

KSMS 2016 12th KSMS Winter Symposium

Systems metabolomics of covariaced multi-component biomarker for different autoimmune diseases

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Index

01 / Abstract

02 / Introduction

03 / Material & Method

04 / Results

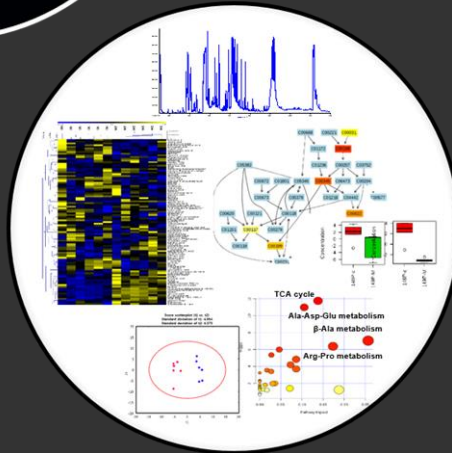
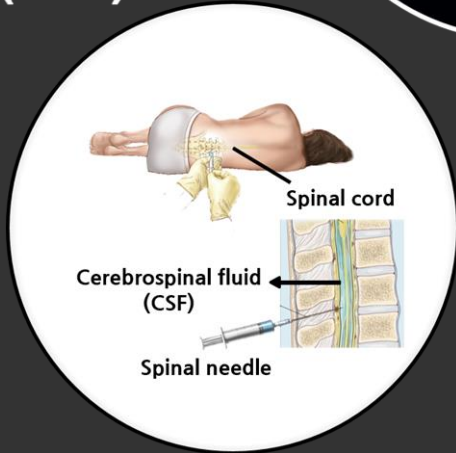
05 / Conclusions

Autoimmune diseases

Cerebrospinal fluid (CSF)



