Biochemical Profiling of Lipids: Applications to Drug Development and Toxicology

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President/CSO

Scientific Approach

Lipomics

- Building technology for understanding lipid metabolism in global and molecular detail.
  - Lipid metabolism in disease
  - Effects of foods and drugs on lipid metabolism
  - Lipids as central components of individual health status

Metabolomics Integrates

Lipomics

Drugs

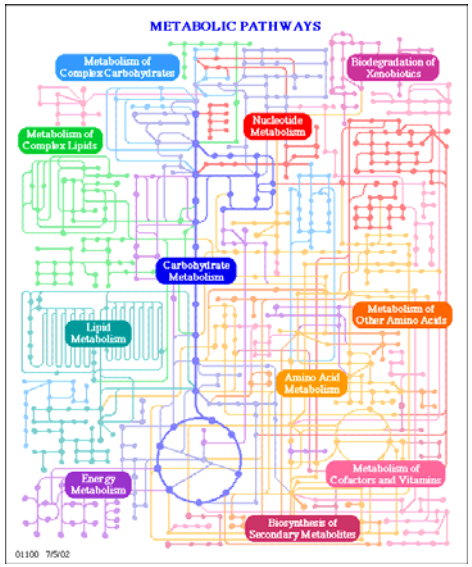
Nutrition

Exercise

Environment

Genes

Metabolism

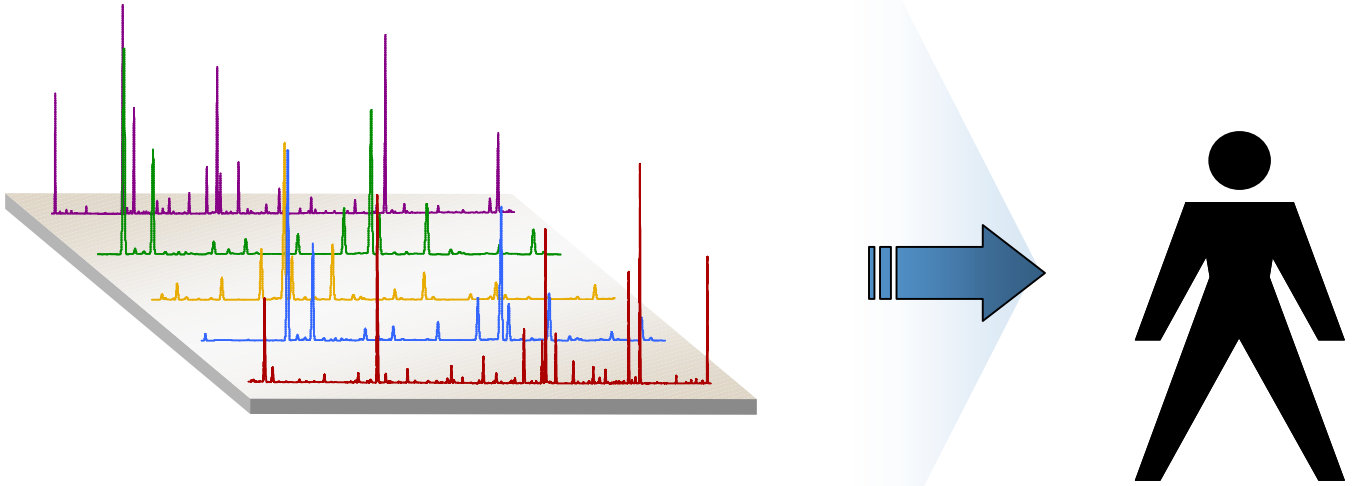


Health

Disease

Metabolic Assessment

- High-content analyses provide *individual* context
- Context allows interpretation



