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Exploring the Biological Characteristics of Thymoma Using Lipidomics: A Pilot Study

Kensuke Takei, Yusuke Takanashi, Yuri Ozawa

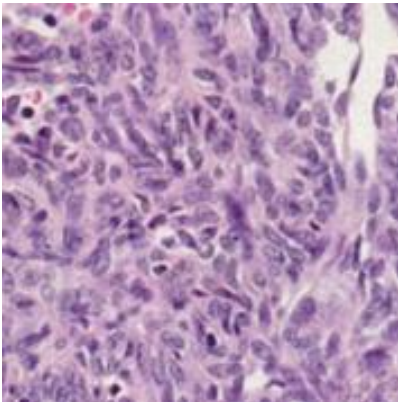
Motohisa Shibata, Keigo Sekihara, Kazuhito Funai

Japan First Department of Surgery, Hamamatsu University School of Medicine

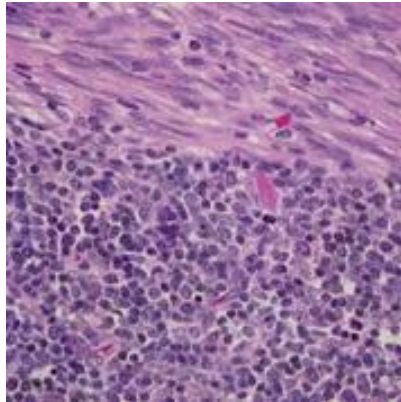
Correspondence: k.takei@hama-med.ac.jp

- Thymoma is a rare neoplasm that can exhibit local invasion and distant metastasis.

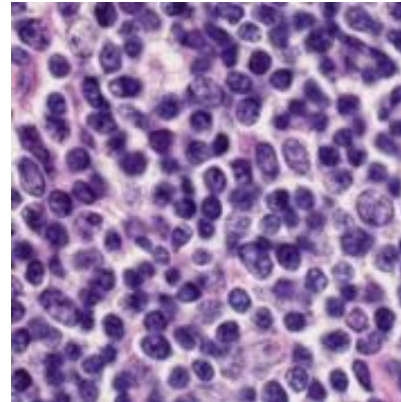
Type A



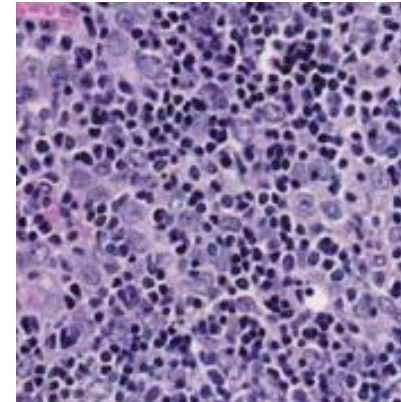
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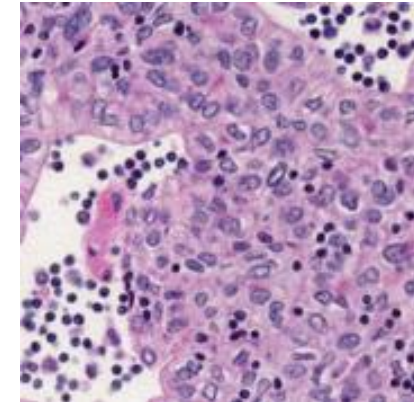
Type B1



