

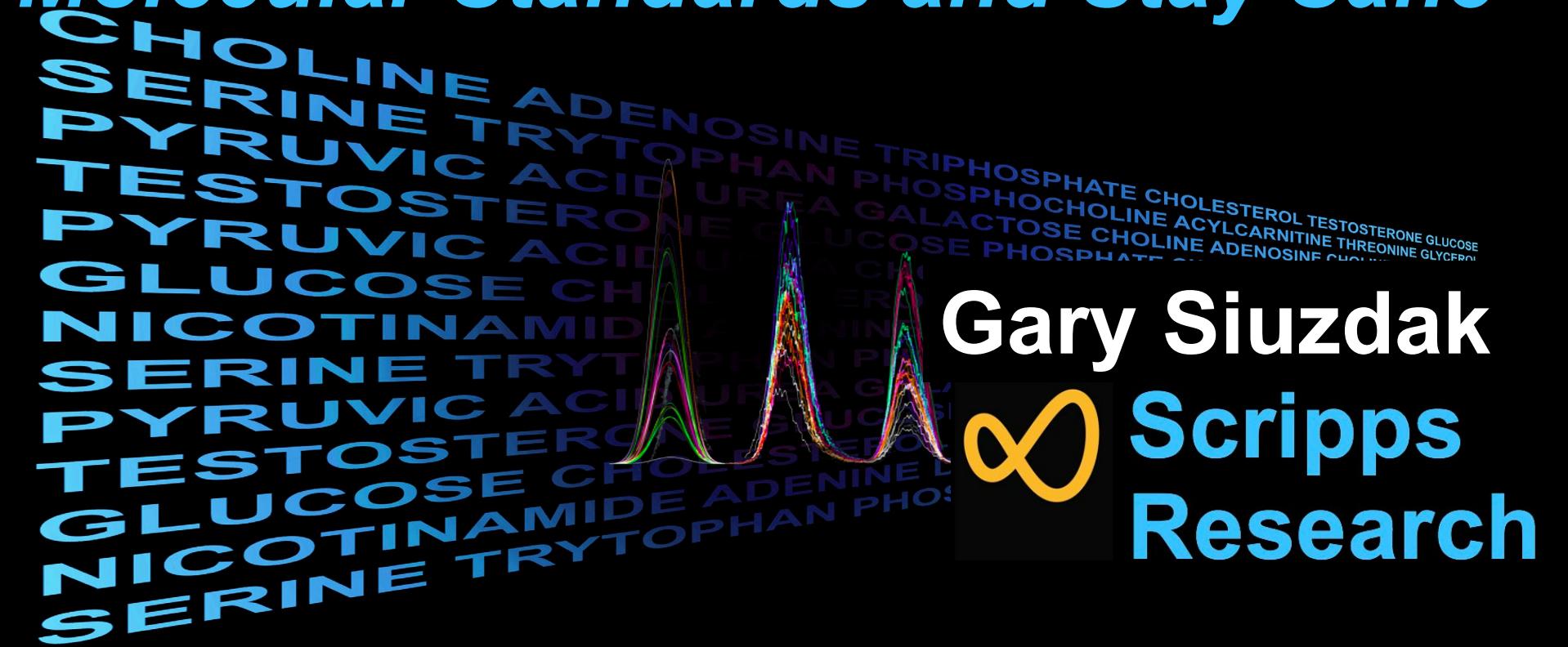
# *METLIN Ion Mobility (downloadable)*



A mass spectrometry peak plot showing several sharp, multi-colored peaks against a black background. The peaks are arranged in three distinct groups along the x-axis. Overlaid on the plot are numerous metabolite names in various colors, rotated diagonally for readability. The labels include: CHOLINE, SERINE, ADENOSINE, PYRUVIC ACID, TESTOSTERONE, PYRUVIC ACID, GLUCOSE, NICOTINAMIDE, SERINE, TRYPTOPHAN, PYRUVIC ACID, TESTOSTERONE, GLUCOSE, CHOLESTEROL, SERINE, TRYPTOPHAN, PYRUVIC ACID, TESTOSTERONE, GLUCOSE, NICOTINAMIDE, and SERINE. To the right of the plot, the name "Gary Siuzdak" is written in large white letters above the Scripps Research logo, which consists of a stylized infinity symbol followed by the text "Scripps Research".

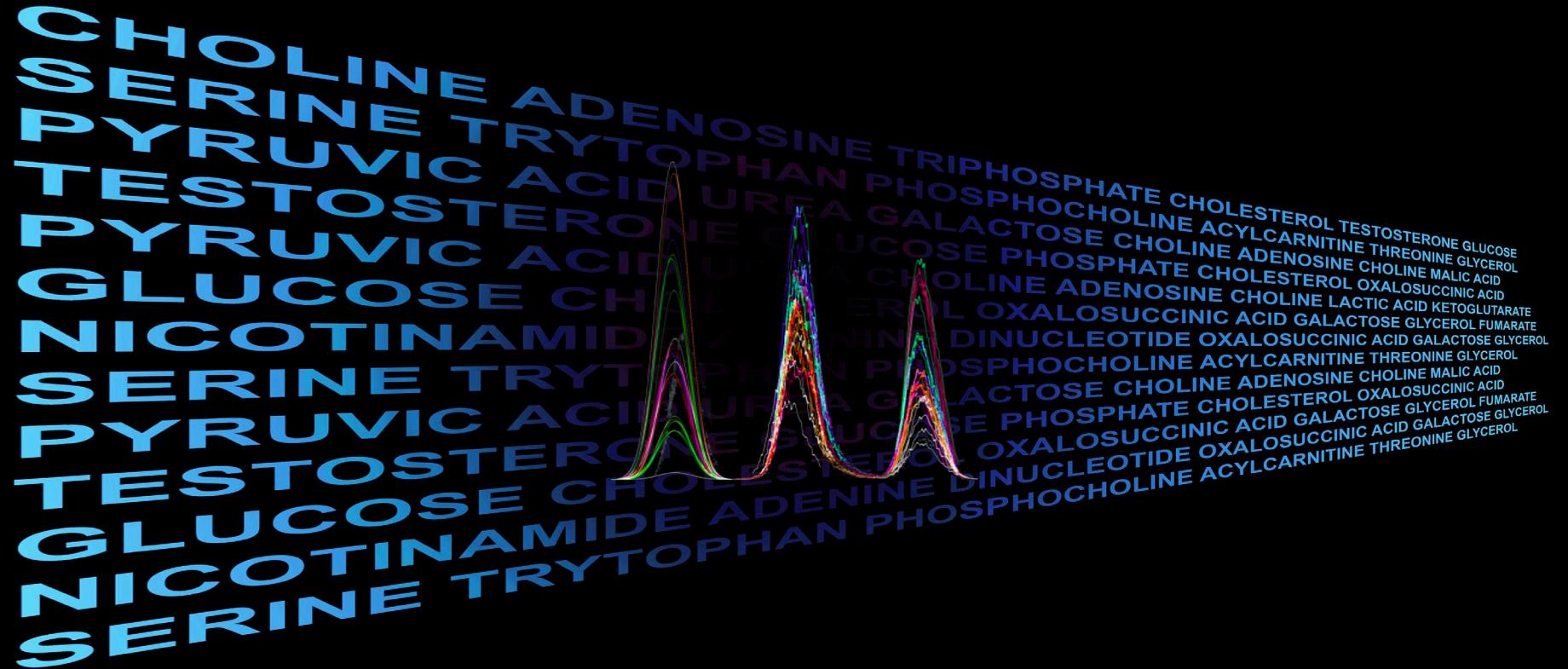
# *METLIN Ion Mobility* *(downloadable)*