Tools for Enabling Metabolic Assessment

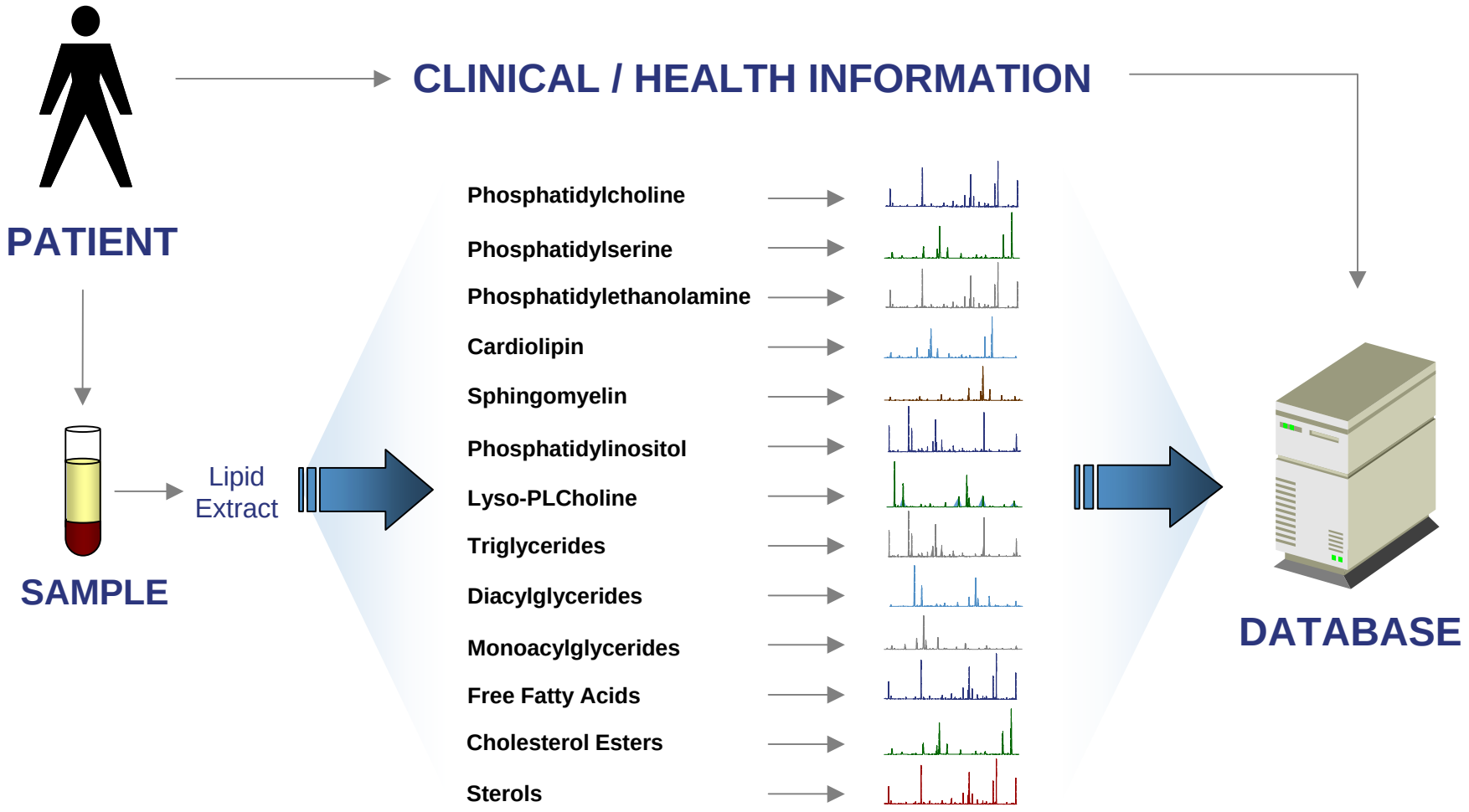
Lipomics

- High-content, quantitative analysis of metabolites
- Analysis of flux through metabolic pathways

