



2026 World Conference on Lung Cancer

SEPTEMBER 12 – 15, 2026 | SEOUL, REPUBLIC OF KOREA

Distinct lipid metabolic profiles associated with SUVmax in lung adenocarcinoma and squamous cell carcinoma

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” Warburg Effect“

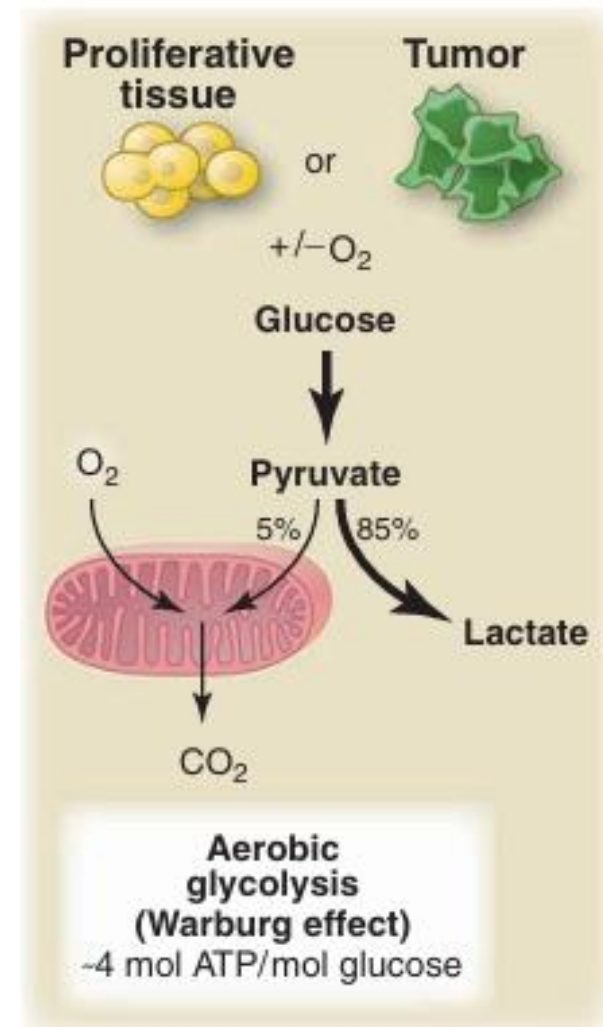
Cancer cells preferentially utilize aerobic glycolysis, despite its low ATP efficiency, and consume large amounts of glucose even under oxygen-rich conditions.

O. Warburg, Biochem. Z. 152, 319 (1924). Science. 2009 22;324(5930):1029-33.

In tumors with a pronounced Warburg effect, lipid synthesis required for cell proliferation is expected to be altered through the utilization of glycolytic intermediates.