Type B2



Type B3



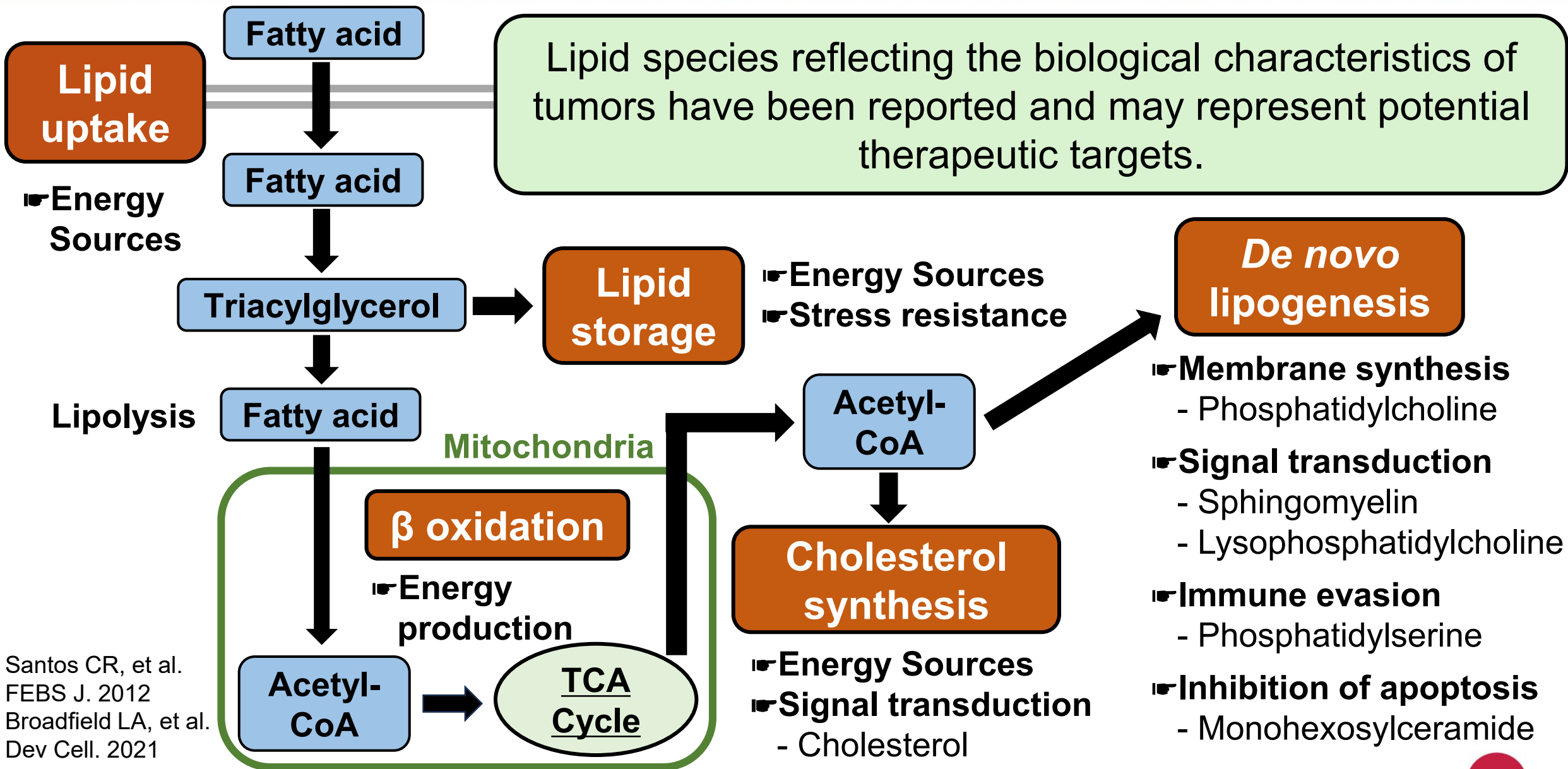
General Rules for Study of Mediastinal Tumors (The 1st Edition),
Japanese Association for Research on the Thymus.

Poor prognosis

➤ For unresectable or recurrent cases, systemic therapy is the standard treatment.

➤ Clinical Problems

1. Treatment options become limited once disease progression or severe adverse events occur.
2. No clearly established criteria exist for selecting optimal therapeutic agents based on histological subtype.



➤ The thymus is progressively replaced by adipose tissue with aging.

Dixit VD. Curr Opin Immunol. 2010

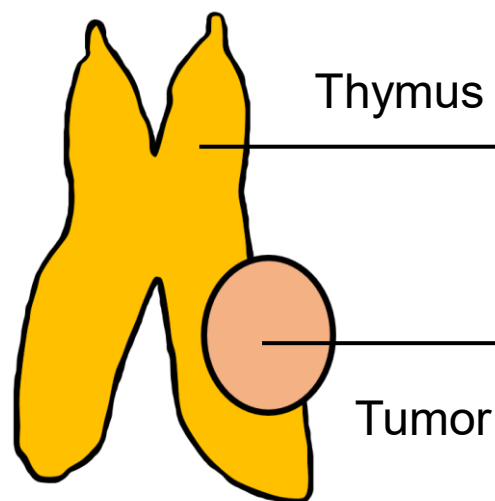
➤ We aimed to investigate the biological characteristics of thymoma toward the identification of potential therapeutic targets and biomarkers for treatment selection using lipid profile analysis (lipidomics).

