

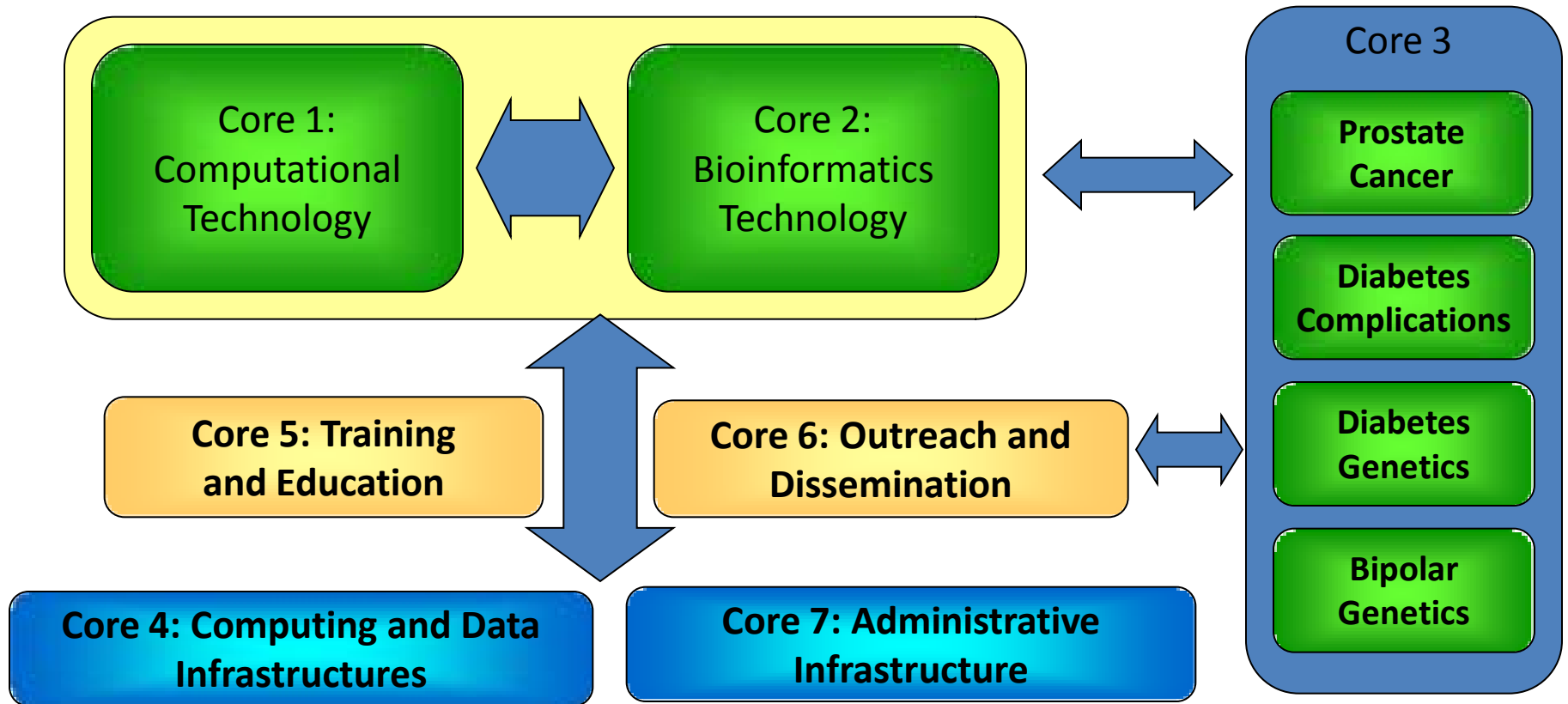
# Driving Biological Problems

## National Center for Integrative Biomedical Informatics, Core 3

Gilbert S. Omenn, M.D., Ph.D.  
Core 3 Director



# National Center for Integrative Biomedical Informatics (NCIBI)



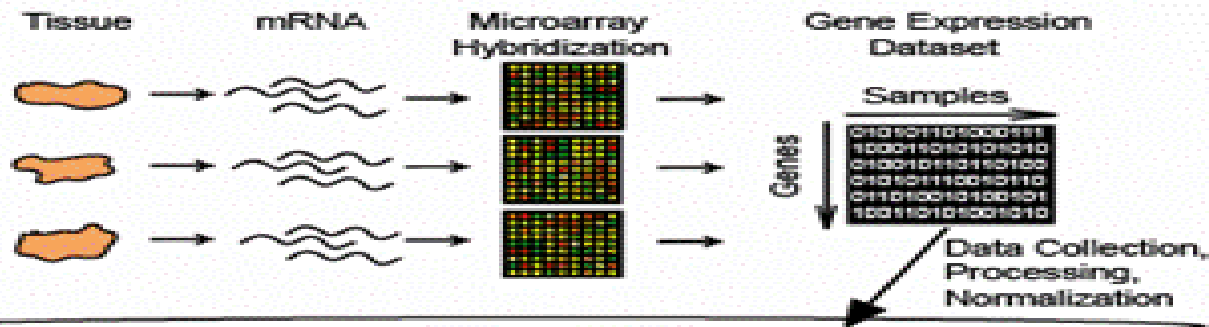
# Prostate Cancer DBP

## Chinnaiyan Lab + ISB/Seattle

- Androgen-mediated signaling
- EZH2/polycomb gene regulation
- Exploitation of Oncomine and of new tools for bioinformatics-based discoveries, then lab confirmation

