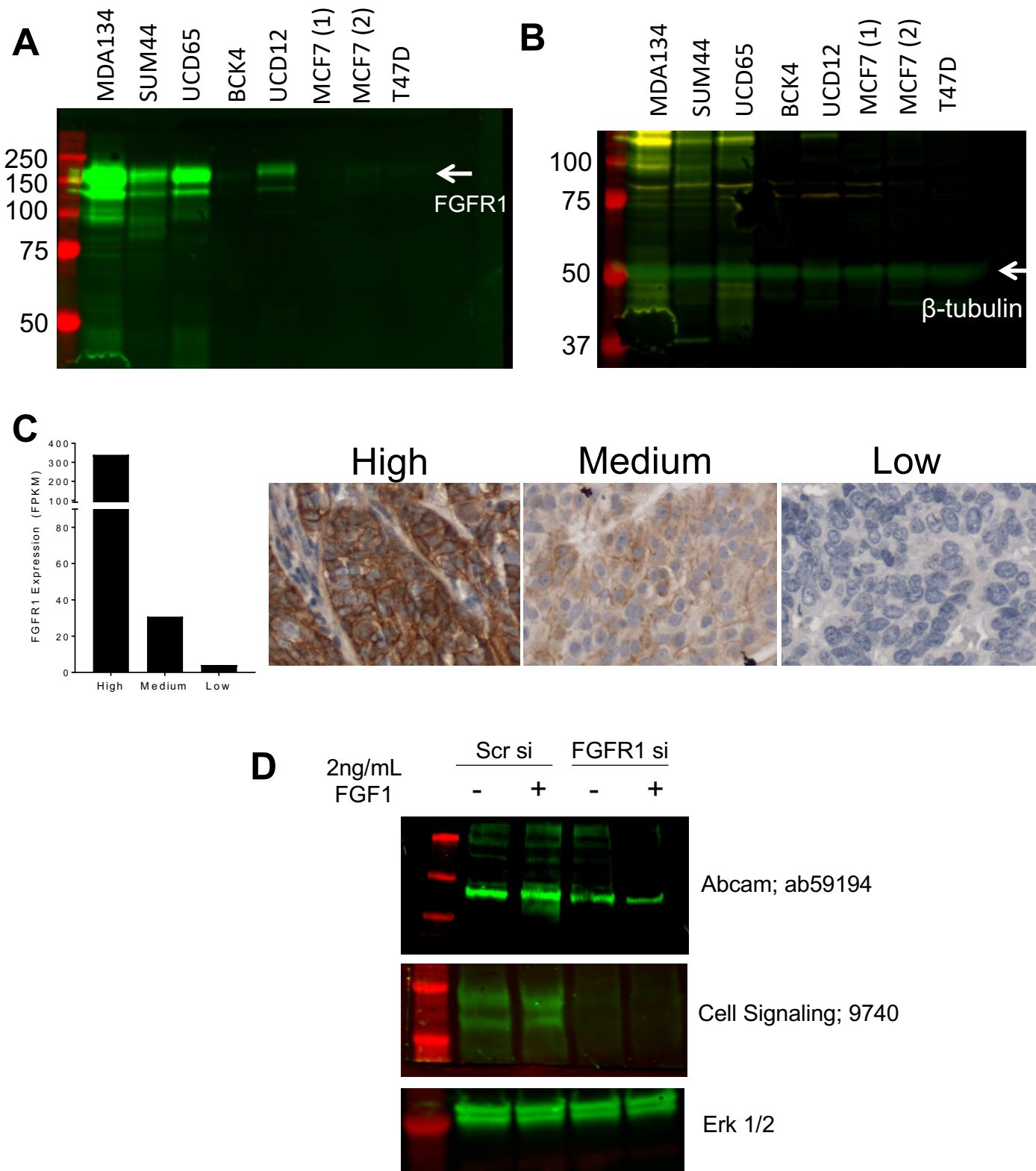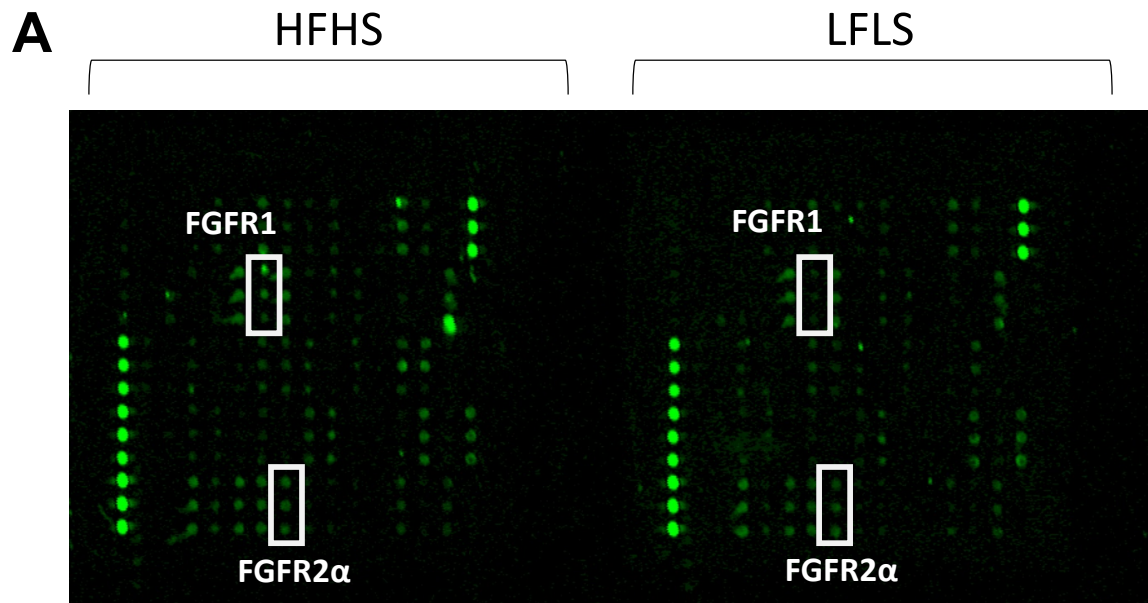**Supplemental Figure 1. NOD-SCID-IL2rγ (NSG) mice are resistant to diet induced obesity.** (A) Body weight of LFLS and HFHS fed NSG mice. Arrow indicates introduction of thermoneutral housing. N=7 per group. Vertical lines indicate times at which body composition was measured. Percent body fat at (i) 86 days old; (ii) 115 days old; and (iii) 189 days old.
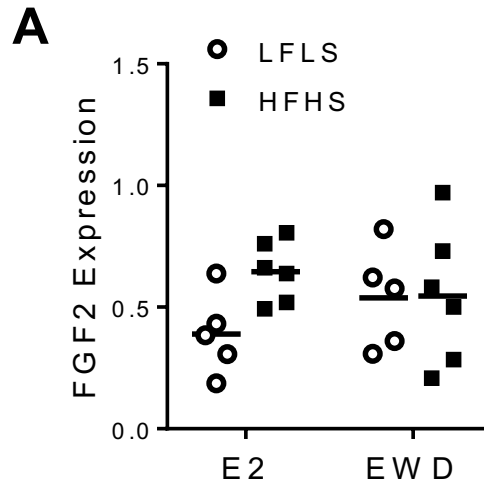
Supplemental Figure 2. Unedited gels showing FGFR1 and β-tubulin. (A) Various cell lines were screened for expression levels of FGFR1 protein. Cell lines that have not been characterized or that were not used in these studies were excluded from the final gel image. (B) β-tubulin expression levels