➤ As a pilot study, we performed lipidomics in a single thymoma case to explore candidate lipid species associated with the biological characteristics of thymoma.

Methods

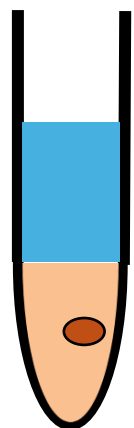
Type B2 thymoma

Frozen tissues



Samples were frozen immediately after intraoperative collection and stored at -80°C until use.

Lipid extraction



Bligh & Dyer method



Liquid chromatography–
tandem mass
spectrometry analysis



Q Exactive™
mass spectrometer



Lipid identification



LipidSearch

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Thermo SCIENTIFIC

Search Result

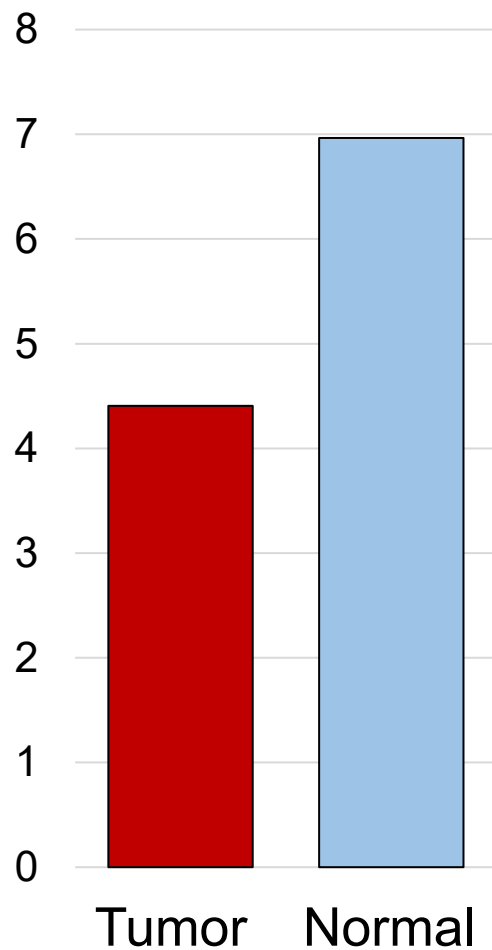
LipidID	LipidGroup...	Grade	IDScore	Rank	Adduct	BaseModif...
SPH(d14:1)...	SPH(d14:1)...	C	0.03	1	M+H	
SPH(d16:0)...	SPH(d16:0)...	C	0.05	1	M+H	
SPH(d16:1)...	SPH(d16:1)...	C	0.51	1	M+H	
LPC(12:0)+H	LPC(12:0)+H	C	1.31	1	M+H	
SPH(d17:0)...	SPH(d17:0)...	C	0.04	1	M+H	
LPC(12:0)+H	LPC(12:0)+H	C	1.80	1	M+H	
DG(9:0,4:0)...	DG(13:0)+N...	C	0.43	1	M+NH4	
AcCa(14:0)+H	AcCa(14:0)+H	A	0.53	1	M+H	
DG(O-24:6)...	DG(O-24:6)...	C	0.05	1	M+H	

LipidSearch Software

Identified lipid species were quantified, and their levels were compared between tumor and normal thymus tissues.