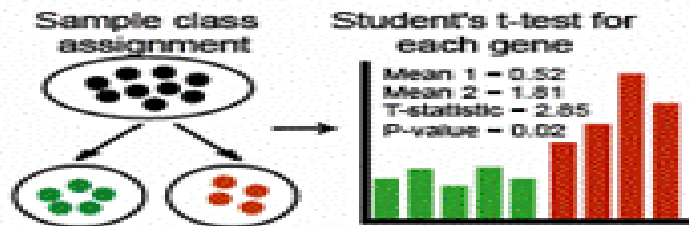


# Cancer gene expression profiling with DNA microarrays

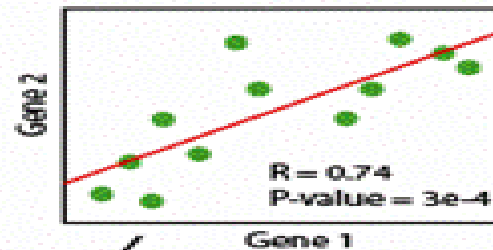


**ONCOMINE Microarray Database**  
90 independent datasets, 15 cancer types  
7,292 microarray experiments  
79,098,564 gene expression measurements

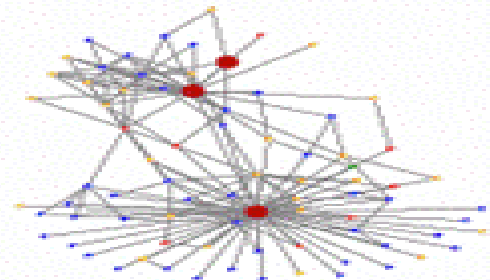
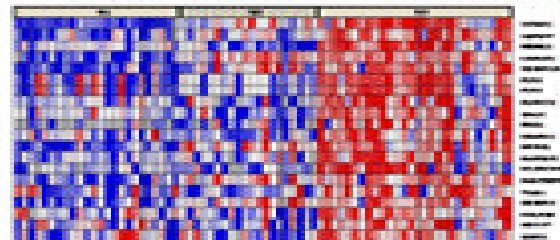
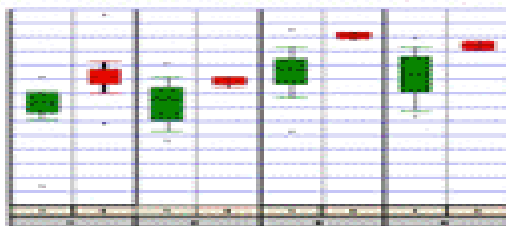
## Differential Expression Analysis (380 to date)



