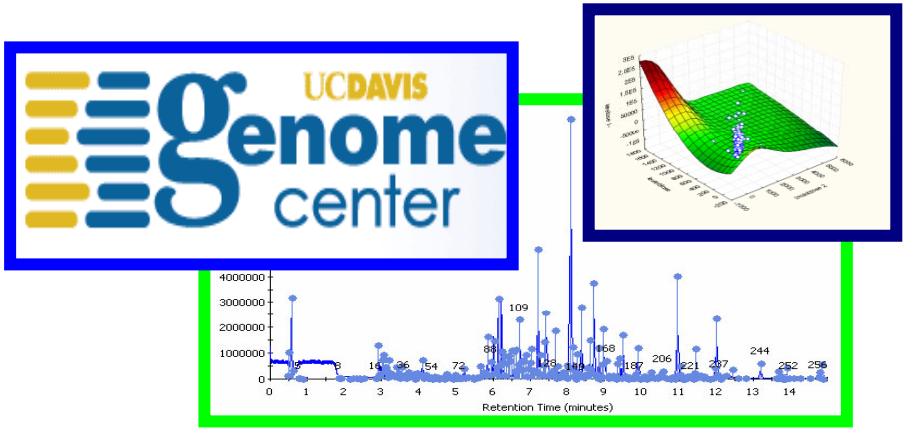


# Metabolomics Core Laboratory at UC Davis

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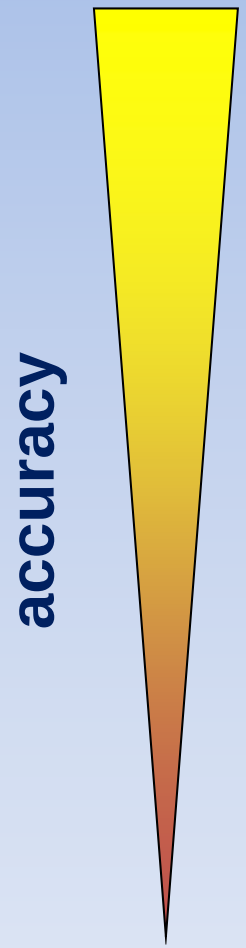
**UC Davis Genome Center**

**http://metabolomics-core.ucdavis.edu**

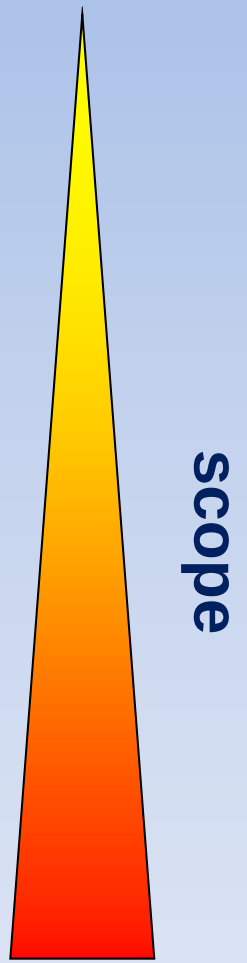
# Metabolomics

- Metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind" - specifically, the study of their small-molecule metabolite profiles. The metabolome represents the collection of all metabolites in a biological cell, tissue, organ or organism, which are the end products of cellular processes.
- Metabolomics reflects the biochemical homeostasis of a biological system, and reports on both genetic and environmental conditions.
- *No single* methodology/technique capable of *coverage* the whole metabolome due to enormous chemical diversity.
- Metabolomics *non-targeted* and *targeted*

