

Supplementary Table S1. Supporting information of each antibody.

Antibodies (abbreviation)	Source	Manufacturer	City, etc	Catalog number
Insulin receptor (INSR)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0681R-TR
BAG family molecular chaperone regulator 1 (BAG1)	Rabbit	Novus Biologicals	Littleton, CO, USA	NB100-56081SS
Integrin beta-3 (ITGB3)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0342R-TR
Transforming growth factor beta-1 proprotein (TGFB1)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-4908R-TR
Insulin-like growth factor-binding protein 3 (IGFBP3)	Rabbit	GeneTex	Irvine, CA, USA	GTX100454
Integrin alpha-1 (ITGA1)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-2095R-TR
Laminin subunit alpha-5 (LAMA5)	Rabbit	EpiGenetek	Farmingdale, NY, USA	#A59602
Nectin-2 (NECTIN2)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-2679R-TR
Extracellular matrix protein 1 (ECM1)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0776R-TR
Hepatocyte nuclear factor 4-alpha (HNF4A)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-3828R-TR
Nuclear factor NF-kappa-B1 p105/p50 (NFκB1)	Rabbit	Cell Signaling technology	Danvers, MA, USA	#12540
Nuclear factor NF-kappa-B2 p100/p52 (NFκB2)	Rabbit	Cell Signaling technology	Danvers, MA, USA	#3017
Clusterin α (CLUα)	Rabbit	GeneTex	Irvine, CA, USA	GTX134435
Insulin-like growth factor-binding protein 2 (IGFBP2)	Rabbit	GeneTex	Irvine, CA, USA	GTX128977
Integrin alpha-3 (ITGA3)	Rabbit	Affinity Biosciences	Cincinnati, OH, USA	AF5182
Collagen alpha-1(XVII) chain (COL17A1)	Rabbit	AVIVA System Biology	San Diego, CA, USA	OACD02624
CD44 antigen (CD44)	Mouse	Thermo Fisher Scientific	Carlsbad, CA, USA	#MS-668-P0
Cdc42 effector protein 5 (CDC42EP5)	Rabbit	Novus Biologicals	Littleton, CO, USA	NBP1-91773
Metalloproteinase inhibitor 1 (TIMP1)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0415R-TR
Neutrophil gelatinase-associated lipocalin (LCN2)	Rabbit	Proteintech	Rosemont, IL, USA	26991-1-AP
Disintegrin and metalloproteinase domain-containing protein 17 (ADAM17)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-4236R-TR
Midkine (MDK)	Rabbit	GeneTex	Irvine, CA, USA	GTX116089
Epithelial cell adhesion molecule (EpCAM)	Mouse	EXBIO Antibodies	Praha, Czech Republic	11-581-C025

Dystroglycan 1 (DAG1)	Rabbit	GeneTex	Irvine, CA, USA	GTX124225
Matrix metalloproteinase-9 (MMP9)	Mouse	Thermo Fisher Scientific	Carlsbad, CA, USA	#MS-817-P0
Mucin-5AC (MUC5AC)	Mouse	Novus Biologicals	Littleton, CO, USA	NBP2-15196
Heme oxygenase 1 (HO1)	Rabbit	StressMarq Biosciences	Victoria, BC, Canada	SPC-112 C/D
FAS-associated factor 1 (FAF1)	Rabbit	Novus Biologicals	Littleton, CO, USA	NBP1-76745
Desmin (DES)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-1026R-TR
Tescalcin (TESC)	Rabbit	Novus Biologicals	Littleton, CO, USA	NBP2-94798
Ras association (RalGDS/AF-6) domain family (N-terminal) member 9 (RASSF9)	Rabbit	ATLAS Antibodies	Stockholm, Sweden	HPA039428
PDZ and LIM domain 3 (PDLIM3)	Rabbit	GeneTex	Irvine, CA, USA	GTX119708
integrin alpha 7 (ITGA7)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-1816R-TR
insulin-like growth factor 2 (IGF2)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0015R-TR
Integrin alpha-5 (Integrin α 5)	Rabbit	GeneTex	Irvine, CA, USA	GTX130705
Integrin beta-5 (Integrin β 1)	Rabbit	GeneTex	Irvine, CA, USA	GTX128839
Phosphorylated focal adhesion kinase(Tyr ³⁹⁷) {pFAK(Tyr ³⁹⁷)}	Rabbit	GeneTex	Irvine, CA, USA	GTX24803
Phosphorylated Paxillin(Tyr ³¹) {pPaxillin(Tyr ³¹)}	Rabbit	Novex	San Diego, CA, USA	44-720G
Phosphorylated protein kinase B(Ser ⁴⁷³) {pAKT(Ser ⁴⁷³)}	Rabbit	Cell Signaling technology	Danvers, MA, USA	#4060
Phosphorylated protein kinase B(Thr ³⁰⁸) {pAKT(Thr ³⁰⁸)}	Rabbit	Cell Signaling technology	Danvers, MA, USA	#2965
Signal transducer and activator of transcription 3(Ser ⁷²⁷) {pSTAT3(Ser ⁷²⁷)}	Rabbit	Cell Signaling technology	Danvers, MA, USA	#9134
Transforming growth factor β 1 (TGF- β 1)	Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-0086R
Phosphorylated-Smad2(Ser ^{465/467}) {pSmad2(Ser ^{465/467})}	Rabbit	GeneTex	Irvine, CA, USA	GTX133614
Phosphorylated-MAPK/ERK kinase 1/2(Ser ^{217/221}) {pMEK1/2(Ser ^{217/221})}	Rabbit	Cell Signaling technology	Danvers, MA, USA	#9154
Phosphorylated-Extracellular-regulated kinase 1/2(Thr ²⁰² /Tyr ²⁰⁴) {pERK1/2(Thr ²⁰² /Tyr ²⁰⁴)}	Rabbit	Cell Signaling technology	Danvers, MA, USA	#4370