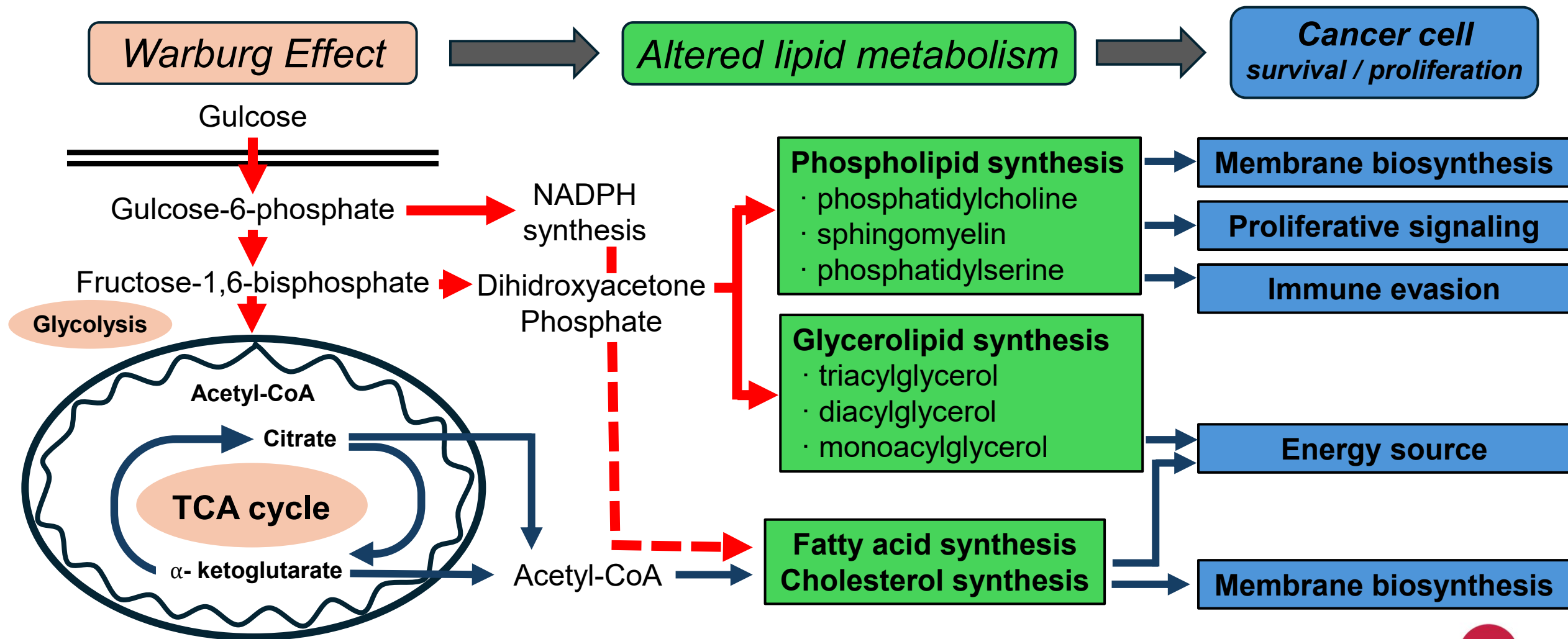
Distinct metabolic profiles may exist that reflect the biological characteristics of tumors.

Front Oncol. 2019 Nov 15;9:1215.



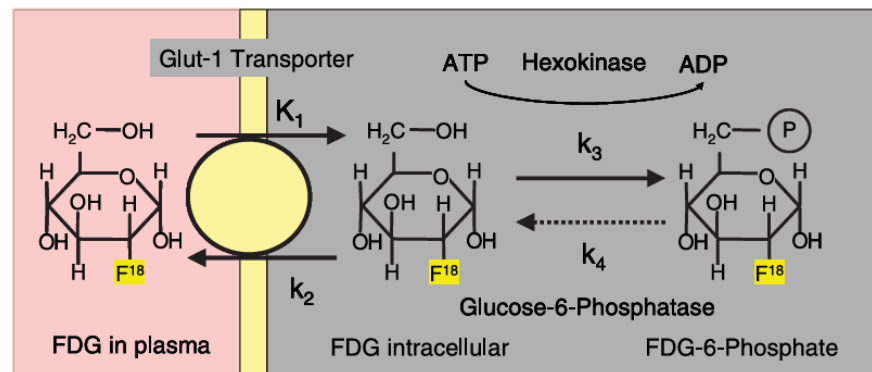
Science. 2009 22;324(5930):1029-33.

Cancer cells drive lipid metabolism through the Warburg effect, supporting survival and proliferation. Metabolic profiles may reflect tumor biology and could help characterize cancer tissue.

