

#### **Biochemical Profiling of Lipids: Applications to Drug Development and Toxicology**

#### Steven M. Watkins, Ph.D. President/CSO

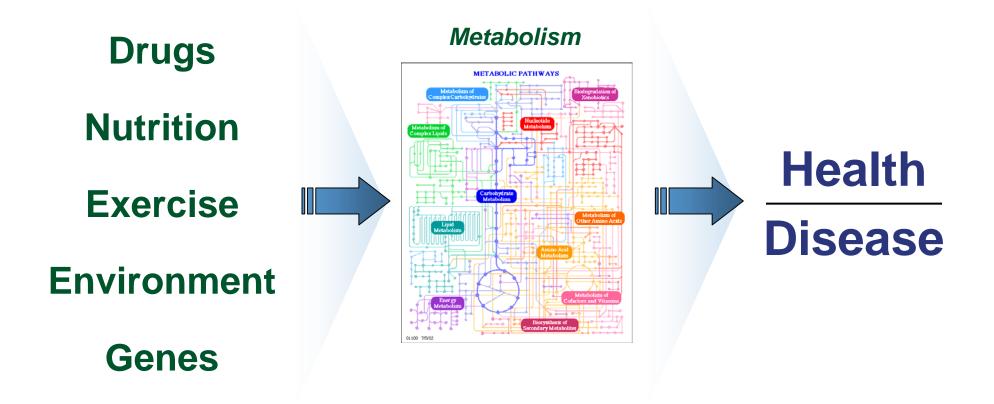
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### **Scientific Approach**



- 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

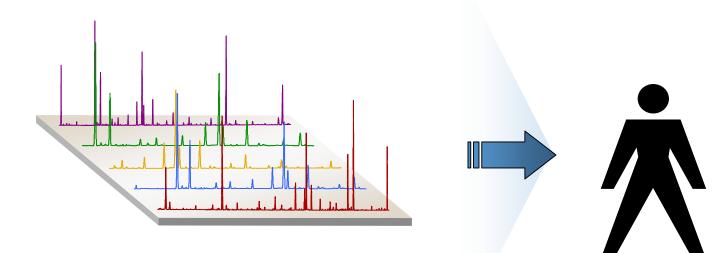


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#### Metabolic Assessment



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



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# Tools for EnablingImage: Construction of the second se

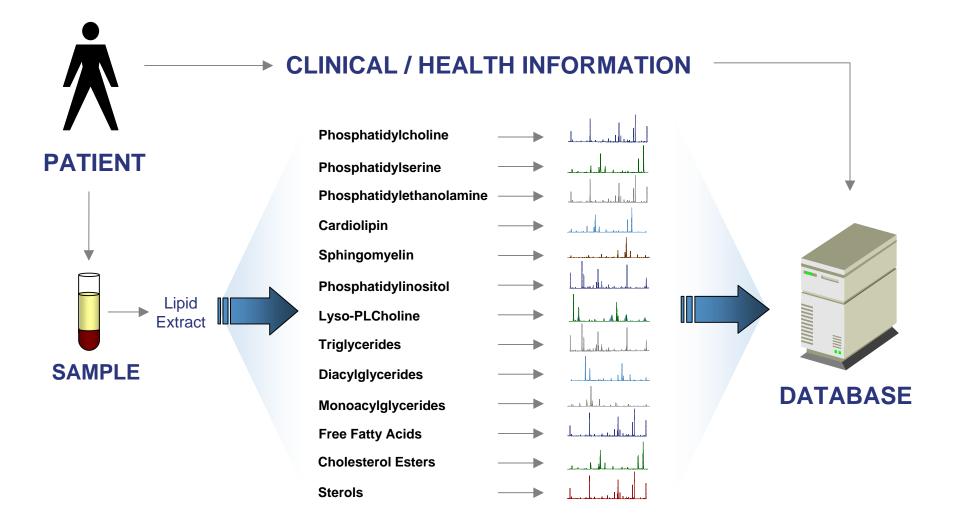
- High-content, quantitative analysis of metabolites
- Analysis of flux through metabolic pathways

## Metabolomics provides both

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#### **Quantitative Analysis**

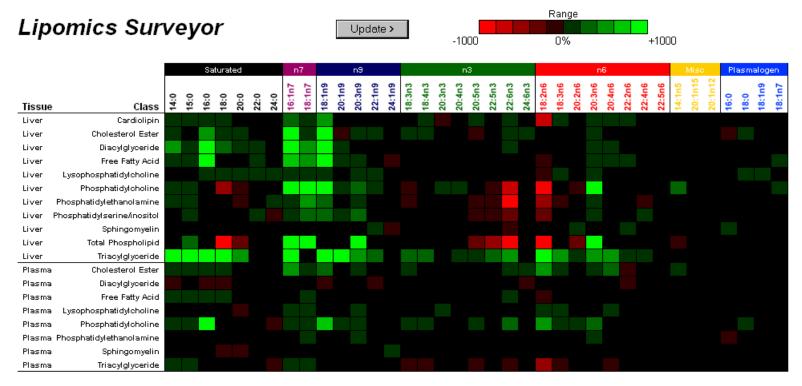




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### Surveyor<sup>®</sup> Data Visualization



