Protein modification	Ratio of means (Leptin/ Mock)
STAT3-phospho (Tyr705)	10.5
mTOR-phospho (Ser2448)	3.2
AKT-phospho (Ser473)	2.2
Caspase-3-cleaved (Asp175)	-3.4

Table S1 List of proteins with expression levels significantly changed in MCF7 cells under leptin treatment using antibody array (>2 fold change, n=3, P<0.05).

Accession	Description	Coverage	# Unique Peptides
Q96KQ7	Histone-lysine N-methyltransferase EHMT2 (G9A)	53.95	28
P63104	14-3-3 protein zeta/delta (14-3-3 ζ/δ)	42.13	17
P52333	Tyrosine-protein kinase (JAK3)	36.93	15
P04412	Epidermal growth factor receptor (EGFR)	33.65	13
Q70UQ0	Inhibitor of nuclear factor kappa-B kinase-interacting protein (IKIP)	25.25	7
F5GXM1	Histone deacetylase 1 (HDAC1)	20.24	3

Table S2 G9a is a new STAT3-associated protein under leptin treatment. LC-MS/MS mass spectrometry analysis identifies a list of proteins that physically interact with STAT3 under leptin treatment (but not under the mock treatment) in MCF7 cells.

Term	Genes	FDR
GO:0045597~positive regulation of cell differentiation	XRCC2, MSR1, THRB, CSF1, PAX6, KITLG, GATA3, FOXA2, NUMB, HOXA5	0.172963
GO:0010719~negative regulation of EMT	FOXA2, NKX2-1, TGFBR3, EFNA1, DAB2IP, HOXA5, HPN, DACT3	0.236285
GO:0051130~positive regulation of cellular junction organization	CAV1, ARF6, PDPK1, NUMB, NPM1, TNKS2, UBE2N, NCK2	0.470977
GO:0010720~regulation of cell development	GATA3, ARHGEF1, LYN, MAP1B, HOXA5, NUMB	0.370416
GO:0022604~regulation of cell morphogenesis	GAS2, TTC3, NRCAM, ANXA7, FYN, NUMB, CDH1	0.482653

Table S3 STAT3-G9a regulates a cohort of genes involved in cell differentiation process. Gene ontology enrichment analysis of gene promoters co-occupied by STAT3 and G9a under leptin treatment in MCF7 cells.

Group	Scale Body Weight	DEXA Body Weight	% Bone Mass	% Fat Mass	% Lean Mass
Western Obese	181.9±4.3	194.9±5.3*	2.7±0.2	8.3±0.7**	91.1±0.7
Western Lean	177.3±6.9	180.5±6.1	2.8±0.2	4.2±0.1	95.8±0.1
Rat Chow	169.2±5.3	178.9±5.8	2.6±0.2	4.3±0.3	95.6±0.4

Table S4 Body composition analysis from DEXA scans. Animals in the Western-obese group showed a significant increase in fat mass compared to animals in the Western-lean group. Values represent mean \pm SEM. n= 9 animals per group. Asterisk indicates P<0.05, double asterisk indicates P<0.0001.

Group	Number of Rats	Total Number of Lesions and Major Lesion Type per Group	Number of Carcinomas per Group
Western Obese	n=9	39* (adenocarcinomas)	27*
Western Lean	n=9	27 (adenomas)	13
Rat Chow	n=9	21 (pre-neoplastic lesions)	12

Table S5 Categorization of tumor number and tumor type in each group of animals. Tumors were classified as malignant carcinomas, benign adenomas, or pre-neoplastic lesions based on the morphology of the epithelial cells. Asterisk indicates P<0.05.

Diet treatment phenotype	Obese	Lean	RD
	7	3	1
LEP+	(78%)	(33%)	(11%)
LEP-	2	6	8
	(22%)	(67%)	(89%)
Total	9	9	9
			P=0.02
DOTAT24	8	1	2
pSTAT3+	(89%)	(11%)	(22%)
	1	8	7
pSTAT3-	(11%)	(89%)	(78%)
Total	9	9	9
			P=0.002
mi D 200at	1	7	P=0.002 8
miR200c+	1 (11%)		
			8
miR200c+ miR200c-	(11%)	(78%) 2	8 (89%)
	(11%) 8	(78%) 2	8 (89%) 1
miR200c-	(11%) 8 (89%)	(78%) 2 (22%)	8 (89%) 1 (11%)
miR200c- Total	(11%) 8 (89%)	(78%) 2 (22%)	8 (89%) 1 (11%) 9
miR200c-	(11%) 8 (89%) 9	(78%) 2 (22%) 9	8 (89%) 1 (11%) 9 P=0.002
miR200c- Total OBR+	(11%) 8 (89%) 9 8	(78%) 2 (22%) 9 2	8 (89%) 1 (11%) 9 P=0.002 1
miR200c- Total	(11%) 8 (89%) 9 8 (89%)	(78%) 2 (22%) 9 2 (22%) 7	8 (89%) 1 (11%) 9 P=0.002 1 (11%)
miR200c- Total OBR+	(11%) 8 (89%) 9 8 (89%) 1	(78%) 2 (22%) 9 2 (22%) 7	8 (89%) 1 (11%) 9 P=0.002 1 (11%) 8

Table S6 Elevated LEP, p-STAT3, and OBR levels are correlated with reduced miR-200c expression in diet-induced obesity and breast cancer rats. Fisher's exact analysis of expression levels of LEP, p-STAT3, miR-200c, and OBR in the mammary tumor sections from the Western diet-treated lean and obese rats and also from the control rats fed with regular diet. (-): negative/low staining, (+): positive/high staining.