Systems metabolomics



Biomarker

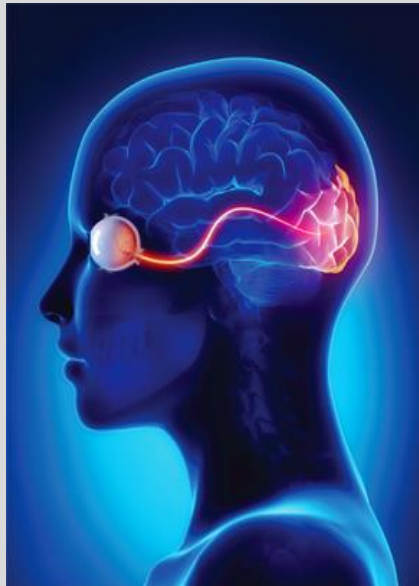


Autoimmune disease

Multiple sclerosis



Neuromyellitis optica spectrum disease

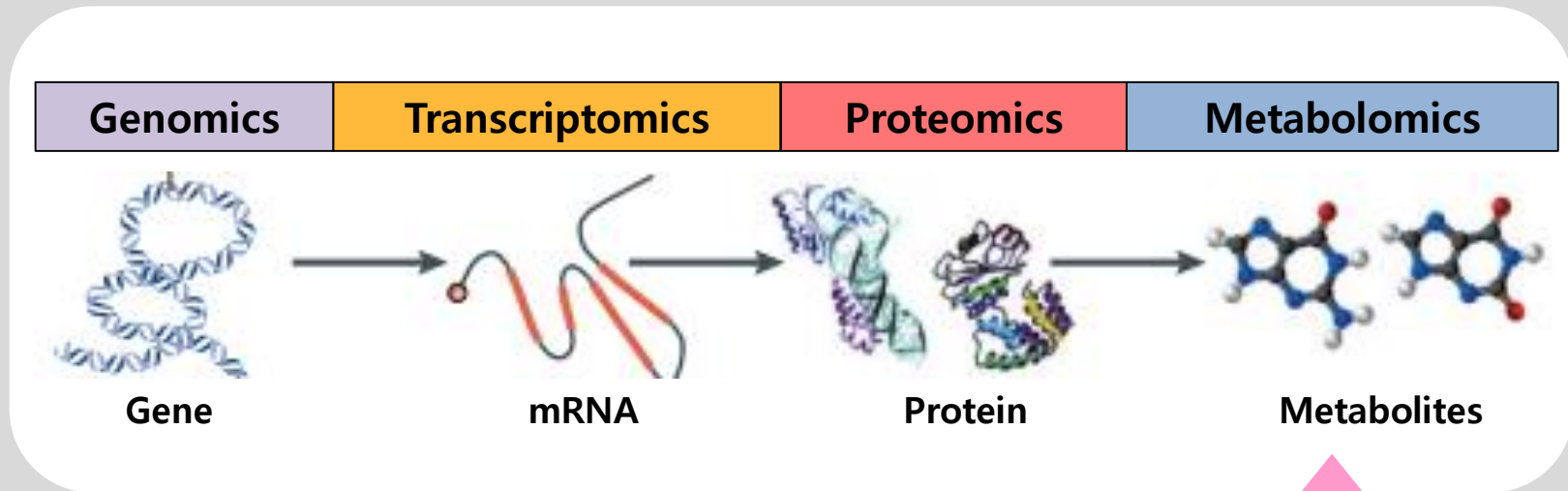


Myelitis

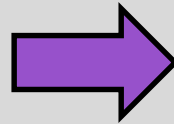


- ✓ **Differentiation** among three diseases is extremely **difficult**

Metabolomics



Separation methods
Detection methods
Statistical methods



Quantify and
Identify
metabolites

Materials

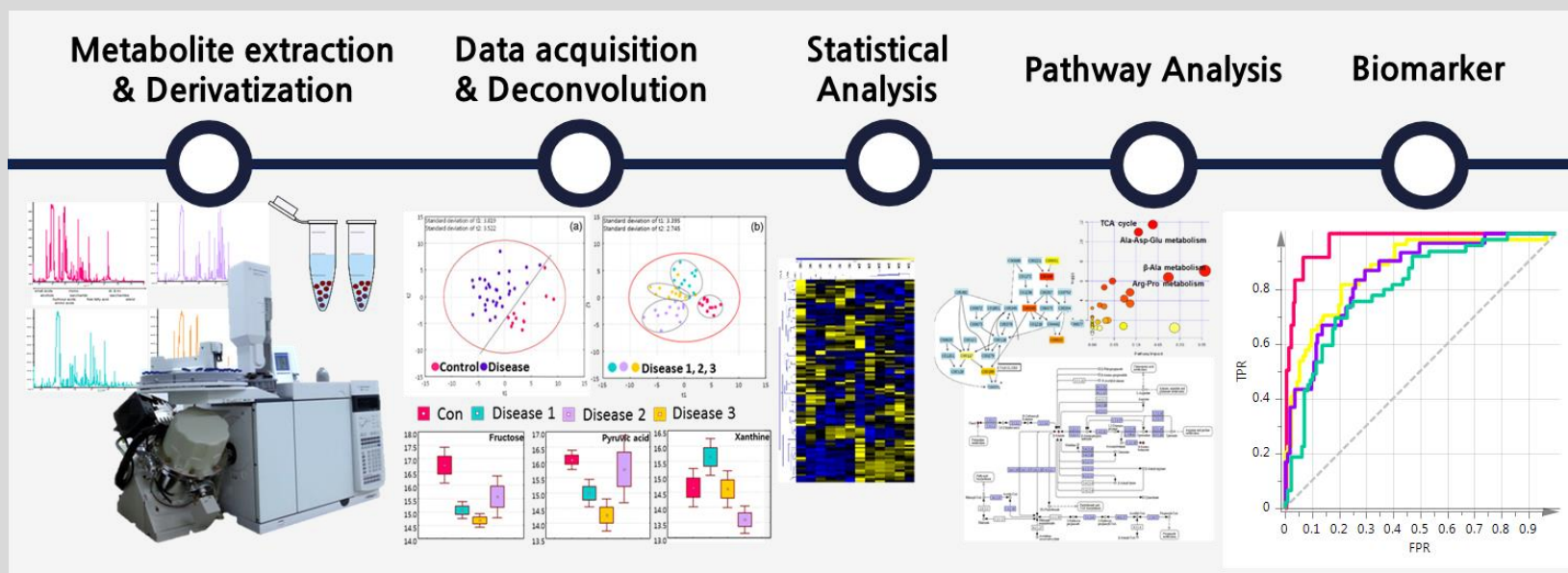
► 145 cerebrospinal fluid (CSF) samples

Control	MS	NMOSD	Myelitis
12	54	49	30

— Clinical data

Age / Gender / Diagnosis / Relapse / Steroid pulse / PD / IFN / Protein / IgG / WBC / OCB

