



Drug and Biomarker Discovery

by HMT's Next-gen Metabolomics

Human Metabolome Technologies (HMT) has been providing metabolome analysis service to researchers worldwide since 2003 and contributed to over 6,000 projects with more than 500 publications. Continuously innovating CE-MS-based metabolomics technology, HMT dramatically improved analytical sensitivity and coverage of target metabolites recently and developed a sophisticated chemoinformatics approach for predicting the structure of unknown compounds, with which dozens of new metabolites were successfully identified. Taken together, HMT introduces a novel solution for elucidating drug efficacy and toxicity mechanisms and discovering patient stratification biomarkers using the cutting-edge metabolomics technologies.

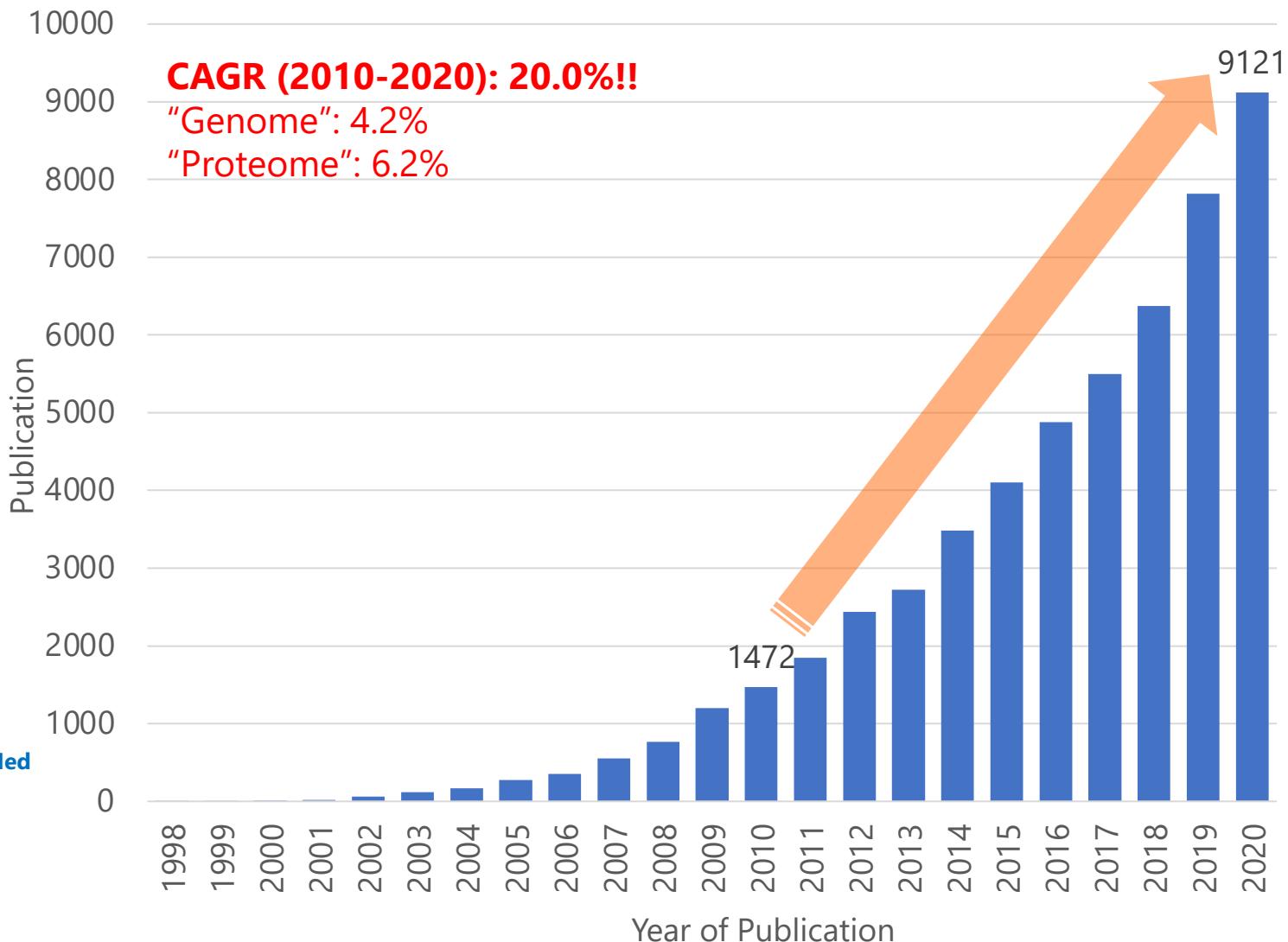
Company Profile

Basic Information

- **Business**
 - ✓ **Metabolome analysis service**
 - ✓ **Biomarker development**
- **Foundation** : July 1st, 2003 from Keio University
- **IPO** : TSE Mothers in 2013
- **Employees** : 78 (As of April 2021)
- **President** : Katsuhito Hashizume
- **Headquarter**: Tsuruoka, Yamagata, Japan
- **Sales office** : Tokyo, Japan
- **Subsidiary** : HMT America (Boston, USA)
HMT Europe (Leiden, Netherlands)
- **Major clients**: Academic institutions, pharma, food and cosmetics companies worldwide



Metabolomics Market Growth

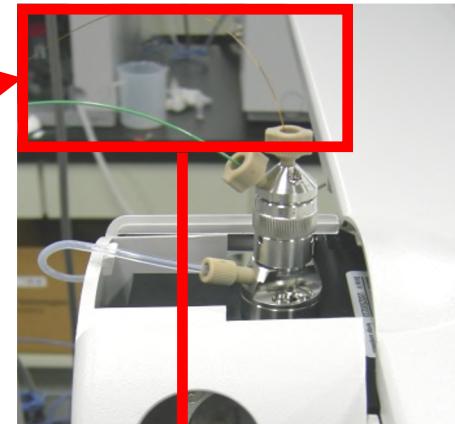
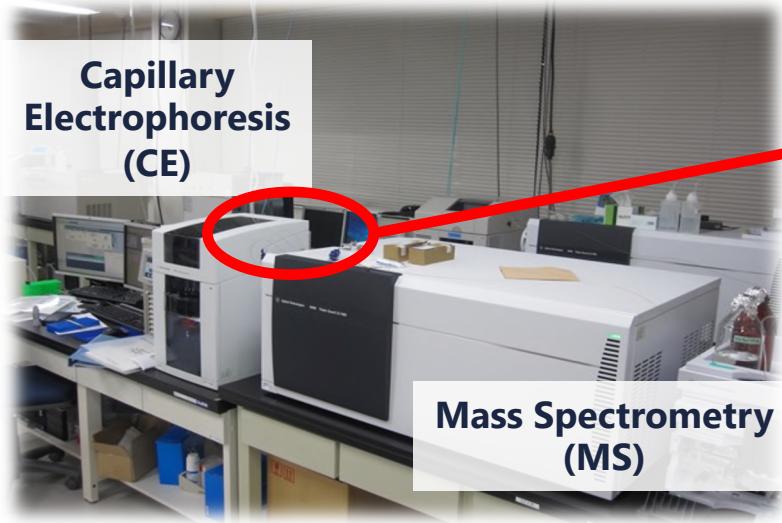


Search key in PubMed
"metabolomic OR
metabolome OR
metabolomics OR
metabonomic OR
metabonomics OR
metabonome"