*How to Analyze a Million  
Molecular Standards and Stay Sane*

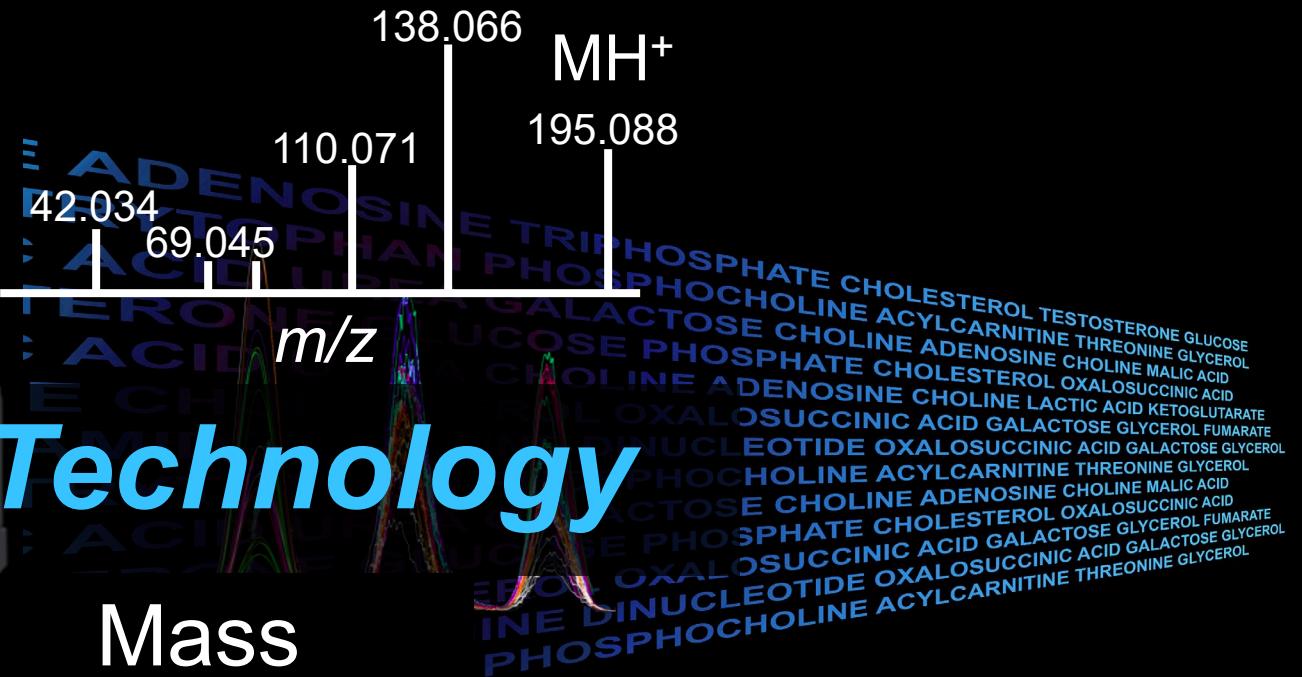


Gary Siuzdak  
Scripps  
Research





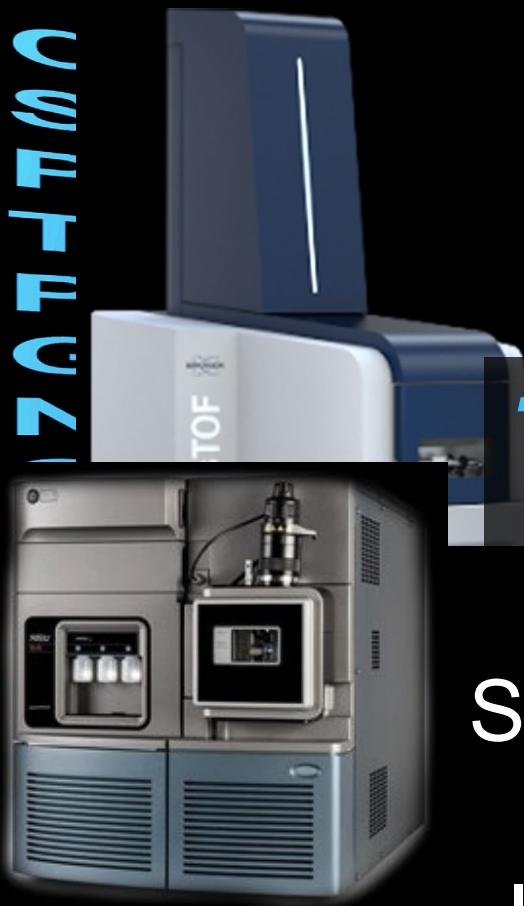
USFTF



# Technology

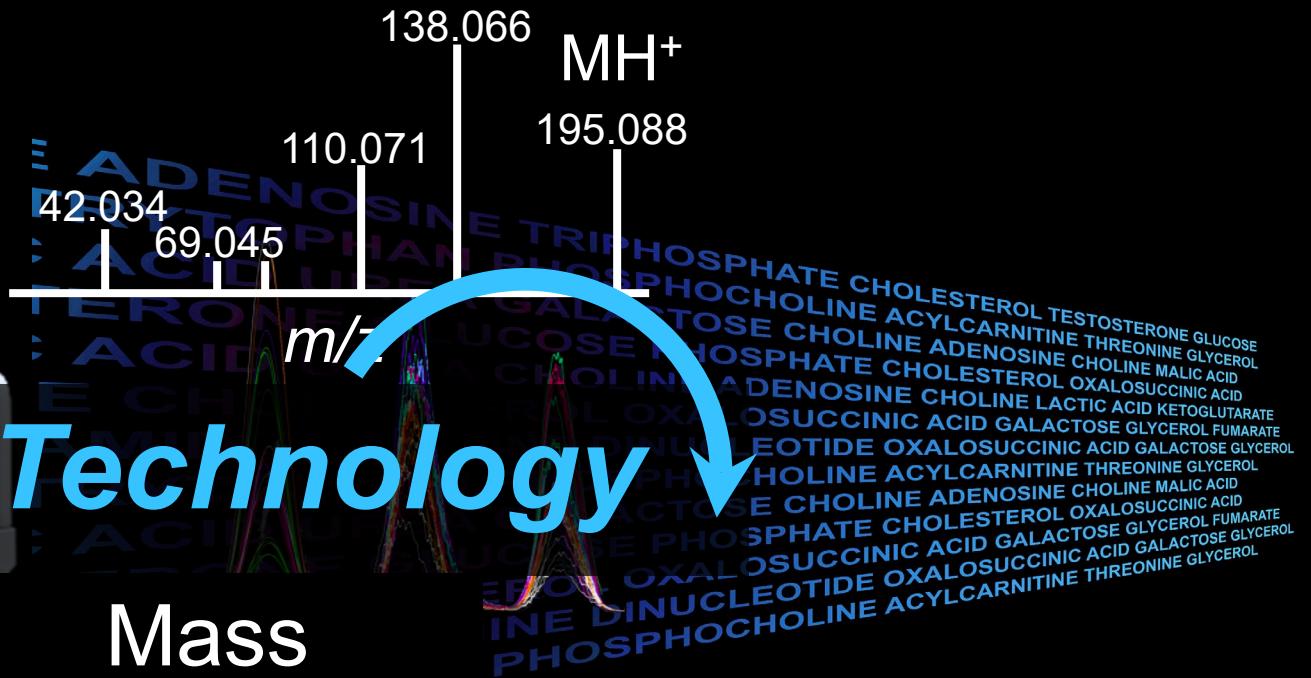
## Mass Spectrometry & Ion Mobility

USFTFC

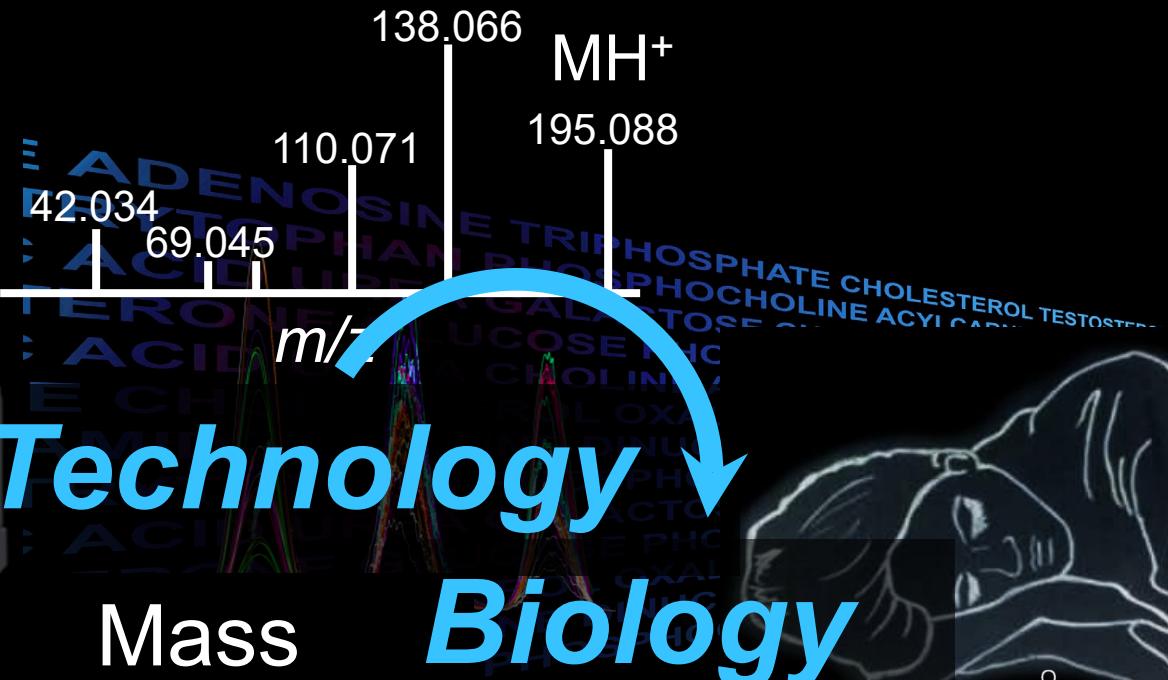


# Technology

## Mass Spectrometry & Ion Mobility

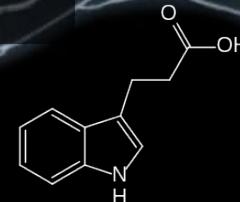
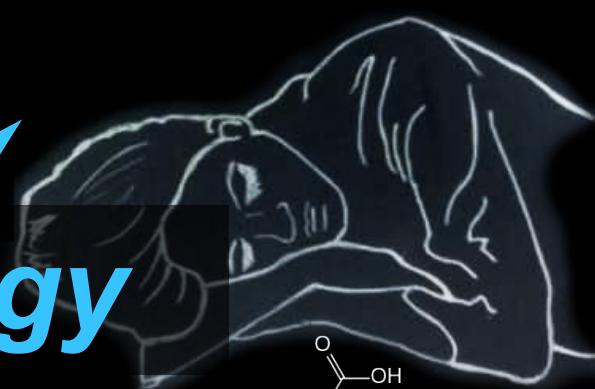


USFTF

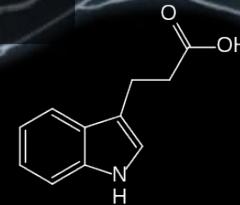
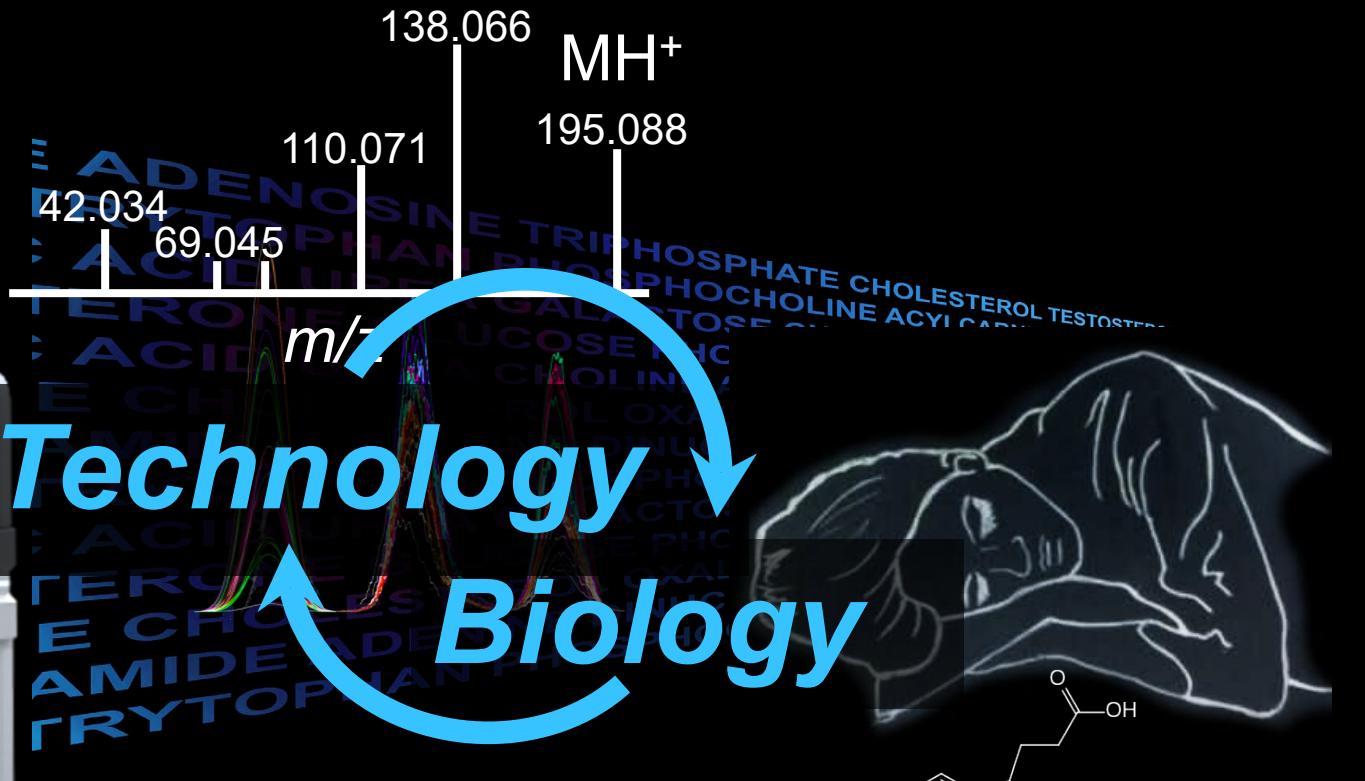
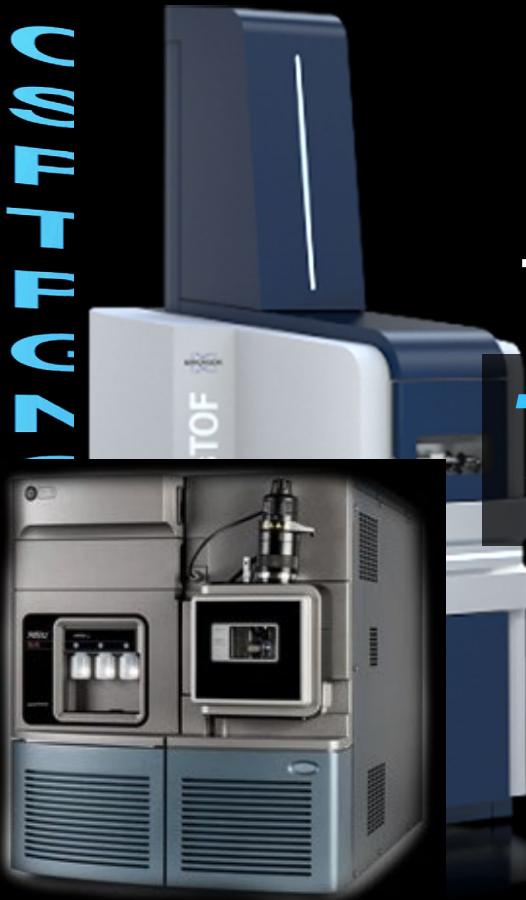


# Technology Mass Spectrometry & Ion Mobility

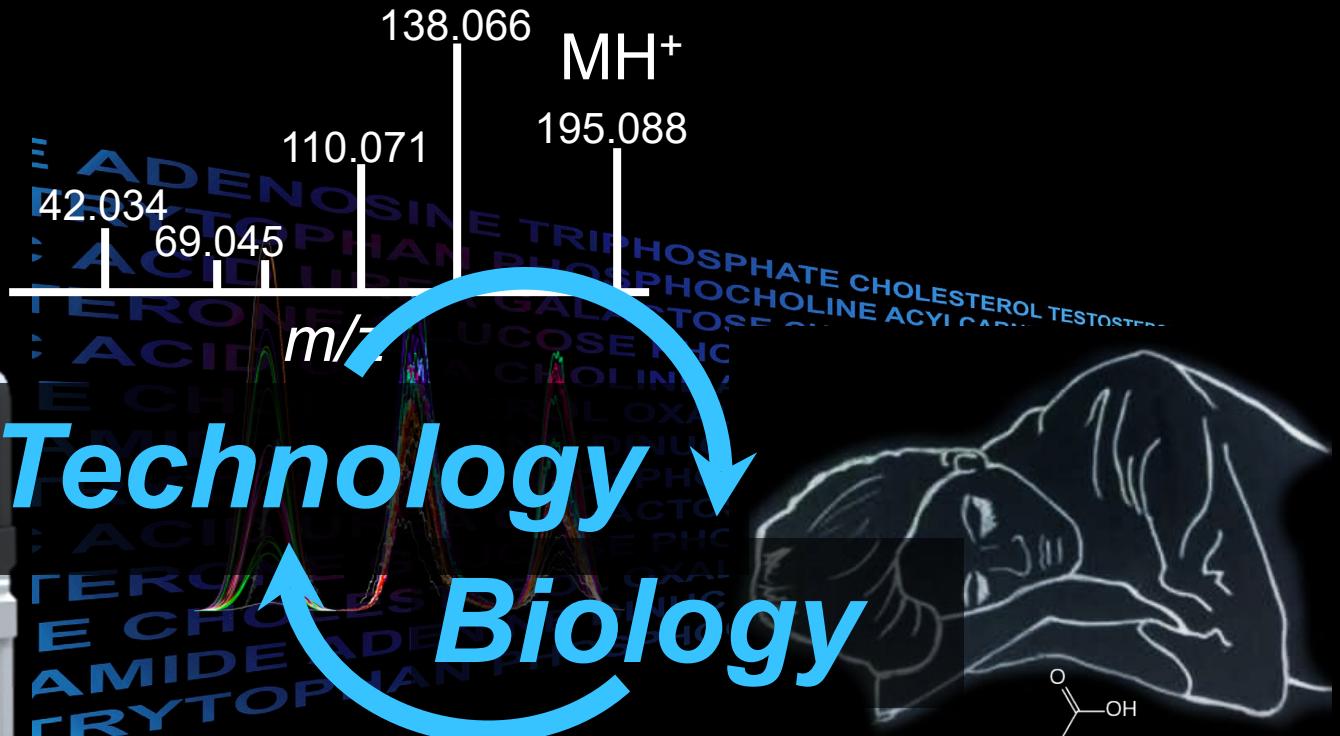
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USFTF

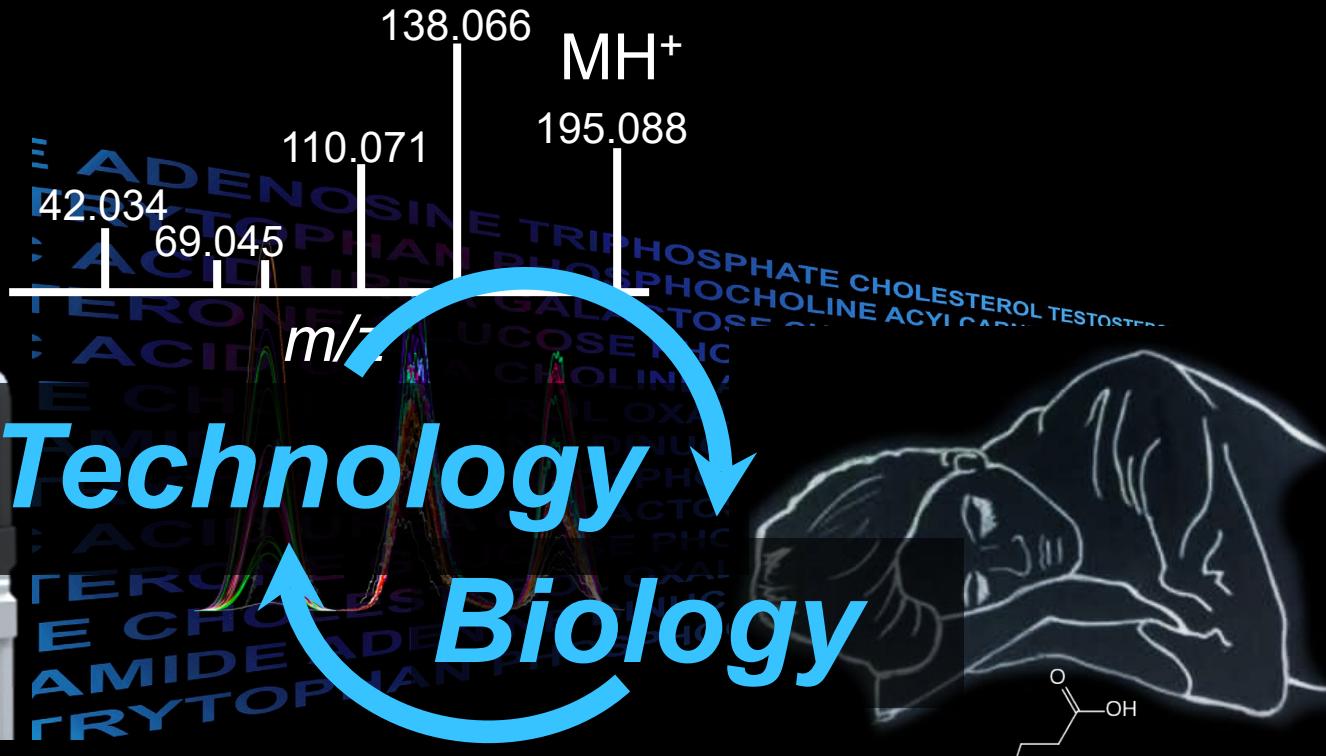


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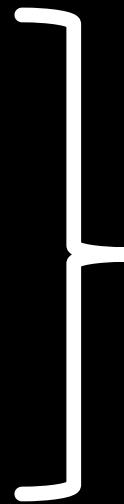


<i>PNAS</i>	1994
<i>Science</i>	1995
<i>Ther. Drug Dis.</i>	2005
<i>Nature Biotech.</i>	2012
<i>Nature Methods</i>	2020
<i>Cell Metabolism</i>	2022
<i>J. Amer. Soc. MS</i>	2022

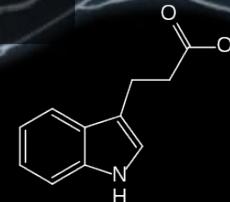
USFTF



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<i>Cell Metabolism</i>	2022
<i>J. Amer. Soc. MS</i>	2022



*One Simple  
Motivation*



CH<sub>3</sub>



# Sleep

CH<sub>3</sub> TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
AN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
EA GALACTOSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
EA CHOLINE ADENOSINE CHOLESTEROL OXALOSUCCINIC ACID  
STEROL OXALOSUCCINIC ACID GALACTOSE LACTIC ACID KETOGLUARATE  
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STEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
DENINE DINUCLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
AN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL