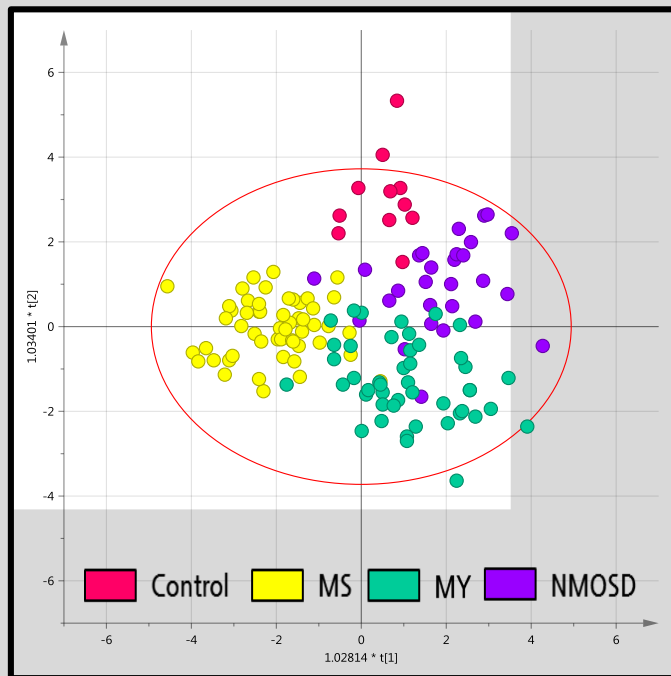
Workflow



Supervised multivariate statistics

► Orthogonal Partial Least Squares Discriminant Analysis (O2PLS-DA)

- Metabolite : 85ea , Clinical Data : 2ea
- Differential metabolic phenotypes according to diseases

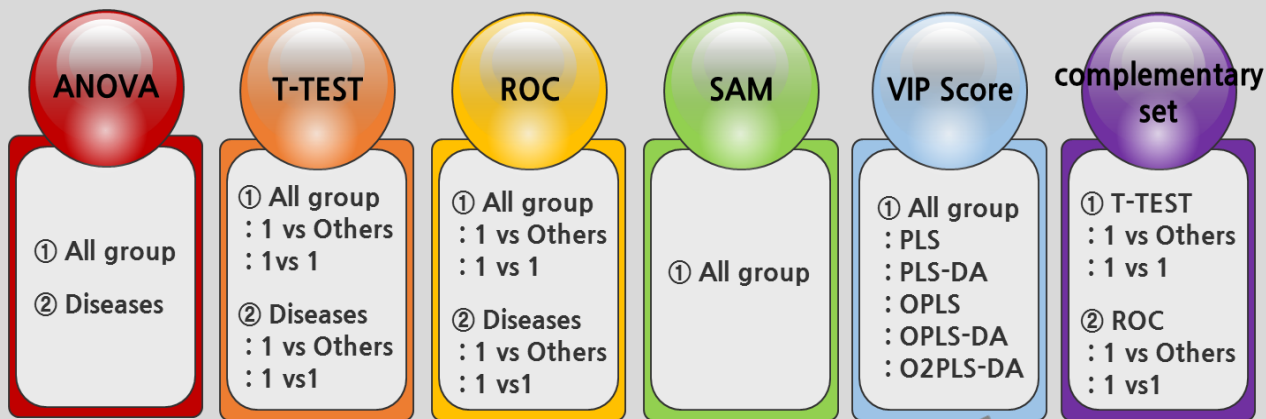


* Misclassification table

	Members	Correct	Control	MS	Myelitis	NMOsD	No class (YPred <= 0)
Control	11	90.91%	10	1	0	0	0
MS	53	98.11%	0	52	0	1	0
Myelitis	28	85.71%	0	1	24	3	0
NMOsD	46	78.26%	0	6	4	36	0
No class	0		0	0	0	0	0
Total	138	88.41%	10	60	28	40	0

