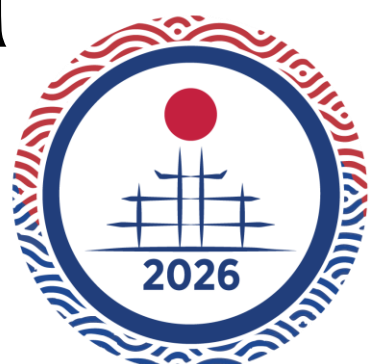


EP02.07: Distinct lipid metabolic strategies in lung and thymic squamous cell carcinoma : a comparative lipidomic analysis

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INTRODUCTION

【Background】

Lung squamous cell carcinoma (lung SCC)
and
Thymic squamous cell carcinoma (thymic SCC)

- Share similar squamous histological features.
- Arise from different organs.
- May have distinct mechanisms of tumorigenesis.

【Lipidomics】

- Lipid metabolism plays an important role in tumor growth and survival.^{1,2}
- Our previous studies suggested that lipidomic profiles may reflect tumor aggressiveness and tissue of origin in SCC.^{3,4}

【Hypothesis】

Lung and thymic SCC would exhibit different lipidomic alterations.

METHODS

Study design

- Exploratory analysis
lung SCC, n=1; thymic SCC, n=1
- Patients selected based on similarities in age, sex, and histological differentiation.(Table 1)

1. Tissue collection : Tumor and matched normal tissue

2. Lipid extraction : Modified Bligh–Dyer method

3. Lipidomic analysis :

- Liquid chromatography–tandem mass spectrometry (LC–MS/MS)
- Peak areas normalization to the internal standard Phosphatidylcholine (PC) (12:0_12:0)
- Summation by lipid class

[Table 1]

Characteristics	Lung SCC case	Thymic SCC case
Age, sex	81, male	76, male
Smoking history	Ex-smoker 41 pack-years	Ex-smoker 30 pack-years
Surgical procedure	Right lower lobectomy	Total thymectomy
Histopathological diagnosis	Squamous cell carcinoma	Squamous cell carcinoma
Differentiation	Moderate	Moderate
Stage	pT2aN0M0, Stage IB	pT1aN0M0, Stage I

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The lung SCC and thymic SCC samples showed different patterns of lipidomic alterations despite their similar squamous histology.
- These findings raise the possibility that lipidomic profiles reflect tissue-of-origin–specific tumor biology that is not apparent from histopathology alone.

Future Direction for Research

- Validate these lipidomic patterns in larger cohorts of lung and thymic SCCs.
- Examine associations between lipid profiles and clinicopathological characteristics, treatment response, and prognosis.
- Determine whether tissue-specific lipid signatures could serve as biomarkers or reveal potential metabolic therapeutic targets.