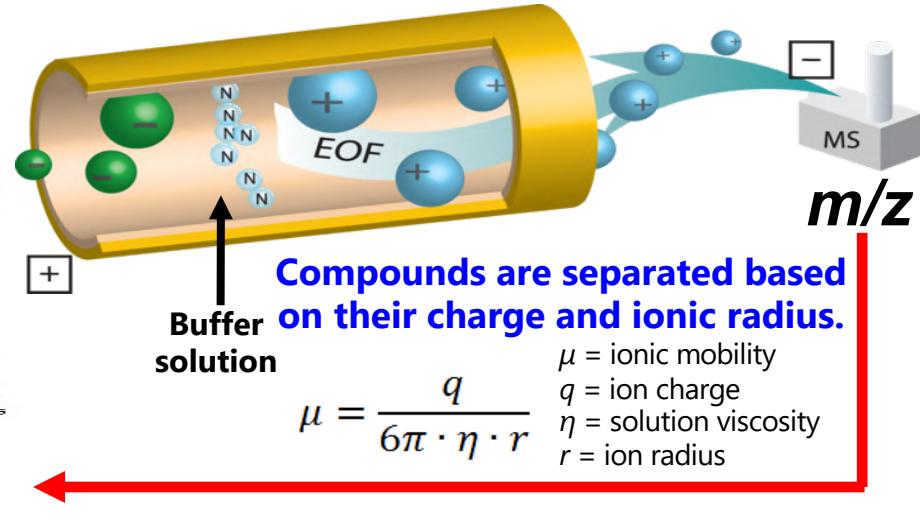
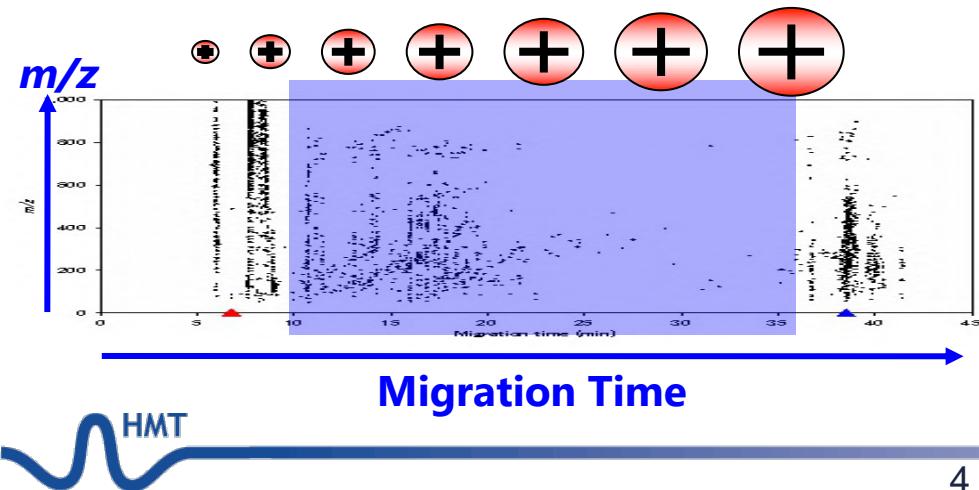


CE-MS-based Metabolomics

Best platform for comprehensive analysis of hydrophilic metabolites

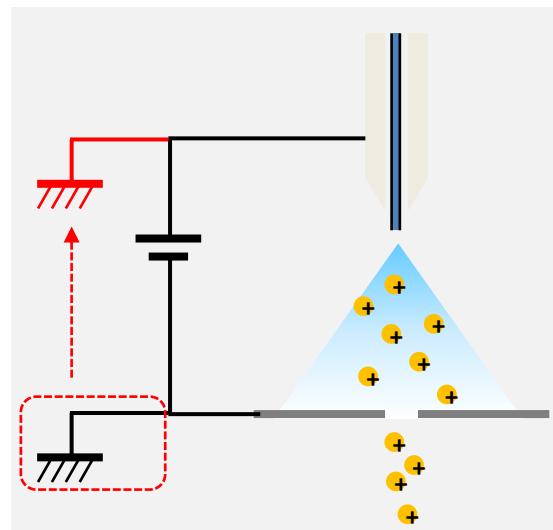


Compounds are measured separately based on their mass and time.



CE-FTMS: World's Only Platform

Agilent's CE &
Thermo's Orbitrap MS
connected by a
patented ESI adaptor



Patented Technology

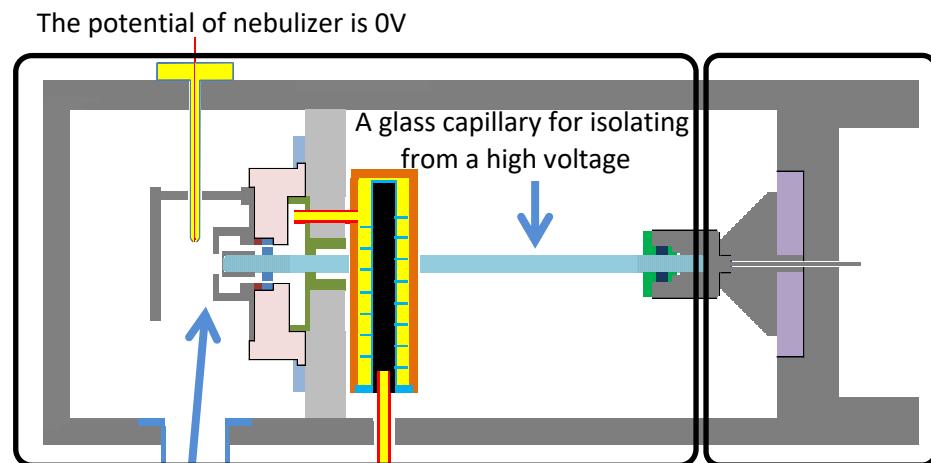
World's only platform combining
CE with high separation power and
Orbitrap with high resolution & sensitivity