# Sleep

***PNAS 1994, Science 1995, & Anal. Chem. 2006***



DINE TRIPHOSPHAN PHOSPHOCHEA GALACTOSE  
GLUCOSE PHOS EA CHOLINE AD  
STEROL OXALO  
DENEINE DINUCLE  
DANE PHOSPHOCHEA GALACTOSE  
GLUCOSE PHOS STEROL OXALO  
DENEINE DINUCLE  
DANE PHOSPHOCH



# Richard Lerner

OSE  
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XCMSOnline.scripps.edu

DINE TRIPHOSPHAT  
EA PHOSPHOC  
EA GALACTOSE  
GLUCOSE PHOS  
EA CHOLINE AD  
STEROL OXALO  
DENEINE DINUCLE  
AN PHOSPHOC  
EA GALACTOSE  
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Richard  
Lerner

# Sleep

PNAS 1994, Science 1995, & Anal. Chem. 2006



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Original approach  
to process and  
statistically assess  
metabolomics data

DINE TRIPHOSPHAT  
EA PHOSPHOC  
EA GALACTOSE  
GLUCOSE PHOS  
EA CHOLINE AD  
STEROL OXALO  
DENEINE DINUCLE  
AN PHOSPHOC  
EA GALACTOSE  
GLUCOSE PHOS  
STEROL OXALO  
DENEINE DINUCLE  
AN PHOSPHOC



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ROL

Richard  
Lerner

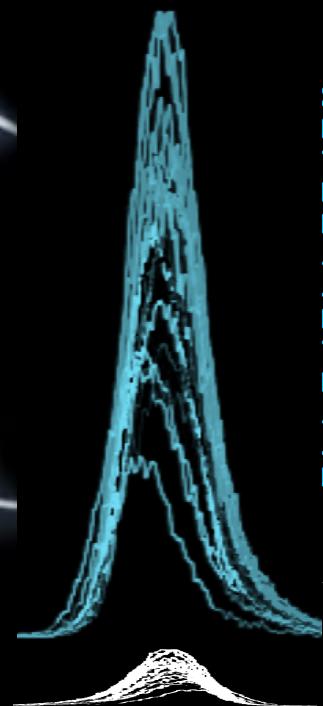
# Sleep

*PNAS 1994, Science 1995, & Anal. Chem. 2006*

CH<sub>3</sub>



SERUM



CH<sub>3</sub>, SPHATE, CHOLESTEROL, TESTOSTERONE, GLUCOSE, IOCHOLINE, ACYLCARNITINE, THREONINE, GLYCEROL, OSE, CHOLINE, ADENOSINE, CHOLINE, MALIC ACID, HOSPHATE, CHOLESTEROL, OXALOSUCCINIC ACID, E, ADENOSINE, CHOLINE, LACTIC ACID, KETOGUTARATE, ALOSUCCINIC ACID, GALACTOSE, GLYCEROL, FUMARATE, JCLEOTIDE, OXALOSUCCINIC ACID, GALACTOSE, GLYCEROL, IOCHOLINE, ACYLCARNITINE, THREONINE, GLYCEROL, OSE, CHOLINE, ADENOSINE, CHOLINE, MALIC ACID, HOSPHATE, CHOLESTEROL, OXALOSUCCINIC ACID, ALOSUCCINIC ACID, GALACTOSE, GLYCEROL, FUMARATE, JCLEOTIDE, OXALOSUCCINIC ACID, GALACTOSE, GLYCEROL, IOCHOLINE, ACYLCARNITINE, THREONINE, GLYCEROL.

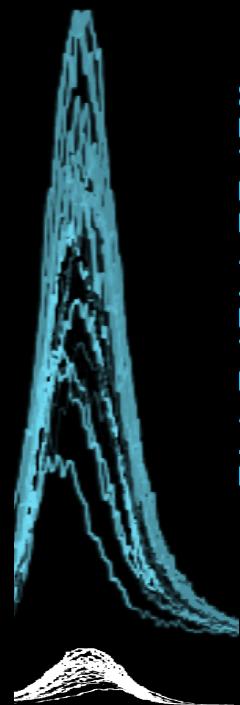
# Metabolite Identification



PHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
CHOLINE ACYLCARNITINE THREONINE GLYCEROL  
OSSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
E ADENOSINE CHOLINE LACTIC ACID KETOGUTARATE  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
JCLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
CHOLINE ACYLCARNITINE THREONINE GLYCEROL  
OSSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
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CHOLINE ACYLCARNITINE THREONINE GLYCEROL

# Metabolite Identification

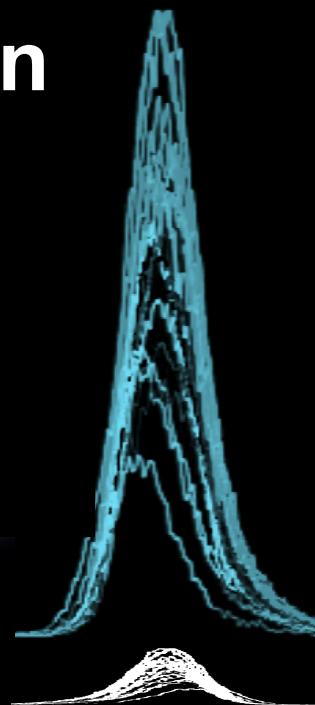
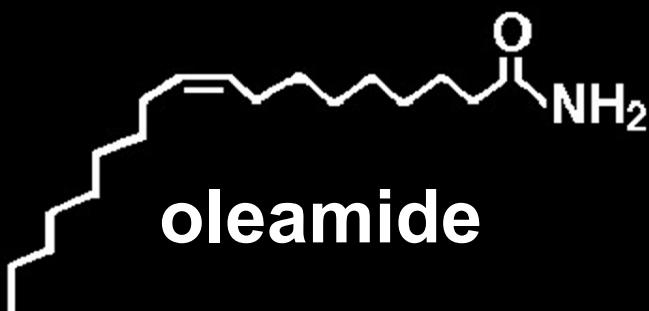
- Accurate  $m/z$
- Tandem MS/MS
- NL Interpretation
- Isotope Pattern
- Preparative LC
- Synthesis



SPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
OCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
OSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
HOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
E ADENOSINE CHOLINE LACTIC ACID KETOGUTARATE  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
JCLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
OCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
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HOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
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OCHOLINE ACYLCARNITINE THREONINE GLYCEROL

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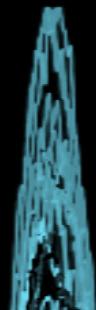
- Accurate  $m/z$
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- NL Interpretation
- Isotope Pattern
- Preparative LC
- Synthesis



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- Isotope Pattern
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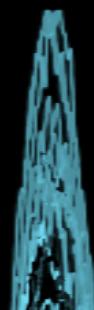


SPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
OCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
OSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
HOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
E ADENOSINE CHOLINE LACTIC ACID KETOGUTARATE  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
CLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
OCHOLINE ACYLCARNITINE THREONINE GLYCEROL

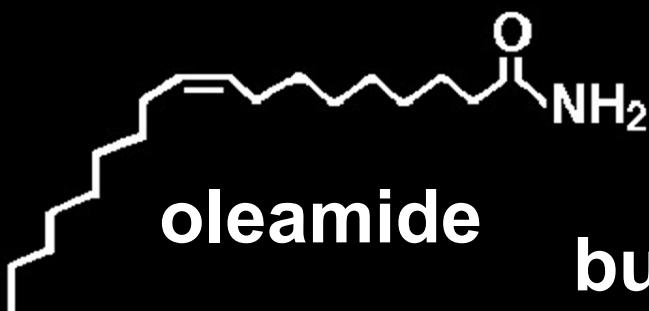


# Metabolite Identification

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- Tandem MS/MS
- NL Interpretation
- Isotope Pattern
- Preparative LC
- Synthesis



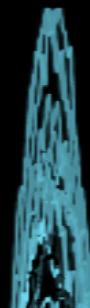
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E ADENOSINE CHOLINE LACTIC ACID KETOGLUARATE  
ALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
CLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
OCHOLINE ACYLCARNITINE THREONINE GLYCEROL



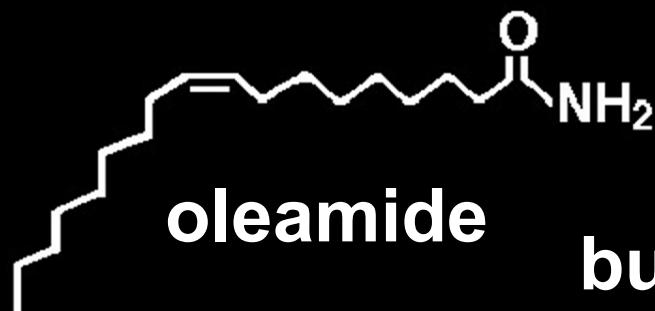
Induces a sleep-like state  
but it took 8 months to identify

# Metabolite Identification

- Accurate  $m/z$
  - Tandem MS/MS
  - NL Interpretation
  - Isotope Pattern
  - Preparative LC
  - Synthesis



**S**PHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
**I**OCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
**O**SE CHOLINE ADENOSINE CHOLINE MALIC ACID  
**H**OSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
**E** ADENOSINE CHOLINE LACTIC ACID KETOGUTARATE  
**A**LOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
**J**CLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
**L**IGULINE ACYLCARNITINE THREONINE GLYCEROL



# Induces a sleep-like state

**but it took 8 months to identify**

*A better way to identify molecules is needed*

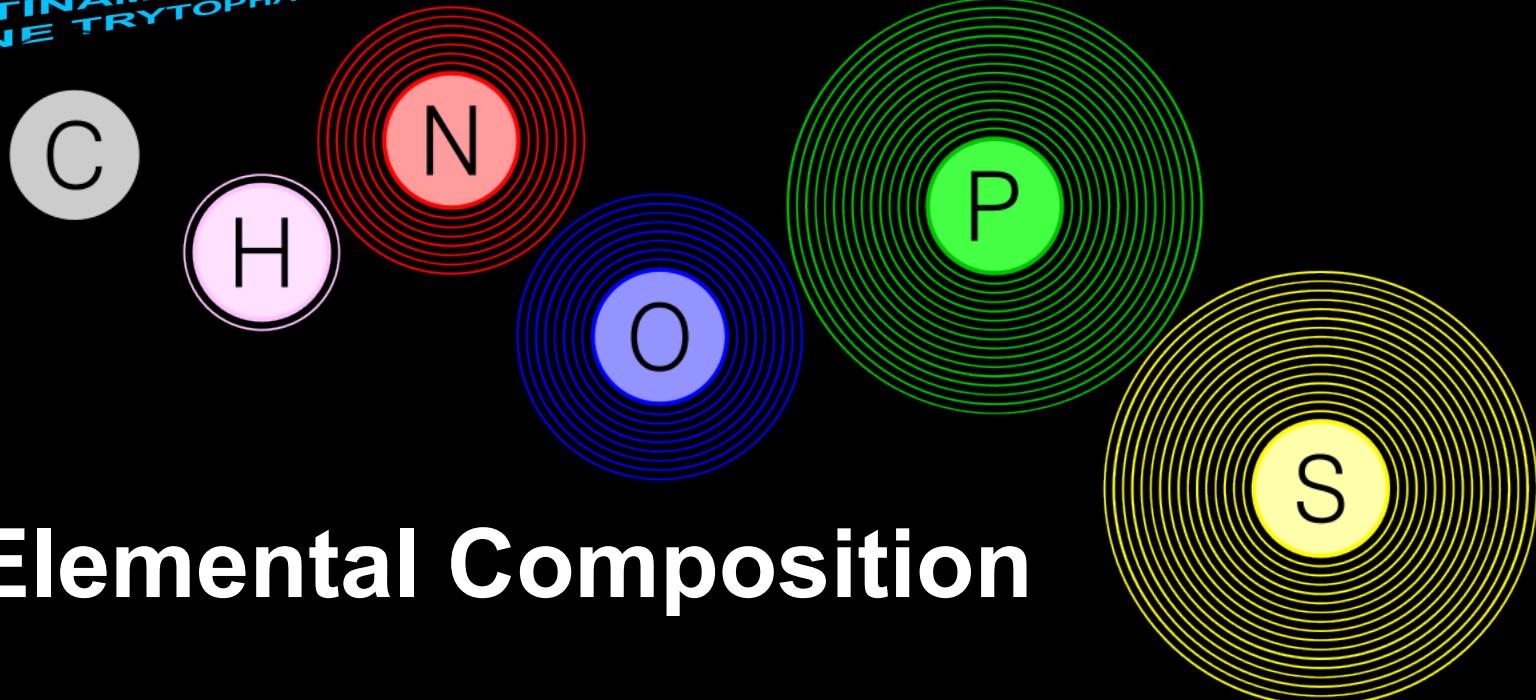
# METLN

# METLIN

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL  
PYRUVIC ACID UREA GALACTOSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
TESTOSTERONE GLUCOSE PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
PYRUVIC ACID UREA CHOLINE ADENOSINE GLUCOSE LACTIC ACID KETOGULATRATE  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID OXALOACETIC ACID  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL  
PYRUVIC ACID UREA GALACTOSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
TESTOSTERONE GLUCOSE PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID GALACTOSE GLYCEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL

# METLIN

*m/z*



**METLIN**

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL  
PYRUVIC ACID UREA GALACTOSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
TESTOSTERONE GLUCOSE PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
PYRUVIC ACID UREA CHOLINE ADENOSINE CHOLINE LACTIC ACID KETOGLUTARATE  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE CHOLINE ADENOSINE CHOLINE CHOLESTEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL  
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NICOTINAMIDE ADENINE DINUCLEOTIDE CHOLINE ADENOSINE CHOLINE CHOLESTEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE THREONINE GLYCEROL

*m/z*

Frag<sub>int</sub> vs *m/z*

# METLIN

*m/z*

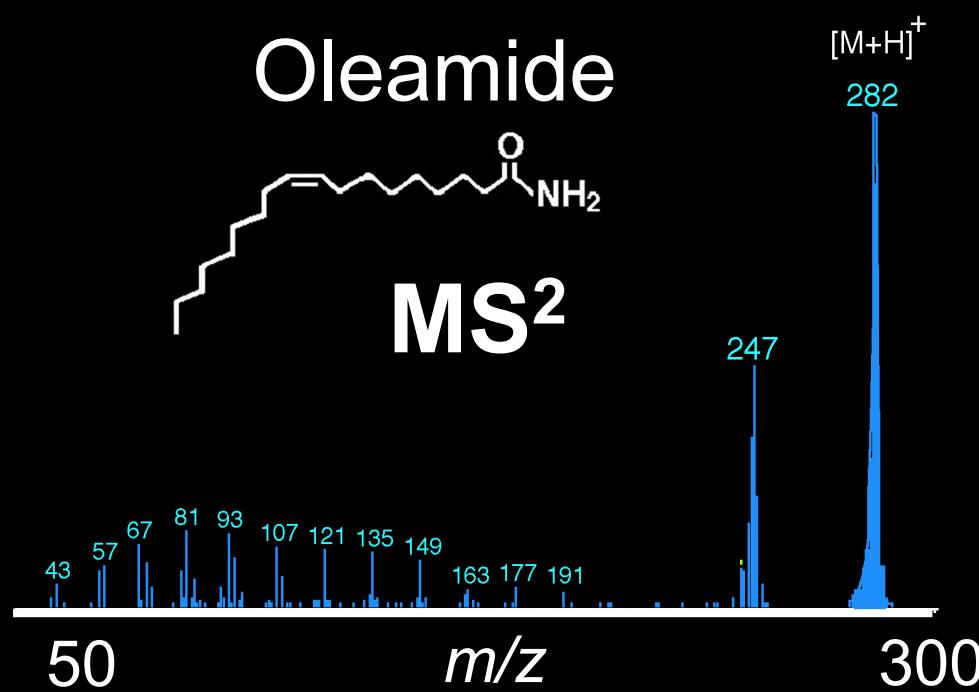
# METLIN-MS<sup>2</sup>

# Frag<sub>int</sub> vs *m/z*

# Oleamide



MS<sup>2</sup>



**METLIN**

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
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TESTOSTERONE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL CARNITINE THREONINE GLYCEROL

