About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS International also organizes 500 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS International Conferences

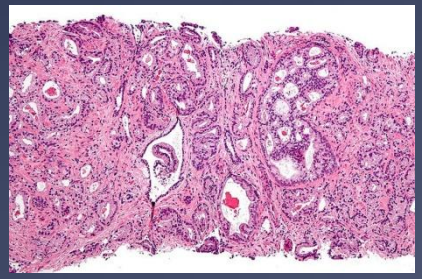
OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS International has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

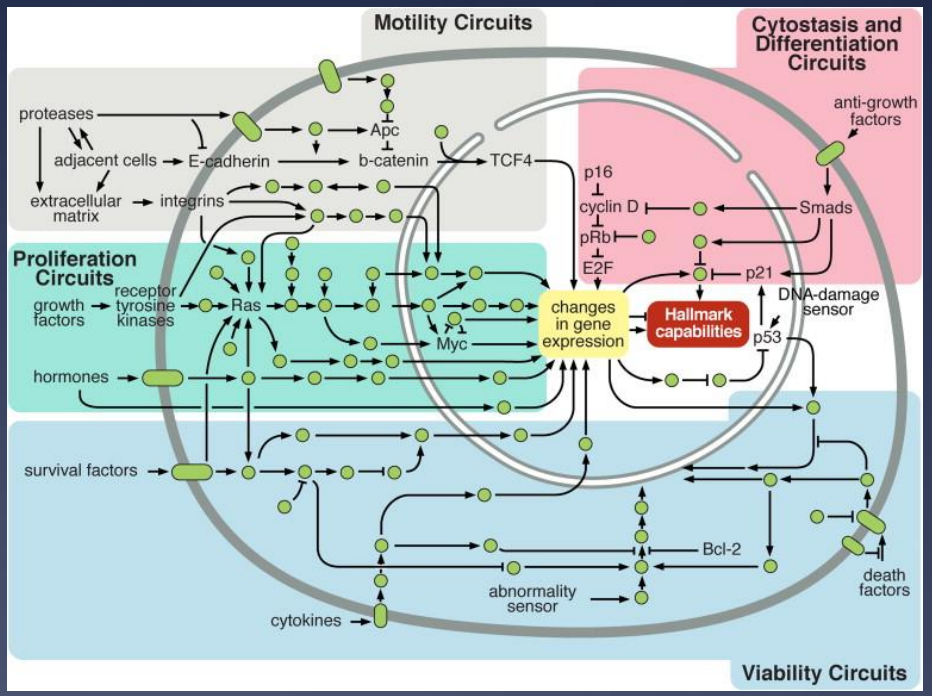
Urinary Metabolome

Jayoung Kim, PhD
Associate Professor, Cedars-Sinai Medical Center
UCLA
Harvard Medical School

Two Grand Challenges in Omics



Biomarker discovery



Hanahan and Weinberg. Cell 2011, 144: 646-74.

Signaling networks

Non-invasive Biomarker to monitor disease progression and drug responses

Waste?

Valuable as a diagnostic biofluid?

Active role by regulating bladder biology?

Urine is an ideal bio-medium to monitor bladder condition

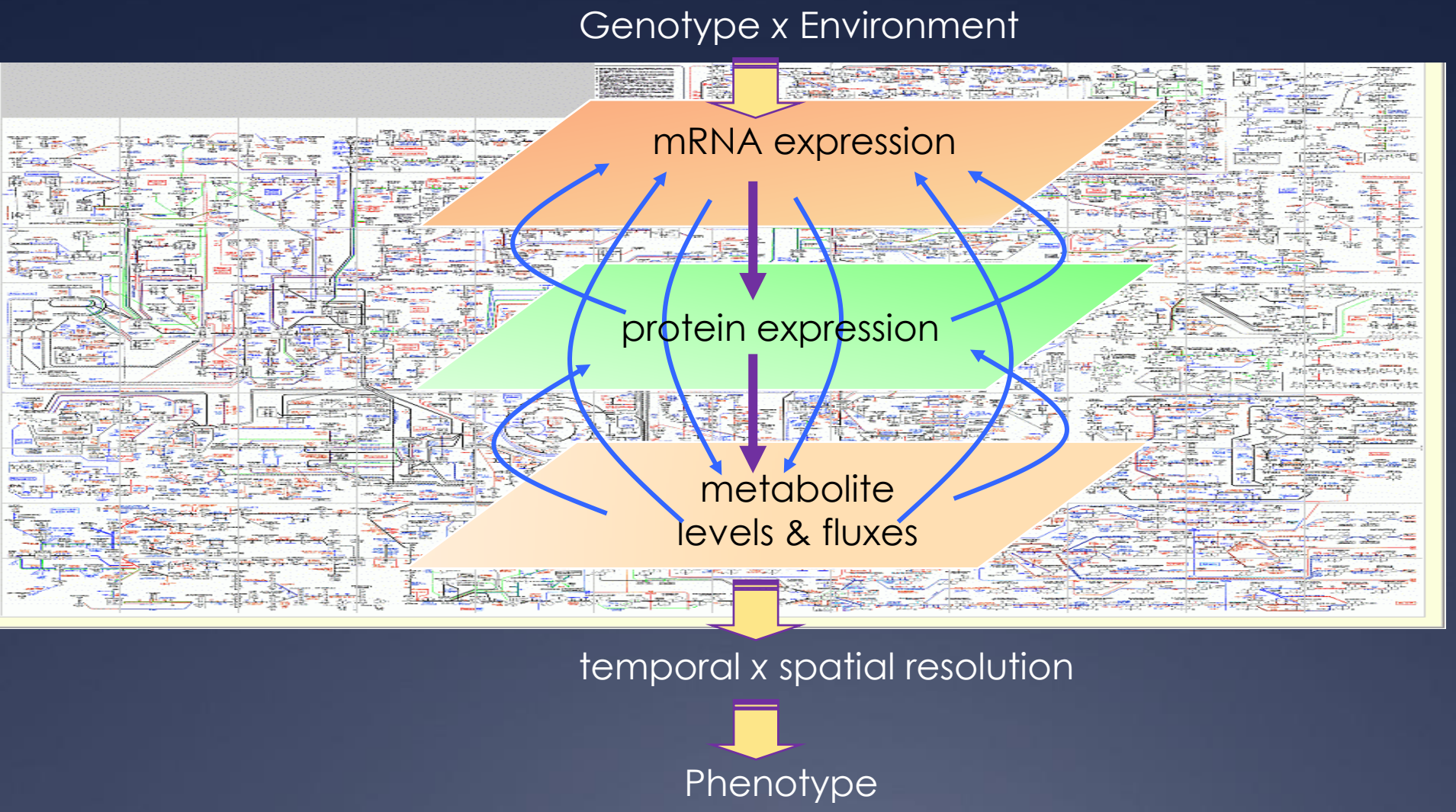
•Readily obtained and available with no required preparation by the patient