Phosphorylated-p38(Thr ¹⁸⁰ /Tyr ¹⁸²)	{p-	Rabbit	GeneTex	Irvine, CA, USA	GTX133460
Phosphorylated-JNK(Thr ¹⁸³ /Tyr ¹⁸⁵)	{p-	Rabbit	GeneTex	Irvine, CA, USA	GTX635799
β-Catenin		Rabbit	Cell Signaling technology	Danvers, MA, USA	#9582
c-MYC		Rabbit	Cell Signaling technology	Danvers, MA, USA	#9402
Cyclin D1		Rabbit	Cell Signaling technology	Danvers, MA, USA	#2978
Cyclin B1		Rabbit	GeneTex	Irvine, CA, USA	GTX100911
P21		Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-10129R-TR
Matrix metalloproteinase-2 (MMP-2)		Rabbit	BIOSS antibodies	Wobum, MA, USA	bs-4605R-TR
α-Smooth muscle actin (αSMA)		Rabbit	Cell Signaling technology	Danvers, MA, USA	#34105
E-Cadherin		Rabbit	GeneTex	Irvine, CA, USA	GTX100443
N-Cadherin		Rabbit	GeneTex	Irvine, CA, USA	GTX127345
Vimentin		Rabbit	GeneTex	Irvine, CA, USA	GTX132610
TP53		Mouse	Thermo Fisher Scientific	Carlsbad, CA, USA	#MS-105-P0
Caspase-3		Rabbit	GeneTex	Irvine, CA, USA	GTX110543
β-Actin		Rabbit	GeneTex	Irvine, CA, USA	GTX109639

Supplementary Table S2. Profile of four amino acid substitution polymorphisms in a pancreatic adenocarcinoma of a patient.¹

Gene symbol	Locus ²	Variant class	Gene Class	Type	Nucleotide Change	Allele frequency (%)	Amino acid Change
<i>TP53</i>	17: 7577568	Hotspot	Loss of function	Snp	c.713G>A	99.5	p.Cys238Tyr
<i>KRAS</i>	12: 25398284	Hotspot	Gain of function	Snp	c.35G>A	49.1	p.Gly12Asp
<i>ARID1A</i>	1: 27105833	Truncating	Loss of function	Del	c.5445delG	17.0	p.Ile1816SerfsTer67
<i>NOTCH2NLC</i>	1: 120612002	Truncating	Loss of function	Del	c.-39436CCG>G	50.2	p. ³

¹ Among all 161 most relevant cancer genes, 2 single nucleotide polymorphisms (Snp) and 2 deletions (Del) were found by using OncoPrint Comprehensive Assay v3 with workflows on Ion Chef System plus Ion Torrent Genexus system. ² Chromosome: its position. ³Not identified.