## Correlation Analysis

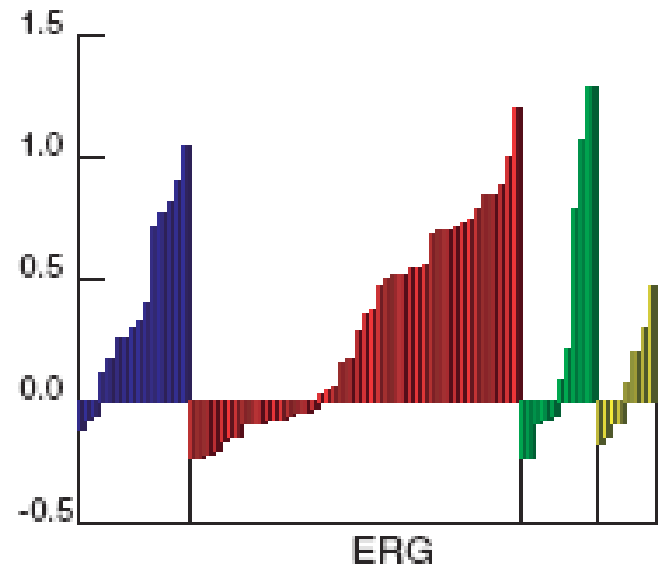
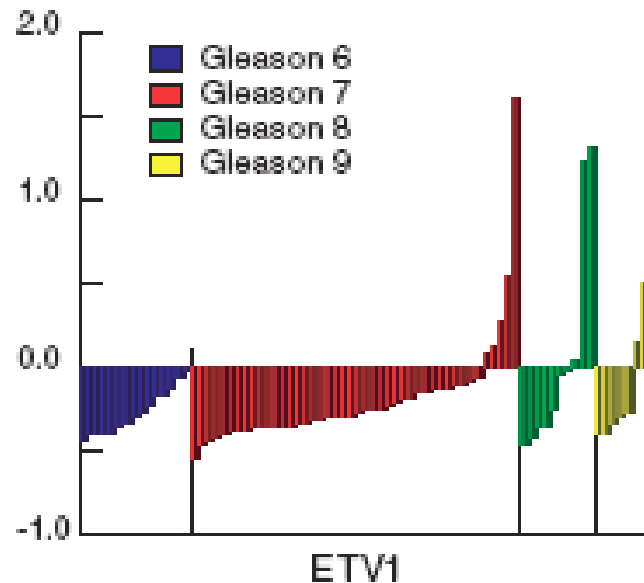
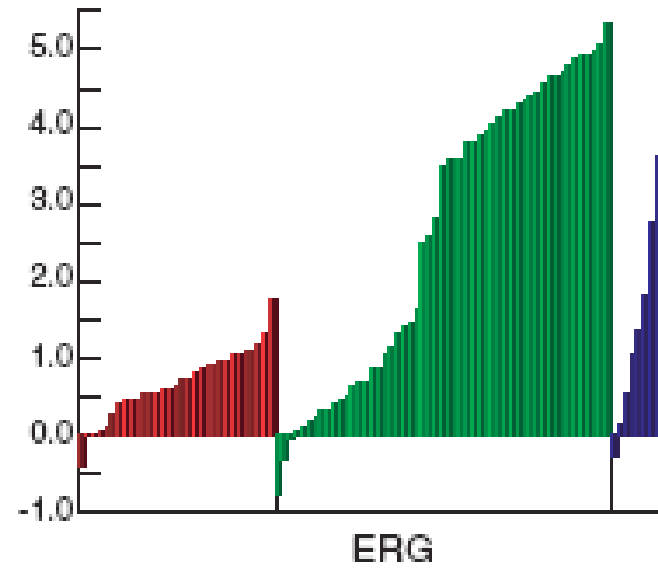
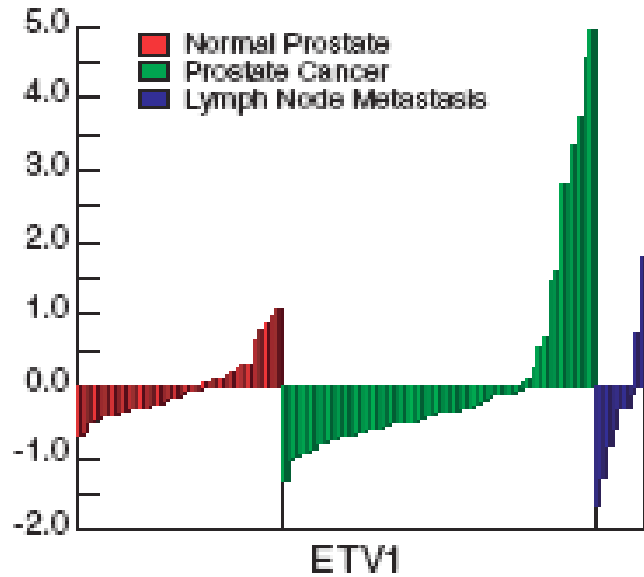


