Supplemental Table S1. Characteristics of the Yale NSCLC cohort: tumor (T) samples (n=72)

Characteristics	ALL-NSCLC
Median age – yr (IQR)	69 (18)
Gender - no.(%)	
Female	42 (58.3%)
Male	30 (41.6%)
Smoking History – no.(%)	
Non-smokers	9 (12.5%)
Former smokers	50 (69.4%)
Current smokers	13 (18.1%)
Type of Procedure – no.(%)	
Surgery	40 (55.5%)
Bronchoscopy	32 (44.4%)
Time of Specimen Acquisition – no.(%)	
New diagnosis	58 (80.5%)
Established diagnosis	12 (16.6%)
Tumor recurrence	1 (1.3%)
Unable to determine	1 (1.3%)
Clinical stage – no.(%)	
Stage I	23 (31.9%)
Stage II	7 (9.7%)
Stage III	8 (11.1%)
Stage IV	26 (36.1%)
not known [A]	8 (11.1%)
Tumor Type – no.(%)	
Adenocarcinoma	39 (54.1%)
Squamous cell carcinoma	22 (30.5%)
Other [B]	11 (15.2%)
Tumor Size – no.(%) [C]	
< 3 cm	25 (34.7%)
> 3 cm	33 (45.8%)
Not available	14 (19.4%)

[A] Unable to determine the accurate clinical stage at the time of biopsy. [B] 'Other' includes poorly differentiated carcinomas, large cell carcinoma, basaloid carcinoma, and sarcomatoid carcinoma. [C] Tumor size was determined by measuring the largest dimension in surgically resected specimens or in CT Scan images (bronchoscopic biopsy patients).

Supplemental Table S2: Characteristics of the Yale NSCLC cohort: Adjacent tissue (AT) samples (n=58)

Characteristics	ALL-NSCLC
Median age – yr (IQR)	69 (19)
Gender - no.(%) Female Male	 34 (58.6%) 24 (41.3%)
Smoking History - n(%) Non-smokers Former smokers Current smokers	 10 (17.2%) 38 (52.8%) 10 (17.2)
Type of Procedure - n(%) Surgery Bronchoscopy	 40 (68.9%) 32 (55.1%)
Time of Specimen Acquisition – n(%) New diagnosis Established diagnosis Tumor recurrence Unable to determine	 49 (84.4%) 7 (12.0%) 2 (3.4%) 0 (0 %)
Clinical stage - n(%) Stage I Stage II Stage III Stage IV not known [A]	 27 (46.5%) 6 (10.3%) 5 (8.6%) 12 (20.6%) 8 (13.7%)
Tumor Type - n(%) Adenocarcinoma Squamous cell carcinoma Other [B]	 34 (58.6%) 8 (13.7%) 16 (27.5%)
Tumor Size - n(%) [C] < 3 cm > 3 cm Not available	 25 (43.1%) 26 (44.8%) 7 (12.0%)

[A] Unable to determine the accurate clinical stage at the time of biopsy. [B] 'Other' includes poorly differentiated carcinomas, large cell carcinoma, basaloid carcinoma, and sarcomatoid carcinoma. [C] Tumor size was determined by measuring the largest dimension in surgically resected specimens or in CT Scan images (bronchoscopic biopsy patients).

Supplemental Table S3: Characteristics of bronchoscopic samples from smokers with NSCLC n=12

Characteristics	**n=12**
Median age – yr (IQR)	67 (20)
Gender - no.(%) Female Male	 8 (66.7%) 4 (33.3%)
Time of Specimen Acquisition – n(%) New diagnosis Established diagnosis	 9 (75%) 3 (25%)
Clinical stage - n(%) Stage I Stage II Stage III Stage IV not known [A]	 1 (8.3%) 0 (0%) 0 (0%) 8 (66.7%) 3 (25.0%)
Tumor Type - n(%) Adenocarcinoma Squamous cell carcinoma	 6 (50%) 6 (50%)
Tumor Size - n(%)[B] < 3 cm > 3 cm Not available	 2 (16.7%) 6 (50.0%) 4 (33.3%)

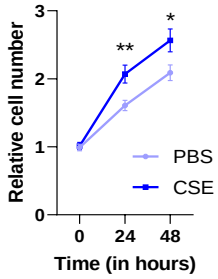
[A] Unable to determine the accurate clinical stage at the time of biopsy.
[B] Tumor size was determined by measuring the largest dimension in surgically resected specimens or in CT Scan images (bronchoscopic biopsy patients).