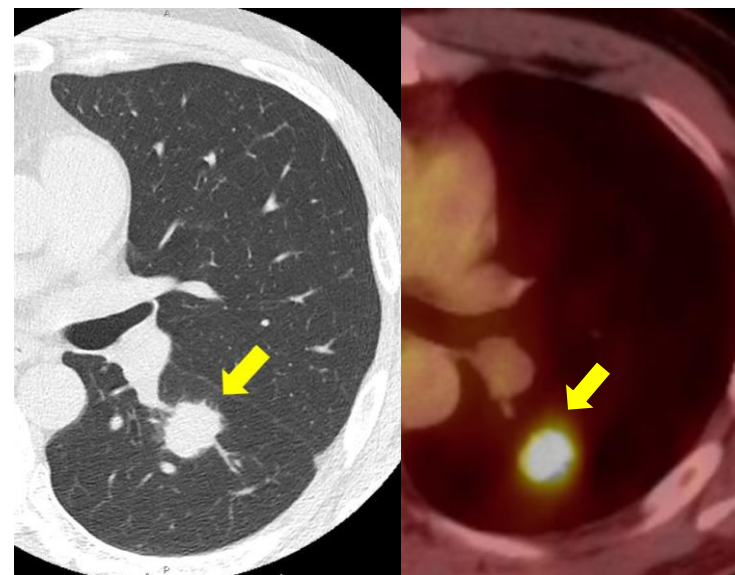


FDG-PET is an imaging modality based on increased glucose uptake by tumor tissues, and SUVmax reflects the extent of the Warburg effect.

Clin Cancer Res. 2005 15;11(8):2785-808.
Expert Rev Mol Med. 2019 27:21:e4.



Clin Cancer Res. 2005 15;11(8):2785-808.



Hypothesis

Non-small cell lung cancer exhibits distinct lipid metabolic characteristics according to histological subtype, namely lung adenocarcinoma (ADC) and lung squamous cell carcinoma (SQCC).

Objective

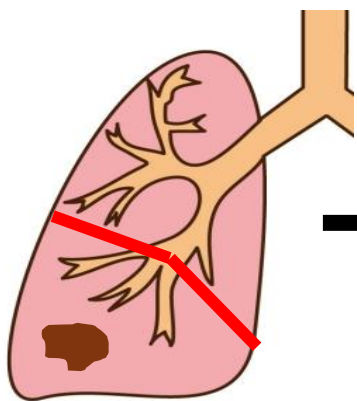
To investigate whether ADC and SQCC exhibit distinct lipid metabolic profiles associated with SUVmax, a surrogate marker of the Warburg effect, we performed lipidomic analyses using LC-MS/MS.