## Data-mining at [www.oncomine.org](http://www.oncomine.org)

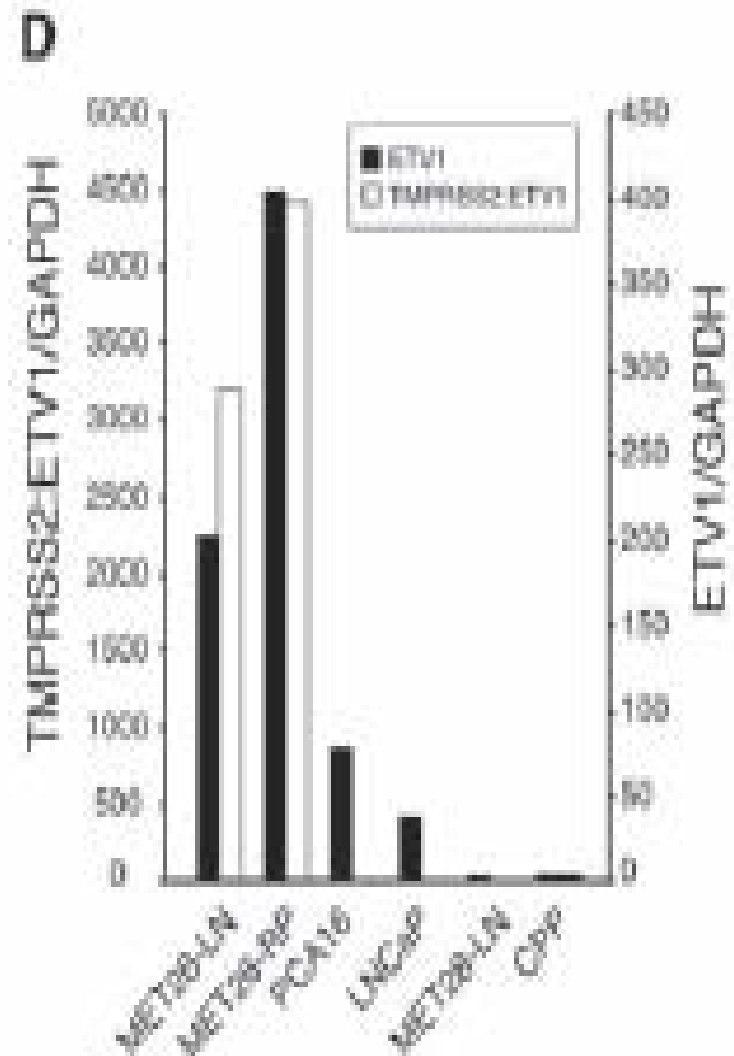
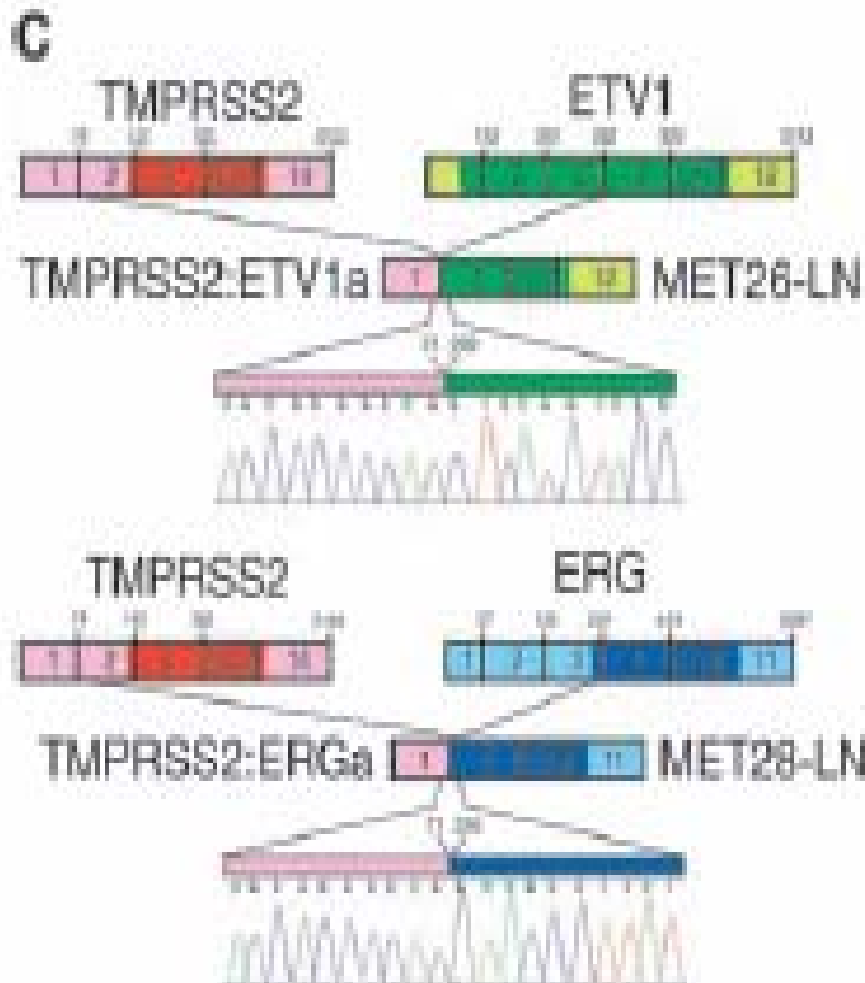


# COPA of Microarray Data Revealed ETV1 and ERG as Outlier Genes across Multiple Prostate Cancer Gene Expression Data Sets

[Tomlins et al., Science 2005, 310: 644 -648]