- **10-fold inc. in sensitivity**
- **2-fold inc. in # metabolites detected**

Potential discovery of novel metabolites
that have never been detected by the
other platforms based on LC- or GC-MS



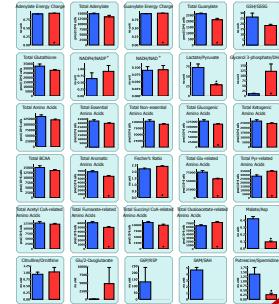
Best-suited to
• **Comprehensive Metabolomics**
• **Biomarker Discovery**



**METABOLOMIC PROFILE OF
MCF-10A CELLS**
IN COLLABORATION WITH PROF BRUGGE & DR. COLOFF
HARVARD MEDICAL SCHOOL, MA, USA
(FROM LEFT TO RIGHT)
DMSO VS MEK INHIBITOR (N=3)

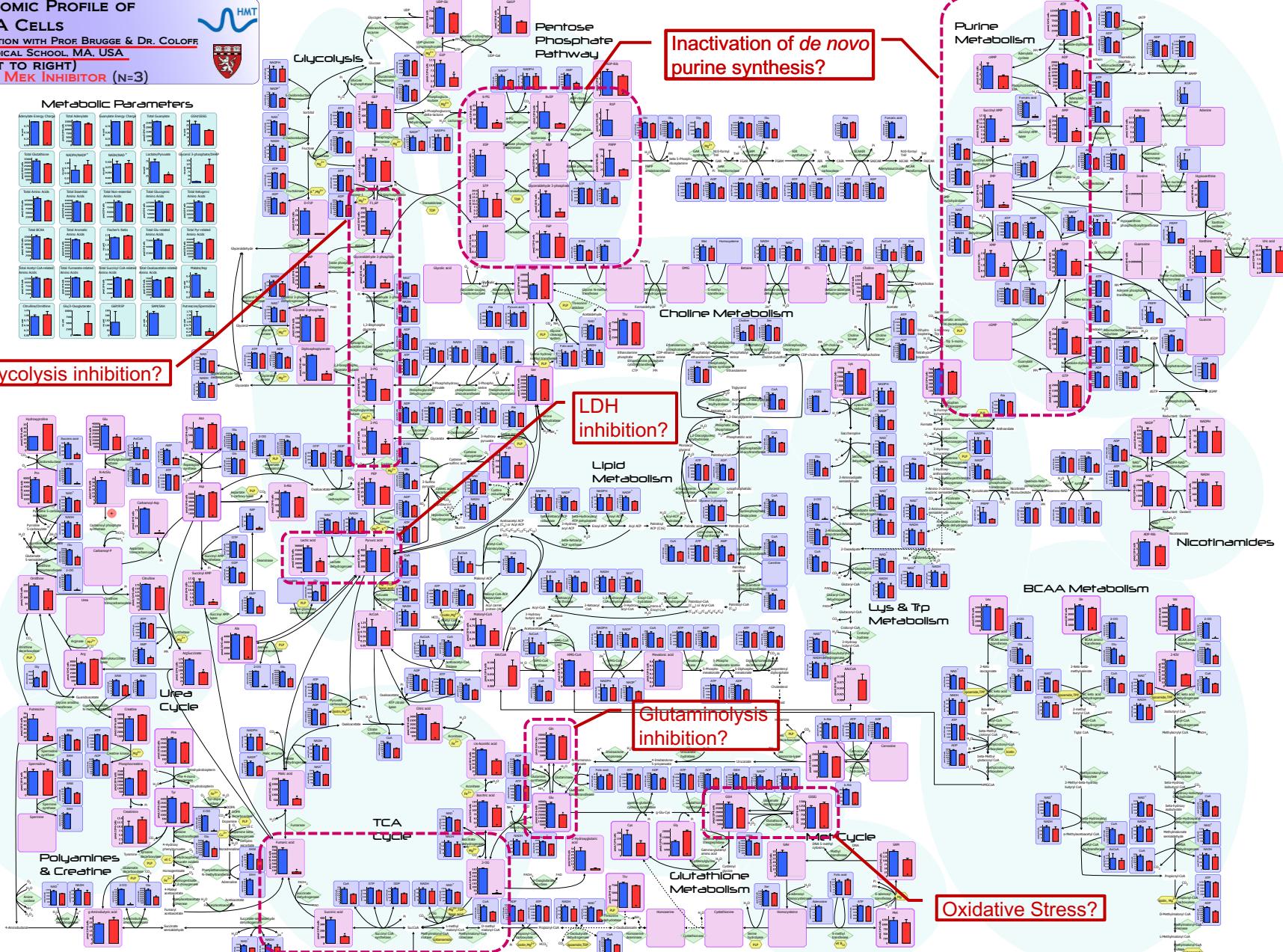


Metabolic Parameters



Glycolysis inhibition?