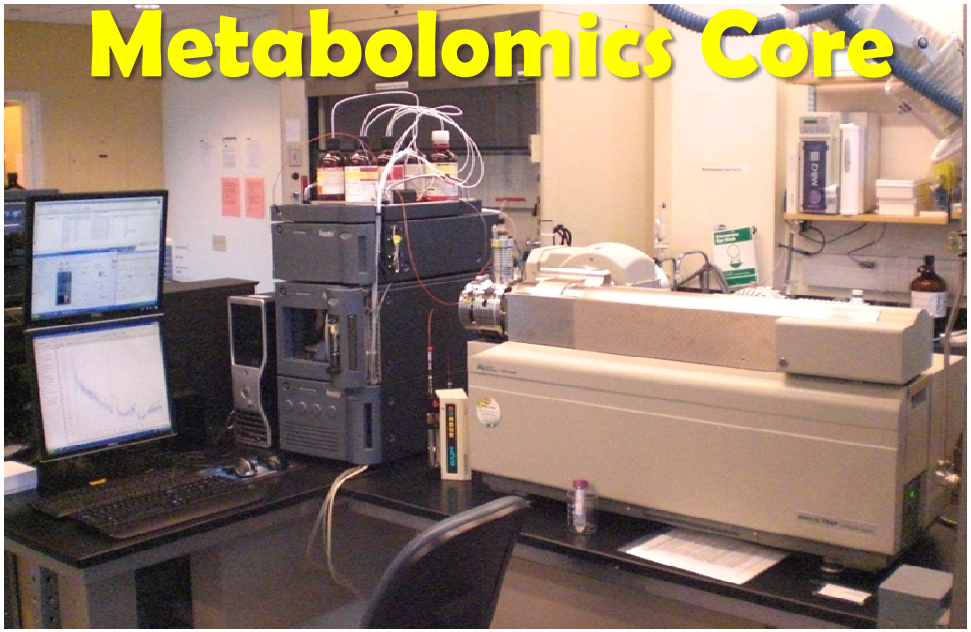
# Metabolomics

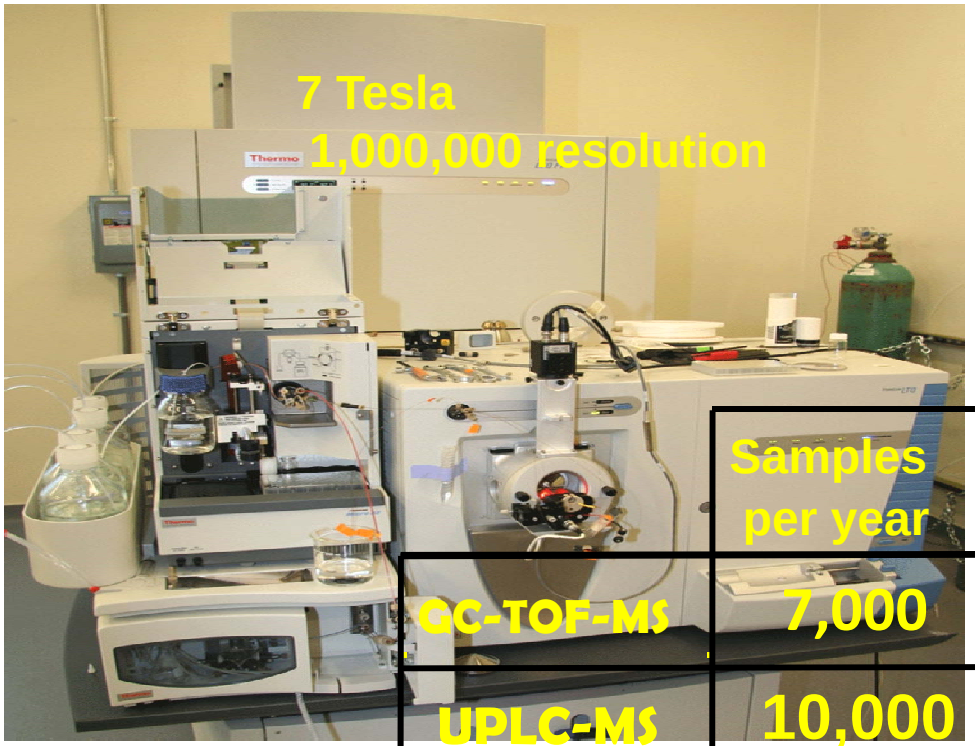



1. **Target analysis**
   **few metabolites**
2. **Metabolite profiling or**
   **targeted Metabolomics**
   **selected metabolites**
3. **Nontargeted Metabolomics**
   **all the metabolites**



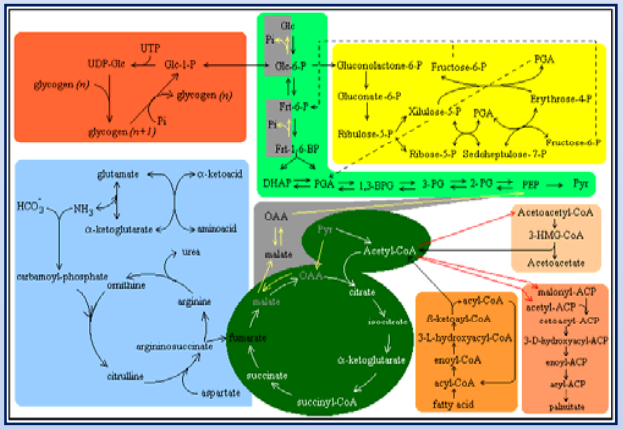
# Metabolomics Core Instrumentation




| | Samples per year | Metabolites detected | dynamic range |
|---|---|---|---|
| GC-TOF-MS | 7,000 | 50 - 700 | $10^{3}$ - $10^{4}$ |
| UPLC-MS | 10,000 | 1 - 1500 | $10^{3}$ - $10^{4}$ |