*LC-MS/MS: liquid chromatography-tandem mass spectrometry

Methods

<Sampling>

Lung cancer tissue



<Lipid extraction>

Bligh & Dyer method



<LC-MS/MS*>



<Lipid identification>

LipidSearch™

LipidSearch
Identification System for Lipidomics

Search Alignment Result Mass List

Alignment Result

Sort Filters Profile Export Quan Column

Job Name 190926_lung cancer alignment

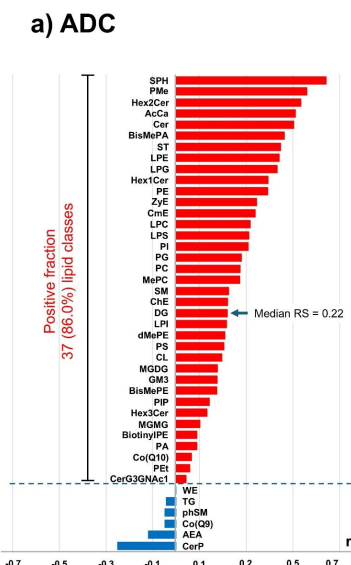
Sample

Result

Rej	LipidMolec	Class	FA	FA Gro
SM(d18:0_24:1)	SM	d18:0_24:1	d42:1	
SM(d18:1_16:0)	SM	d18:1_16:0	d34:1	
SM(d18:1_16:1)	SM	d18:1_16:1	d34:2	
SM(d18:1_18:0)	SM	d18:1_18:0	d36:1	
SM(d18:1_18:3)	SM	d18:1_18:3	d36:4	
SM(d18:1_20:3)	SM	d18:1_20:3	d38:4	
SM(d18:1_22:0)	SM	d18:1_22:0	d40:1	
SM(d18:1_23:0)	SM	d18:1_23:0	d41:1	
SM(d18:1_23:1)	SM	d18:1_23:1	d41:2	
SM(d18:1_24:0)	SM	d18:1_24:0	d42:1	
SM(d18:1_24:1)	SM	d18:1_24:1	d42:2	
SM(d18:1_24:1)	SM	d18:1_24:1	d42:2	
SM(d18:1_24:2)	SM	d18:1_24:2	d42:3	
SM(d18:1_24:2)	SM	d18:1_24:2	d42:3	
SM(d18:1_24:3)	SM	d18:1_24:3	d42:4	
SM(d18:2_18:1)	SM	d18:2_18:1	d36:3	
SM(d18:2_18:3)	SM	d18:2_18:3	d36:5	
SM(d18:2_24:0)	SM	d18:2_24:0	d42:2	

<Correlation analysis>

Lipid level vs SUVmax



- Patients who received radical surgery
- ADC (n=22)
- SQCC (n=16)

- Q Exactive™ Hybrid Quadrupole-Orbitrap™ Mass Spectrometer
- Ultimate 3000 system

- Spearman's rank correlation coefficient

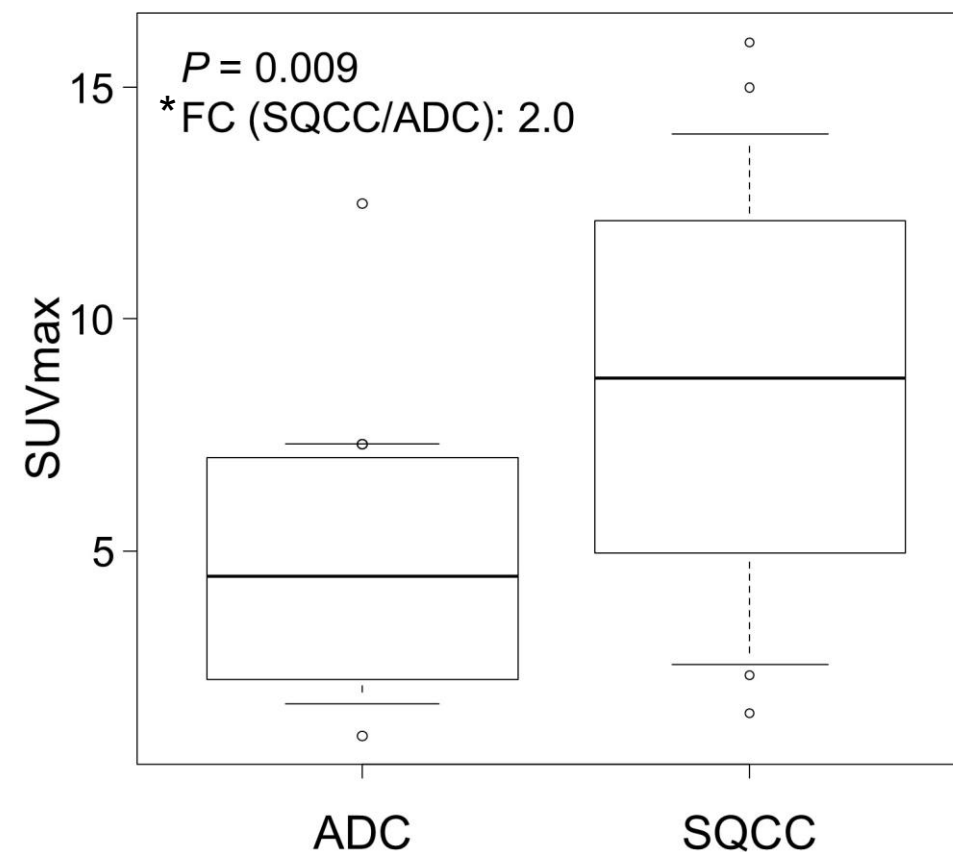
*LC-MS/MS: liquid chromatography-tandem mass spectrometry