Inactivation of de novo purine synthesis?



HMT CARCINOSCOPE

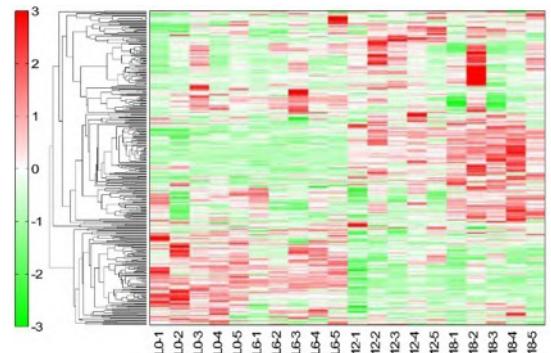
TCA inactivation?

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* HMT's C-SCOPE contributed to this study.

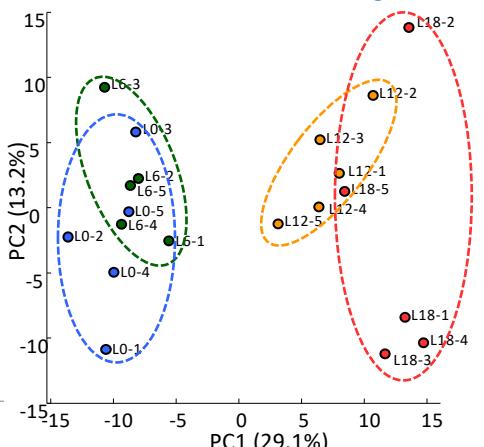
Data Analysis & Interpretation Support

Statistical Analysis

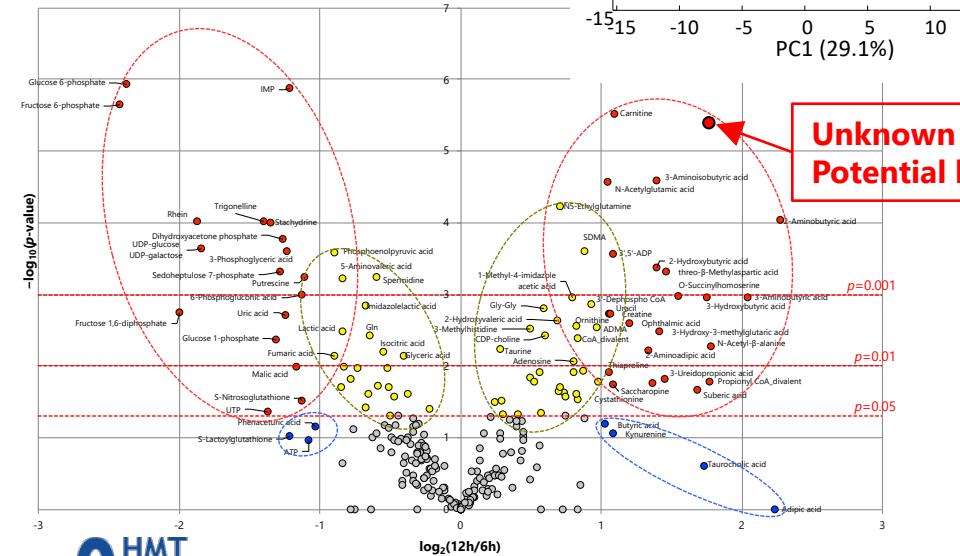


Cluster Analysis

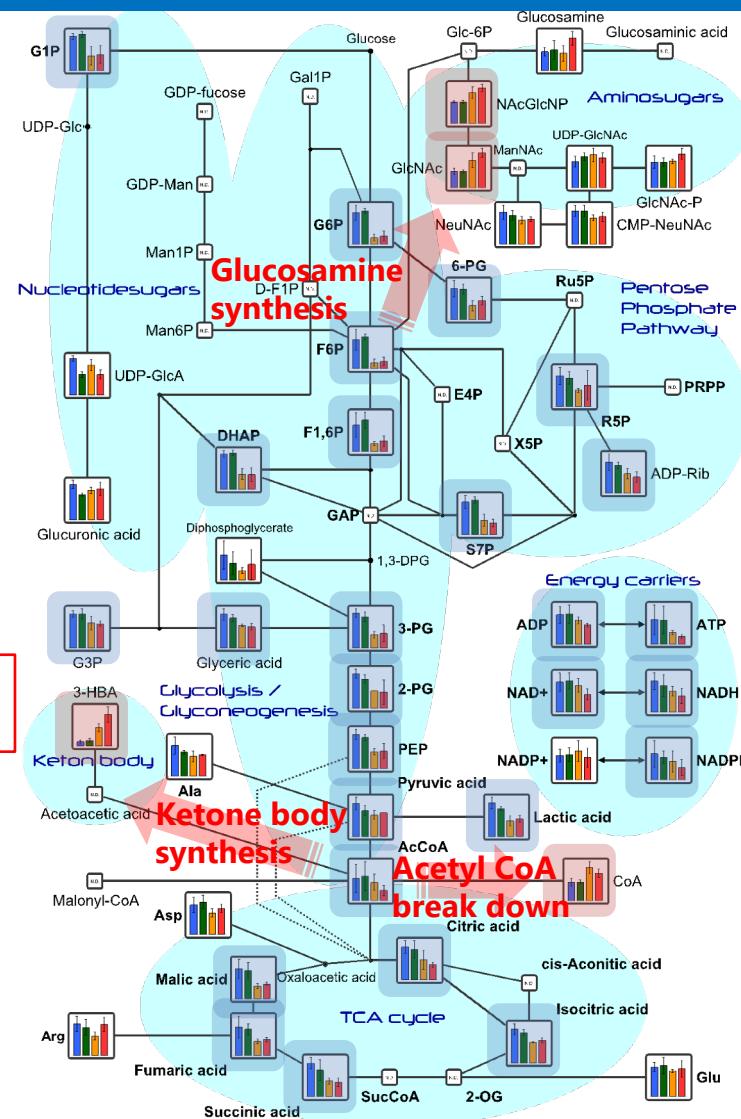
Principal Component Analysis



Volcano Plot



Pathway Map



Unexplored Metabolomic Space

Comprehensive Metabolome
???,???,???

PubChem DB
109,908,881

Human Metabolome DB
Detected & Predicted
115,398

Human Metabolome DB
Detected
9,419