# Metabolomics workflow



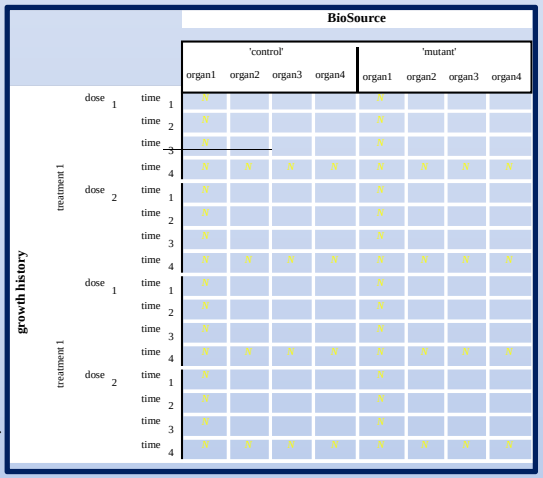

Pathways Analysis

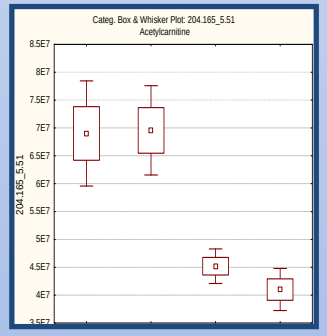
hypotheses

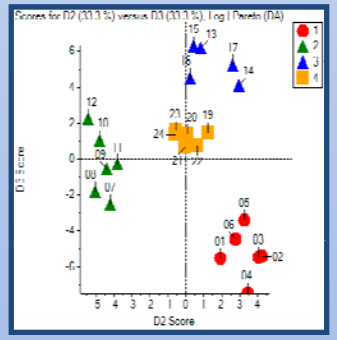
interpretation

experiments

data



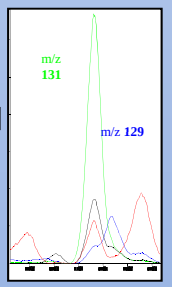




Data Analysis
( Multivariate Statistics )

Experimental design
SetupX

Sample Preparation
( wet chemistry )




Data Annotation
BinBase

Data Acquisition
( Mass Spectrometry )

| | Name | Provider | URL | Publication |
|---|---|---|---|---|
| Freely available | XCMS | SCRIPPS | http://masspec.scripps.edu/xcms/xcms.php | (Smith *et al.*, 2006) |
| | MZmine2 | VTT & OIST | http://mzmine.sourceforge.net | (Katajamaa *et al.*, 2006) |
| | MSFACTs | Noble Foundation | http://www.noble.org/plantbio/ms/msfacts/msfacts.html | (Duran *et al.*, 2003) |
| | metAlign | Plant research International | http://www.metalign.wur.nl/UK | (Lommen, 2009) |
| | MathDAMP | Keio University | http://mathdamp.iab.keio.ac.jp | (Baran *et al.*, 2006) |
| Commercially available | MarkerLynx | Waters Ltd. | http://www.waters.com | |
| | Matlab bioinformatics toolbox | MathWorks | http://www.mathworks.com | |
| | MarkerView | AppliedBiosystems | http://www3.appliedbiosystems.com | |
| | MsXelerator | MsMetrix | http://www.msmetrix.com | |
| | AnalyzerPro | SpectralWorks | http://www.spectralworks.com/analyzerpro.asp | |

Table 1.3: Available deconvolution software. Various software packages are available for the peak deconvolution and alignment of the LC-MS data. This Table lists several freely and commercially available packages together with the information about the provider, URL addresses and available original publications.