Patient characteristics

Characteristics	ADC (n=22)	SQCC (n=16)	P-value
Median age (range)	70 (48-89)	71 (54-83)	0.407
Sex (male/female)	15/7	15/1	0.106
Smoking history (+/-)	16/6	16/0	*0.030
Median Brinkman index (range)	345 (0-1600)	1590 (180-3000)	*< 0.001
Median SUVmax (range)	4.5 (1.0-12.5)	8.8 (1.5-16.0)	*0.009
Pathological stage			0.607
I A	9	8	
I B	6	5	
II A	0	1	
II B	5	2	
III A	2	0	
Lmph node metastasis (N0/N1/N2)	16/5/1	14/2/0	0.812
Degree of differentiation (G1/G2/G3)	3/14/5	4/10/2	0.583
Pleural invasion (pI0/pI1/pI2/pI3)	11/9/1/1	10/5/1/0	0.921
Lymphatic vessel invasion (+/-)	11/11	7/9	0.752
Blood Vessel invasion (+/-)	12/10	12/4	0.309
Spread through air space (+/-)	6/16	2/14	0.426
Histologic subtype of ADC			-
Lepidic	3	-	
Papillary	12	-	
Acinar	5	-	
Solid	2	-	
Recurrent (+/-)	10/12	4/12	0.309

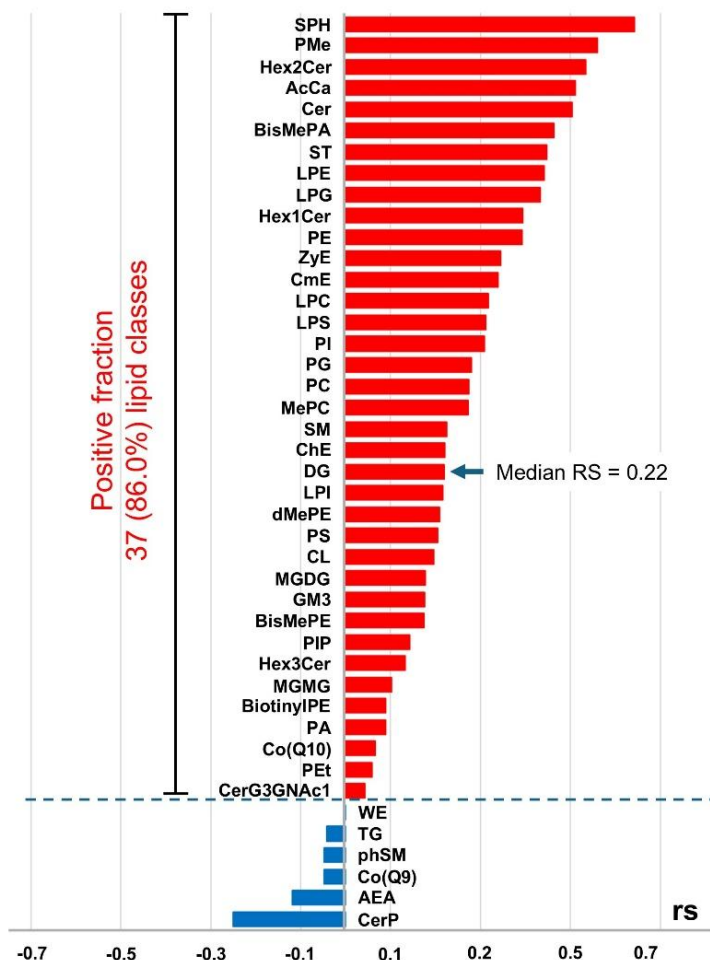
Abbreviations: ADC, adenocarcinoma; SQCC, squamous cell carcinoma, SUVmax; maximum standardized uptake value

Lung SQCC shows
twofold higher FDG uptake than lung ADC.