Supplementary Table S3. Incidence (%) of different differentiated adenocarcinoma (ADC) in patient-derived pancreatic cancer tissue-transplanted xenograft (PC-PDX) mice administered fucoxanthin (Fx).

Group no.	Treatment (No. of mice)	Well-moderately differentiated ADC ^a	Moderately differentiated ADC ^b	Moderately-poorly differentiated ADC ^c	Total ADC
1	Fx (9)	55.6%*	44.4%	0%**	100%
3	Control (9)	0%	33.3%	66.7%	100%

^a It is comprised of well > moderately (4 mice) and well < moderately (1 mouse) differentiated ADCs. These lesions were only detected in group 1 ^b It is moderately differentiated ADC alone. ^c It is comprised of poorly (2 mice) and poorly > moderately (4 mice) differentiated ADCs. These lesions were only detected in group 3. Significant difference for Fisher's exact probability test: * $P < 0.05$ and ** $P < 0.01$ from group 3. Group 1, fucoxanthin-high diet administered mice; group 3, control diet administered mice.

Supplementary Table S4. Profile of upregulated proteins identified by LC-MS/MS in whole tumor tissue of patient-derived pancreatic cancer tissue-transplanted xenograft (PC-PDX) mice administered fucoxanthin (Fx).¹

Gene symbol	Description	Fold change ²
HSPA1L	Heat shock 70 kDa protein 1-like	76.6
PRMT5	Protein arginine N-methyltransferase 5	24.6
TBC1D2B	TBC1 domain family member 2B	15.5
TNXB	Tenascin-X	15.5
NEK9	Serine/threonine-protein kinase Nek9	14.9
NAAA	N-acylethanolamine-hydrolyzing acid amidase	14.8
TGFBR2	TGF-beta receptor type-2	11.7
MTOR	Serine/threonine-protein kinase mTOR	9.5
HSBP1	Heat shock factor-binding protein 1	7.7
ILVBL	2-hydroxyacyl-CoA lyase 2	7.5
F13A1	Coagulation factor XIII A chain	7.1
APBB1IP	Amyloid beta A4 precursor protein-binding family B member 1-interacting protein	7.0
UNC119B	Protein unc-119 homolog B	6.7
PEX1	Peroxisome biogenesis factor 1	6.7
GFPT2	Glutamine--fructose-6-phosphate aminotransferase [isomerizing] 2	5.8
KRI1	Protein KRI1 homolog	5.7
PCOLCE	Procollagen C-endopeptidase enhancer 1	5.5
CCDC90B	Coiled-coil domain-containing protein 90B, mitochondrial	5.5
ISG20	Interferon-stimulated gene 20 kDa protein	5.5
YKT6	Synaptobrevin homolog YKT6	5.4
DOCK2	Dedicator of cytokinesis protein 2	5.1
COL6A6	Collagen alpha-6(VI) chain	5.1
TACO1	Translational activator of cytochrome c oxidase 1	4.9
FUT8	Alpha-(1,6)-fucosyltransferase	4.8
OSBPL9	Oxysterol-binding protein-related protein 9	4.8

PRORS1P	Putative prolyl-tRNA synthetase associated domain-containing protein 1	4.8
CMTR1	Cap-specific mRNA (nucleoside-2'-O-)-methyltransferase 1	4.7
NHLRC2	NHL repeat-containing protein 2	4.5
AXL	Tyrosine-protein kinase receptor UFO	4.3
HTRA2	Serine protease HTRA2, mitochondrial	4.2
VAV2	Guanine nucleotide exchange factor VAV2	3.9
DCUN1D5	DCN1-like protein 5	3.9
HAL	Histidine ammonia-lyase	3.9
TNS1	Tensin-1	3.8
MINDY3	Ubiquitin carboxyl-terminal hydrolase MINDY-3	3.8
DDC	Aromatic-L-amino-acid decarboxylase	3.7
MAP2K3	Dual specificity mitogen-activated protein kinase kinase 3	3.7
DPT	Dermatopontin	3.6
SEC24D	Protein transport protein Sec24D	3.5
KDM1A	Lysine-specific histone demethylase 1A	3.5
AFAP1	Actin filament-associated protein 1	3.4
CPSF1	Cleavage and polyadenylation specificity factor subunit 1	3.4
ZFP36L2	mRNA decay activator protein ZFP36L2	3.3
ACSM3	Acyl-coenzyme A synthetase ACSM3, mitochondrial	3.1
HDAC6	Histone deacetylase 6	3.1
AGPAT1	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha	3.1
VTI1A	Vesicle transport through interaction with t-SNAREs homolog 1A	3.0
AP1S1	AP-1 complex subunit sigma-1A	2.9
FILIP1L	Filamin A-interacting protein 1-like	2.9
SNTB2	Beta-2-syntrophin	2.8
DCN	Decorin	2.6
HO1	Heme oxygenase 1	2.5
FAF1	FAS-associated factor 1	1.8

