



**ProFACT**  
**PROTEOMICS**  
MAKING A FUNCTIONAL DIFFERENCE

# **Functional Proteomic Profiling for Biomarker and Drug Discovery**

**BioPartnering 2011**

**May 23, 2011**

# About ProFACT Proteomics, Inc.

**1 Deer Park Drive, Suite P  
Monmouth Junction, NJ 08852  
[www.profactproteomics.com](http://www.profactproteomics.com)**

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- **Founded in 2004**
- **3 Patents Pending**
- **5 NJ Commission on Science and Technology Grants, 2006-09; QTDC Grants, 2009, 2010**
- **High Throughput Functional Proteomics Infrastructure**
- **Molecular Profiling and Discovery Services with transferable protocols & Consumable Reagents**
- **One Major Biopharma Service Agreement**
- **Three Institutional Consortium arrangements**
- **Seeking client-sponsored research, collaborations, partnerships**
- **Ongoing public and private (one-on-one) tech webinars by subscription.**

# **Lack of Productivity in BioPharma**

## **An Opportunity for Functional Proteomics**

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- **A wealth of cellular response-based pre-clinical drugs are not well-characterized *vis* mechanism of action and off-target effects.**
- **Proteomics platforms reliant on sequence annotation do not provide functional characterization.**

**BioPharma needs new means to amass productive early stage proteomic data that:**

- **can access natural cellular sources**
- **functionally characterize protein-drug interaction**
- **functionally discriminate to the level of conformational variants**

# Competitive Advantages

- **Specificity, the Functional Proteomics Advantage:**
  - A sufficiently functionally characterized and enriched protein can yield a **Sequence ID** whereas **Sequence Annotation** cannot be reconciled to a functioning protein.
  - Key to specificity is the quality and manner of separations.
- **ProFACT Drug Discovery and Development Advantages:**
  - Drug discovery from **natural cellular sources**, not recombinant proteins
  - Conformational variant compartmentalization and characterization
  - Dimension: Multiple (a customizable number) sub-proteomic comparisons at once, then drill-down by analysis and iterative redistribution and then target enrichment vs single-ply pattern generation platforms
  - Pattern Profiling and Drug Responsiveness in one platform

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## New Functional Proteomics Strategies for Drug Discovery and Functional Biomarkers

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### Conformerics™ Bioactive Target/Drug Assays

- Compartmentalize functional variants
- Challenge variants with small molecules
- *Kinetics-based drug response from natural cellular sources*

### Functional Proteome Prospecting™

- Find drug targets and functional biomarkers from some or no foreknowledge.
- Enrich and optimize discoveries for further characterization, screening, and sequence annotation.