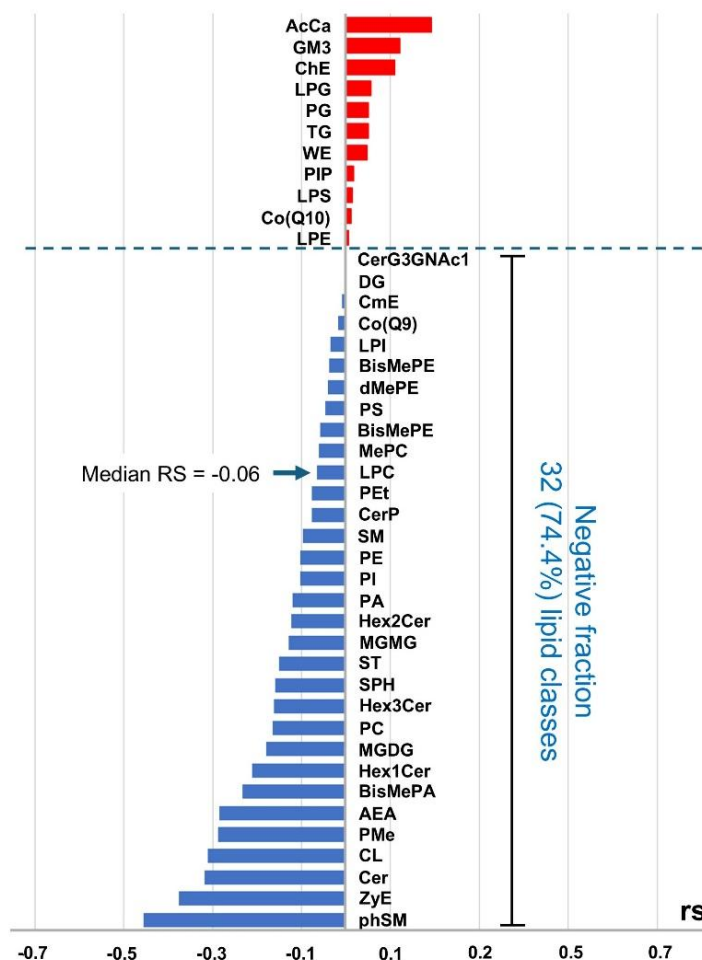


*FC: fold change

a) ADC



b) SQCC



ADC (left panel):

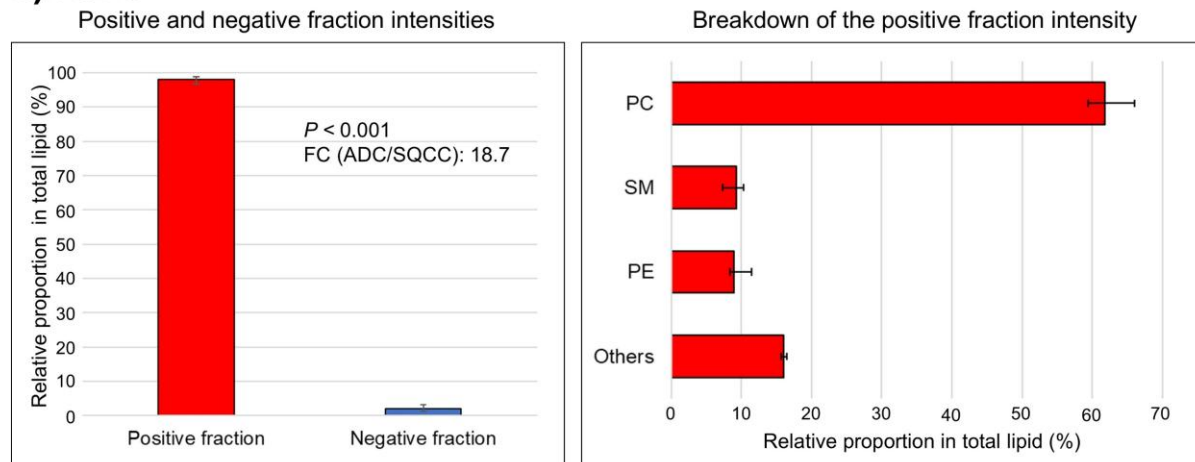
86.0% of lipid classes were
positively correlated with SUVmax (red).