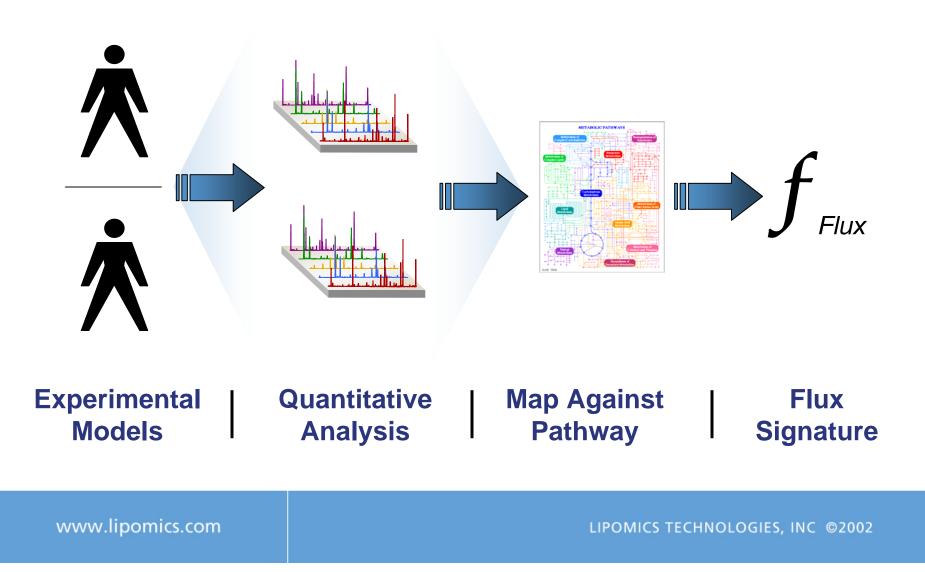


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#### Steady-State Flux Analyses







#### **Building Diagnostics for Metabolic Disease Therapy**

#### Edward Leiter The Jackson Laboratory

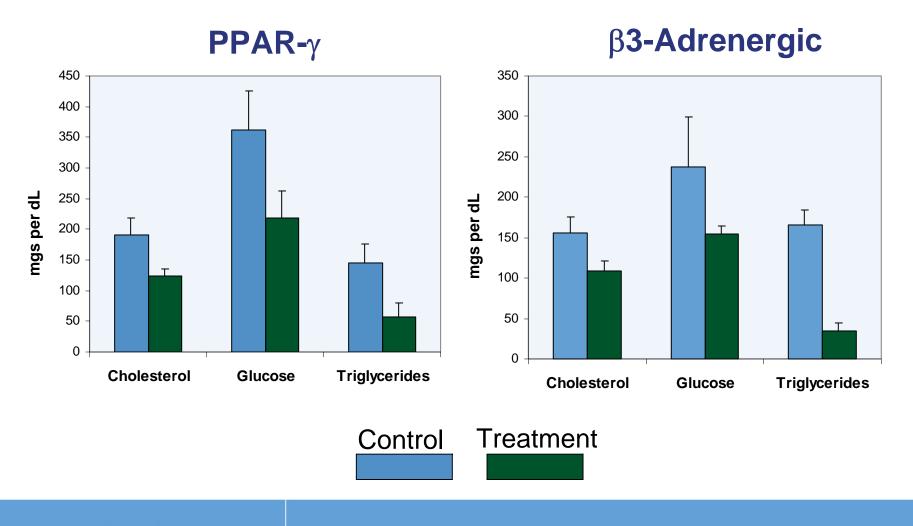
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## Profiling the Effects of Lipomics Insulin-Sensitizing Drugs

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

#### **Clinical Biomarkers**

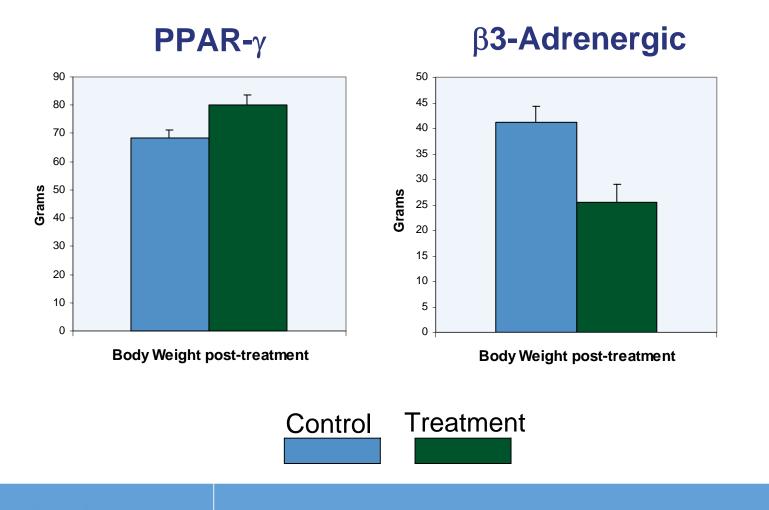




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#### **Body Weight Following Treatment**