**METLIN-MS<sup>2</sup>**

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SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
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NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID CHOLINE GLYCEROL  
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TESTOSTERONE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL KETOGULARATE  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID CHOLINE GLYCEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL

**METLIN-NI**

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
PYRUVIC ACID UREA GALACTOSE CHOLINE ADENOSINE CHOLINE MALIC ACID  
TESTOSTERONE GLUCOSE PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
PYRUVIC ACID UREA CHOLINE ADENOSINE CHOLINE LACTIC ACID KETOGULARATE  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID CHOLINE GLYCEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
PYRUVIC ACID UREA GLUCOSE PHOSPHATE CHOLESTEROL OXALOSUCCINIC ACID  
TESTOSTERONE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL KETOGULARATE  
GLUCOSE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL FUMARATE  
NICOTINAMIDE ADENINE DINUCLEOTIDE OXALOSUCCINIC ACID CHOLINE GLYCEROL  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL

$m/z$

Frag<sub>int</sub> vs  $m/z$

NL<sub>int</sub> vs  $\Delta m/z$

JASMS 2022  
Nature Methods 2020

**METLIN**

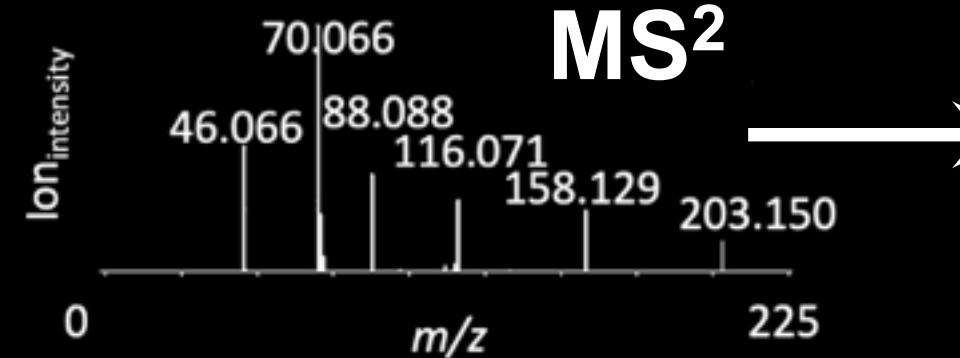
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TESTOSTERONE CHOLESTEROL OXALOSUCCINIC ACID GALACTOSE GLYCEROL CARNITINE THREONINE GLYCEROL

**METLIN-MS<sup>2</sup>**

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
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**METLIN-NL**

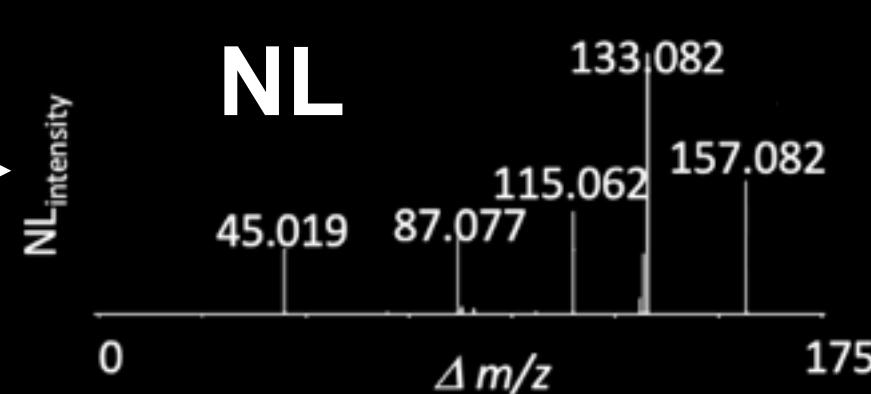
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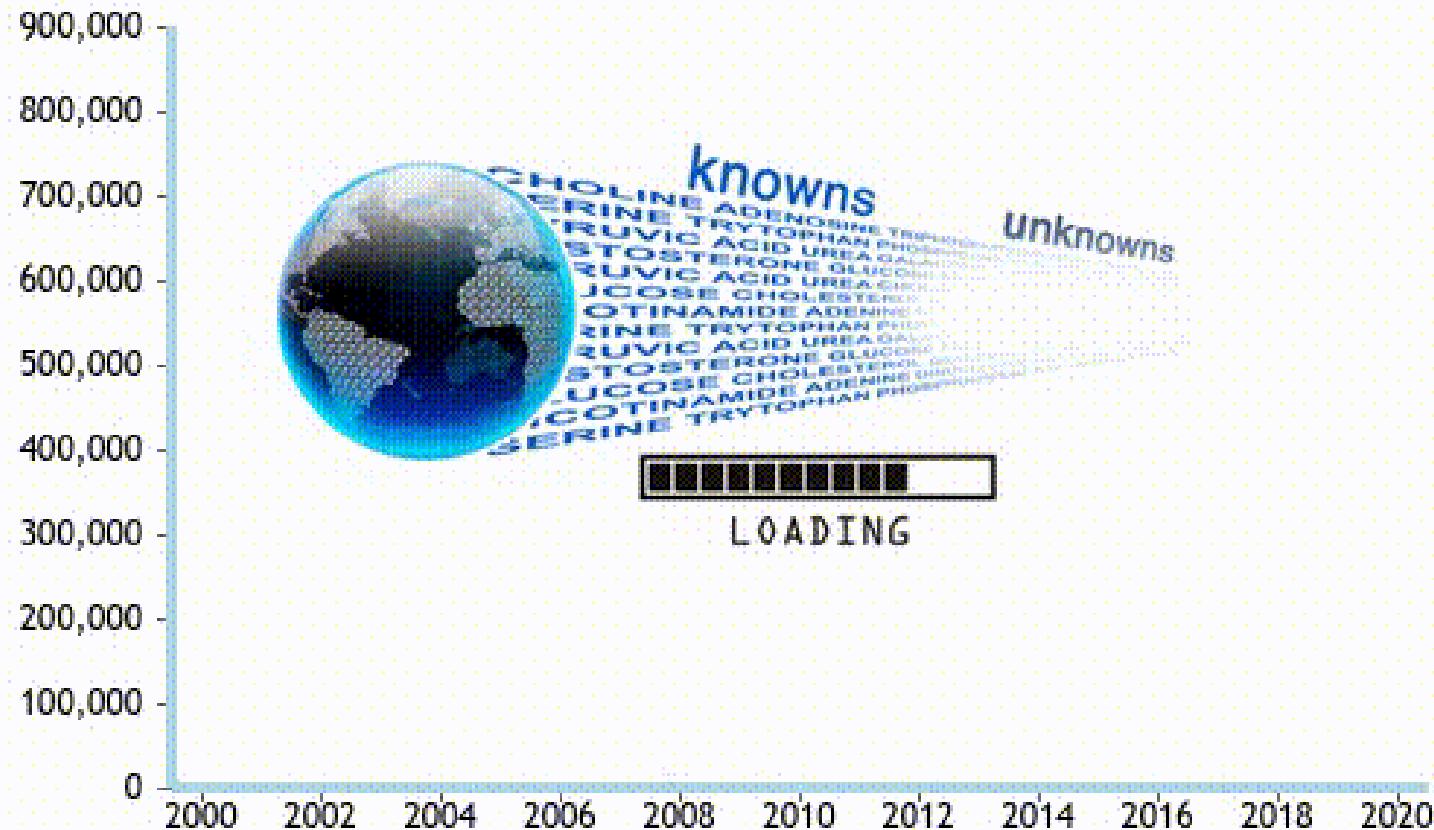
$m/z$