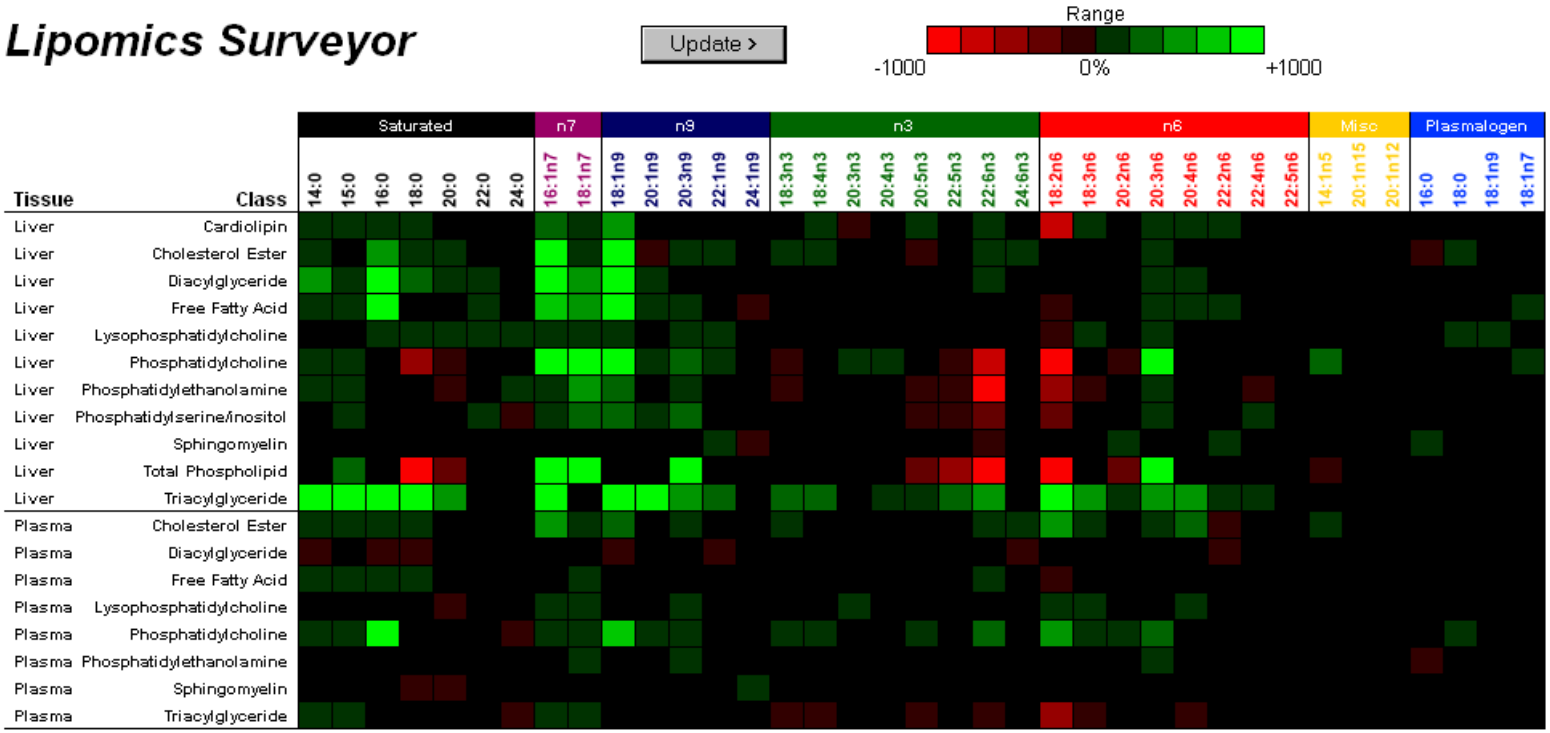
Metabolomics provides both

Quantitative Analysis

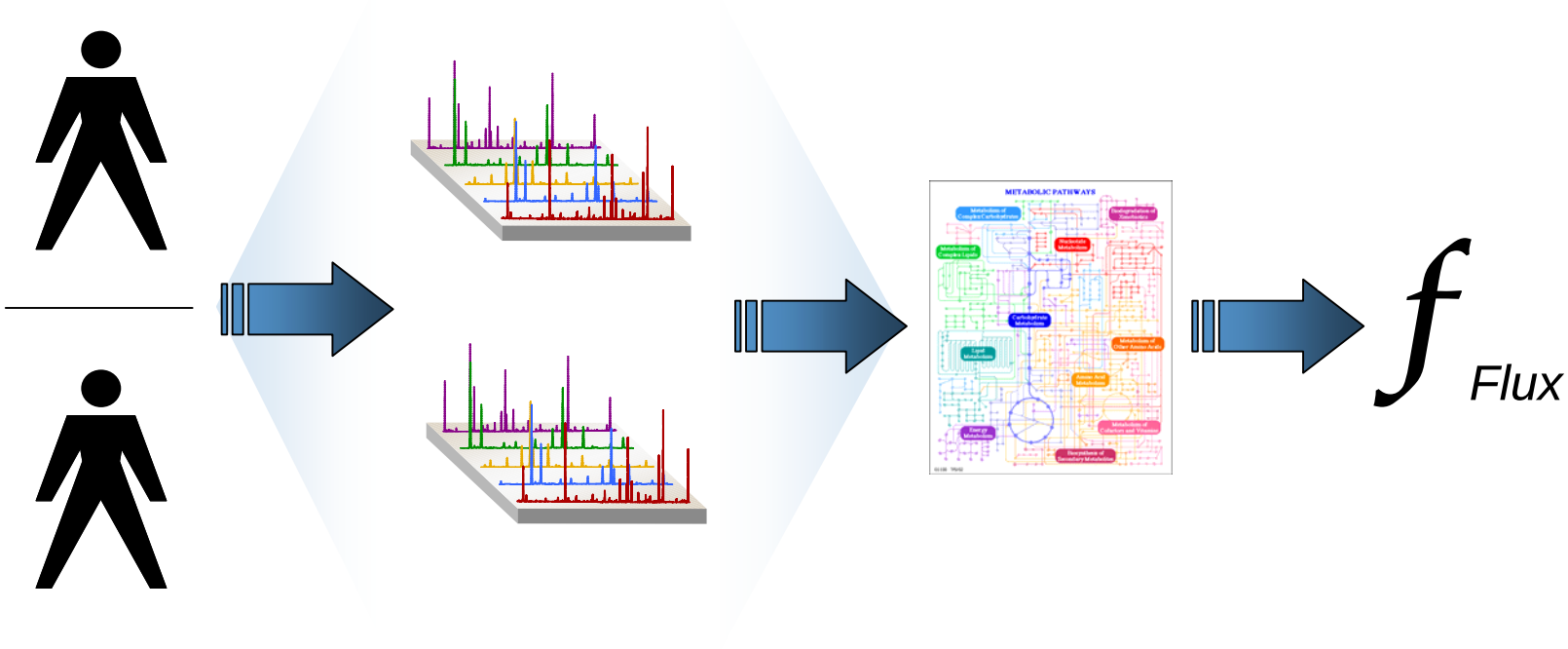
Lipomics



Surveyor® Data Visualization



Steady-State Flux Analyses



Experimental Models | **Quantitative Analysis** | **Map Against Pathway** | **Flux Signature**