### Rational Genome to Proteome Prospecting™

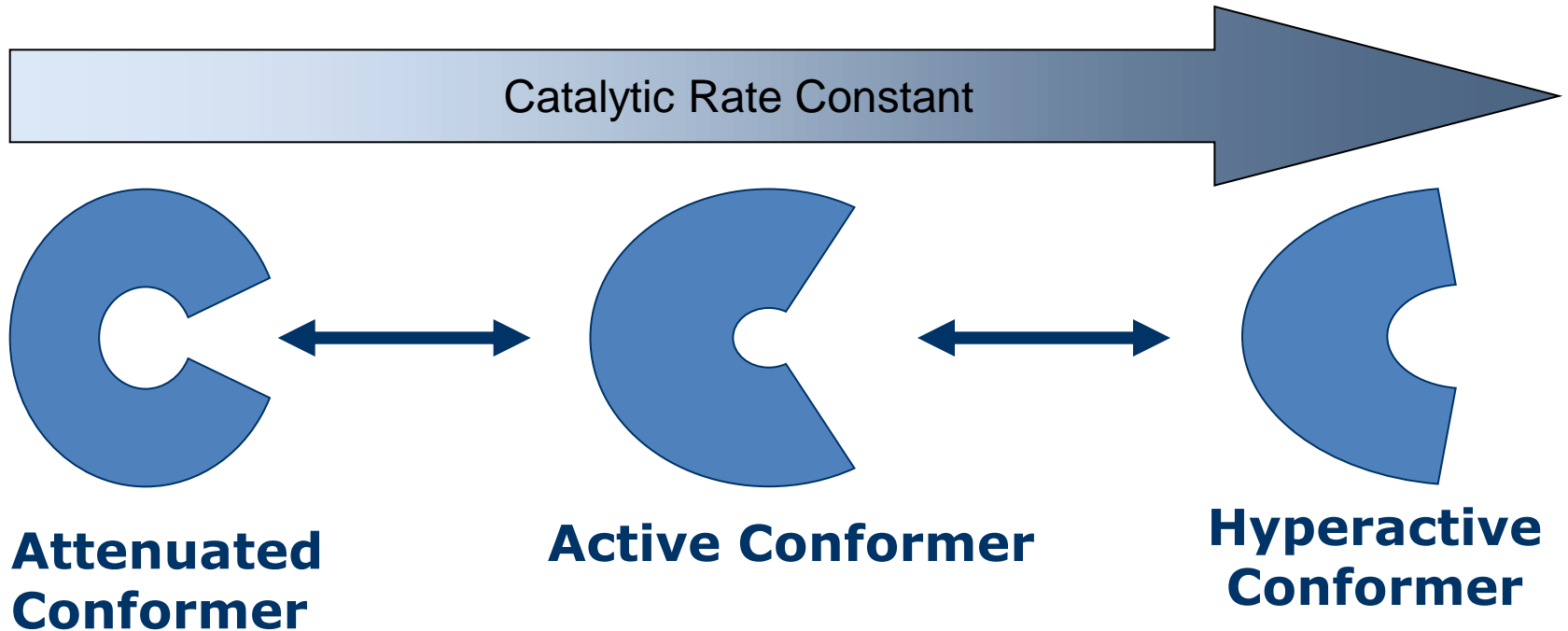
- Reconcile gene and protein expression for biomarker discovery.

### DeepSee™

- SeraFILE™-based kits for entry level functional profiling.