SQCC (right panel):

74.4% of lipid classes were
negatively correlated with SUVmax (blue).

The relative abundance of lipid classes showed opposite correlations with SUVmax in ADC and SQCC.

rs: Spearman's rank correlation coefficient

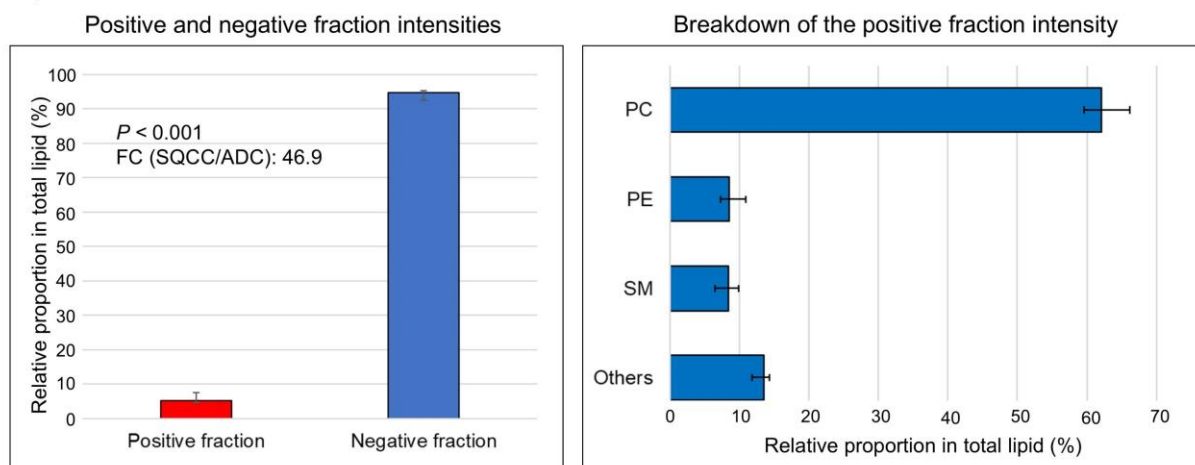
a) ADC

ADC (upper panel):

97% of relative lipid abundances showed
a positive correlation (red).

The top-3 abundant lipid classes within
the **positive fraction** were

- 1: Phosphatidylcholine (PC)
- 2: Sphingomyelin (SM)
- 3: Phosphatidylethanolamine (PE)

b) SQCC

SQCC (lower panel):

95% of relative lipid abundances showed
a negative correlation (blue).

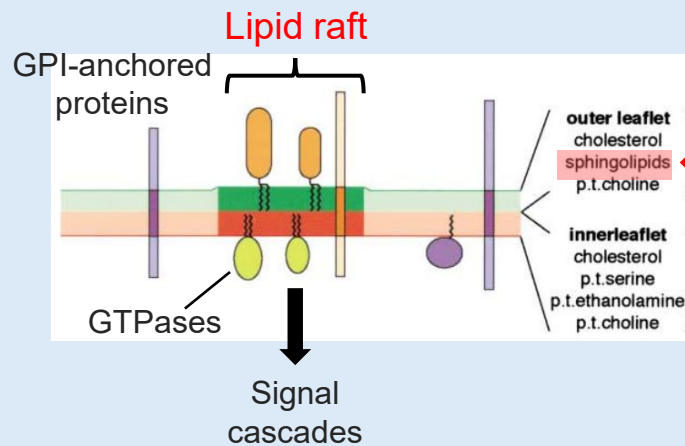
The top-3 abundant lipid classes within
the **negative fraction** were