Supplemental Table S4: MiR-1 targets in NSCLC smokers

ARHGAP22	Rho GTPase Activating Protein 22
MOCOS	Molybdenum Cofactor Sulfurase
SH3PXD2B	SH3 And PX Domains 2B
MTL5	Testis Expressed Metallothionein Like Protein
NFRKB	Nuclear Factor Related To KappaB Binding Protein
FGD6	FYVE, RhoGEF And PH Domain Containing 6
VPS33A	VPS33A Core Subunit Of CORVET And HOPS Complexes
PUS1	Pseudouridine Synthase 1
GOLGA3	Golgin A3
SEMA4B*	Semaphorin 4B
TRAP1*	TNF Receptor Associated Protein 1
TFAP4*	Transcription Factor AP-4
XYLT2	Xylosyltransferase 2
NOTCH3*	Notch Receptor 3
NPAS2	Neuronal PAS Domain Protein 2
COL5A2*	Collagen Type V Alpha 2 Chain
CEP250*	Centrosomal Protein 250
BCAS4	Breast Carcinoma Amplified Sequence 4
CPT1B*	Carnitine Palmitoyltransferase 1B
SEC61A1*	SEC61 Translocon Subunit Alpha 1
WHSC1*	Nuclear Receptor Binding SET Domain Protein 2
HS3ST1*	Heparan Sulfate-Glucosamine 3-Sulfotransferase 1
ITGA2*	Integrin Subunit Alpha 2
SDCCAG3	Endosome Associated Trafficking Regulator 1

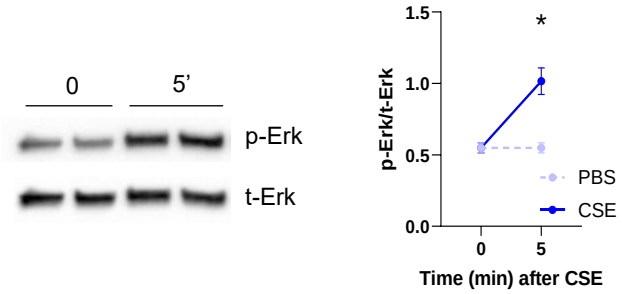
* Genes previously shown to be related to tumor progression in NSCLC, (1-12).

Supplemental Figure S1



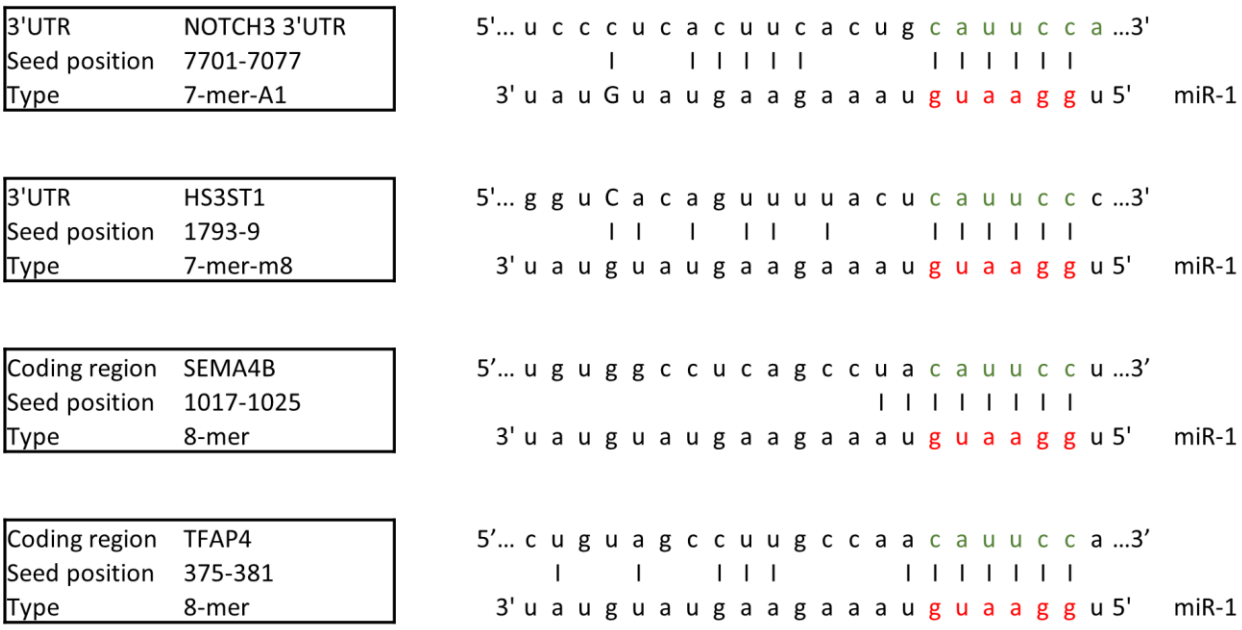
HUVECs were exposed to 10% CSE (or PBS, control) at the indicated times (in minutes) and cell numbers determined by counting using a hemocytometer. Relative cell numbers were presented after normalizing to values at time '0'(n>12 from 3 experiments, *p= 0.021, **p=0.0065)

Supplemental Figure S2:



HUVECs were starved and treated with CSE for indicated time and cells were harvested for Western analysis. Graphs represent ratio of band intensities (phospho to total ERK) after normalizing with time 0 value (n=3, *p= 0.0257).