Building Diagnostics for Metabolic Disease Therapy

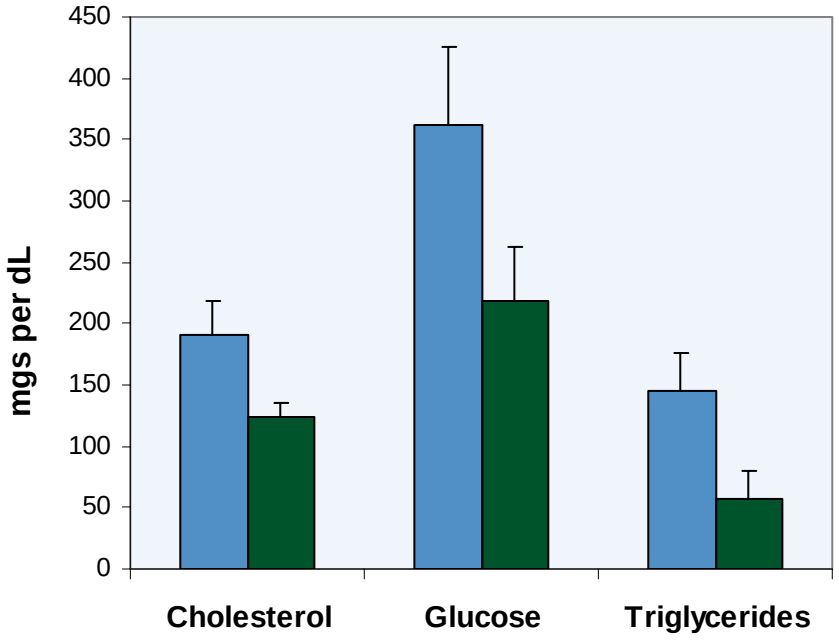
Edward Leiter
The Jackson Laboratory

Profiling the Effects of Insulin-Sensitizing Drugs

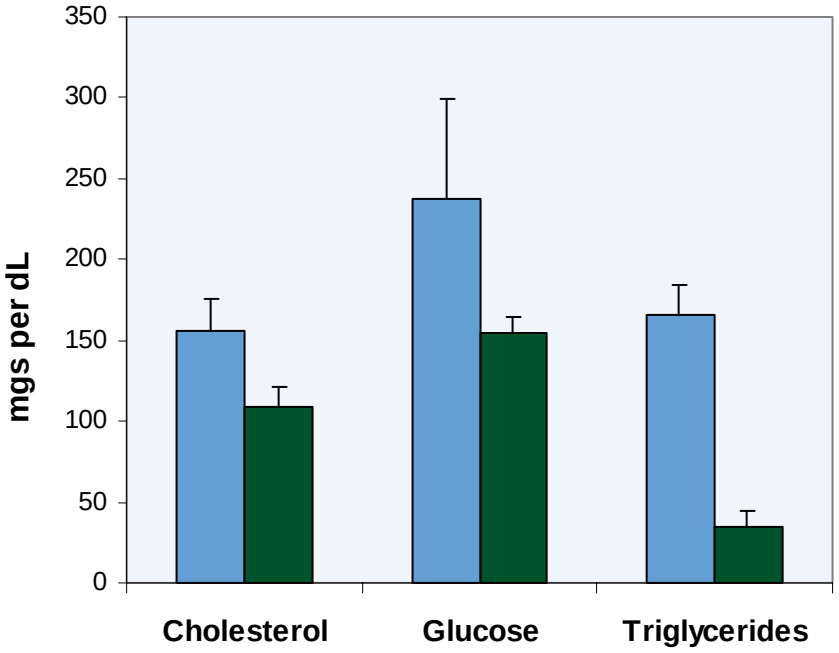
- **Investigated the effects of two diabetes drugs on lipid metabolism in a obese-diabetic model**
- **PPARγ agonist:** Rosiglitazone
- **β-3 adrenergic agonist**: CL316,243