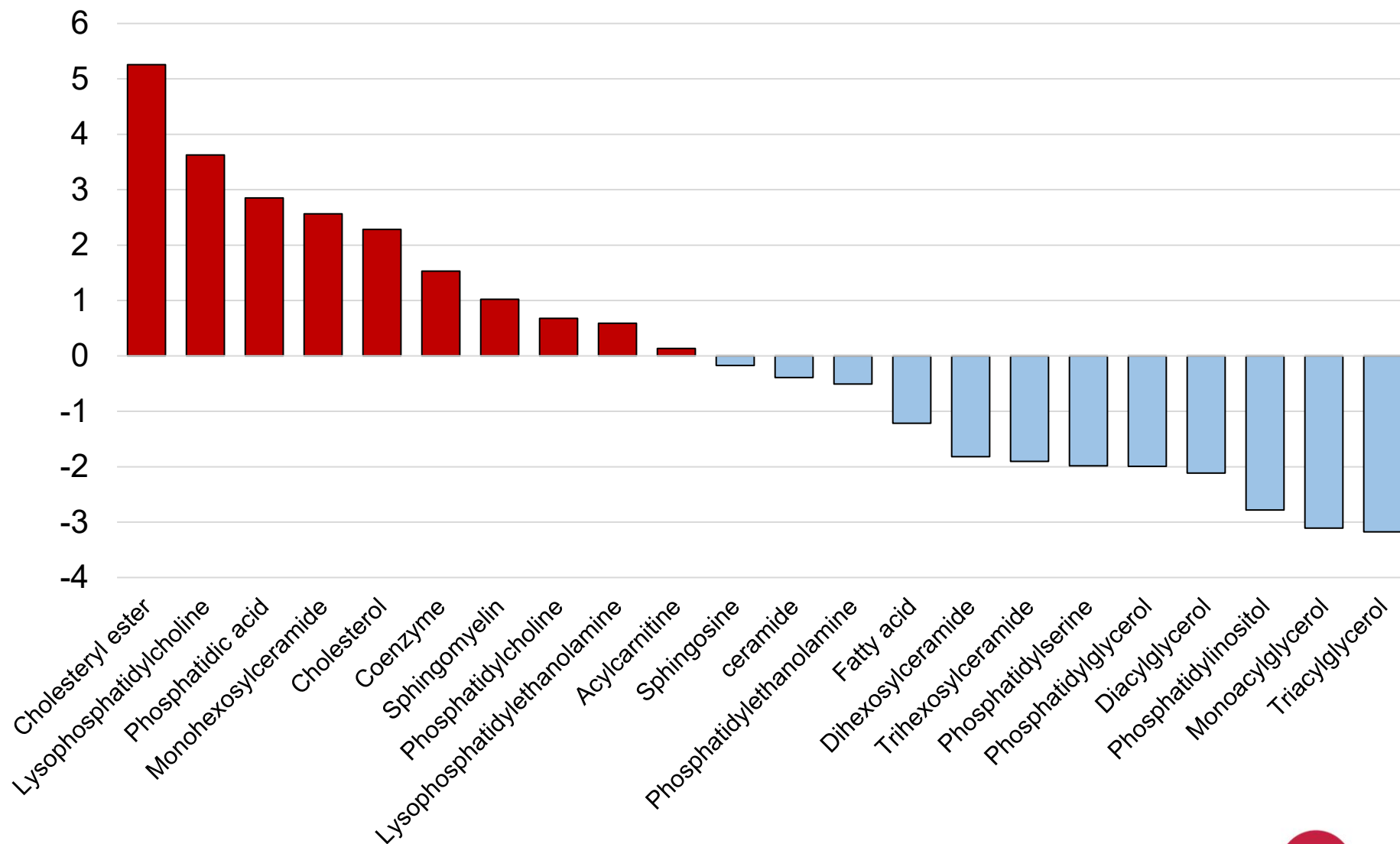
Results

($\times 10^7$) Total lipid levels



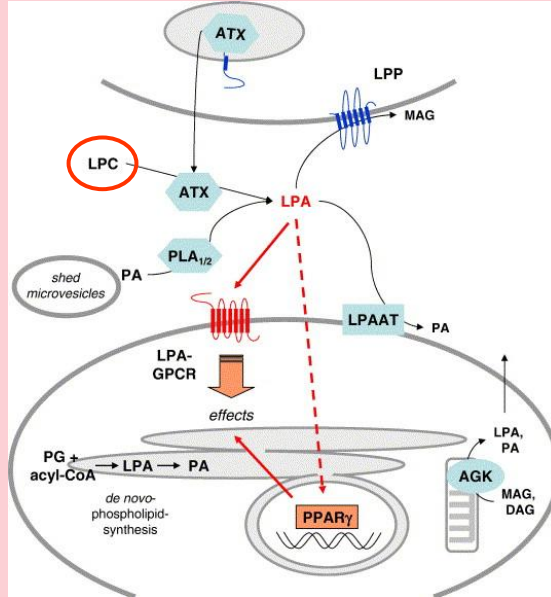
(log2)