in the same cell lines. (C) Validation of FGFR1 antibody (Cell Signaling; 9740) in a panel of breast cancer PDX tumors. Expression of the FGFR1 gene (left) and immunohistochemical analysis of FGFR1 protein (right 3 panels) in high, medium, and low-expressing tumors. (D) Immunoblot validation of antibody in PT12 cells treated with Scrambled siRNA (Scr si) or FGFR1 siRNA (FGFR1 si) and then treated with Veh or 2 ng/mL human FGF1. Erk ½ was used as a loading control.
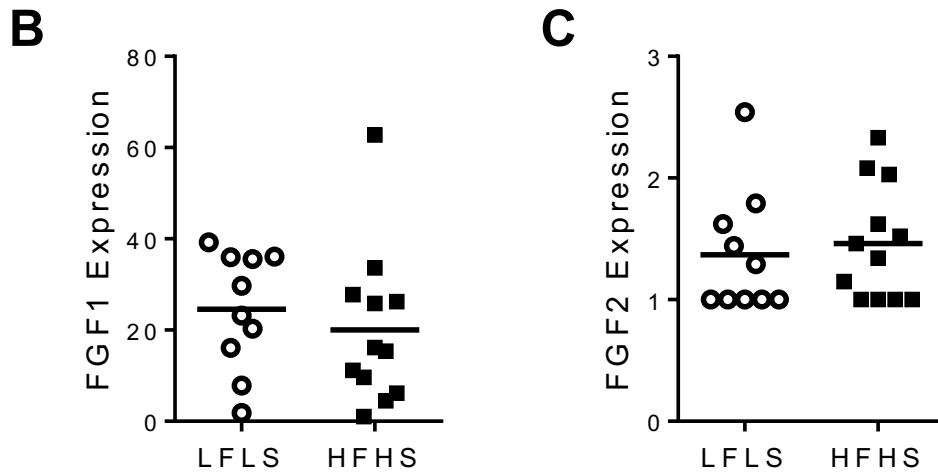
Supplemental Figure 3. Phosphorylated FGFR1 distinguishes tumors from HFHS vs LFLS fed mice. Glass slide phospho-receptor tyrosine kinase array performed on UCD12 tumor lysates LFLS and HFHS EWD mice. Note that pFGFR1 is elevated with HFHS feeding, but pFGFR2α is not.