Compounds
unknown

Compounds
reported

Metabolome
in human



Source:
<https://hmdb.ca/>
<https://pubchem.ncbi.nlm.nih.gov/>
as of 2021/5/24

ω Search – Structure Prediction

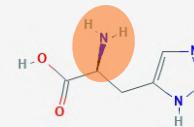
MS/MS × Chemoinformatics
= Structure Elucidation

“Michi-taro”
Precursor
search

MT
estimation

MS/MS
Finger-
printing

Precursor



Histidine

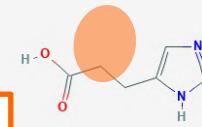


-NH

Score 0.96

Almost identical
except -NH₂ group

Candidate structure

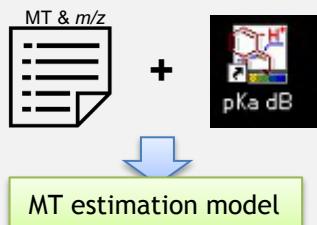


1H-Imidazole-
4-propionic acid

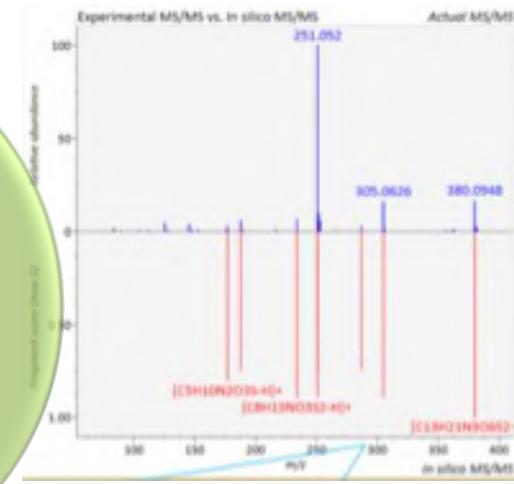
Ranking based on the structural
similarity of candidates & targets