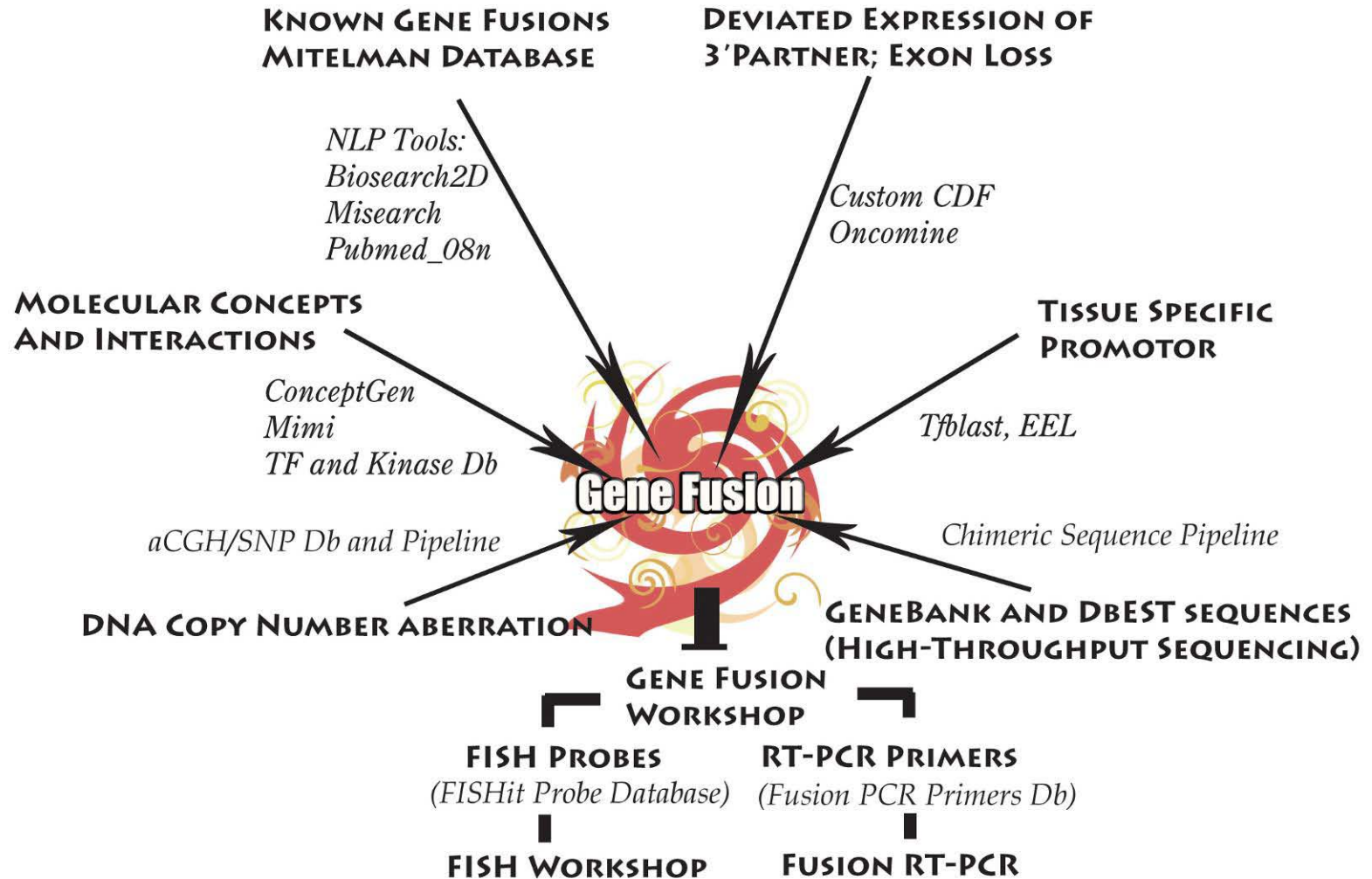


# COPA Unveils Androgen-Responsive Transcription Factor Fusion Genes [TMPRSS2;ETS: t21q22;17q21]



# Integrative Model for Translation of Bio-Data into Novel Gene Fusions

(Xiaosong Wang)



# *Application of NCIBI Tools and Technologies in Cancer Fusion Studies*

- Biosearch2D (<http://biosearch2D.ncibi.org>). Conceptual query tools for gene and mesh terms mapping.
- Custom CDF (<http://brainarray.mbni.med.umich.edu>). Probe-level microarray analysis.
- MiSearch (<http://misecond.ncibi.org>). Flexible query tools for pubmed (Better than Entrez)
- Gene2Mesh (<http://Gene2Mesh.ncibi.org>). Search for the significant mesh terms of interested gene.
- Oncomine and MCM (<http://www.oncomine.org>). Cancer profiling data and molecular concepts collection.
- Mimi (<http://mimi.ncibi.org>). Molecular interactions map.
- MBI-nextgen (Oracle Server). Data Warehouse for NCIBI.
- Con-Sig, Concept signatures. Compares mutation and fusion mechanisms.