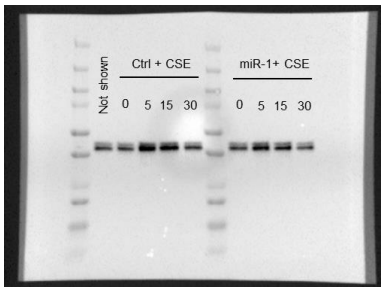
Supplemental Figure S3:



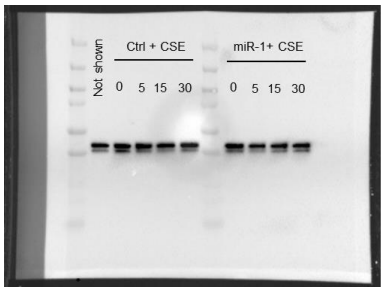
MiR-1 targets (A) NOTCH3 (B) HS3ST1 (C) SEMA4B (D) TFAP4 in this study. Predicted miR-1 binding sites are depicted in green in target sequence and corresponding nucleotides in miR-1 mature sequence are in red. Vertical lines shows complementary bases.

Supplementary Figure S4: Uncropped Gel #2 for Figure 6B (used in the main figure and analysis)

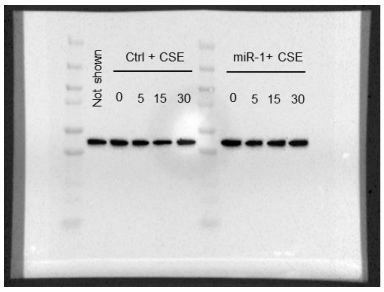
p-ERK

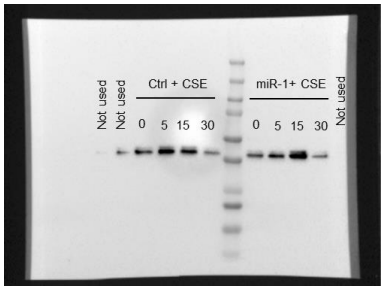


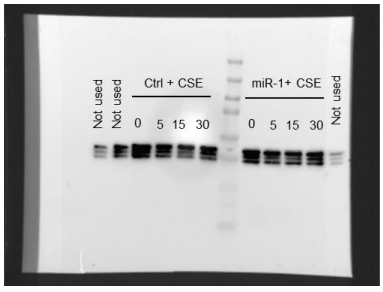
t-ERK

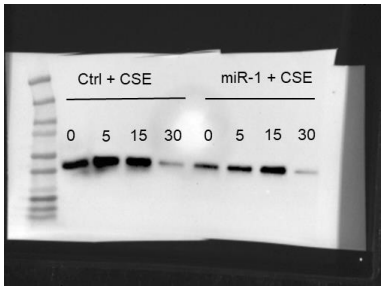


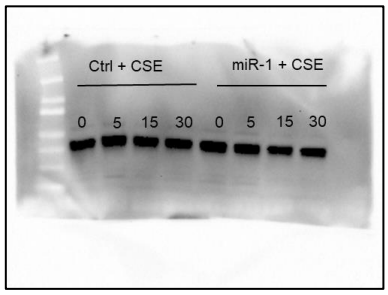
β-actin





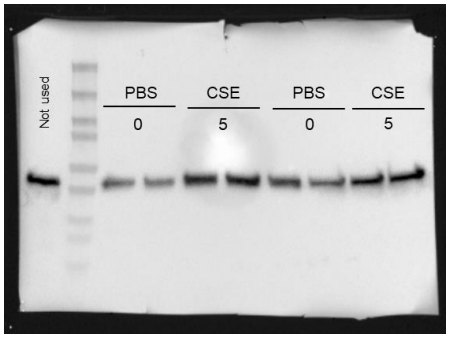




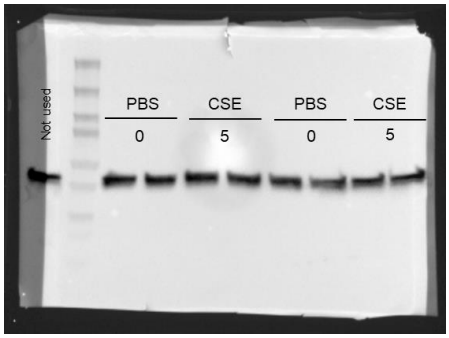


Supplemental Figure S5: **Uncropped western blots for Figure S2 (used in the supplemental figure and analysis)**

p-ERK



t-ERK



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