#### **PPAR-** $\gamma$ **Treatment**

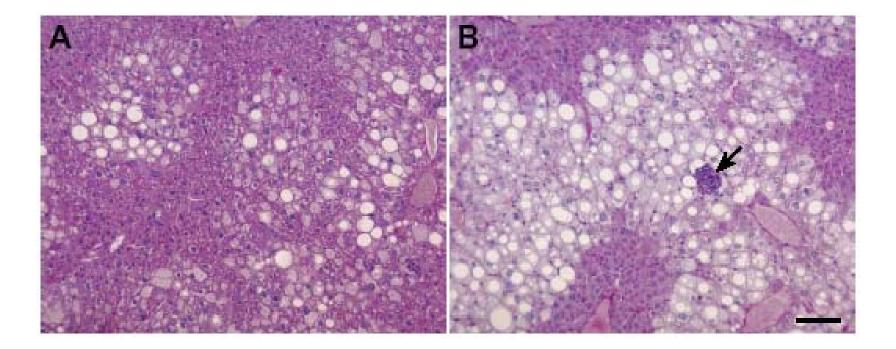


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#### Hepatic Lipid Accumulation





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#### **PPAR-***γ* **Treatment**



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### β**3-Adrenergic Agonist**



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### Hepatic Lipid Synthesis 🛛 📢 Lipomics



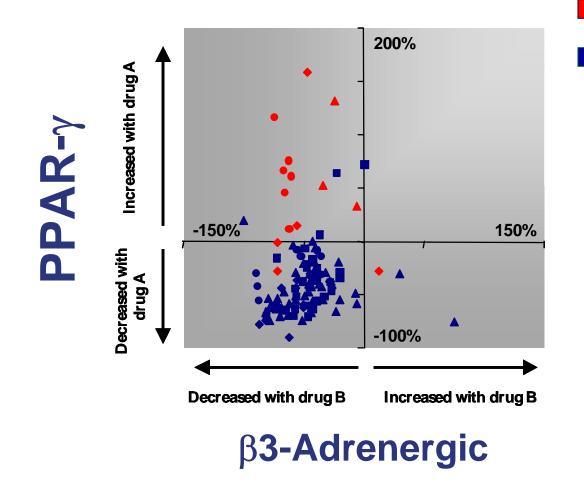
#### **PPAR-**γ

#### β**-3 Agonist**

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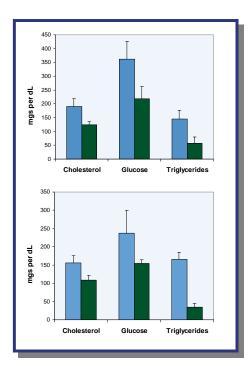
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## Plasma Metabolome Reveals Lipomics Mechanism



Signature of lipogenesis

All other metabolites



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#### **Metabolic Assessment**



- 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

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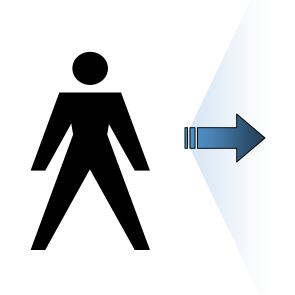
### **Building Diagnostics**

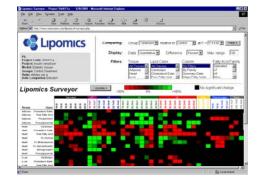


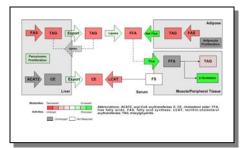
- Single chronic diseases have more than one metabolic (or environmental) cause
- Next generation diagnostics need to provide actionable information.
  - What dysregulation needs treatment?
- Metabolic assessment enables actionable, individual-specific diagnoses.

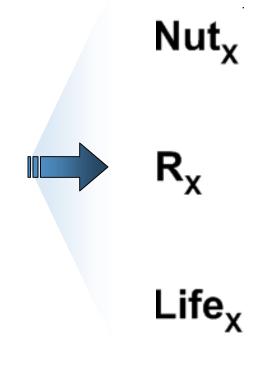
## **Delivering Health to the Individual**











## Individual Dx Map to Pathway Action

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