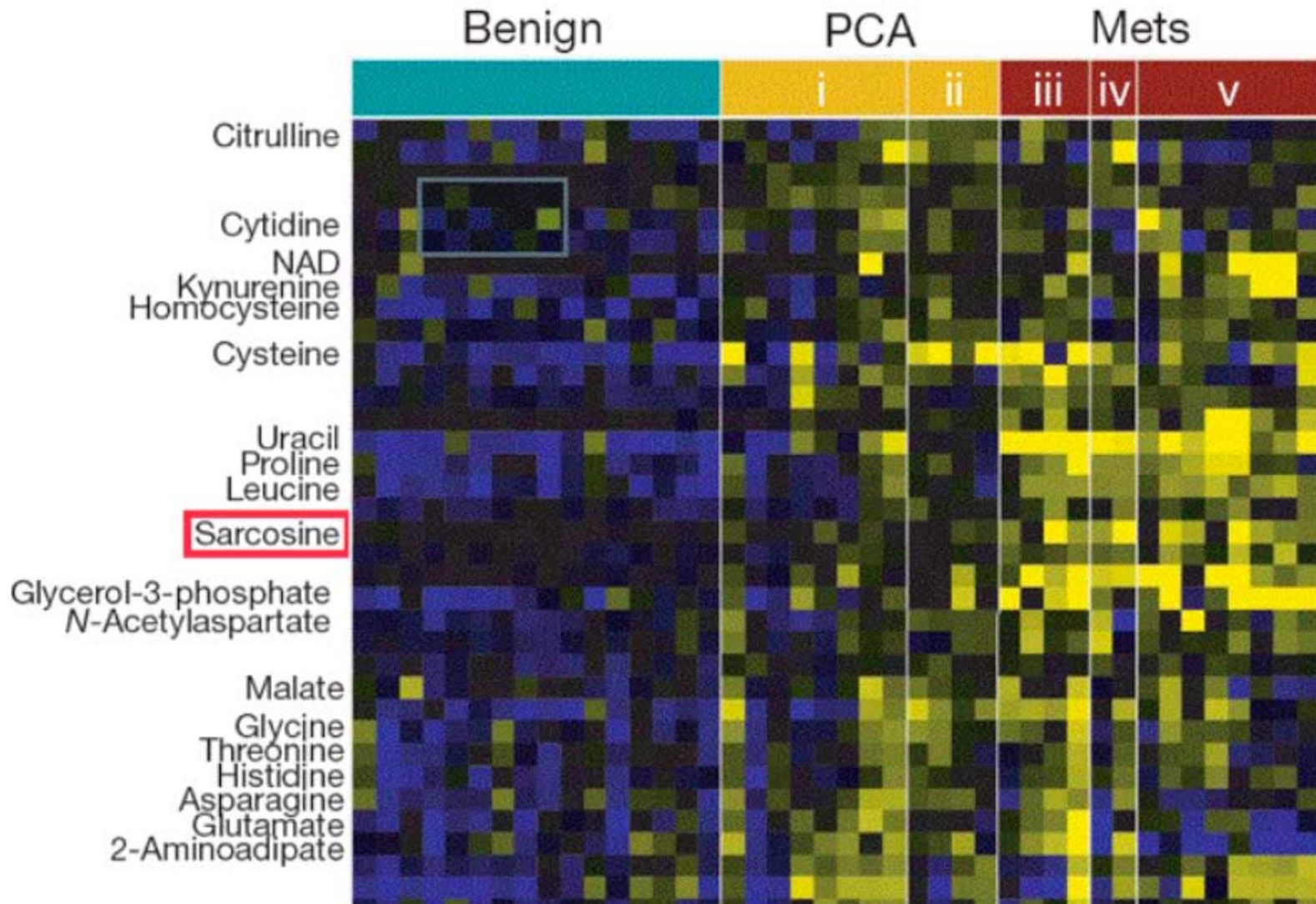
# “Metabolic Profiles Delineate Potential Role for Sarcosine in Prostate Cancer Progression”

(Sreekumar et al, Nature 2009)

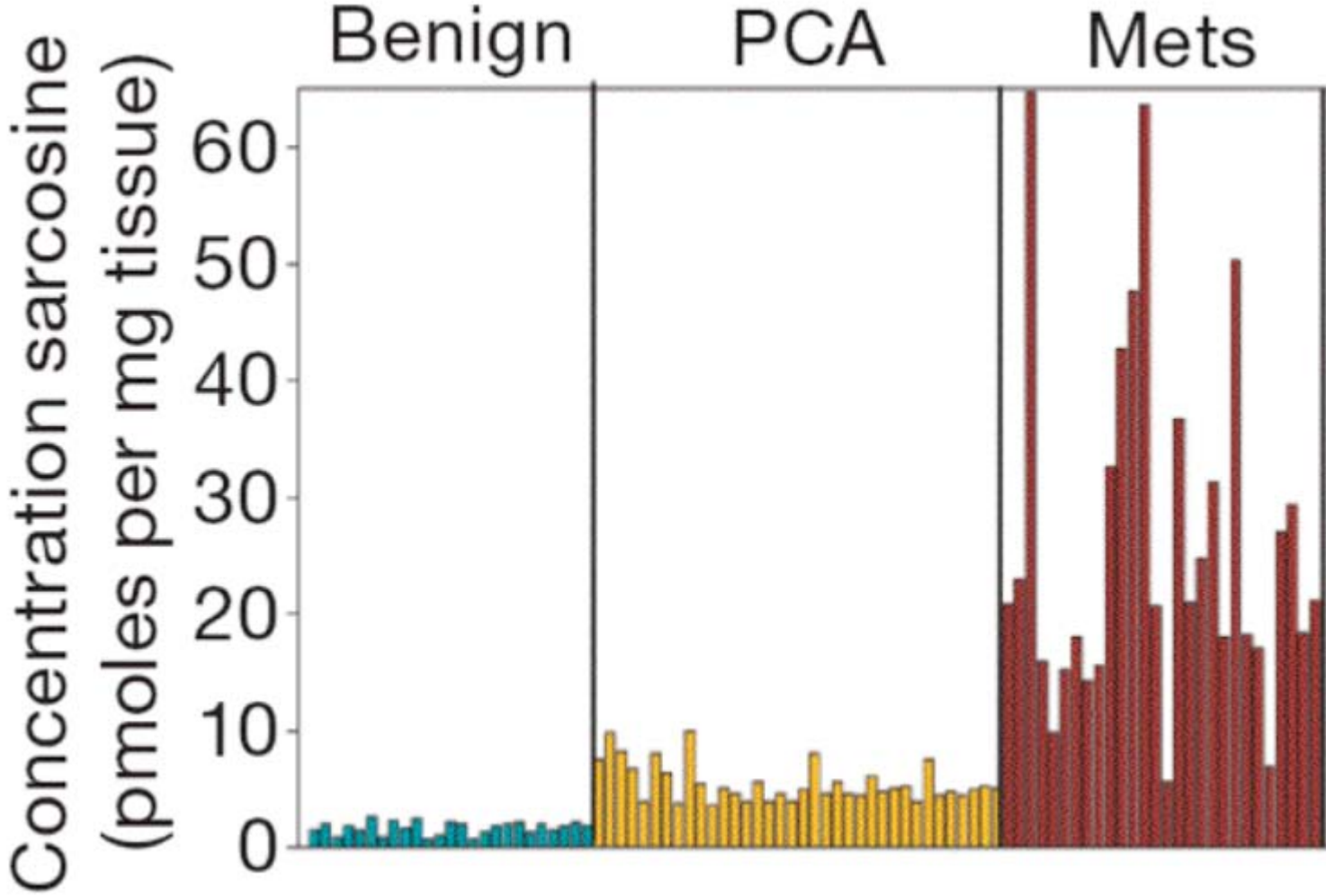
Combined HPLC & Mass Spec to profile 1126 metabolites across 262 samples (tissue, urine, plasma)