Tumor-to-normal tissue ratio

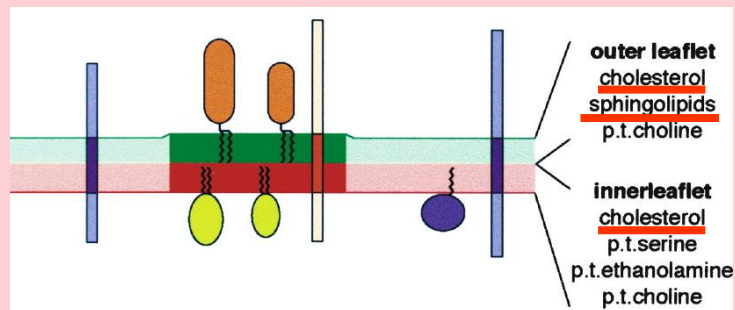


Increased lipids in tumor tissue

➤ Lysophosphatidylcholine



Meyer zu Heringdorf D, et al.
Biochim Biophys Acta. 2007

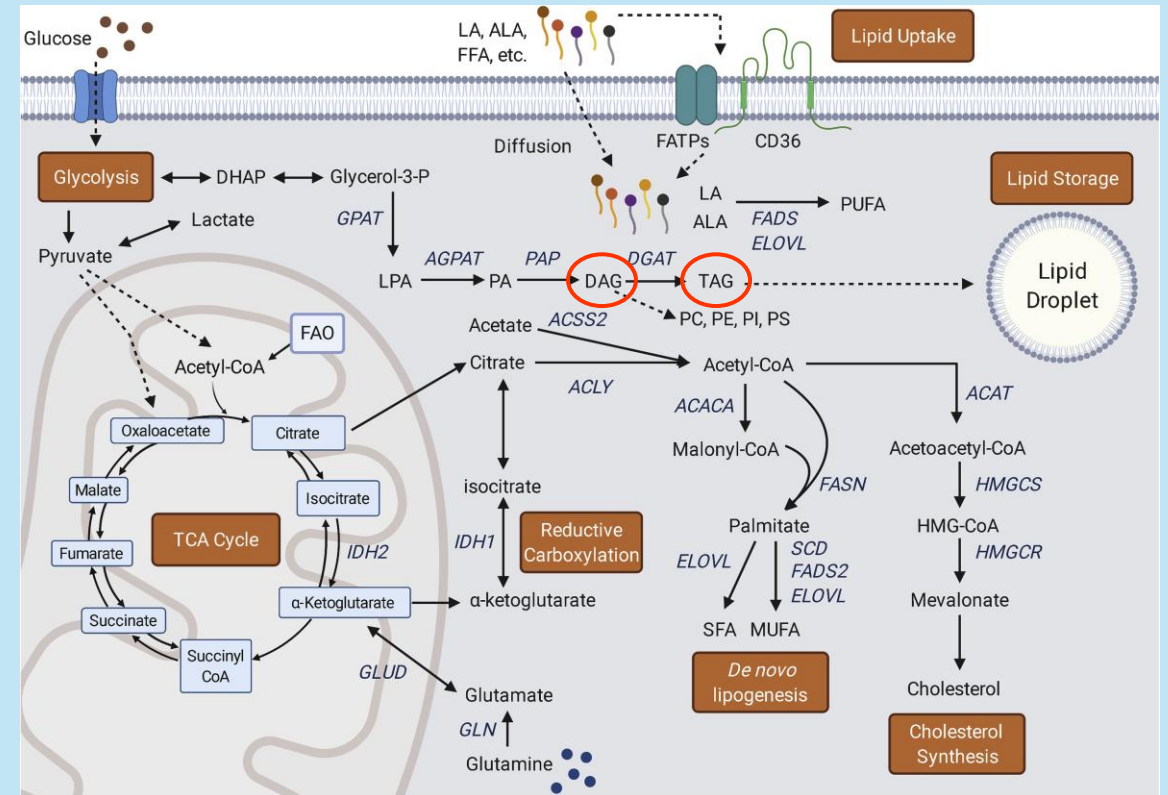


Munro S. Cell. 2003

Signal transduction

Decreased lipids in tumor tissue

➤ Glycerides



Broadfield LA, et al. Dev Cell. 2021

Energy Sources

Conclusions

- Lipid profiles differ between thymoma and normal thymus tissue, suggesting distinct biological characteristics of thymoma.
- Further studies with larger cohorts of thymoma patients using lipidomics are warranted to elucidate biological characteristics toward the identification of potential therapeutic targets and biomarkers for treatment selection .