MT estimation model

Model prepared by MT, m/z & theoretical
pKa of metabolites in the HMT library



Ranking based on the similarity
of actual & estimated MTs

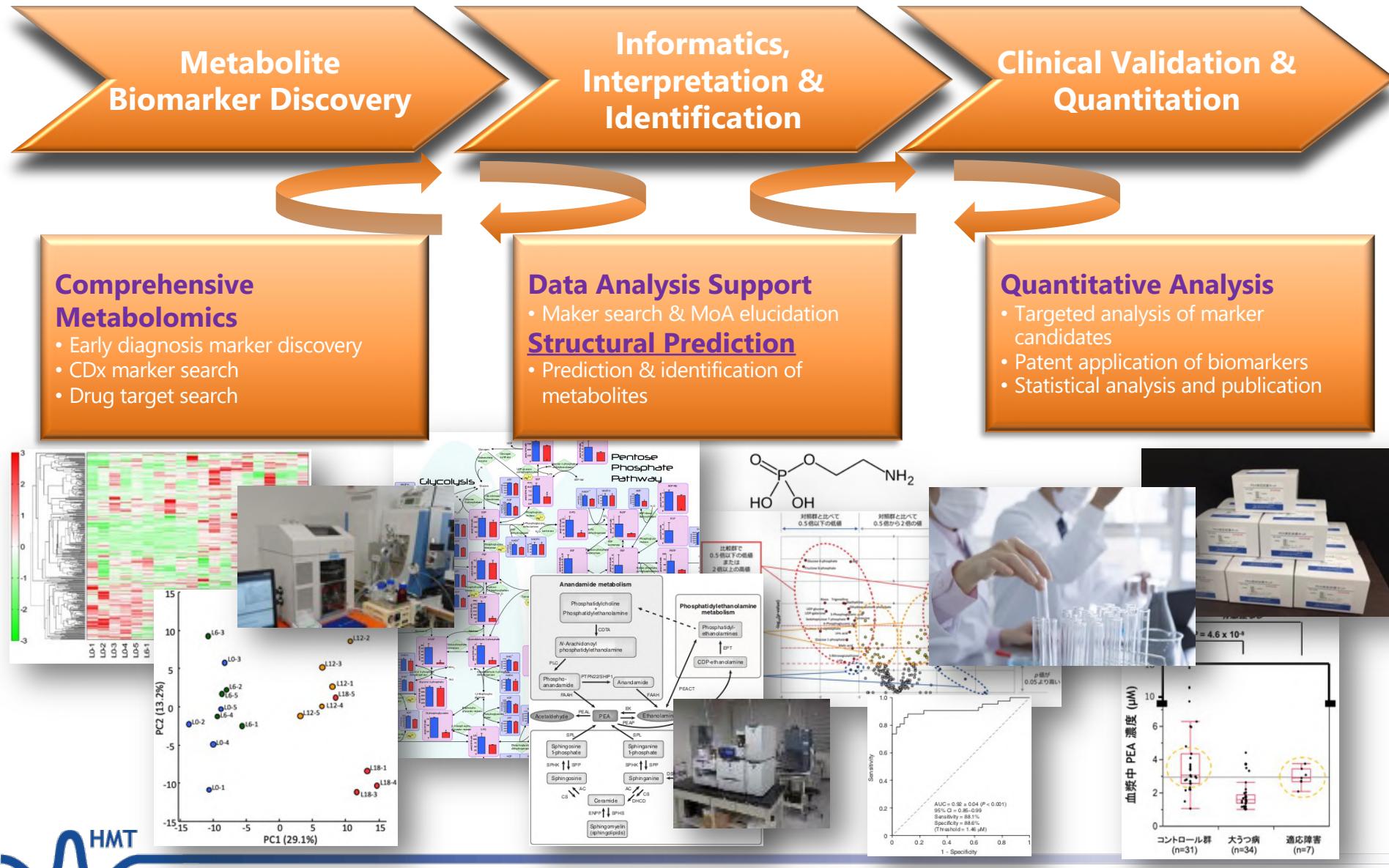


Ranking based on the similarity of
actual & simulated MS/MS spectra

Combining the 3 results for extracting the most likely structure



Total Solution for Drug Dev. & Biomarker Discovery



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