| Name | URL | Compounds | Note |
|---|---|---|---|
| **PubCHEM** | http://pubchem.ncbi.nlm.nih.gov | > 37.300,000 | Literature based collection of various chemical compounds (including non-biological) |
| **MassBank** | http://www.massbank.jp | >22,000 | Experimental mass spectra metabolite data from different MS technologies |
| **ChEBI** | http://www.ebi.ac.uk/chebi/init.do | ~ 18,000 | Literature based collection of small molecule information (biologically active compounds) |
| **KEGG** | http://biocyc.org | ~16,000 | Literature based, organism specific information on the level of genome, pathway and compound |
| **METLIN** | http://metlin.scripps.edu | >15,000 | Experimental mass spectral metabolite data from FTMS, LC/MS and MS/MS |
| **BioCyc** | http://biocyc.org | ~8,000 | Literature based, primarily microorganisms and plants, pathway and compound information |
| **HMDB** | http://www.hmdb.ca | >6,500 | Literature based collection of small molecules present in human body |

Table 1.4: Available databases containing information on metabolites. The databases vary in their purpose and scope. They range from the listing of a broad catalogue of chemical compounds to being highly specialised on small molecules from a specific organism with associated experiment and literature-reported information.

# Data Analysis

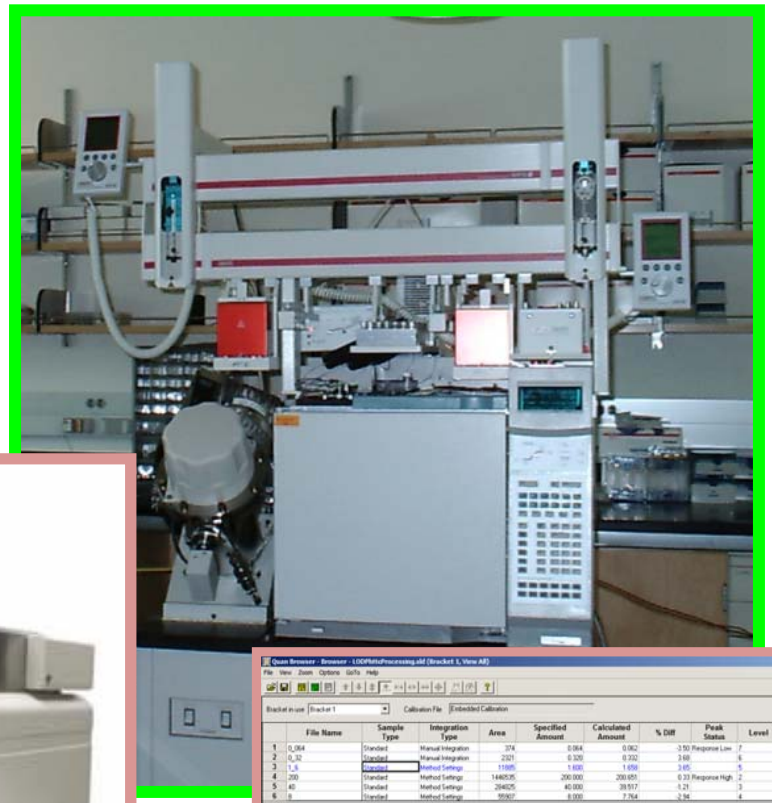
**The challenge is that the total number of measured compounds, *Nc*, is much larger than the number of available distinct samples, *Ns*.**

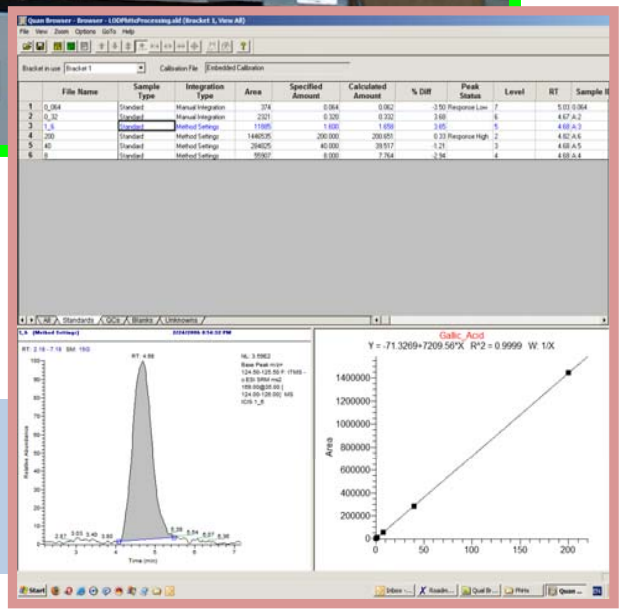
$$Nc >> Ns$$

**This is quite opposite to large clinical studies.**

- Unbiased unsupervised methods – reduction of irrelevant information
- **Biased (Supervised learning) – Identification of the optimal multivariate biomarkers**
- **T-test ,One Way ANOVA, PCA, PCA-DA**
- **Metabolic Pathways Analysis**