Clinical Biomarkers

PPAR-γ



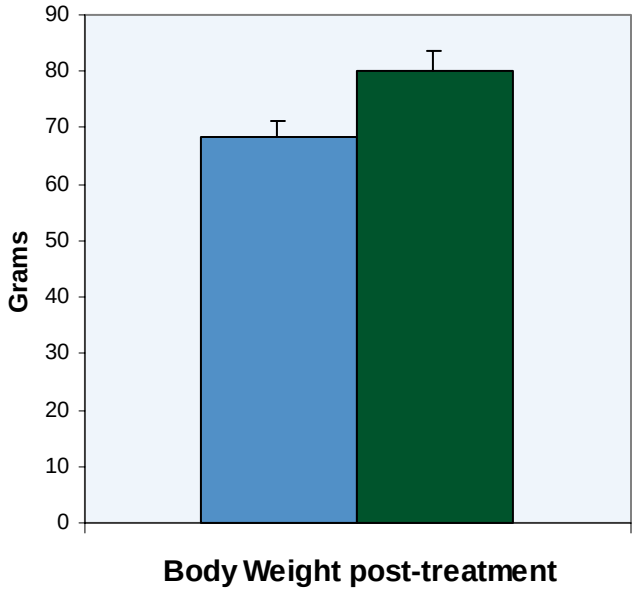
β3-Adrenergic



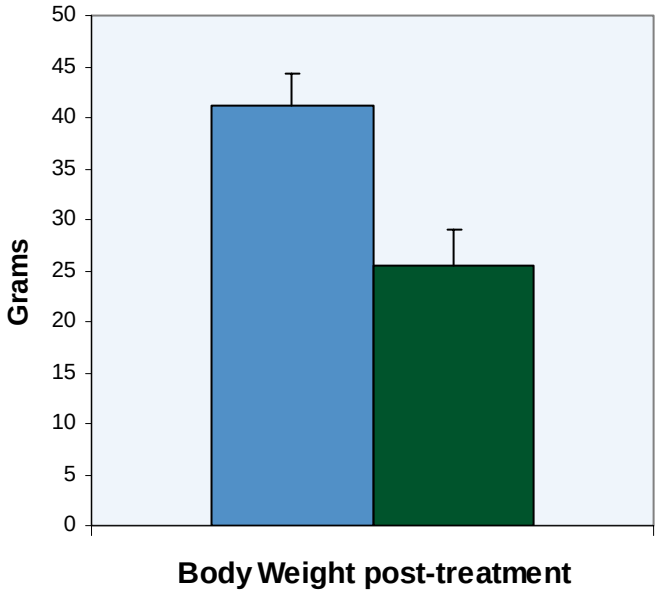
Control Treatment

Body Weight Following Treatment

PPAR-γ

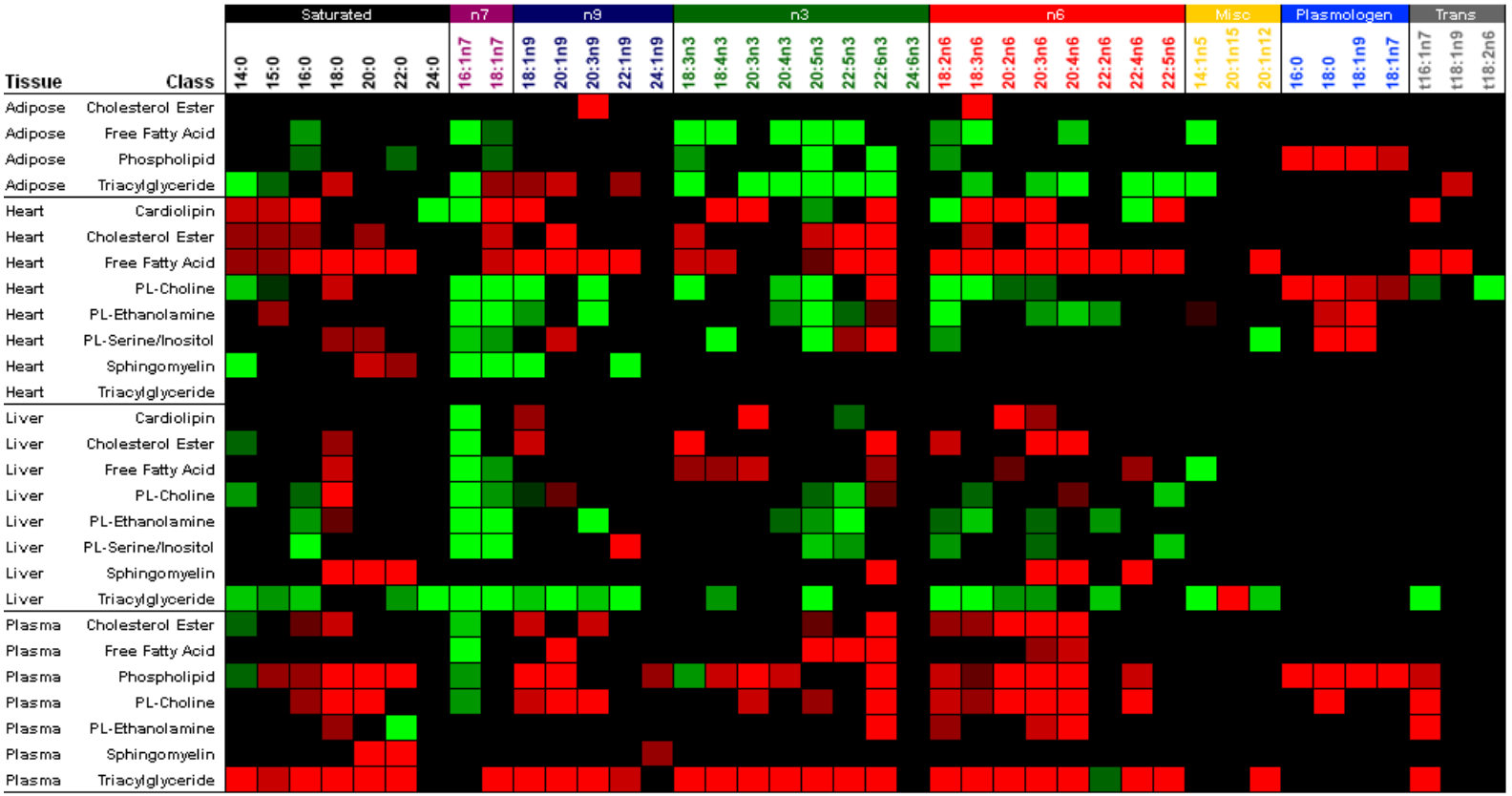


β3-Adrenergic

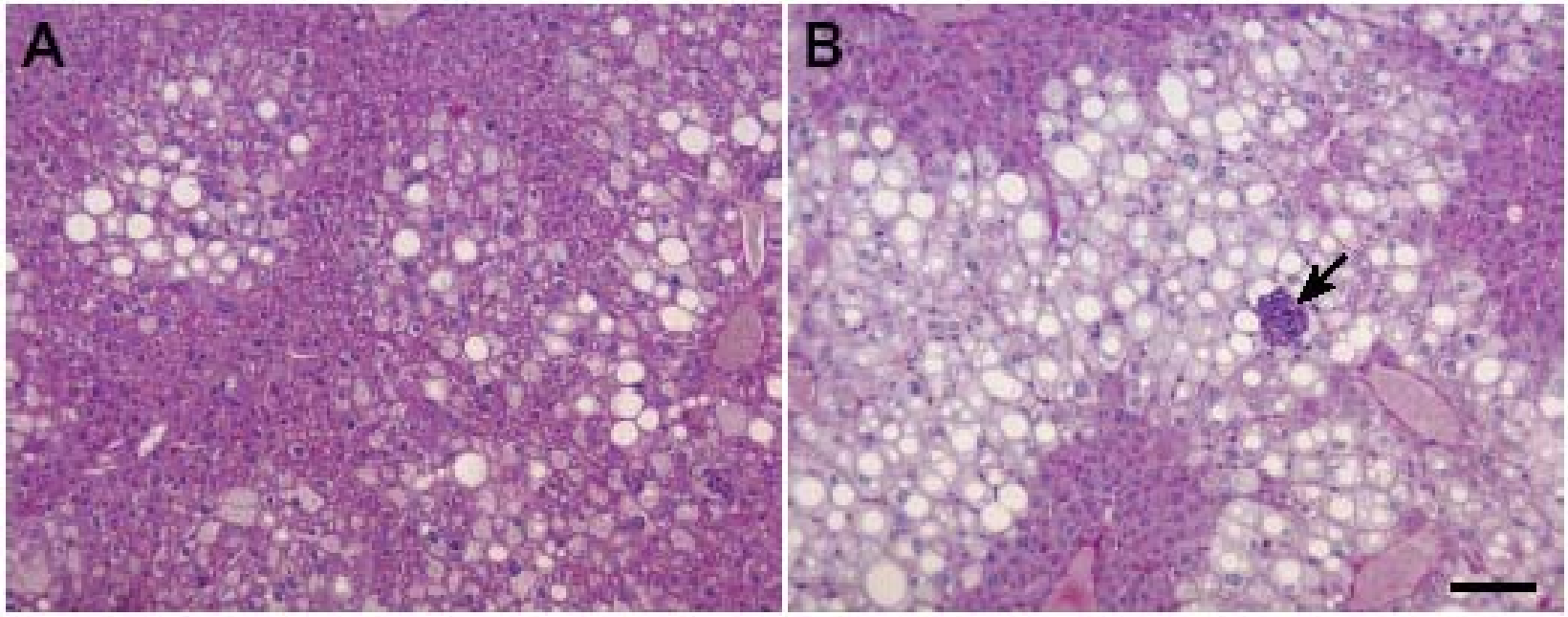


Control Treatment

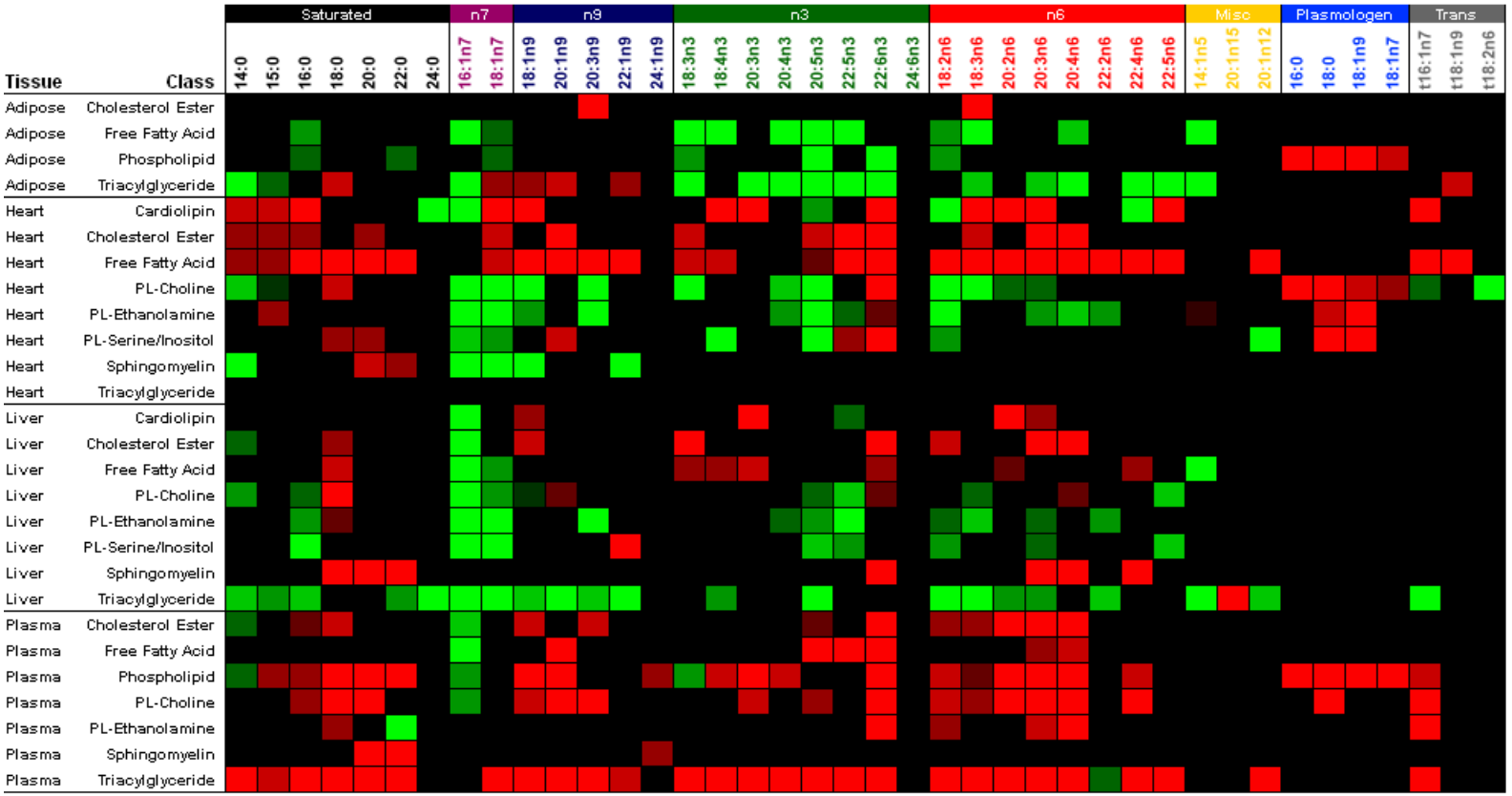
PPAR-γ Treatment



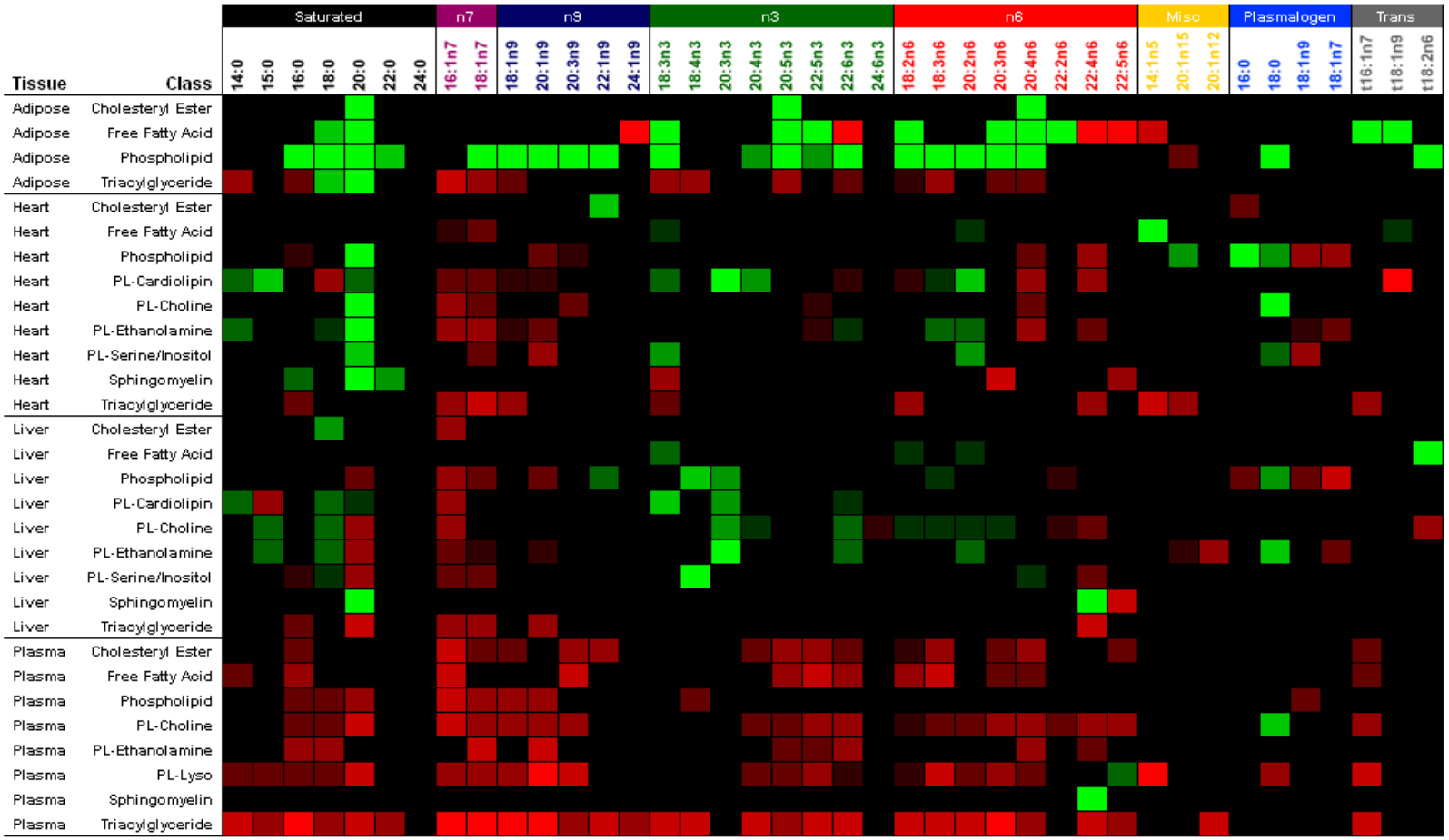