Frag<sub>int</sub> vs  $m/z$

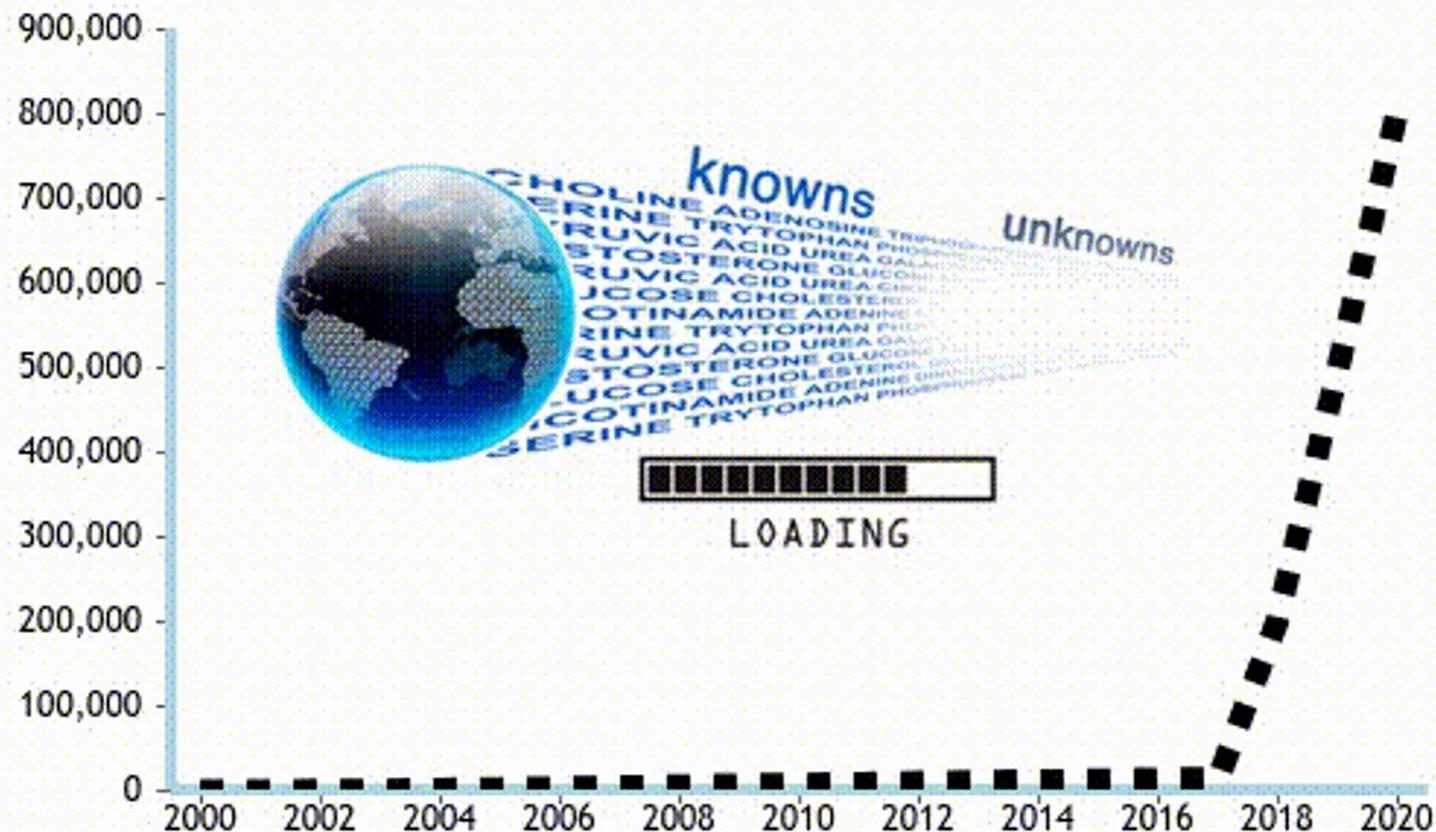
NL<sub>int</sub> vs  $\Delta m/z$



# METLIN MS/MS Data

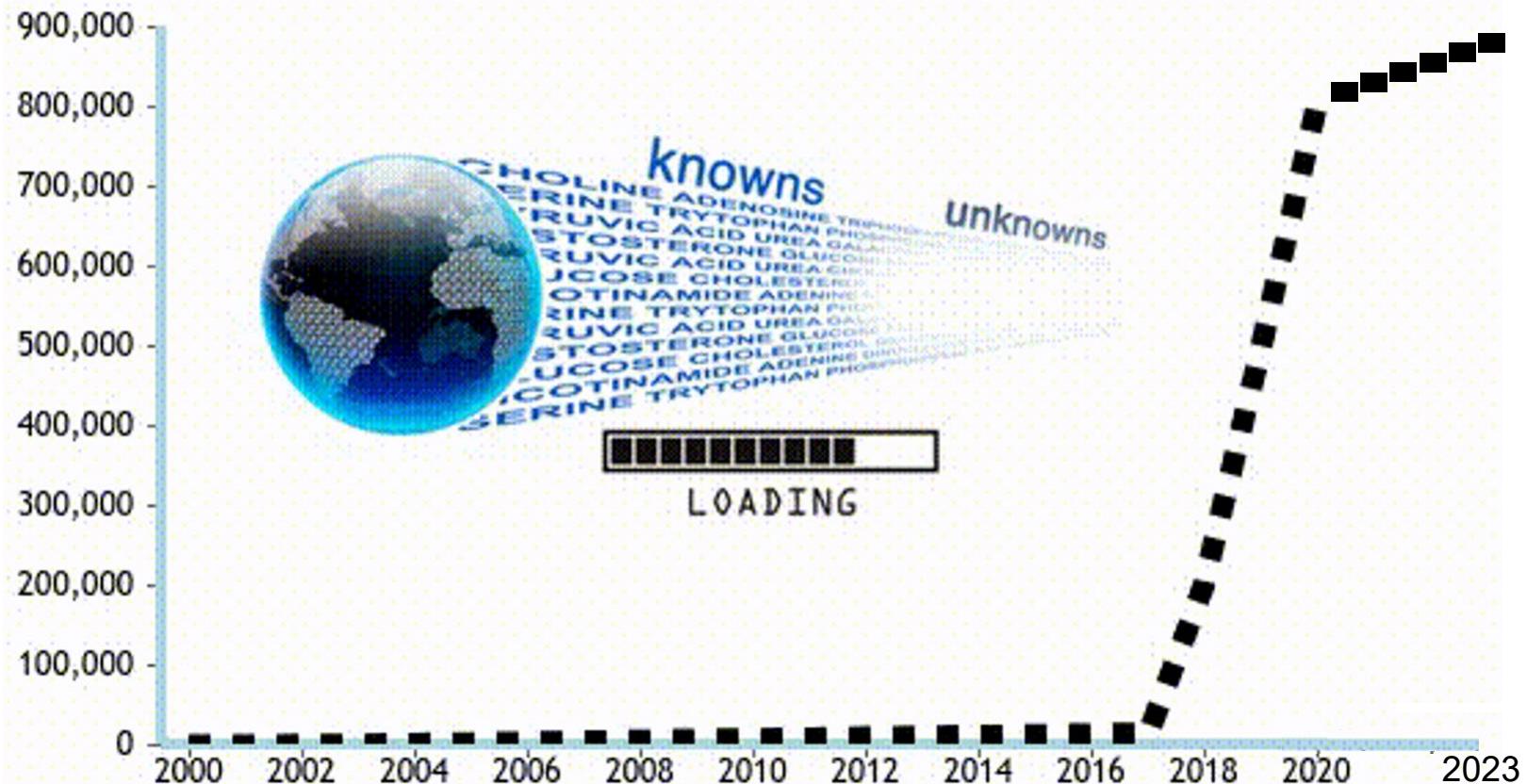


# METLIN MS/MS Data



850,000

# METLIN MS/MS Data



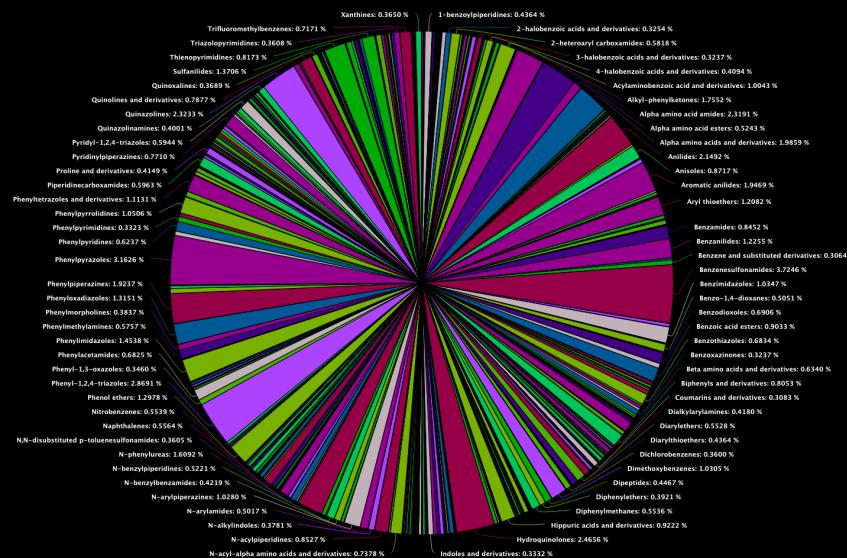
900,000

# METLIN-MS<sup>2</sup> & NL Statistics

*Nature Methods 2020  
Cell Metabolism 2022*

# METLIN-MS<sup>2</sup> & NL Statistics

- 1.17 Million Standards Analyzed

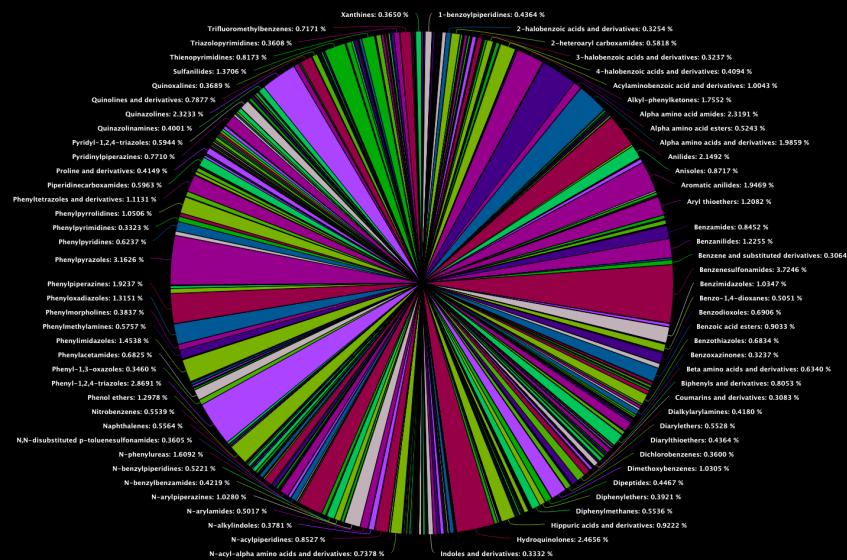


350 chemical  
classes

*Nature Methods* 2020  
*Cell Metabolism* 2022

# METLIN-MS<sup>2</sup> & NL Statistics

- 1.17 Million Standards Analyzed
- 77% Success: 23% failed filter
- 900K Standards each with MS/MS

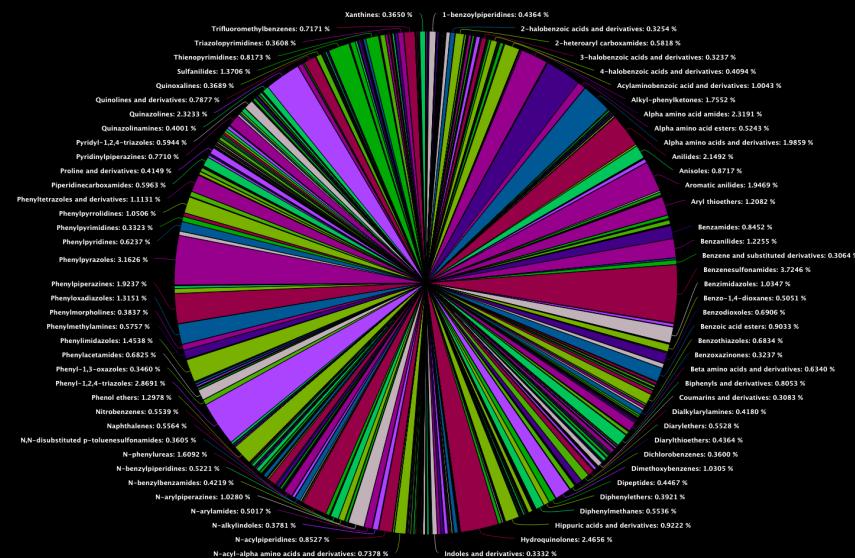


350 chemical  
classes

*Nature Methods* 2020  
*Cell Metabolism* 2022

# METLIN-MS<sup>2</sup> & NL Statistics

- 1.17 Million Standards Analyzed
  - 77% Success: 23% failed filter
  - 900K Standards each with MS/MS acquired at 4 collision energies in pos & neg ionization modes

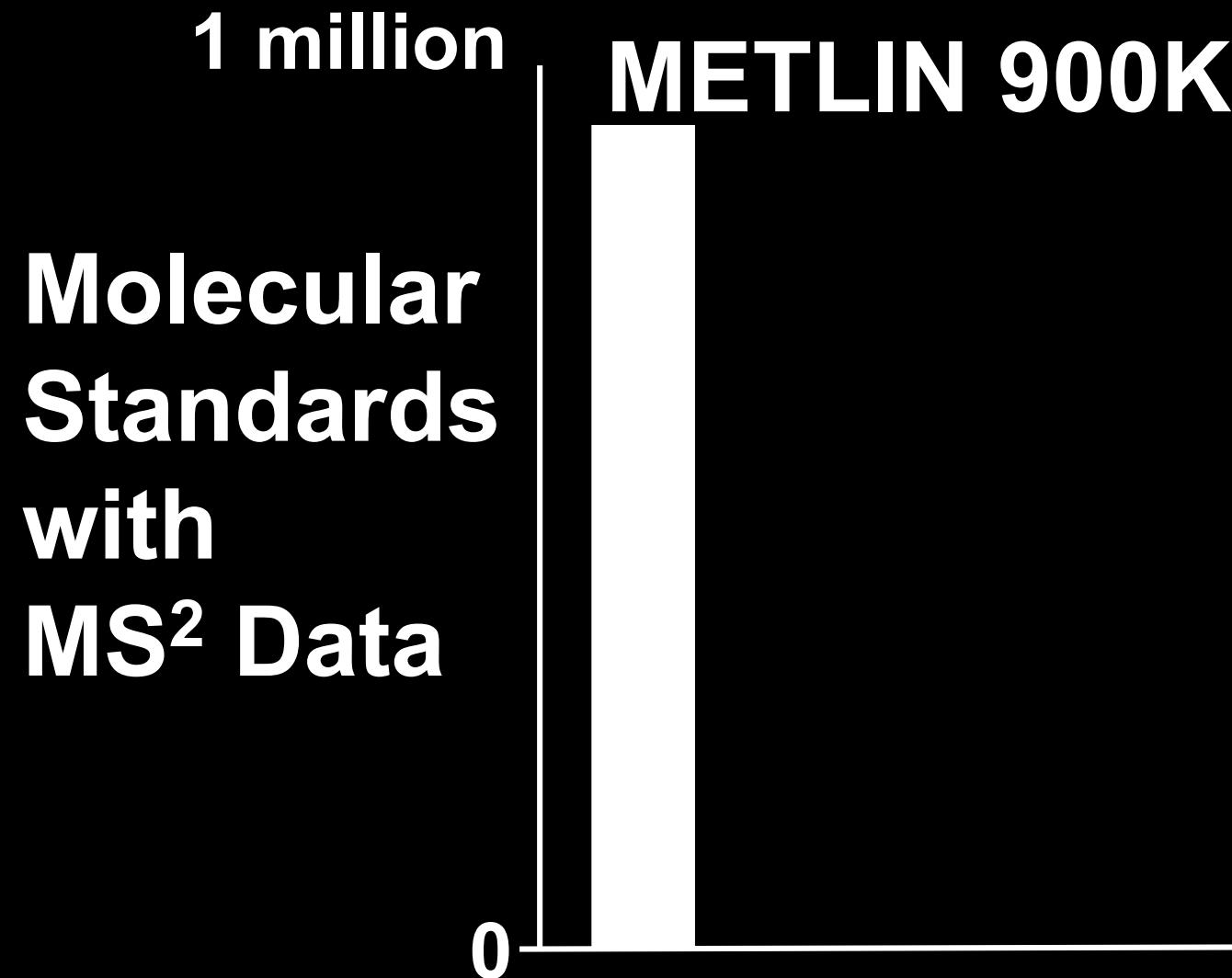


# 350 chemical classes

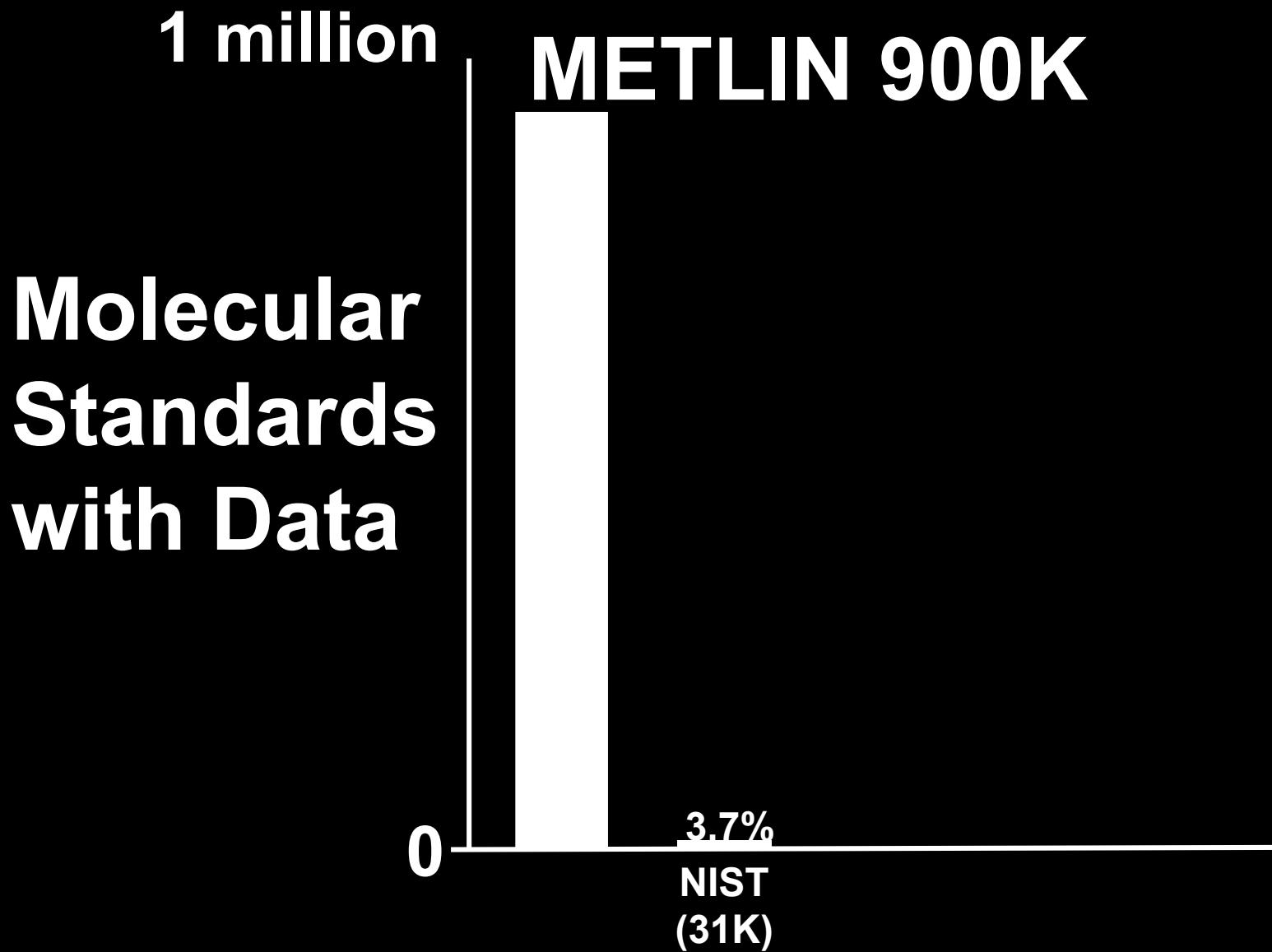
# **Nature Methods 2020**

# **Cell Metabolism 2022**

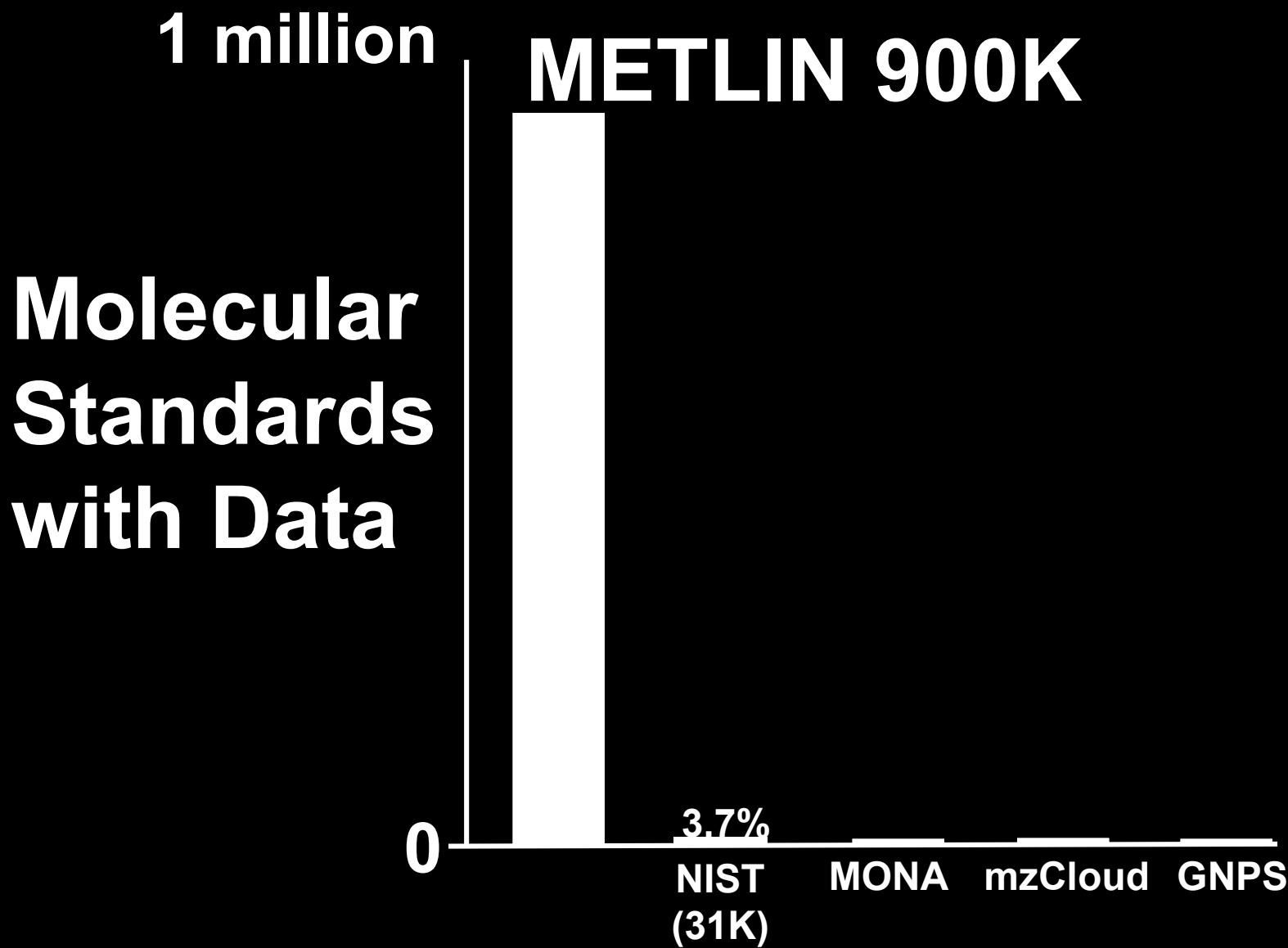
# METLIN-MS<sup>2</sup> & NL Statistics



# METLIN-MS<sup>2</sup> & NL Statistics



# METLIN-MS<sup>2</sup> & NL Statistics





**METLIN**

CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE GLUCOSE  
SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYLCARNITINE THREONINE GLYCEROL  
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**METLIN-MS<sup>2</sup>**