- Able to distinguish normal, BPH, local cancer and metastatic cancer from metabolomic signatures (tissue)
- Oncomine Concept Maps highlighted amino acid metabolism and methylation metabolism; ?link
- Sarcosine (methyl glycine) is increased in invasive prostate cancers compared with benign or localized
- Injection of sarcosine, over-expression of GNMT or EZH2, and knockdown of sarcosine dehydrogenase lead to invasive phenotype from benign cells

# Metabolite Levels



# Sarcosine Levels with Sensitive Assay



# Next-Gen Sequencing: Platforms, Informatics, Cancer Applications

Arul M. Chinnaiyan, M.D., Ph.D.

Christopher Maher, Ph.D.

Michigan Center for Translational Pathology

Jim Cavalcoli, Ph.D., NCIBI/CCMB

NCIBI DBP on Prostate Cancer and Gene Fusions





# Bipolar Disease DBP

- Genome association & pathways studies
- Pharmacogenomic studies of variation in responses (efficacious and toxic) to Lithium Rx
- Analyses of co-morbidities of BPD

Melvin McInnis, M.D., Ben Keller, Ph.D.,  
Rich McEachin, PhD, Haimin Chen, Ph.D.

Depression Research Center, Dept of Psychiatry





# Mechanisms of Complications of Diabetes: Neuropathy/Nephropathy

- Differential diagnosis of glomerular disease by transcription factor binding site patterns
- Bayesian analyses of time course and risk factors for chronic kidney disease
- Mechanisms and prevention of reactive oxygen species-mediated damage to nerves





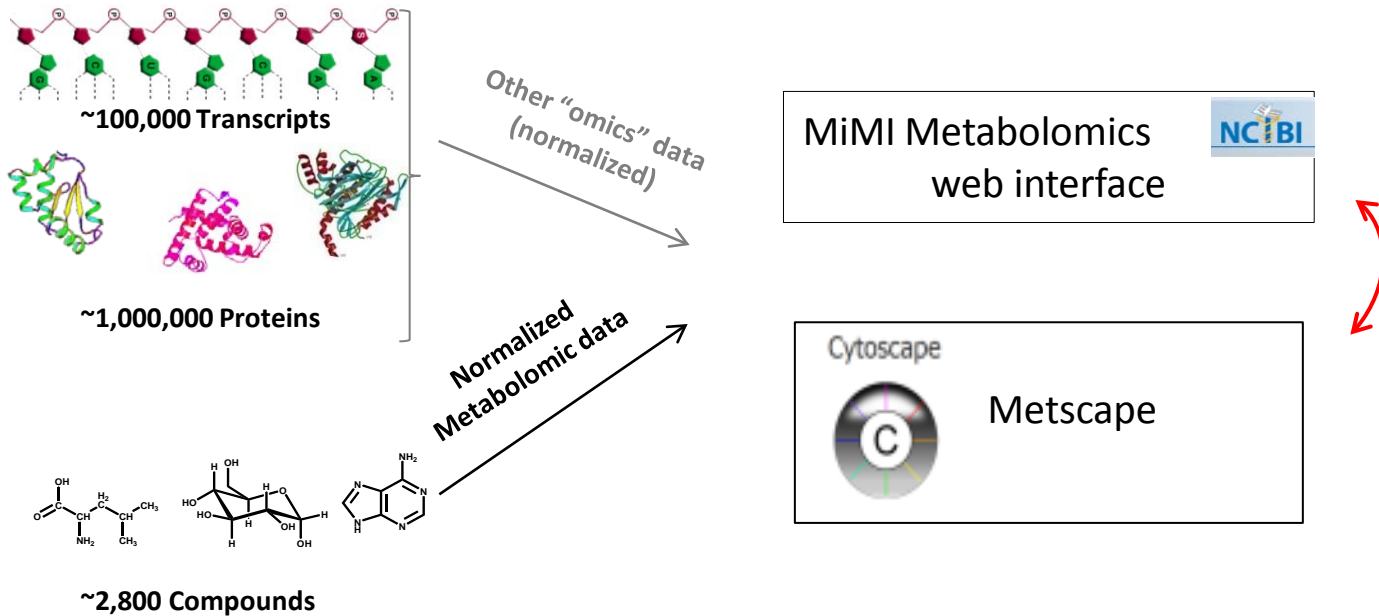
# Mechanisms of Complications of Diabetes: Neuropathy/Nephropathy