Hepatic Lipid Accumulation



PPAR-γ Treatment



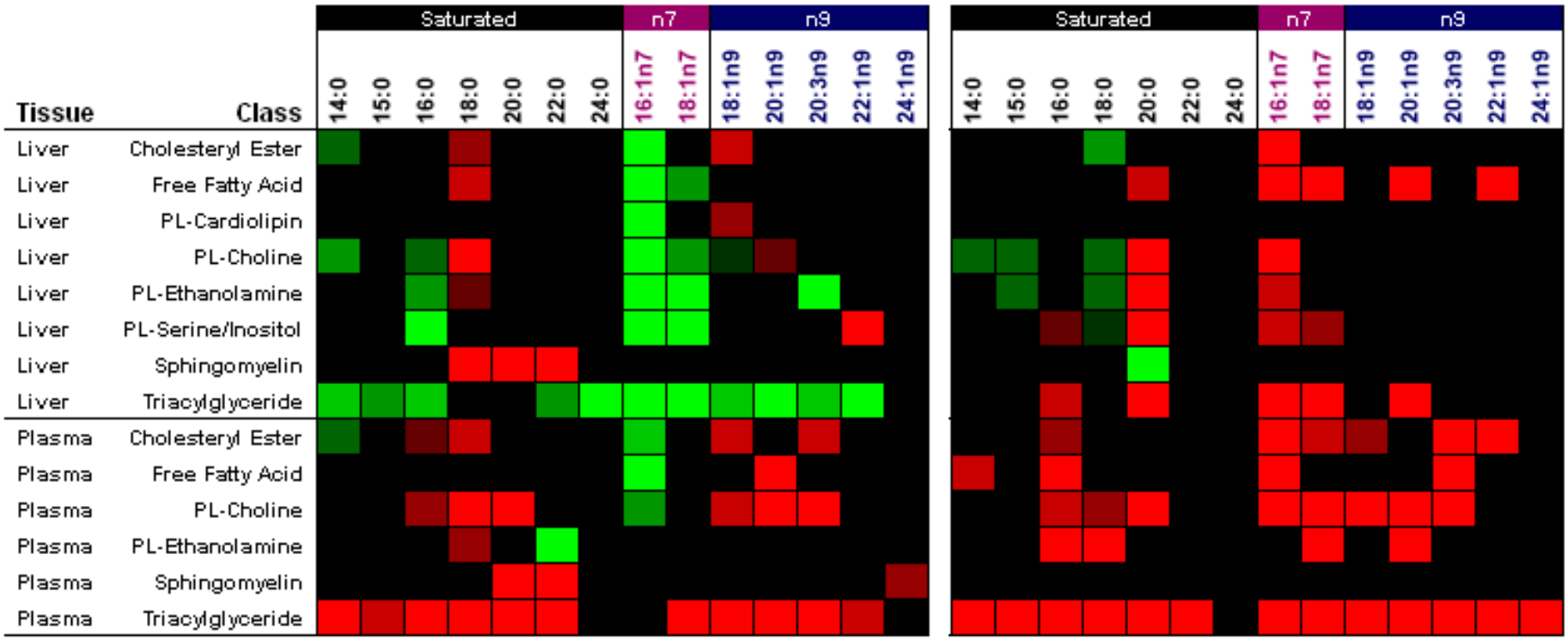
β3-Adrenergic Agonist



Hepatic Lipid Synthesis

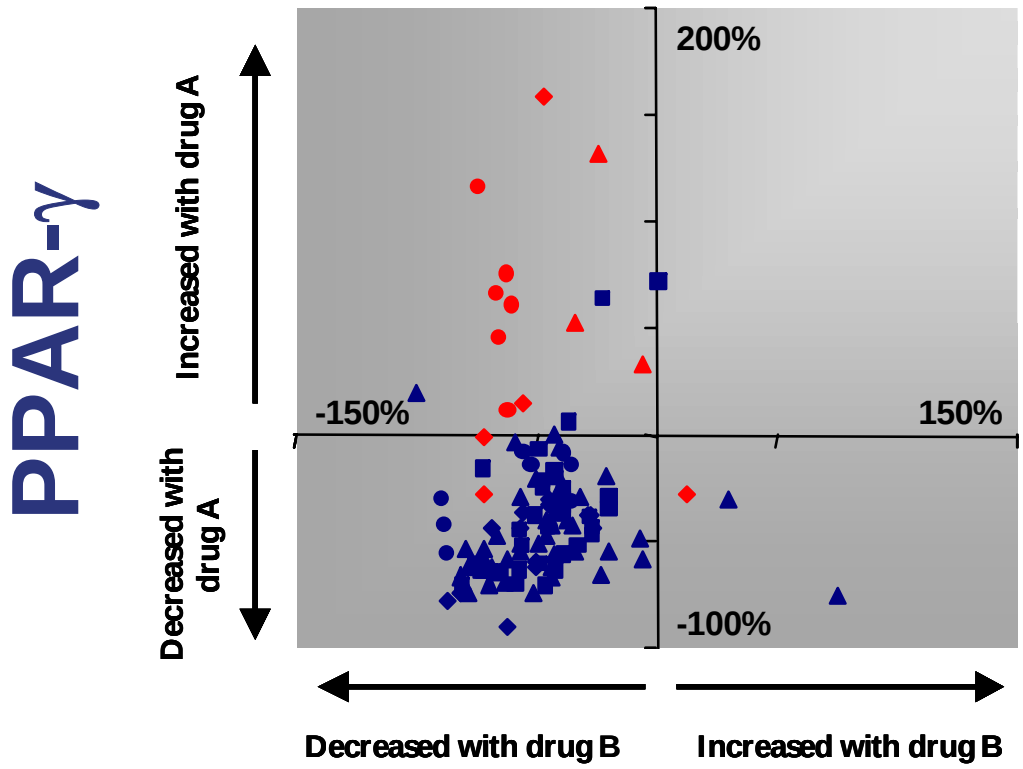
PPAR-γ

β-3 Agonist



Plasma Metabolome Reveals Mechanism

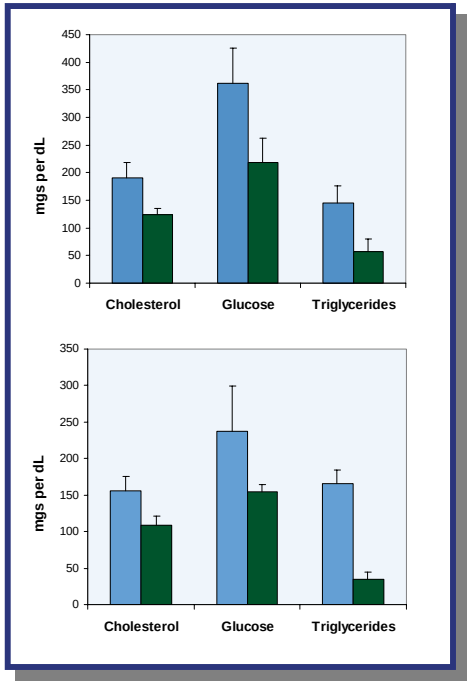
Lipomics



β3-Adrenergic

Signature of lipogenesis

All other metabolites



Metabolic Assessment