# Conformerics™ Bioactive Target/Drug Assays

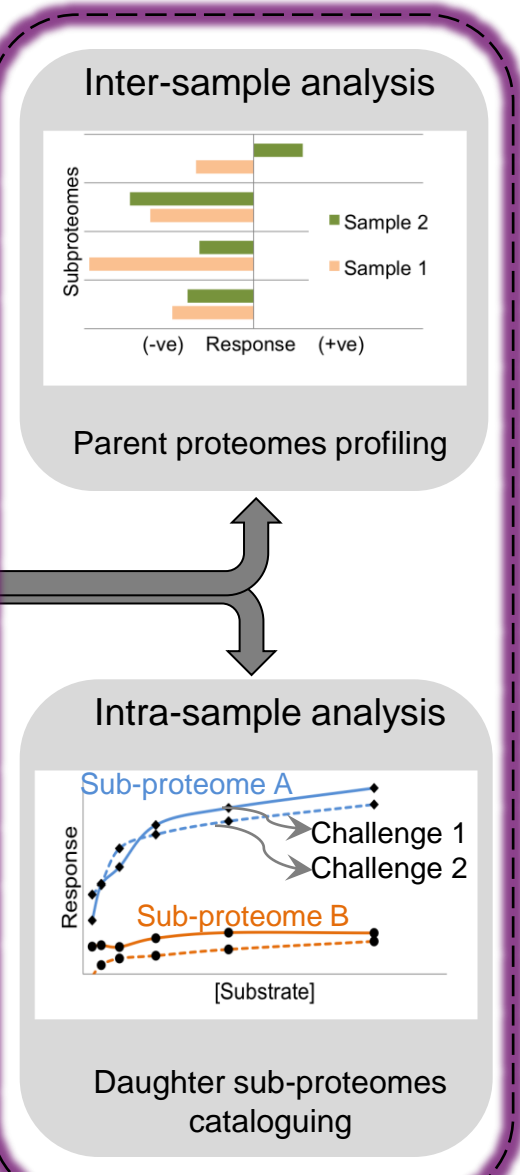
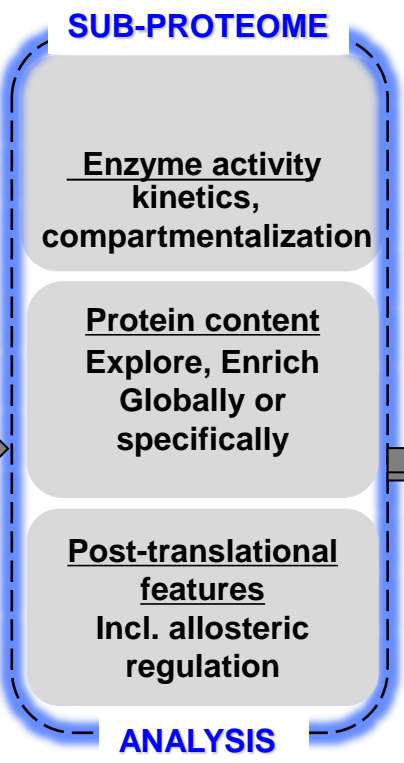
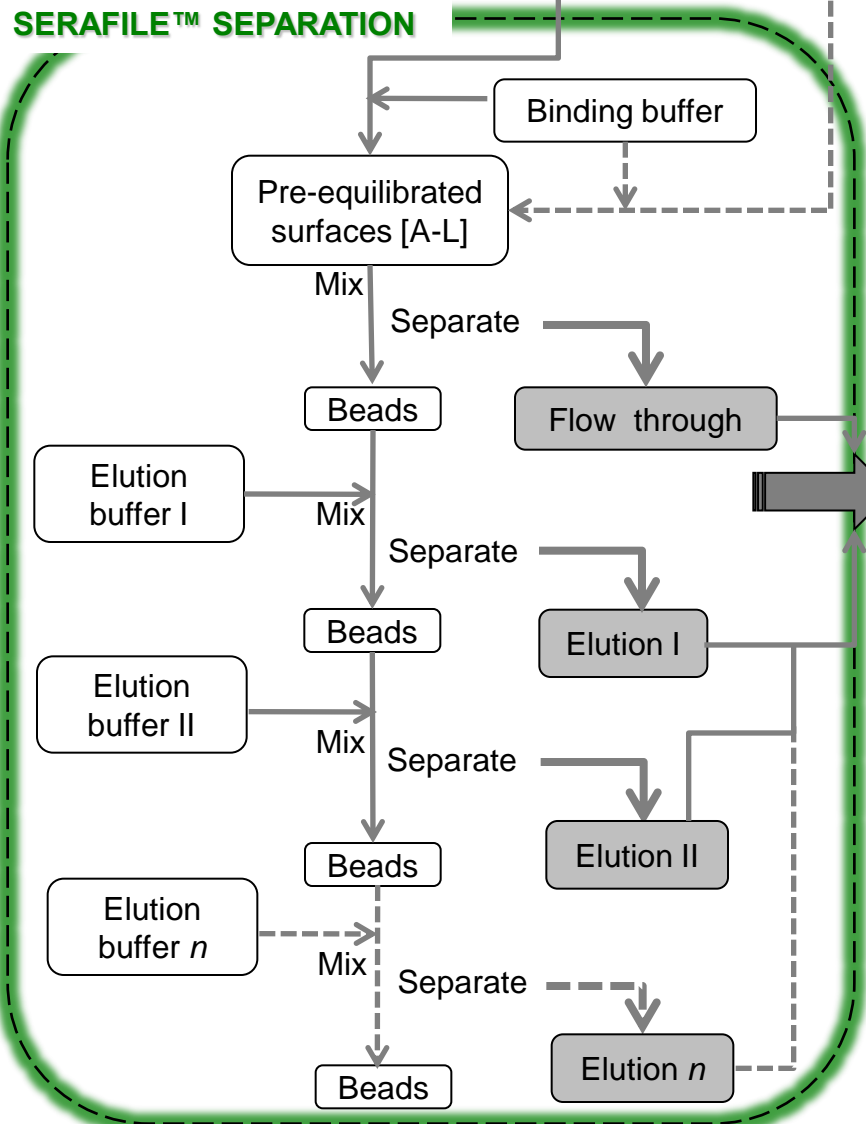
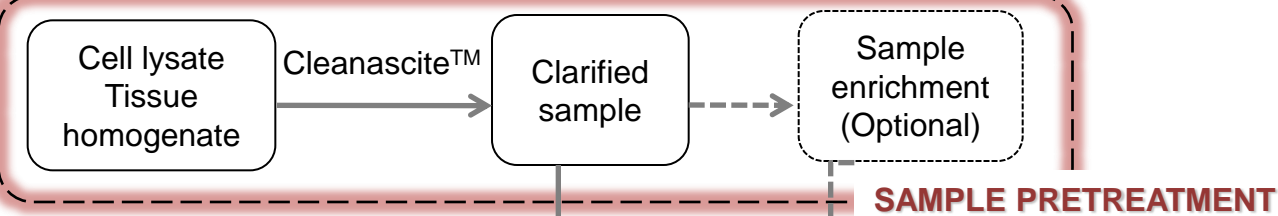
- Compartmentalize functional variants
- Challenge specifically pooled variants with small molecules
- Kinetics-based drug response indexing from natural cellular sources