Selection of Important Differential Metabolites

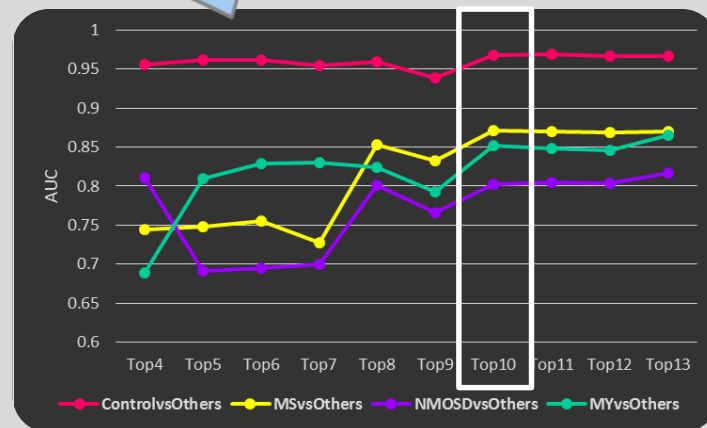
► Screen the Metabolite composite



► Variable Importance score of PLS-DA

— Top 10

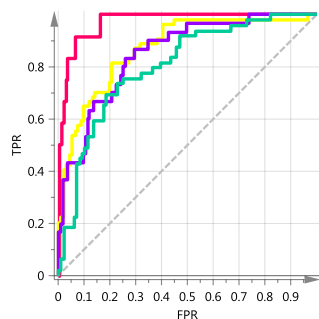
Threose	Inosine
Lactic acid	Phenylacetic acid
1-monostearin	Phenylalanine total
1-monopalmitin	Leucine
3-hydroxypropionic acid	Myristic acid



Biomarker

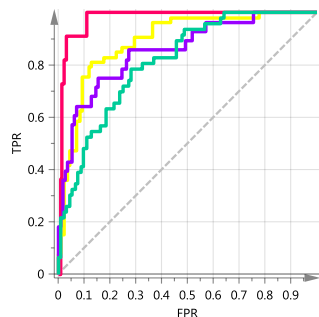
► Receiver operating characteristic curve (ROC)

Metabolite : 10ea (VIP Score Top 10)



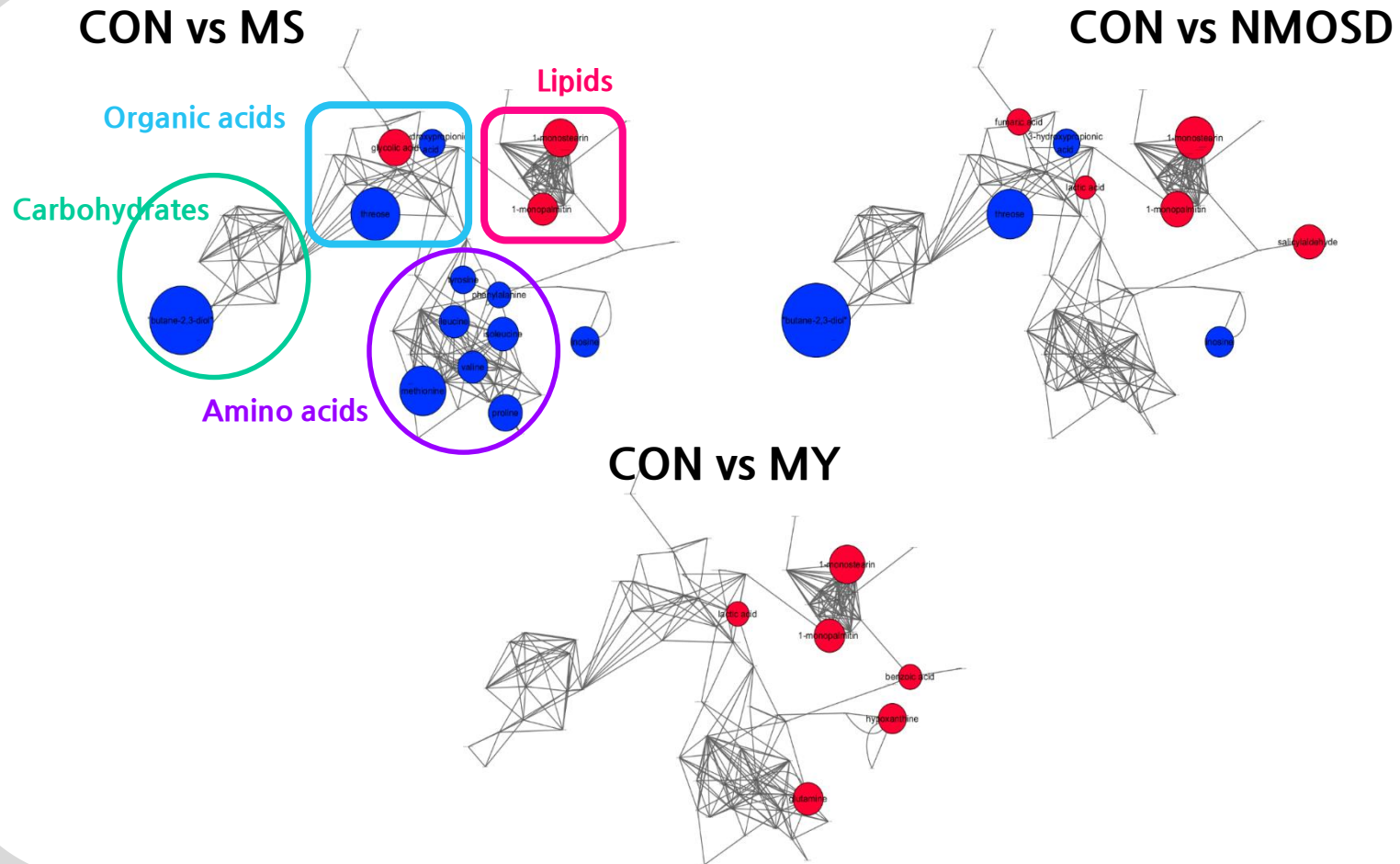
	AUC
Control vs Others	0.968
MS vs Others	0.872
NMOSD vs Others	0.803
MY vs Others	0.852

