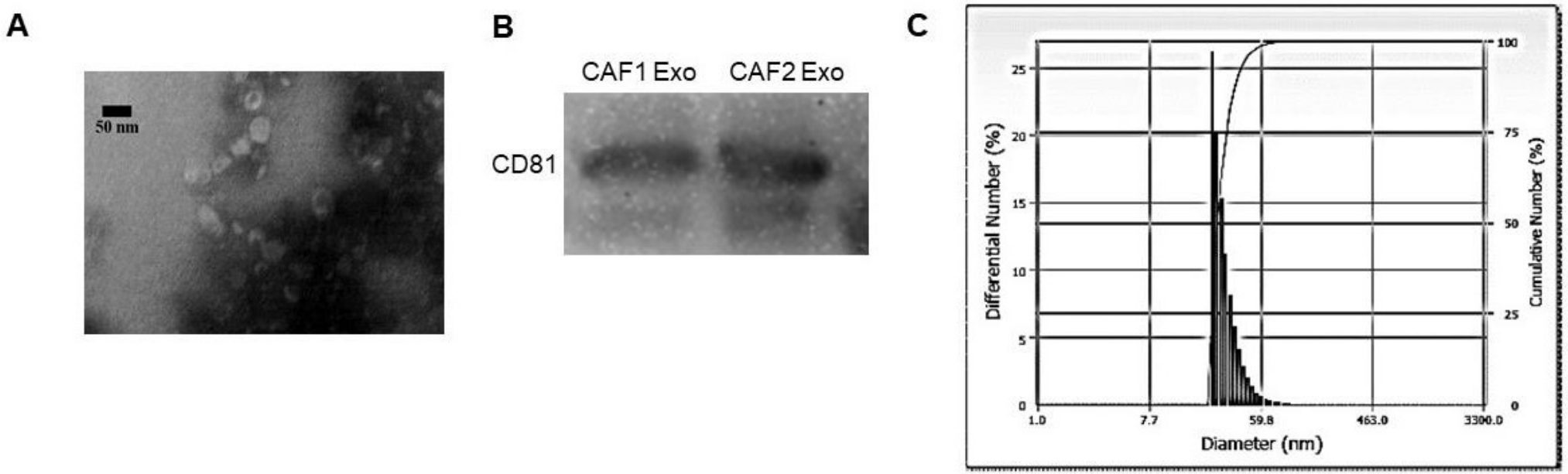
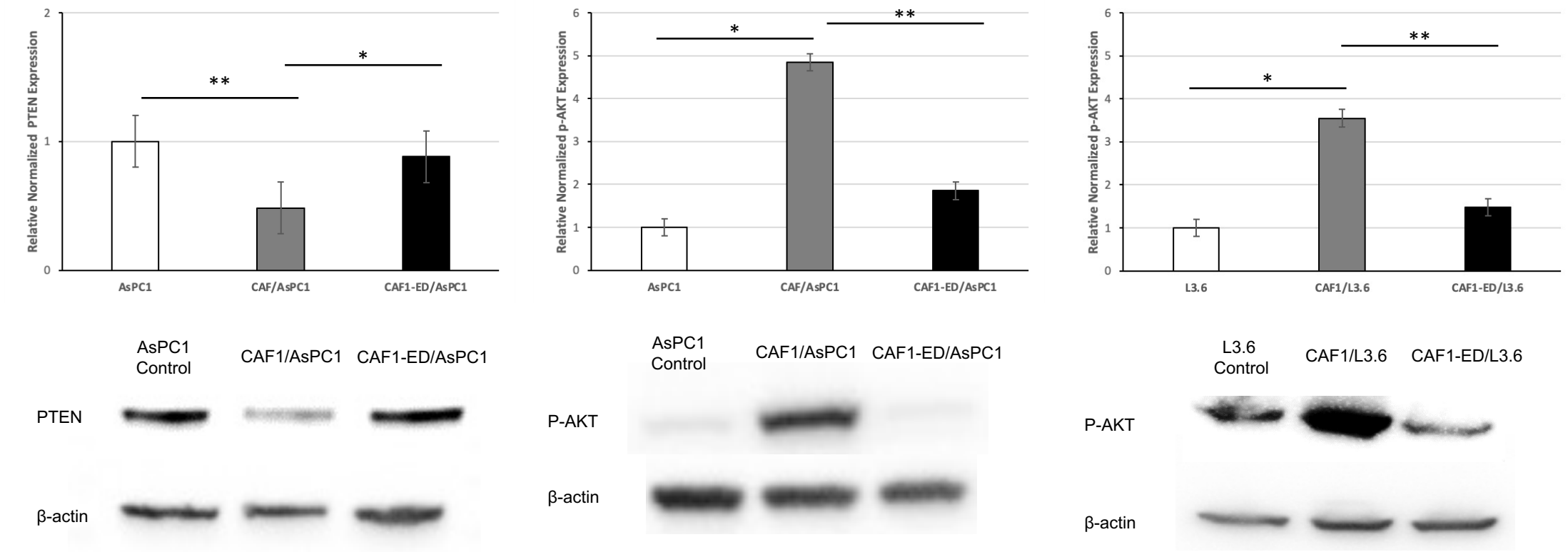


Supplemental Figure S1: **Verification of exosome samples.** CAF-secreted exosomes were analyzed for the correct shape and size via transmission electron microscopy (**a**) as well as for exosome protein markers such as CD81 (**b**). Average diameter of exosomes was analyzed via dynamic light scattering particle size analysis which showed a peak diameter size at 37nm (**c**).