Recombinant strategies do not consider the transitions of enzymes in their natural environment

Conformerics™ screens small molecules against the most kinetically responsive (disease specific) enzyme variants

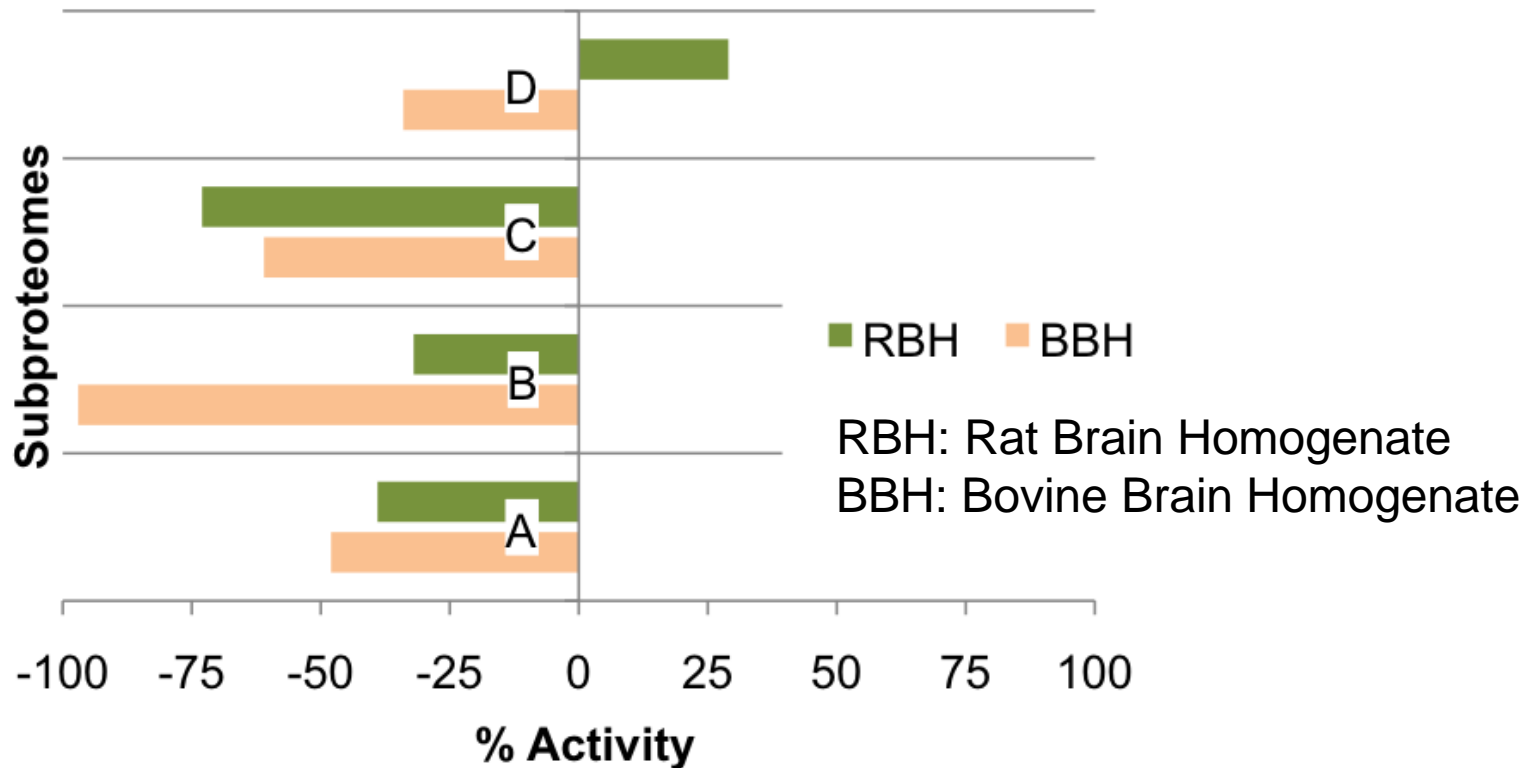
# SeraFILE™ Profiling & Cataloging



# SeraFILE™

## Comparison of Parent Proteomes

Profiles of cyclic AMP hydrolysis activity modulated by cyclic GMP in Phosphodiesterase