¹ Proteins passed both peptide false discovery rate (FDR, cutoff < 1%) and protein FDR (cutoff < 1%) were detected. Among all 318 upregulated proteins (≥ 1.5 -fold change), top 50 upregulated proteins, and three proteins, DCN (2.6-fold), HO1 (2.5-fold) and FAF1 (1.8-fold) were showed. ² Fold change in human protein expressions in whole tumor tissue of PC-PDX mice with Fx-high diet administration (group 1) compared to that of control mice (group 3). Proteins colored gray were the proteins that were applied to western blot analysis as noteworthy cancer-related molecules (Figure 4).

Supplementary Table S5. Profile of downregulated proteins identified by LC-MS/MS in whole tumor tissue of patient-derived pancreatic cancer tissue-transplanted xenograft (PC-PDX) mice administered fucoxanthin (Fx).¹

Gene symbol	Description	Fold change ²
INSR	Insulin receptor	N.D. ³
BAG1	BAG family molecular chaperone regulator 1	N.D.
NTS	Neurotensin/neuromedin N	N.D.
MT2A	Metallothionein-2	N.D.
ITGB3	Integrin beta-3	N.D.

TNIP1	TNFAIP3-interacting protein 1	N.D.
CCDC12	Coiled-coil domain-containing protein 12	N.D.
SIPA1L3	Signal-induced proliferation-associated 1-like protein 3	N.D.
RTN2	Reticulon-2	N.D.
MAP3K7	Mitogen-activated protein kinase kinase kinase 7	N.D.
IL1R2	Interleukin-1 receptor type 2	N.D.
CD47	Leukocyte surface antigen CD47	N.D.
VEZT	Vezatin	N.D.
TUFT1	Tuftelin	N.D.
WDR49	WD repeat-containing protein 49	N.D.
CEMIP2	Cell surface hyaluronidase	N.D.
HRNR	Hornerin	N.D.
IFIT5	Interferon-induced protein with tetratricopeptide repeats 5	N.D.
TTK	Dual specificity protein kinase TTK	-10.2
CTDSPL2	CTD small phosphatase-like protein 2	-7.6
TGFB1	Transforming growth factor beta-1 proprotein	-6.0
SCFD2	Sec1 family domain-containing protein 2	-5.5
LPXN	Leupaxin	-4.7
LAMTOR2	Ragulator complex protein LAMTOR2	-4.4
IGFBP3	Insulin-like growth factor-binding protein 3	-4.0
MIF	Macrophage migration inhibitory factor	-3.8
TFF3	Trefoil factor 3	-3.8
TFCP2L1	Transcription factor CP2-like protein 1	-3.7
ITGA1	Integrin alpha-1	-3.6
TERF2IP	Telomeric repeat-binding factor 2-interacting protein 1	-3.6
LAMA5	Laminin subunit alpha-5	-3.2
REG4	Regenerating islet-derived protein 4	-3.2
SP3	Transcription factor Sp3	-3.1
NECTIN2	Nectin-2	-3.1
ECM1	Extracellular matrix protein 1	-3.0
MUC5B	Mucin-5B	-2.8
HNF4A	Hepatocyte nuclear factor 4-alpha	-2.7
PCID2	PCI domain-containing protein 2	-2.5
GPX2	Glutathione peroxidase 2	-2.5
NFKB1	Nuclear factor NF-kappa-B p105 subunit	-2.4
NFKB2	Nuclear factor NF-kappa-B p100 subunit	-2.3
CLU	Clusterin	-2.3
IGFBP2	Insulin-like growth factor-binding protein 2	-2.3
ABRACL	Costars family protein ABRACL	-2.3
AAGAB	Alpha- and gamma-adaptin-binding protein p34	-2.2
CNOT2	CCR4-NOT transcription complex subunit 2	-2.2
SEC62	Translocation protein SEC62	-2.1