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**METLIN-NI**

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$m/z$

Frag<sub>int</sub> vs  $m/z$

NL<sub>int</sub> vs  $\Delta m/z$

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METLIN

$m/z$

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METLIN-MS<sup>2</sup>

Frag<sub>int</sub> vs  $m/z$

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METLIN-NI

NL<sub>int</sub> vs  $\Delta m/z$

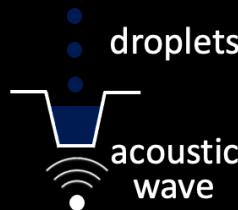
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METLIN-IMS

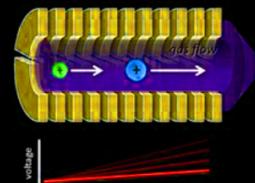
CCS values

# METLIN - Ion Mobility Spectrometry

**Step 1:** Sample Plate Preparation

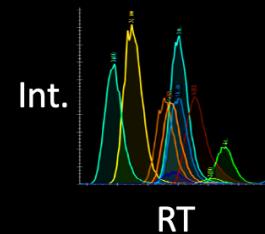


**Step 2:** Collect LC-IMS Data



TIMS and TWIMS

**Step 3:** Generate Raw IMS Data

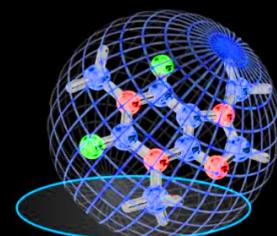


**Step 4:** Skyline IMS Data Input to CCS Values



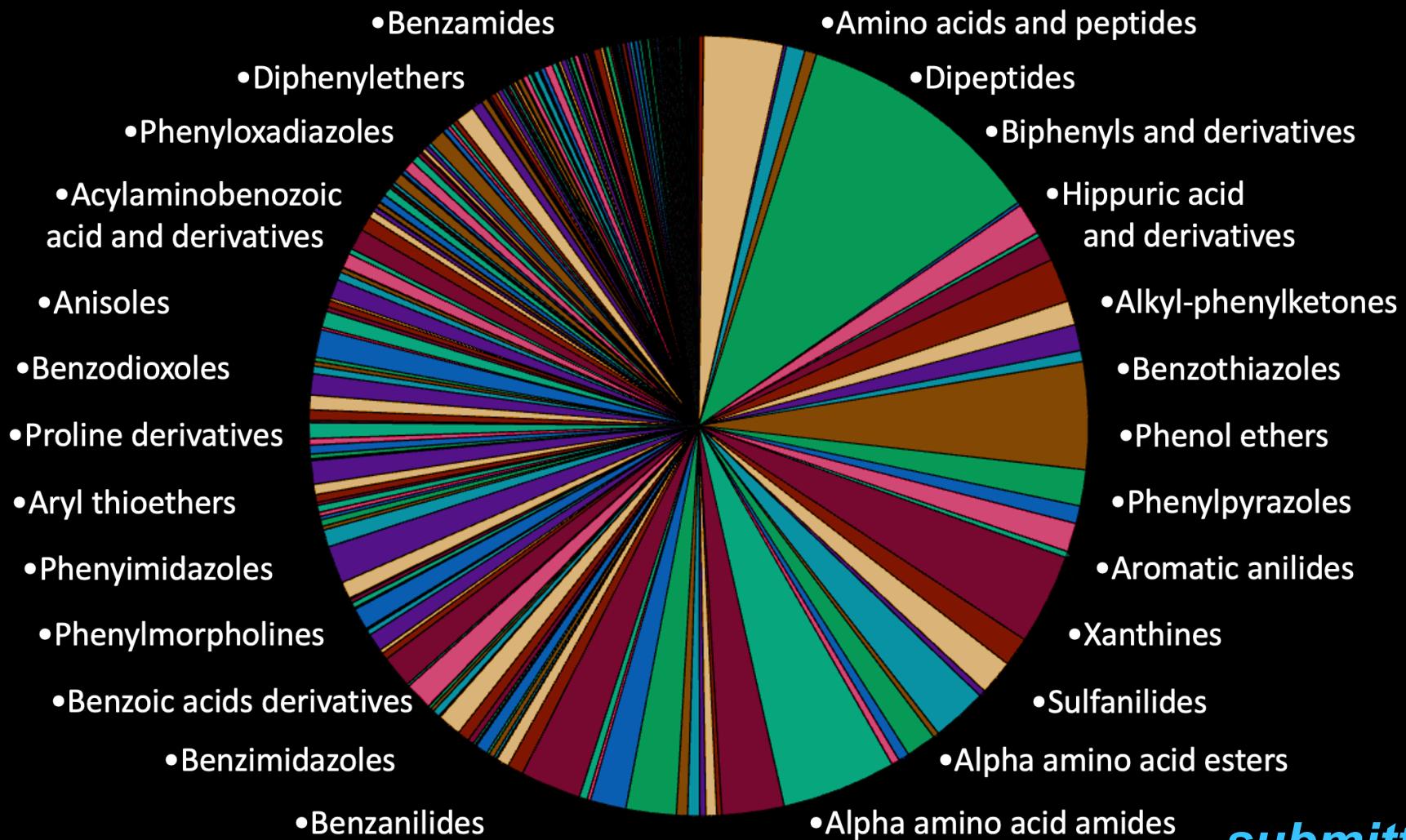
Automated 600,000 Data Sets Conversion to CCS

**Step 5:** Generate & Export CCS Values



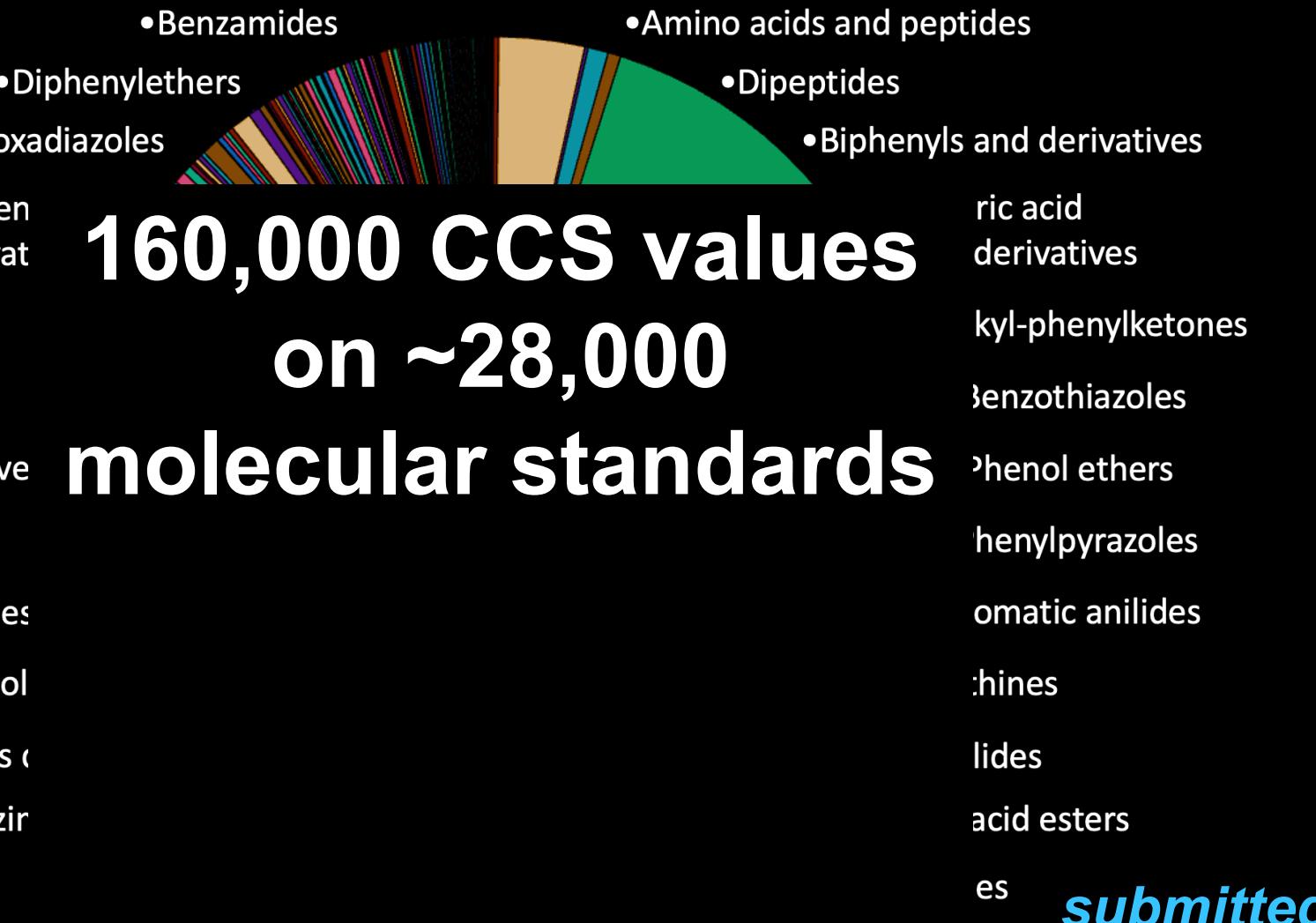
*submitted*

# METLIN - Ion Mobility Spectrometry



*submitted*

# METLIN - Ion Mobility Spectrometry



# METLIN - Ion Mobility Spectrometry



160,000 CCS values  
on ~28,000  
molecular standards

$\text{MH}^+$

$\text{MNa}^+$

$\text{MNH}_4^+$

$\text{M}-\text{H}^-$

$\text{M}+\text{Cl}^-$

$\text{M}+\text{TFA}^-$

*submitted*

# METLIN - Ion Mobility Spectrometry

- 
- Benzamides
  - Amino acids and peptides
  - Dipeptides
  - Biphenyls and derivatives
  - Phenyloxadiazoles
  - Diphenylethers
  - Acylaminobenzoic acid and derivatives
  - Anisoles
  - Benzodioxoles
  - Proline derivative
  - Aryl thioethers
  - Phenylimidazoles
  - Phenylmorphol
  - Benzoic acids
  - Benzir

160,000 CCS values  
on ~28,000  
molecular standards

Freely downloadable

$\text{MH}^+$

$\text{MNa}^+$

$\text{MNH}_4^+$

$\text{M}-\text{H}^-$

$\text{M}+\text{Cl}^-$

$\text{M}+\text{TFA}^-$

*submitted*

# METLIN - Ion Mobility Spectrometry

- 
- Benzamides
  - Diphenylethers
  - Phenyloxadiazoles
  - Acylaminobenzoic acid and derivatives
  - Anisoles
  - Benzodioxoles
  - Proline derivative
  - Aryl thioethers
  - Phenylimidazoles
  - Phenylmorpholines
  - Benzoic acids
  - Benzirines
  - Amino acids and peptides
  - Dipeptides
  - Biphenyls and derivatives

160,000 CCS values  
on ~28,000  
molecular standards

Freely downloadable  
In collaboration with  
Erin Baker & Skyline

$\text{MH}^+$   
 $\text{MNa}^+$   
 $\text{MNH}_4^+$   
 $\text{M}-\text{H}^-$   
 $\text{M}+\text{Cl}^-$   
 $\text{M}+\text{TFA}^-$   
*submitted*

# METLIN - Ion Mobility Spectrometry

Brian Pratt

Michael MacCoss

Brendan MacLean

(Skyline)

Heino Heyman

(Bruker)



# The Two Hows?







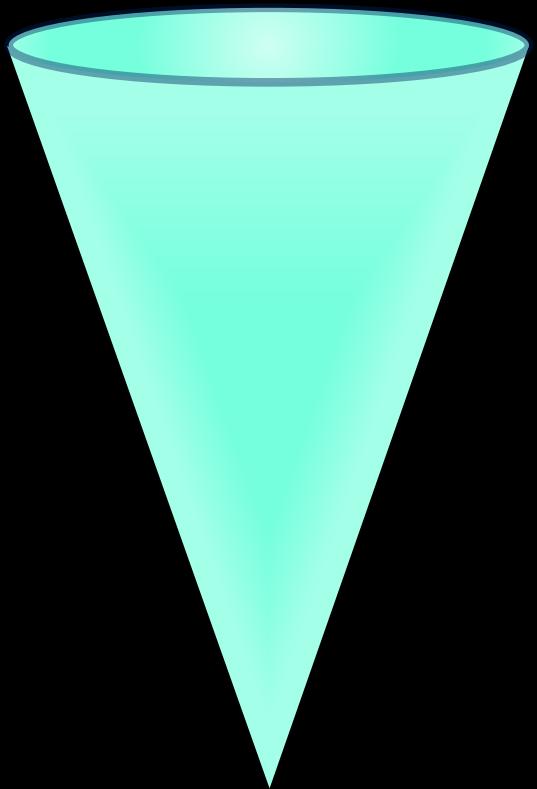






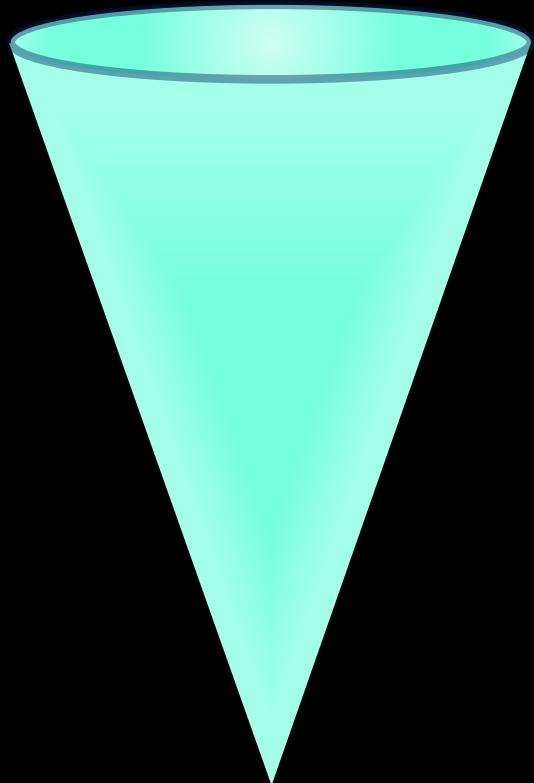
*One Simple  
Motivation*

30,000 features detected



*One Simple  
Motivation*

# 30,000 features detected



- Experimental Design
- Fold change
- Statistics (p-value)

*One Simple  
Motivation*

# 30,000 features detected



- Experimental Design
- Fold change
- Statistics (p-value)