Lipomics

- High-content assays are required to elucidate metabolic basis for phenotype
- Want data on both metabolite concentrations and metabolic flux

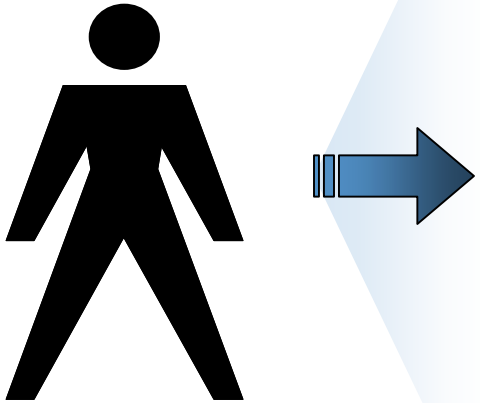
Must know both the identity and quantity of each metabolite

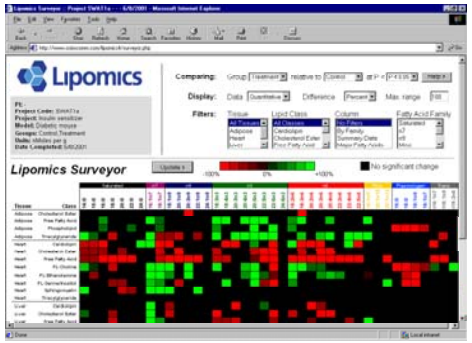
Building Diagnostics

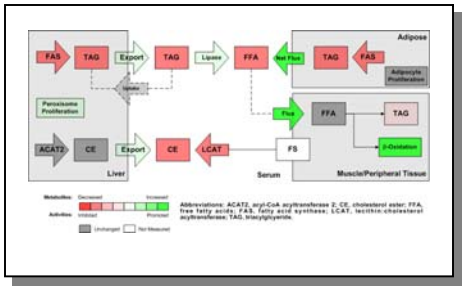
- Single chronic diseases have more than one metabolic (or environmental) cause
- Next generation diagnostics need to provide actionable information.
  - What dysregulation needs treatment?
- Metabolic assessment enables actionable, individual-specific diagnoses.

Delivering Health to the Individual

Lipomics







Nut_x

R_x

$Life_x$

Individual Dx | **Map to Pathway** | **Action**

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