DBP Lead Investigators:

- Matthias Kretzler, Dept of Medicine/Nephrology
- Eva Feldman, Dept of Neurology and Taubman Stem Cell Institute
- Chuck Burant, Dept of Medicine/ Metabolomics and Obesity Center
- Christopher Beecher, Dept of Pathology

# Bioinformatics Framework for the Analysis and Interpretation of Metabolomic Data

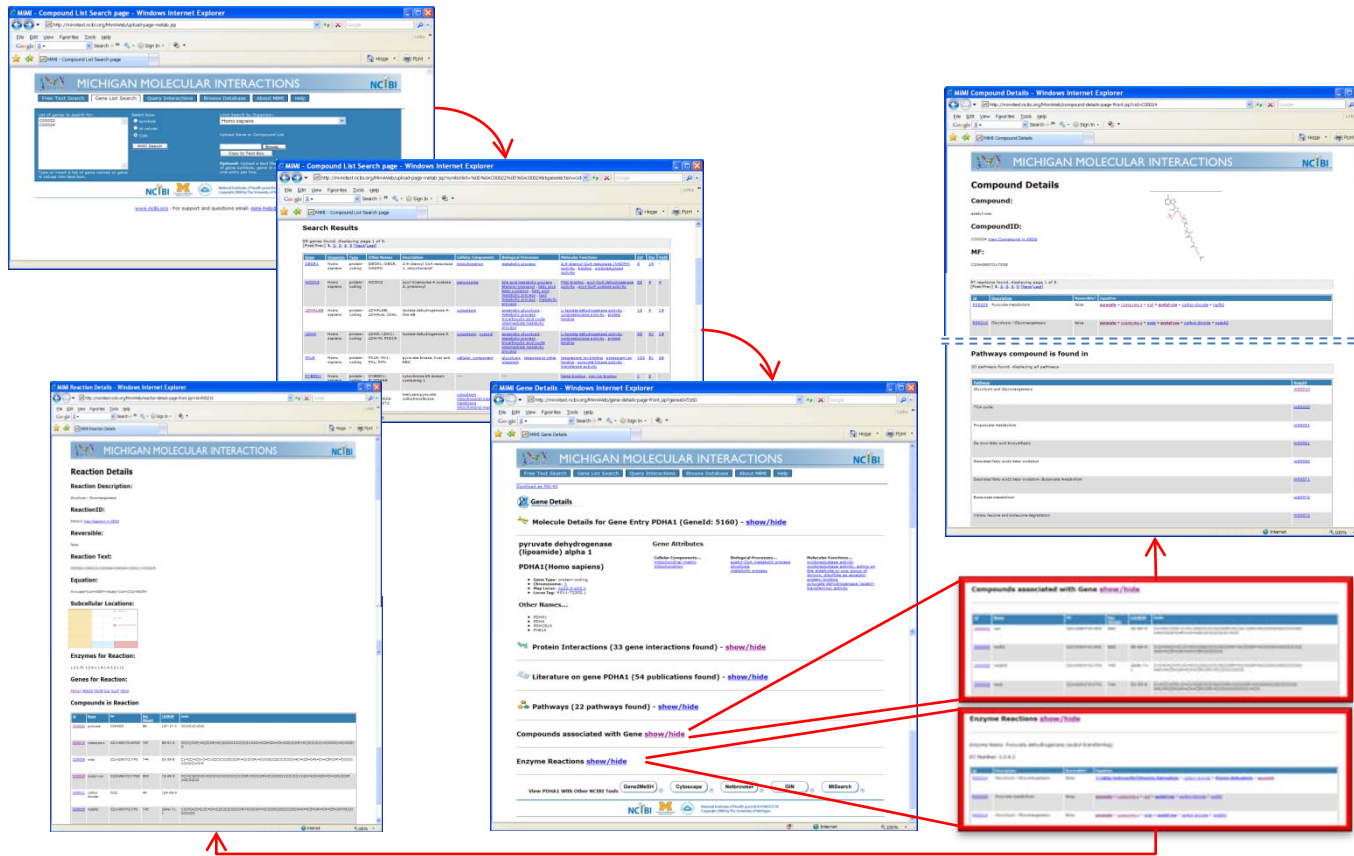
(Karnovsky, Burant, Beecher, Kretzler, Cavalcoli, Omenn)



<http://mimi.ncibi.org/MimiWebBeta/upload-page-metab.jsp>

<http://www.cytoscape.org/> (A beta version of Metscape can be downloaded via Cytoscape plug-in manager under Network and Attribute I/O category)

# Extending MiMI-Web to Include Metabolites



[KEGG](#) (Kanehisa et al., 2008) and [EHMN](#) (Ma et al., 2007) databases were used to trace the connections between metabolites and genes, and provide the framework for data analysis