ZMYND8	Protein kinase C-binding protein 1	-2.1
SYNE2	Nesprin-2	-2.1
CMC1	COX assembly mitochondrial protein homolog	-2.1
CFL2	Cofilin-2	-2.1
FKBP5	Peptidyl-prolyl cis-trans isomerase FKBP5	-2.1
PROM1	Prominin-1	-2.0
PIEZO1	Piezo-type mechanosensitive ion channel component 1	-2.0
VSNL1	Visinin-like protein 1	-2.0
SCIN	Adseverin	-2.0
OCLN	Occludin	-1.9
UXT	Protein UXT	-1.9
GATA6	Transcription factor GATA-6	-1.9
ITGA3	Integrin alpha-3	-1.9
COL17A1	Collagen alpha-1(XVII) chain	-1.9
CST3	Cystatin-C	-1.9
PKP2	Plakophilin-2	-1.9
CD44	CD44 antigen	-1.9
XRCC4	DNA repair protein XRCC4	-1.9
FXD3	FXD domain-containing ion transport regulator 3	-1.9
LAMTOR5	Ragulator complex protein LAMTOR5	-1.9
CD55	Complement decay-accelerating factor	-1.9
NCAPH	Condensin complex subunit 2	-1.9
CDC42EP5	Cdc42 effector protein 5	-1.8
AGRN	Agrin	-1.8
TIMP1	Metalloproteinase inhibitor 1	-1.8
LCN2	Neutrophil gelatinase-associated lipocalin	-1.8
PPP1R1B	Protein phosphatase 1 regulatory subunit 1B	-1.7
QSOX1	Sulfhydryl oxidase 1	-1.7
ADAM17	Disintegrin and metalloproteinase domain-containing protein 17	-1.7
RASAL1	RasGAP-activating-like protein 1	-1.7
NFATC2IP	NFATC2-interacting protein	-1.7
FAM83B	Protein FAM83B	-1.7
HNF1B	Hepatocyte nuclear factor 1-beta	-1.7
MDK	Midkine	-1.7
DKK1	Dickkopf-related protein 1	-1.7
MAPK13	Mitogen-activated protein kinase 13	-1.7
FHL2	Four and a half LIM domains protein 2	-1.7
PTGES2	Prostaglandin E synthase 2	-1.7
EPCAM	Epithelial cell adhesion molecule	-1.7
GRN	Progranulin	-1.7
RHOC	Rho-related GTP-binding protein RhoC	-1.7
MMP9	Matrix metalloproteinase-9	-1.7

CD99	CD99 antigen	-1.7
DAG1	Dystroglycan 1	-1.7
PTP4A1	Protein tyrosine phosphatase type IVA 1	-1.7
ANKRD22	Ankyrin repeat domain-containing protein 22	-1.7
NUCKS1	Nuclear ubiquitous casein and cyclin-dependent kinase substrate 1	-1.6
MUC5AC	Mucin-5AC	-1.6
OXR1	Oxidation resistance protein 1	-1.6
RPA3	Replication protein A 14 kDa subunit	-1.6
STUB1	E3 ubiquitin-protein ligase CHIP	-1.6
SUMO3	Small ubiquitin-related modifier 3	-1.6
TGFB1I1	Transforming growth factor beta-1-induced transcript 1 protein	-1.6
MSLN	Mesothelin	-1.6
LTBR	Tumor necrosis factor receptor superfamily member 3	-1.6
HAT1	Histone acetyltransferase type B catalytic subunit	-1.6
CDK9	Cyclin-dependent kinase 9	-1.6
GAB1	GRB2-associated-binding protein 1	-1.6
COL15A1	Collagen alpha-1(XV) chain	-1.6
F11R	Junctional adhesion molecule A	-1.5
CDH3	Cadherin-3	-1.5
CAT	Catalase	-1.5

¹ Proteins passed both peptide false discovery rate (FDR, cutoff < 1%) and protein FDR (cutoff < 1%) were detected. Among all 888 downregulated proteins (≤ -1.5 -fold change), 109 downregulated involving in proteins growth, inflammation, and cancer development, were showed. ² Fold change in human protein expressions in whole tumor tissue of PC-PDX mice with Fx-high diet administration (group 1) compared to that of control mice (group 3). ³ N.D., Proteins were not detected in group 1 and detected in group 3. Proteins colored gray were the proteins that were applied to western blot analysis as noteworthy cancer-related molecules (Figure 4).