*One Simple  
Motivation*

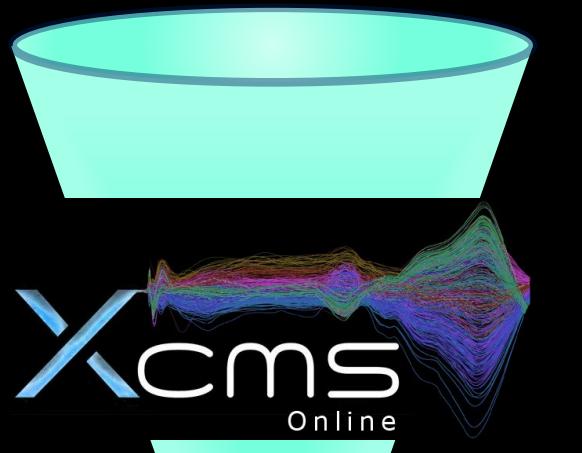
# 30,000 features detected



- Experimental Design
  - Fold change
  - Statistics (p-value)  
  - MS, IMS, & MS/MS data

# *One Simple Motivation*

# 30,000 features detected



CHOLINE  
SERINE TRYPTOPHAN TRIPHOSPHATE CHOLESTEROL ACYL CARNITINE  
PYRUVIC ACID UREA PHOSPHOCHOLINE ACYL CARNITINE  
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METLIN

Metabolites



Phenotype

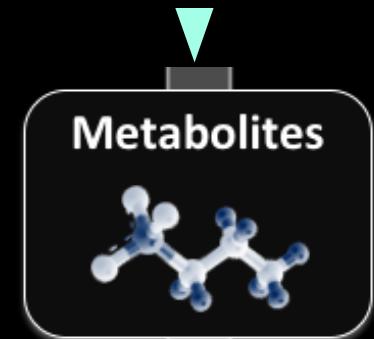
- Experimental Design
- Fold change
- Statistics (p-value)
- MS, IMS, & MS/MS data

*One Simple  
Motivation*

# *Central Dogma of Biology*



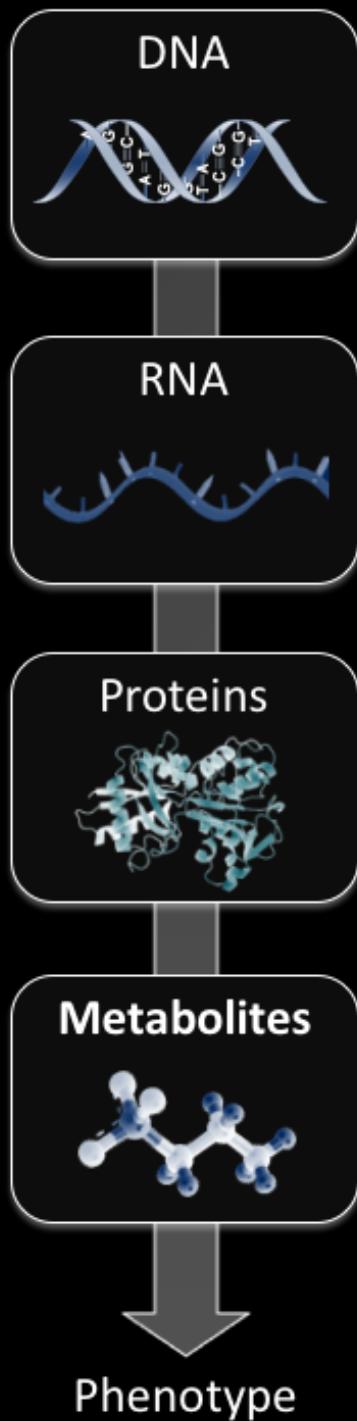
CHOLINE ADENOSINE TRIPHOSPHATE CHOLESTEROL TESTOSTERONE  
SERINE TRYPTOPHAN PYRUVIC ACID UREA PHOSPHOCHOLINE ACV  
TESTOSTERONE GLUCOSE CHOLESTEROL OXALIC ACID  
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SERINE TRYPTOPHAN PHOSPHOCHOLINE ACYL CARNITINE



Phenotype

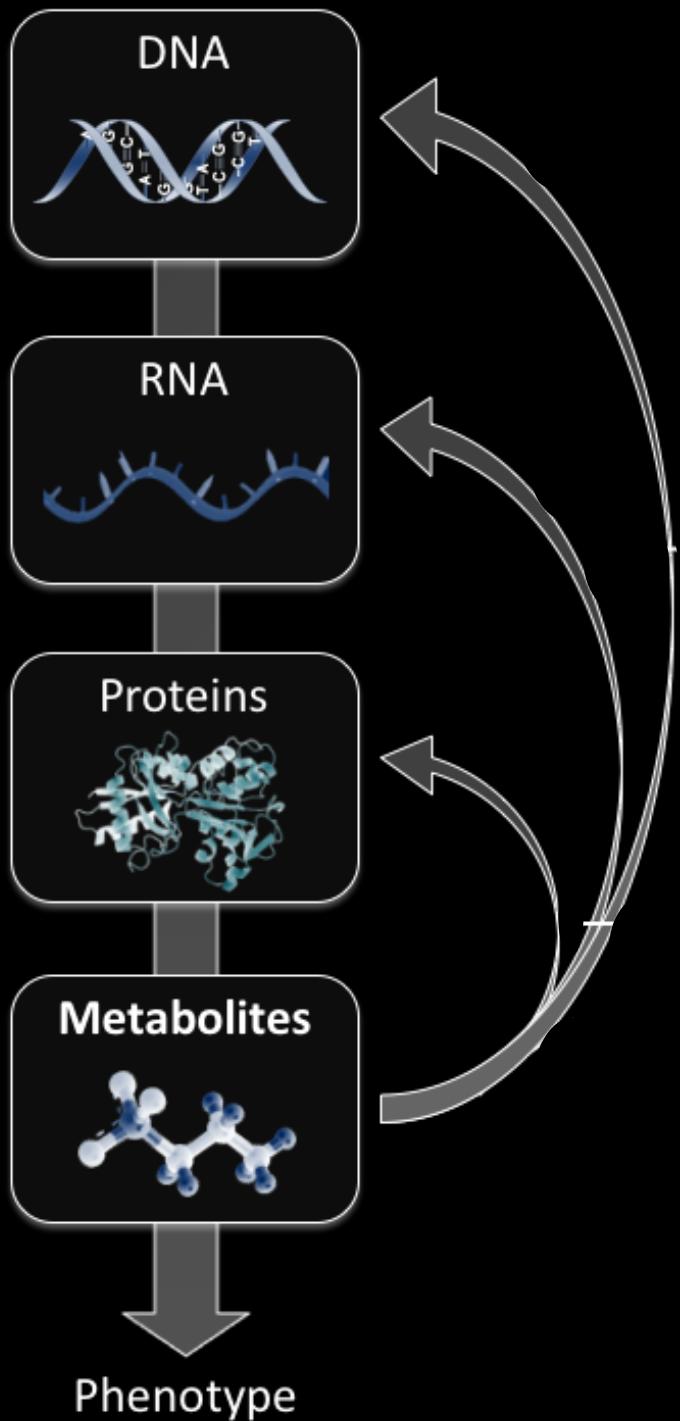
*Nature Biotech. 2018  
Nature Reviews 2019  
Cell Metabolism 2022*

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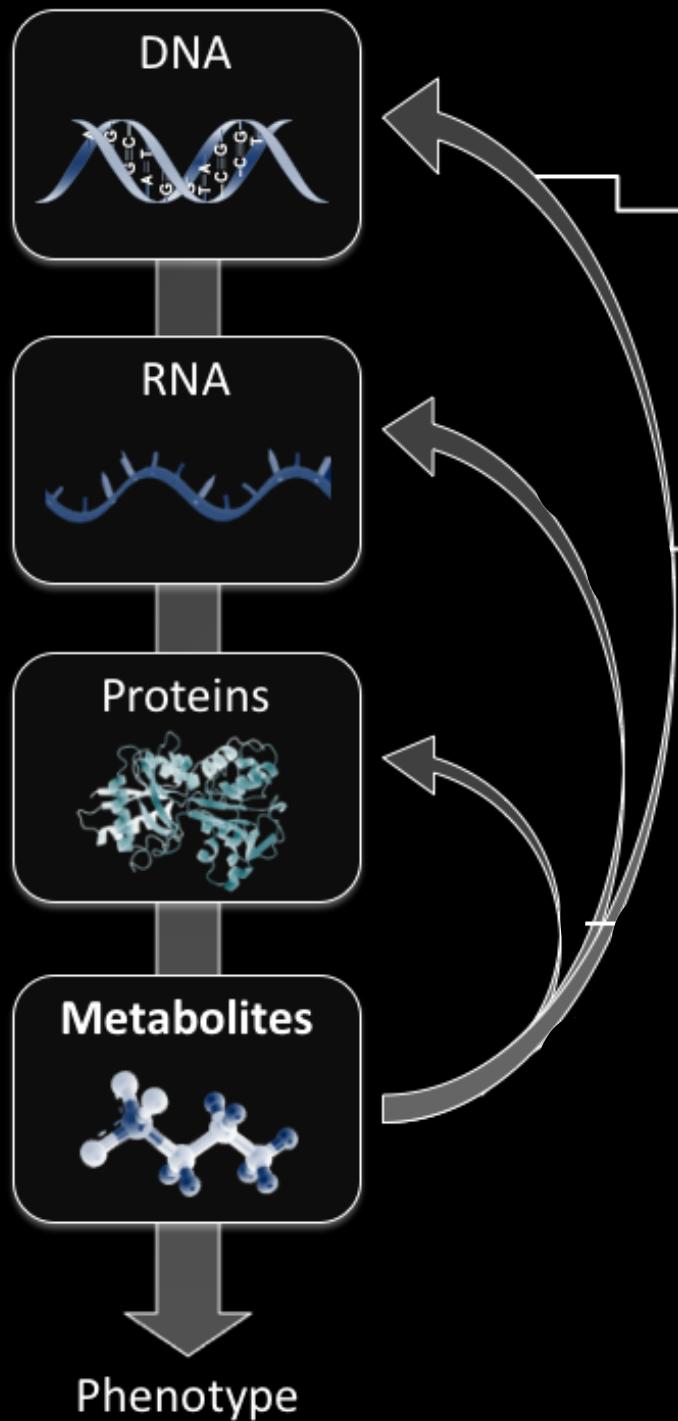


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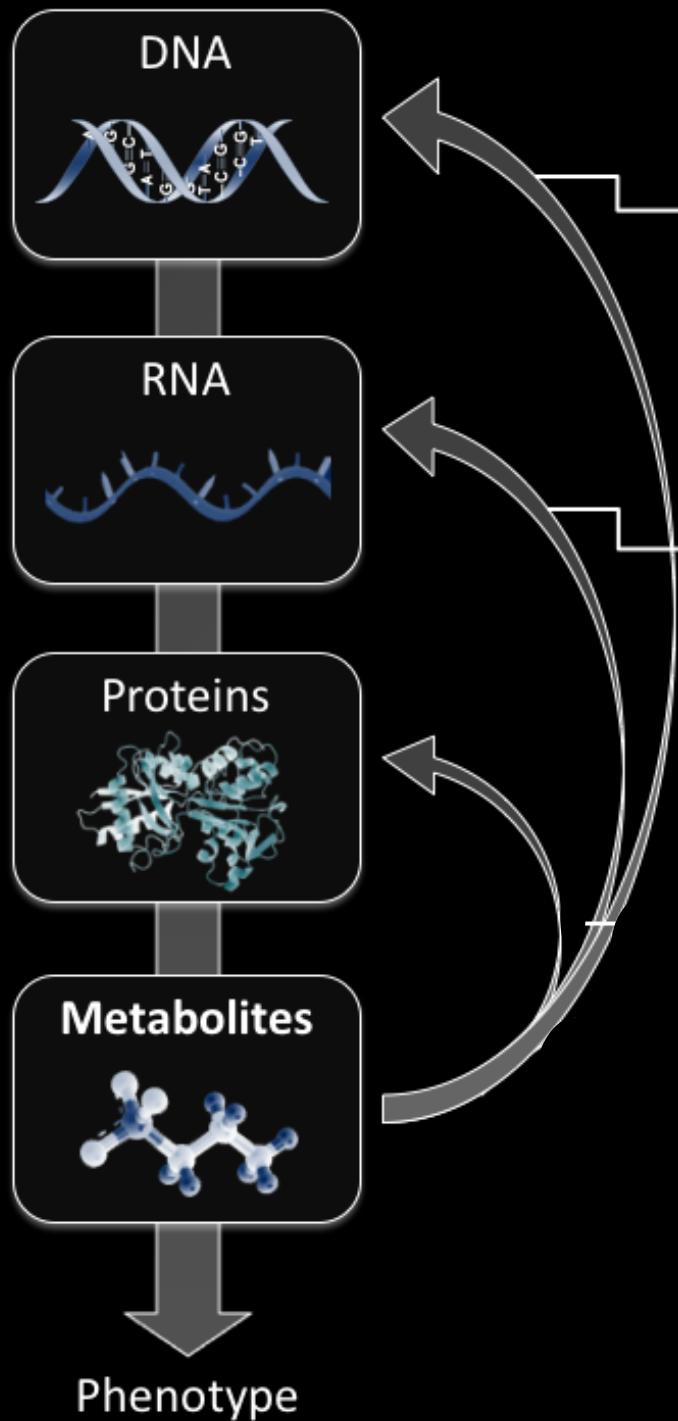
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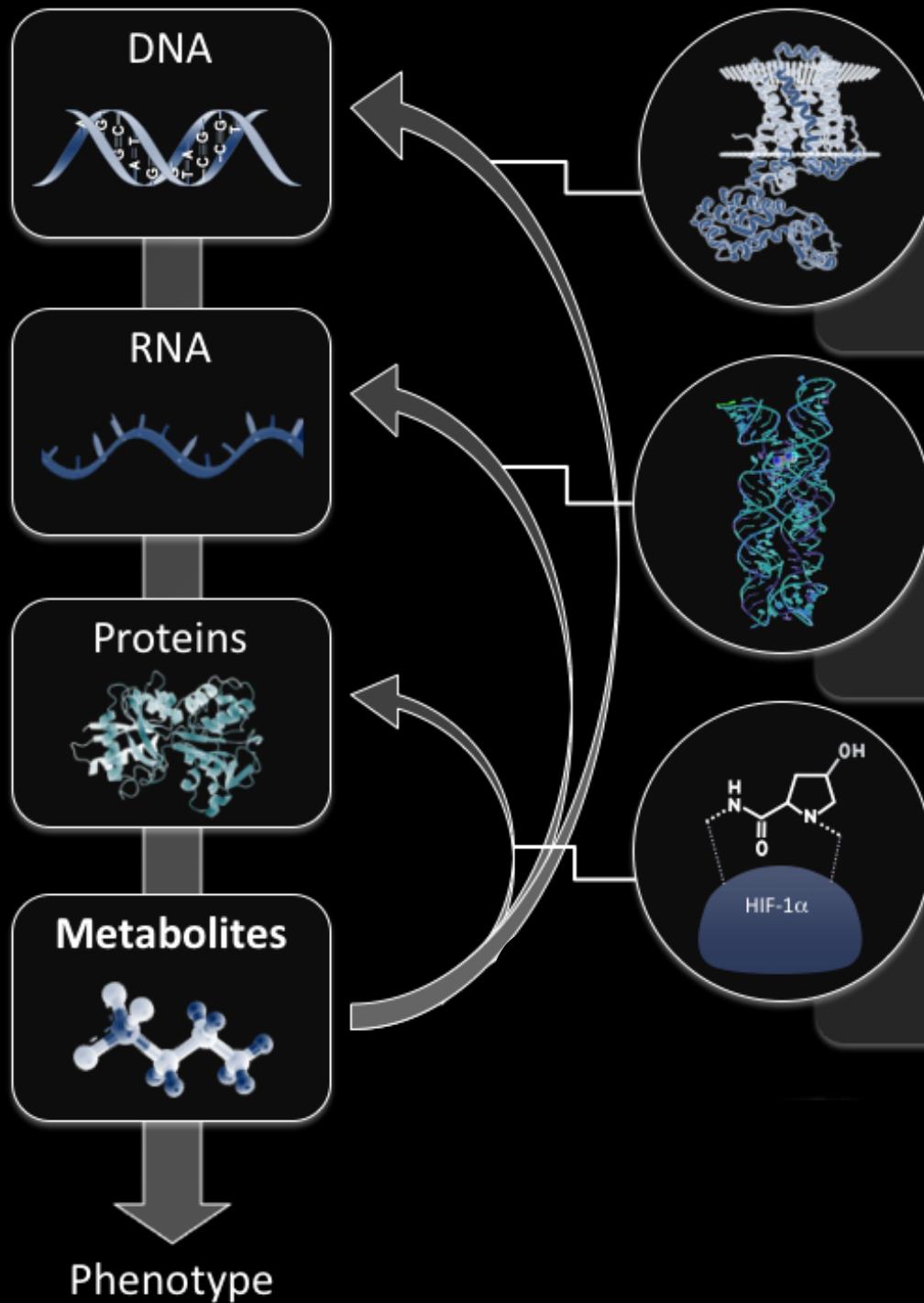
### Gene expression