# GC-TOF-MS and LC-MS/MS Target Analysis






**Identification and calibration are performed with authentic standards.**

# Structure elucidation


**Highest resolution: 1000000**

**High mass accuracy**

**Hybrid IT-FT-ICR**

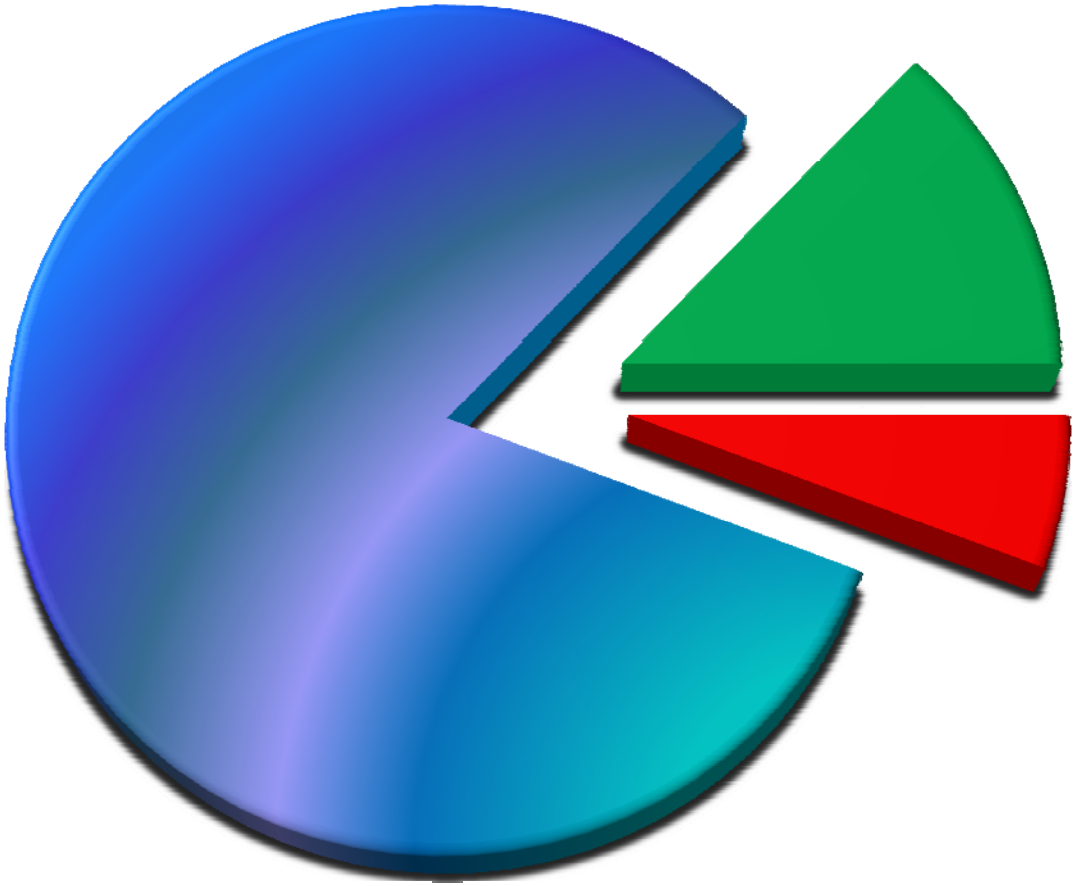
**API ion sources**

**Elemental composition assignment**

**Biomarkers identification**

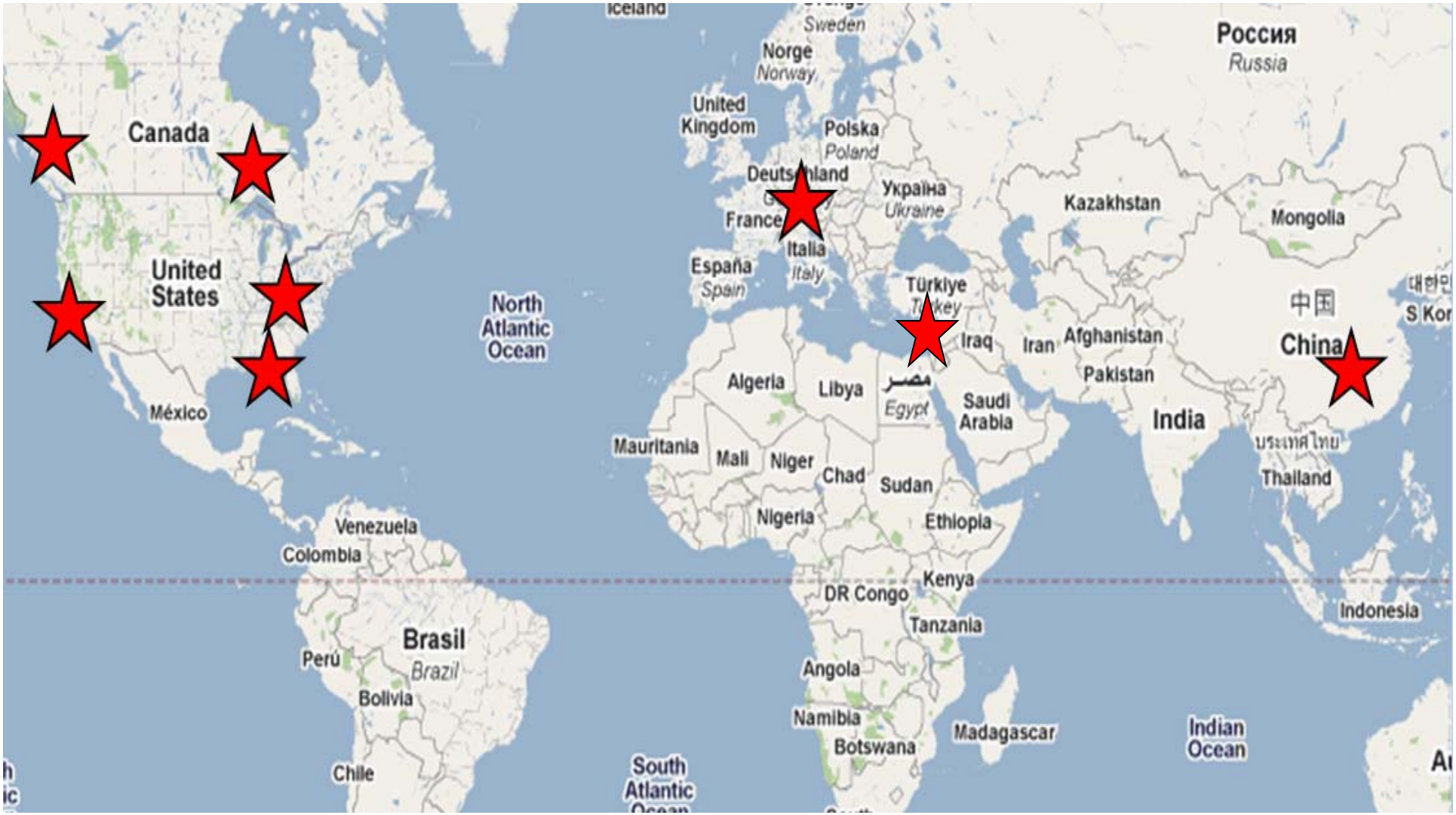
**Instrument is in share with Proteomics Core** **30%**

# Services on campus



- Metabolites Profiling
- Quantitation
- Identification of unknowns

- Dept Plant Sciences
- Dept Evolution & Ecology
- Genome Center
- Cancer Center
- Berkeley
- UCSD
- Stanford
- USDA
- UCSF
- Off State Universities
- Industry


Canada
United States
México
North Atlantic Ocean
Venezuela
Colombia
Brasil
Brazil
Perú
Bolivia
Chile
South Atlantic Ocean
Iceland
Sweden
Norge
Norway
United Kingdom
Polska
Poland
Deutschland
France
Україна
Ukraine
Italia
Italy
España
Spain
Türkiye
Algeria
Libya
مصر
Egypt
Mauritania
Mali
Niger
Chad
Sudan
Nigeria
Ethiopia
Kenya
DR Congo
Tanzania
Angola
Namibia
Botswana
Madagascar
Indian Ocean
Iraq
Iran
Afghanistan
Pakistan
India
Saudi Arabia
Kazakhstan
Mongolia
Россия
Russia
中国
China
S Kor
Thailand
Indonesia

# Acknowledgments


UC Davis Genome Center



Metabolomics Fiehn Lab