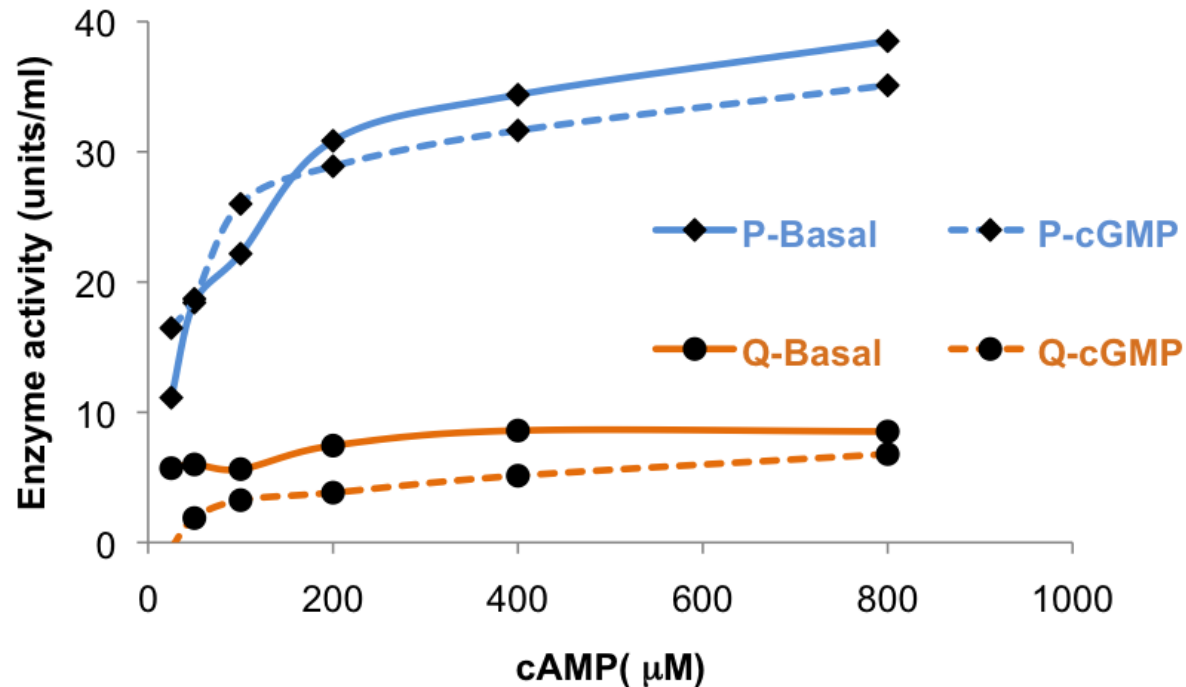




# SeraFILE™

## Comparison of Derivative Proteomes

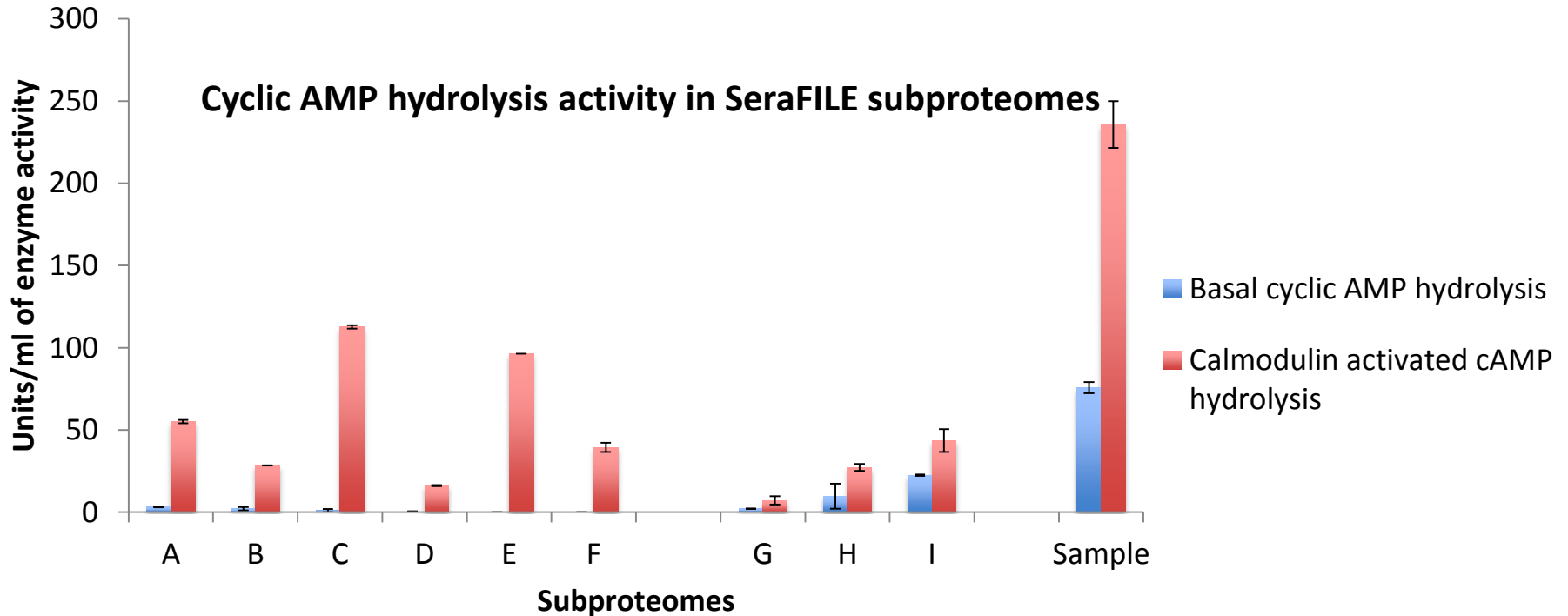
Profiles of cyclic AMP hydrolysis activity modulated by cyclic GMP in Phosphodiesterase