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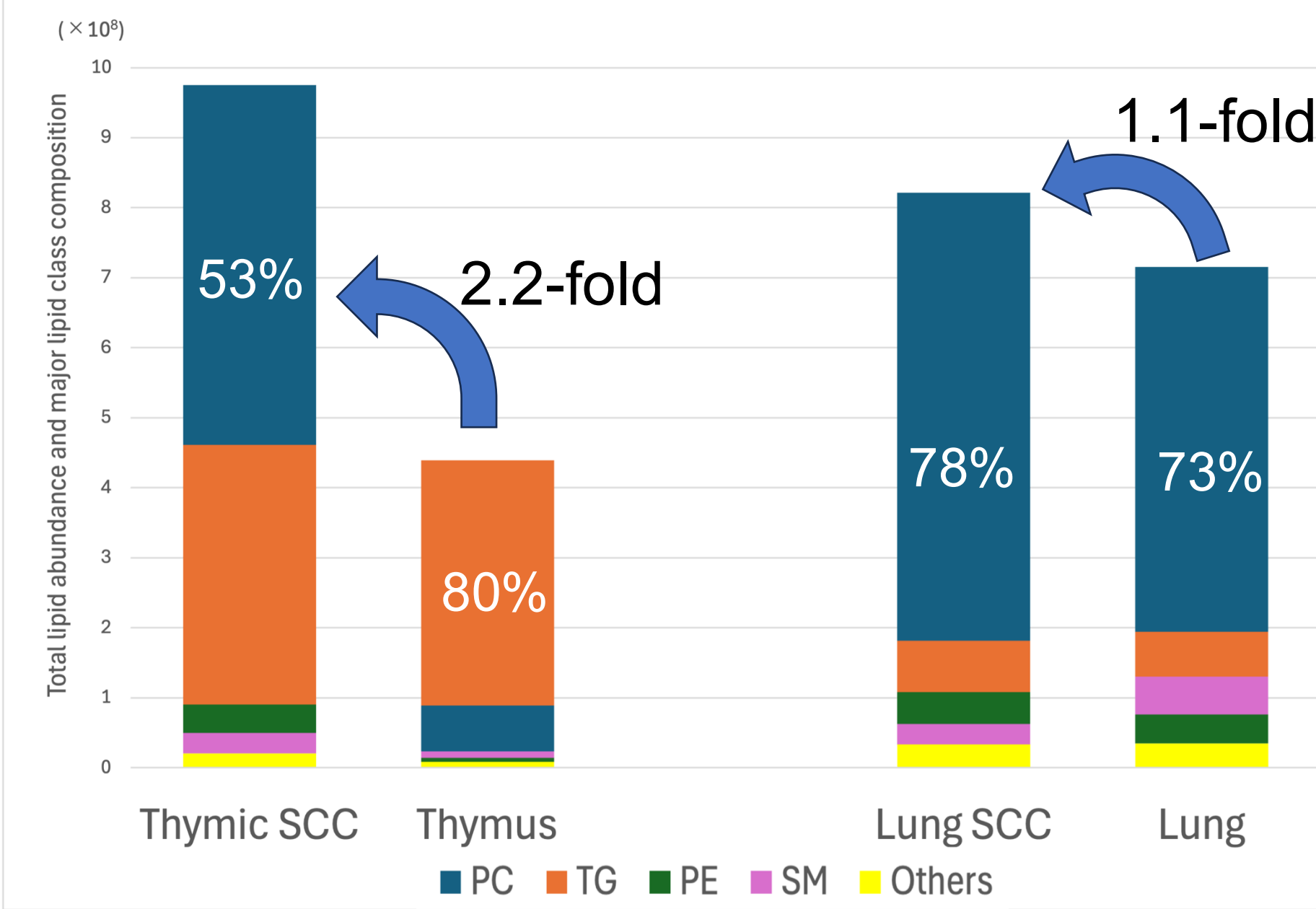
Potential biological relevance of key lipid classes

PC, PE, SM	Major phospholipid components of cellular membranes
TG	Energy storage lipid
Ch, ChE	Membrane structure, cholesterol homeostasis, and storage
PG	Key phospholipid in the mitochondrial inner membrane
CoQ10	Mitochondrial electron transport and oxidative phosphorylation
Hex2Cer, Hex3Cer	Complex glycosphingolipids involved in membrane organization
AcCa	Mitochondrial fatty-acid metabolism
CL	Essential for mitochondrial respiratory chain function

RESULTS

Total lipid abundance and major lipid class comparison between tumor and normal tissues

- A total of 23 lipid classes were identified.
- Phosphatidylcholine (PC), triglycerides (TG), phosphatidylethanolamine (PE), and sphingomyelin (SM) were the predominant lipid classes in both tumor types and their matched normal tissues.
- PC was the predominant lipid class in both tumors and normal lung tissue, whereas TG predominated in normal thymic tissue.
- Total lipid abundance was higher in tumor tissues than in matched normal tissues, with a greater increase in thymic SCC (2.2-fold) than in lung SCC (1.1-fold).



Lipid class comparison between tumor and normal tissues

【Thymic SCC/normal tissue】

Overall changes	Major increases	Major decreases
22 classes increased; only FA decreased	ChE : 24.0-fold PG : 18.1-fold CoQ10 : 10.5-fold	None

FA: fatty acids, ChE: cholesteryl esters, PG: phosphatidylglycerol, CoQ10: coenzyme Q10

→Thymic SCC showed broad increases(22/23) across lipid classes.

【Lung SCC/normal tissue】

Overall changes	Major increases	Major decreases
15 classes increased 8 decreased	Hex2Cer : 11.1-fold AcCa : 3.8-fold	ChE : 0.7-fold SM : 0.5-fold Hex3Cer: 0.4-fold

HexCer2: dihexosylceramide , AcCa : acylcarnitine , SM: sphingomyelin , Hex3Cer: trihexosylceramide

→Lung SCC exhibited more selective increases and decreases than thymic SCC.

Lipid class comparison between lung and thymic tumor tissues

【Thymic SCC/Lung SCC】

Higher in lung SCC	Higher in thymic SCC
ChE, CoQ10, Ch, Hex2Cer, AcCa, CL	TG, Hex3Cer

Ch: cholesterol, CL: cardiolipin

→The two SCCs exhibited distinct lipid-class profiles despite their similar squamous histology.