- Signal transduction control of transcription
- Epigenetic regulation by cofactors of chromatin enzymes

### RNA metabolism

- Metabolite sensing by riboswitches
- Post-transcriptional modifications

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## Gene expression

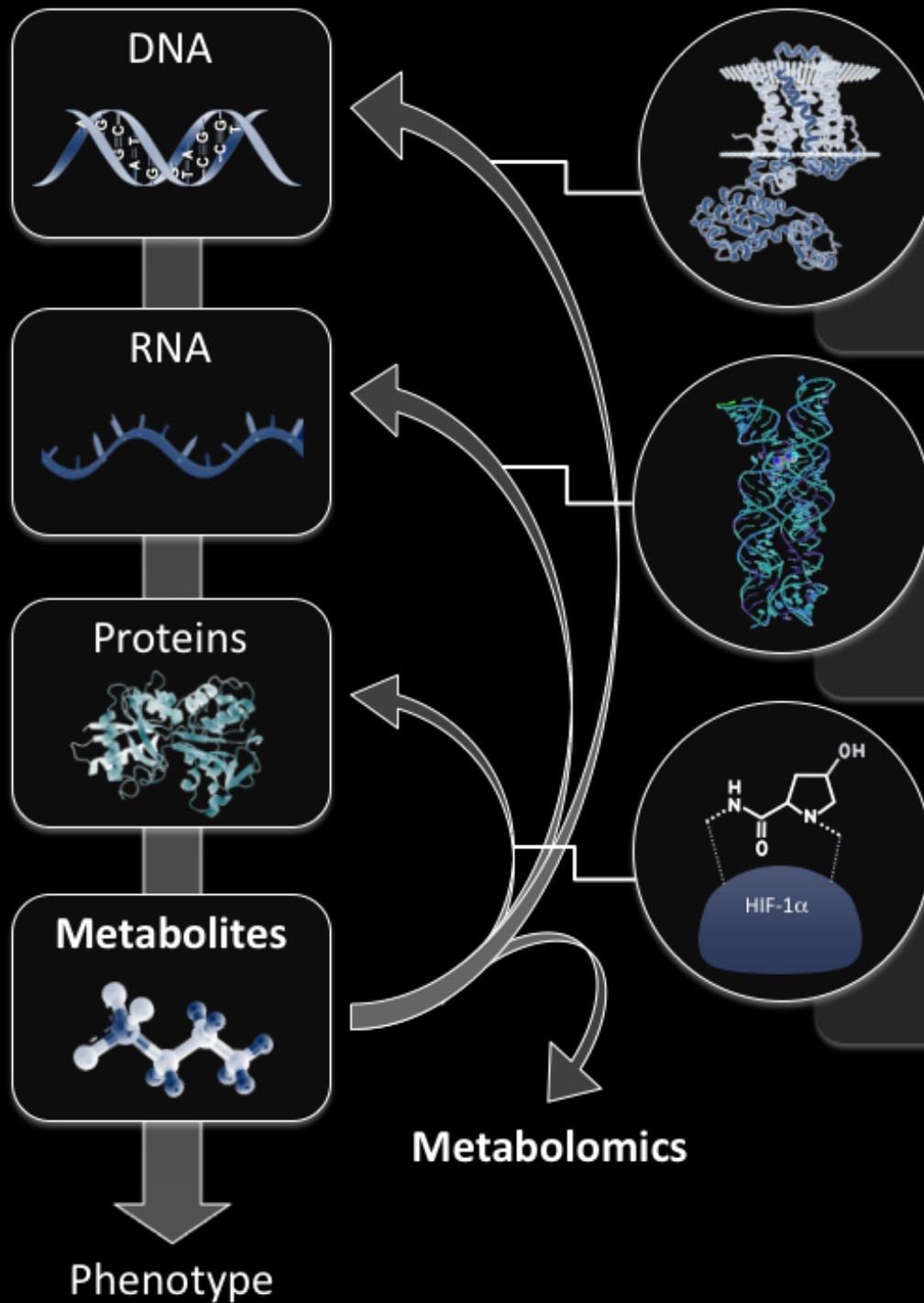
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## RNA metabolism

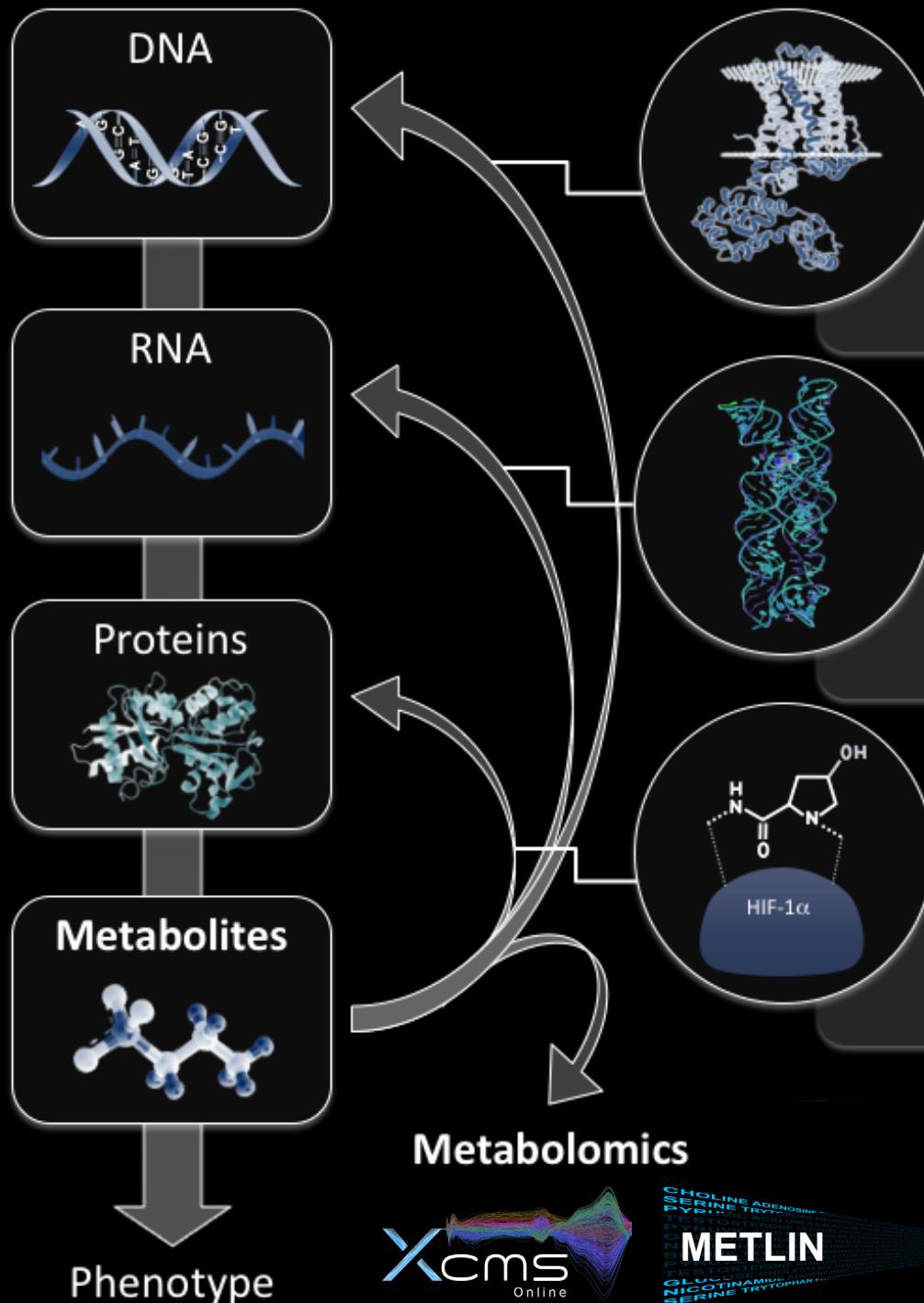
- Metabolite sensing by riboswitches
- Post-transcriptional modifications
- Ribosome sensing

## Protein activity

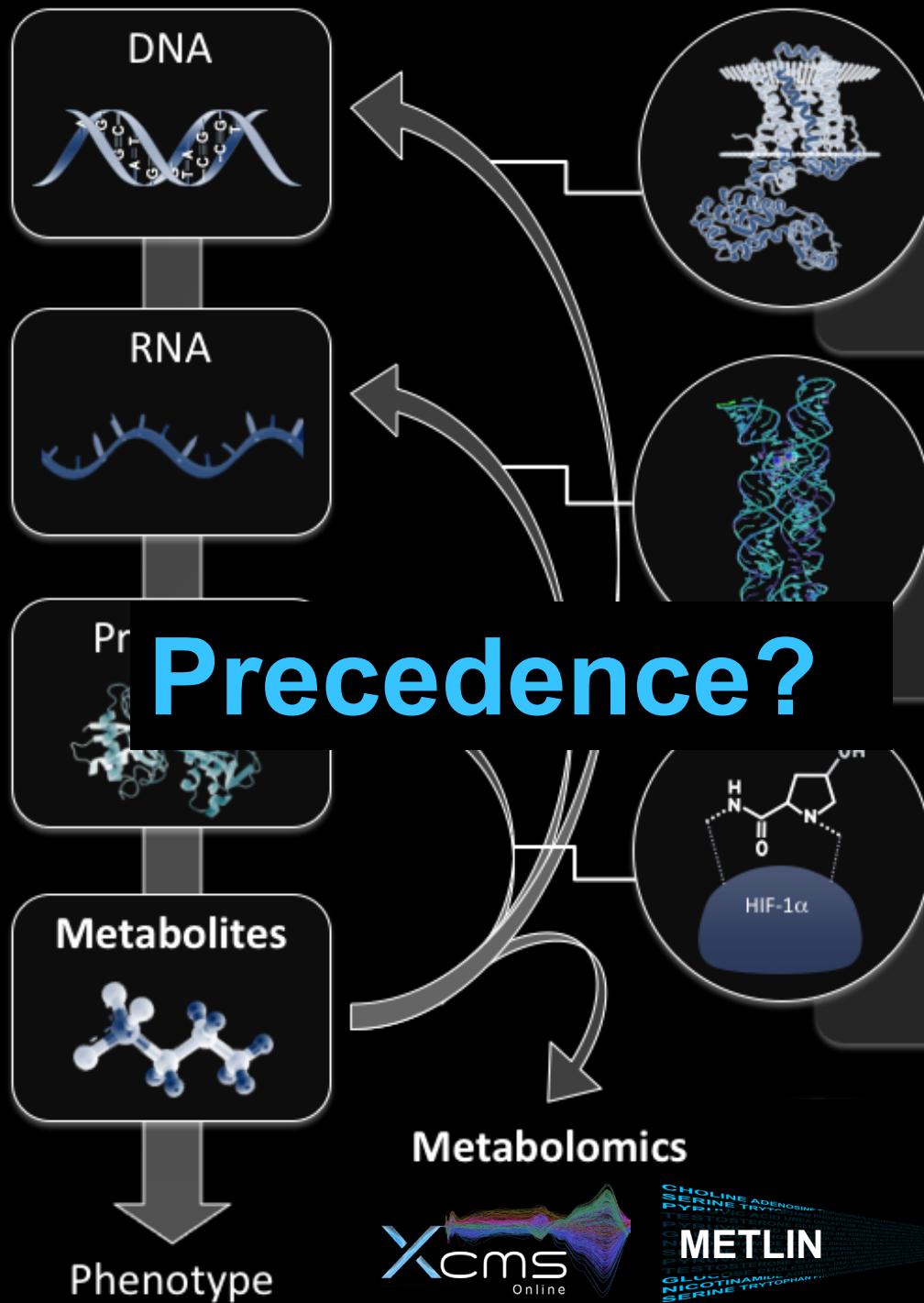
- Allosteric regulation of receptors/transcription factors
- Catalysis by co-factors/substrates
- Post-translational modifications



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# Precedence?

# Metabolite System Journal

Taurine	Multiple Sclerosis	Nature Chemical Biology
Microbial metabolites	Plant Assembly	Nature Microbiology
Itaconate	Anti-Inflammatory	Nature
Itaconate	Anti-Inflammatory	Nature
Ribonucleotide	Antiviral	Nature
Indole Propionic Acid	Immune Response	PNAS with Pete Schultz
Kynurenine depletion	Cancer therapeutic	Nature Biotechnology
Histidine	Cancer therapeutic	Nature
Succinate	Thermogenesis	Nature
Glutamine	Sickle Cell Disease	NEJM
Apelin peptide	Sarcopenia	Nature Medicine
Sterols	Multiple Sclerosis	Nature
Succinate	Intestinal Remodeling	Cell
Inositol Phosphates	Viral Capsid Co-factors	Nature
5-Aminovaleric Acid	Reduces B-Oxidation	Scientific Reports
Nicotinamide	Acute Kidney Injury	Nature Medicine
Microbiota metabolites	Immune Response	Immunity
$\beta$ -Hydroxybutrate	Hypertension	Cell Reports
BH4-tetrahydrobiopterin	T-cell proliferation	Nature
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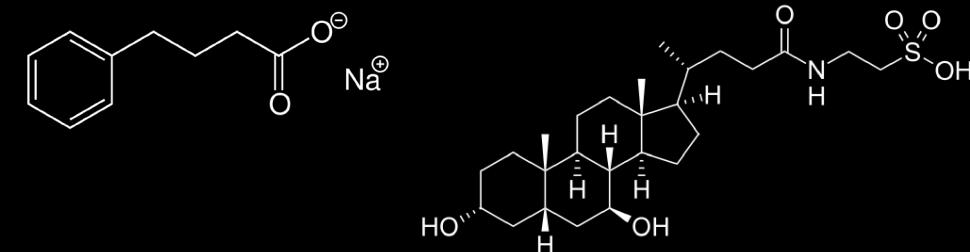
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## Precedence?



# One Simple Motivation



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## *Metabolomics*



# One Simple Motivation

*Metabolomics*

## beyond biomarkers



# One Simple Motivation

*Metabolomics*

## beyond biomarkers



toward identifying  
endogenous  
metabolites  
that  
modulate  
physiology

# Acknowledgements

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NIH   DOE   DoD

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NIH   DOE   DoD



# METLIN



# METLIN



Winnie Heim



Aries Aisporna



# METLIN



Winnie Heim



Aries Aisporna

# Sleep



Richard Lerner



Ben Cravatt

# Acknowledgements