# SeraFILE™

## Functional Profiles of Phosphodiesterase

### PDE 1 Activation with Calmodulin

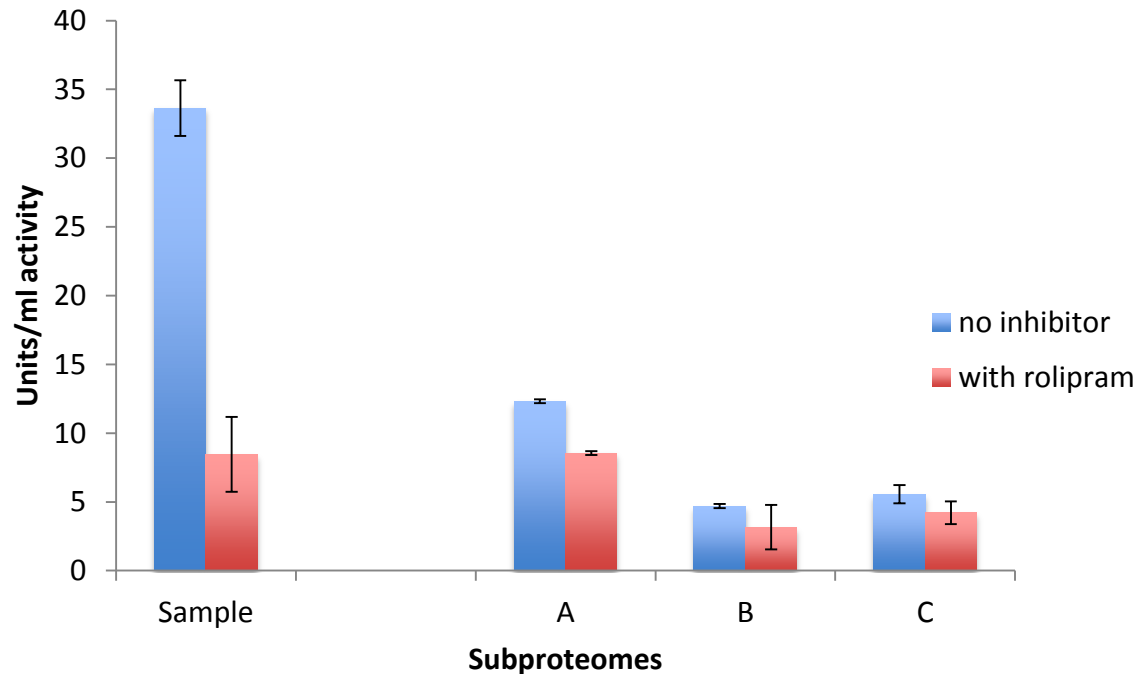


**SeraFILE™ generates a profile of enzyme activities and compartmentalizes those activities in subproteomes.**

# SeraFILE™

## Functional Profiles of PDE Activity

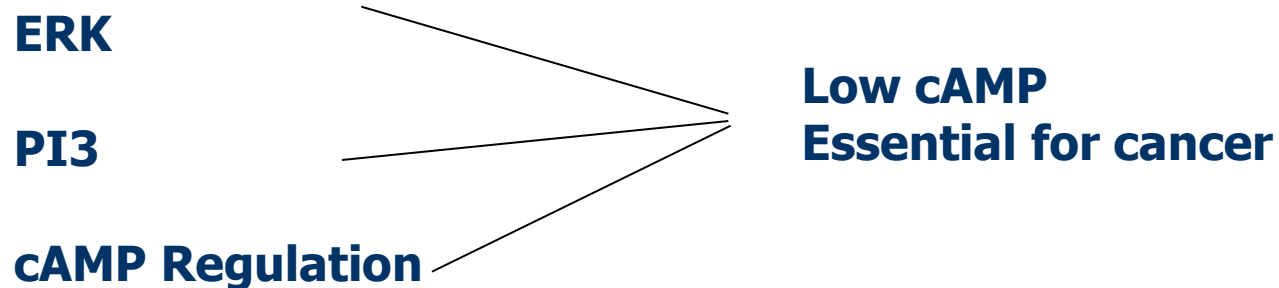
**Inhibition of cyclic AMP hydrolysis activity in bovine brain homogenate (BBH) with rolipram, a PDE4 specific inhibitor.**



**SeraFILE™ generates a profile of enzyme activities and compartmentalizes those activities in subproteomes.**

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## A Commercial Direction For Cancer Targets



**PDE inhibitors, though clinically promising,  
often fail due to adverse events and toxicity generally  
attributable to lack of specificity**

**Functional Phosphodiesterase Variants Could Be Significant  
Cancer Targets**

**with the assistance of ProFACT's proteomics strategies**

# SeraFILE™

## Proteomic connections to function, small molecule modulation, and gene expression

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### Enrichment Strategies

#### Specific Activity

- Immunological
- Catalytic Rates
- Conformation Variants
- Cellular Response

#### Purification

#### Identification/Characterization

### Discovery

#### Comparisons - Cell Models

- Environmental Stimuli
- Oxygen Stress
- Interfering RNA
- Drugs

#### Comparison of Normal/Disease

- Tissue
- Blood/Serum

# Call to Action

## Collaborations & Partnerships

### **Biomarker Discovery**

**Gene Expression to Protein Reconciliation**  
**Functional Protein Profiling**  
**Targeted Enrichment**

### **Drug Discovery**

**Protein classes in progress:**  
**Phosphodiesterases**  
**Kinases**  
**Proteasome**  
**p53**

**Platform is open to others**  
**Allosteric Regulation and Kinetics**  
**Enzyme Variant Cataloging/Characterization**  
**Small Molecule Screening/Indexing Drug Responsiveness**

**We invite you to help build ProFACT's vision for new candidates functionally optimized at the cellular, mechanistic and clinical levels.**



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