Pathways Manipulated by all 5 microRNAs (miR-21- 5p, miR-92a-3p, miR-221- 3p, miR-181a-5p, and miR-222-3p)	Putative Gene Targets
Wnt Signaling Pathway	GSK3B, PPP2R5E, LRP6, TCF4, WNT5A, FZD6, SKP1, FRAT2, CAMK2A, NLK, SENP2, FZD10, AXIN2, CXXC4, WIF1, NFATC3, DAAM1, TBL1XR1
MAPK Signaling Pathway	FOS, NTF3, RASA2, CRK, CACNB4, RAP1A, FASLG, TAOK1, CACNA1I, NLK, DUSP10, RASGRP1, PPM1A, DUSP8, CDC42, FGF18, RPS6KA3, AKT3, MAP2K1, STMN1, MAP3K2, MEF2C, DUSP5, MAP2K4, RAP1B, TGFBR2
PI3K-AKT Signaling	PHLPP2, PRLR, GSK3B, TSC1, PPP2R5E, ITGA8, PIK3CB, CREB5, YWHAG, COL27A1, ANGPT2, ITGA5, PIK3AP1, CDKN1B, FASLG, ITGAV, DDIT4, PIK3R3, COL5A1, KIT, PIK3R1, JAK3, FGF18, COL1A2, AKT3, PIK3CA, MAP2K1, ITGA6, PTEN, SGK3, KDR, SPP1, BCL2L11, RPS6KB1, COL4A1, IL6R
HIF-1 Signaling	STAT3, PIK3CB, ARNT, ANGPT2, CDKN1B, CAMK2A, PIK3R3, PIK3R1, AKT3, PIK3CA, MAP2K1, PDHB, PFKFB4, RPS6KB1, EGLN1, IL6R
Focal Adhesion	GSK3B, CRK, ITGA8, PIK3CB, PIP5K1C, RAP1A, COL27A1, ITGA5, VCL, ITGAV, PPP1R12A, PIK3R3, COL5A1, PIK3R1 CDC42, COL1A2, AKT3, PIK3CA, MAP2K1, ITGA6, PTEN, KDR, RAP1B, SPP1, COL4A1
T cell Receptor Signaling	FOS, GSK3B, PIK3CB, PIK3R3, RASGRP1, PIK3R1, CDC42, AKT3, CD4, PIK3CA, MALT1, MAP2K1, CARD11, NFATC3
VEGF Signaling	PIK3CB, PIK3R3, PTGS2, PIK3R1, CDC42, AKT3, PIK3CA, MAP2K1, NFATC3, KDR
Endocytosis	CHMP7, DNAJC6, GRK5, GRK7, PIP5K1C, PDCD6IP, EEA1, ITCH, VPS36, ASAP1, ZFYVE16, RAB11FIP2, GIT2, SMURF1, RAB11A, KIT, CDC42, SMAD7, RAB11FIP1, KDR, TGFBR2, ADRB1
Jak-Stat Pathway	PRLR, STAT3, PIK3CB, CSF2RB, CNTFR, SPRED2, PIK3R3, LIFR, PIK3R1, JAK3, SPRY1, PIAS4, AKT3, PIK3CA, SPRY2, IL6R
Endoplasmic Reticulum Protein Processing	UBE2E3, SAR1B, YOD1, HSPA5, UBE2J1, SKP1, EDEM1, EDEM3, MAN1A2, SVIP, SEC62, SEC24A, LMAN1, UBE2D3, SEC24B, UBE2G1, DNAJB12, DERL1, ATXN3, RRBP1, PARK2
Ubiquitin Mediated Proteolysis	UBE2E3, WWP2, FBXW7, ITCH, UBE2J1, SKP1, CUL5, SKP2, BIRC6, SMURF1, PIAS4, UBE2D3, CDC27, UBE2G1, UBE2W, PARK2
B Cell Receptor Signaling	FOS, GSK3B, PIK3CB, PIK3AP1, PIK3R3, PIK3R1, AKT3, PIK3CA, MALT1, MAP2K1, CARD11, NFATC3

Supplemental Table S1

Cellular pathways and genetic targets of identified microRNAs.



Supplemental Figure S2: Western blot analysis of PTEN/p-AKT expression in cells where exosomes are retained or depleted from CAF-derived media. (Top row) Quantification of relative PTEN protein levels or phosphorylated AKT protein levels (p-AKT) within cell lysates of epithelial cells cultured in normal media (control), CAF-conditioned media, or exosome-depleted CAF-conditioned media (CAF1-ED). (Bottom Row) Representative images of western blots used for protein quantification. Protein levels were normalized and quantified using ImageJ software. $^{**}p<0.01$. $^{*}p<0.05$.