Metabolite : 8ea (VIP Score Top 8) + Clinical Data : 2ea (Protein, IgG)



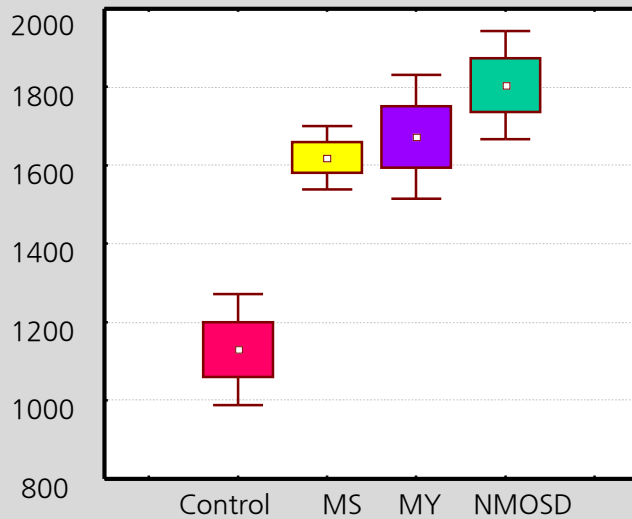
	AUC
Control vs Others	0.976
MS vs Others	0.892
NMOSD vs Others	0.813
MY vs Others	0.855

Multi-factor interactive disease metabolic network

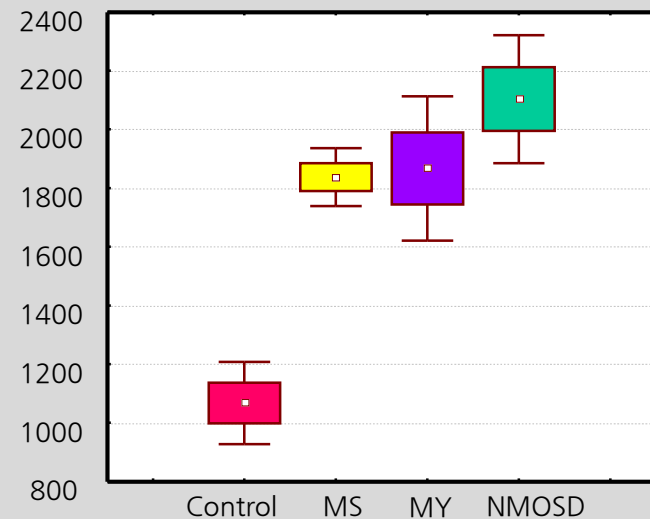


Disease-shared and -specific biomarkers

1-monopalmitin



1-monostearin



Conclusions

- ▶ **Unique metabolic phenotype of different type of AI diseases**
- ▶ **Construction of multivariate statistical discriminant model**
- ▶ **Discovery of authentic biomarker panel and validation**
- ▶ **Biochemical characterization of AI disease at the metabolic network level**

Thank you