- 1: Phosphatidylcholine (PC)
- 2: Phosphatidylethanolamine (PE)
- 3: Sphingomyelin (SM)

SM

(Sphingomyelin)

- Major component of lipid rafts.
- Recruit functional proteins, such as receptors, thereby enhancing signaling efficiency.

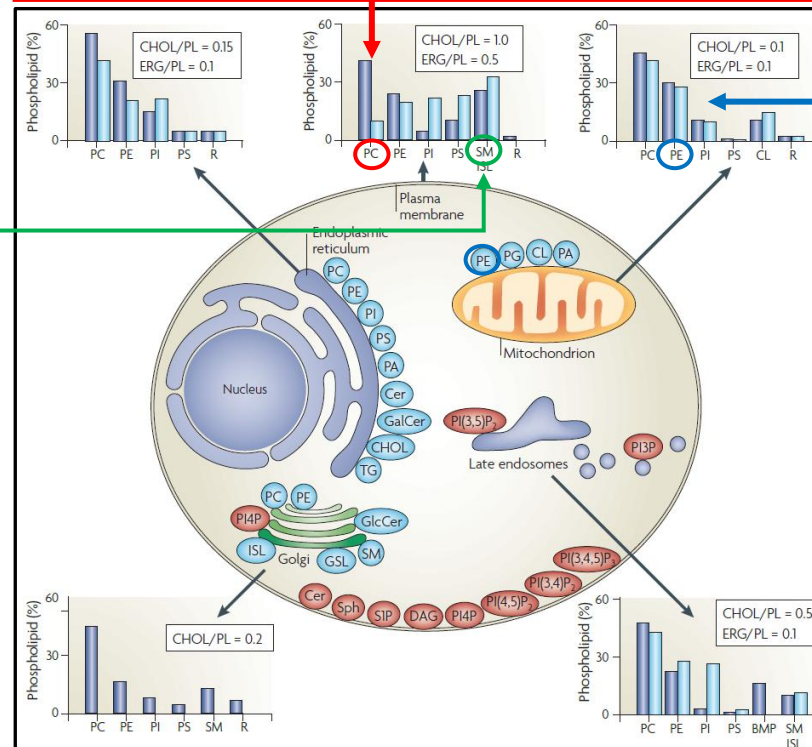


Cell. 2003 Nov 14;115(4):377-88.

PC

(Phosphatidylcholine)

- The most abundant lipids in cellular and organelle membranes.
- Support the rapid proliferation of cancer cells.



Nat Rev Mol Cell Biol. 2008;9(2):112–24.

PE

(Phosphatidylethanolamine)

- Maintenance of the mitochondrial inner membrane and electron transport chain.
- Induction of autophagy
 - removal of oxidized proteins
 - suppression of ROS accumulation

Nat Cell Biol. 2010 Sep;12(9):823-30.

- In ADC, increased glycolytic activity may be coupled with lipid synthesis to support membrane biogenesis and tumor proliferation.
- In SQCC, the opposite correlation suggests that enhanced glycolysis is not coupled with the accumulation of these major lipids, possibly reflecting increased lipid utilization/turnover or diversion of glycolytic metabolic substrates.
- These findings suggest histology-specific coupling between glucose and lipid metabolism in lung cancer.

Conclusions

- Lung ADC and SQCC showed opposite correlations between lipid profile changes and SUVmax, suggesting that these histological subtypes possess distinct lipid metabolic characteristics.
- Our findings may contribute to the identification of novel biomarkers for therapeutic stratification and provide insights that could support the development of new therapeutic targets.