Mouse Mammary Adipose

Human PDX Tumors

Supplemental Figure 4. FGF ligand expression in mouse and human tissues. (A) FGF2 gene expression in mammary adipose tissue from LFLS and HFHS mice with E2 or after EWD N=5 per group. No significant effects of adiposity or estradiol treatment. (B-C) Expression of FGF1 (b) and FGF2 (c) in lysates from human UCD12 PDX tumors. Expression level of 1 is the lowest limit of detection.

Supplemental Figure 5. Crown-like structures in mammary adipose tissue of Rag1-null females.
Quantification of crown-like structures (CLS) in mammary tissue of LFLS and HFHS mice with or without E2 supplementation. E2 effect p=0.0002;; Adiposity effect p=0.007;; Interaction p=0.007; 2-way ANOVA. Representative image is shown on the right;; scale is 50 μm.

Supplemental Table 1. Summary of patient characteristics

Variables	All (n=154)
Age	
Median (IQR)	48.5 (42, 54)
BMI	
Median (IQR)	25.7 (22.5, 29.7)
Diabetes mellitus, n (%)	
No	148 (96.1%)
Yes	6 (3.9%)
Dyslipidemia, n (%)	
No	136 (88.3%)
Yes	18 (11.7%)
Hypertension, n (%)	
No	130 (84.4%)
Yes	24 (15.6%)
Race, n (%)	
Asian	7 (4.5%)
Black	12 (7.8%)
Other	4 (2.6%)
White	117 (76.0%)
Not reported	14 (9.1%)
Tumor subtype, n (%)	
HR+	85 (55.2%)
HER2+	19 (12.3%)
Triple-negative	18 (11.7%)
Noninvasive or benign histology	32 (20.8%)