•The ease of collection allows for serial sampling to monitor disease and therapeutic response.

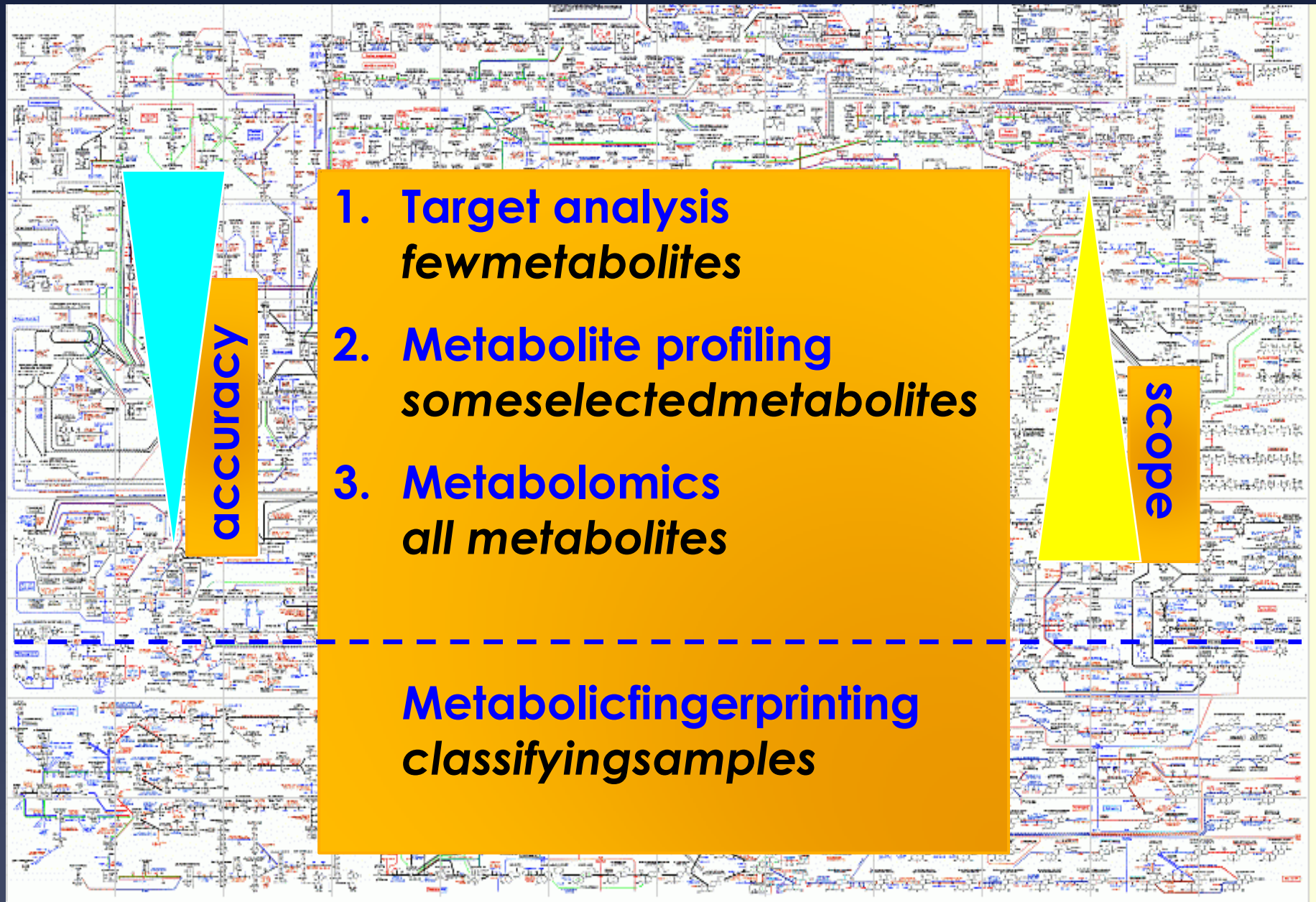
•Less complex than other body fluids.

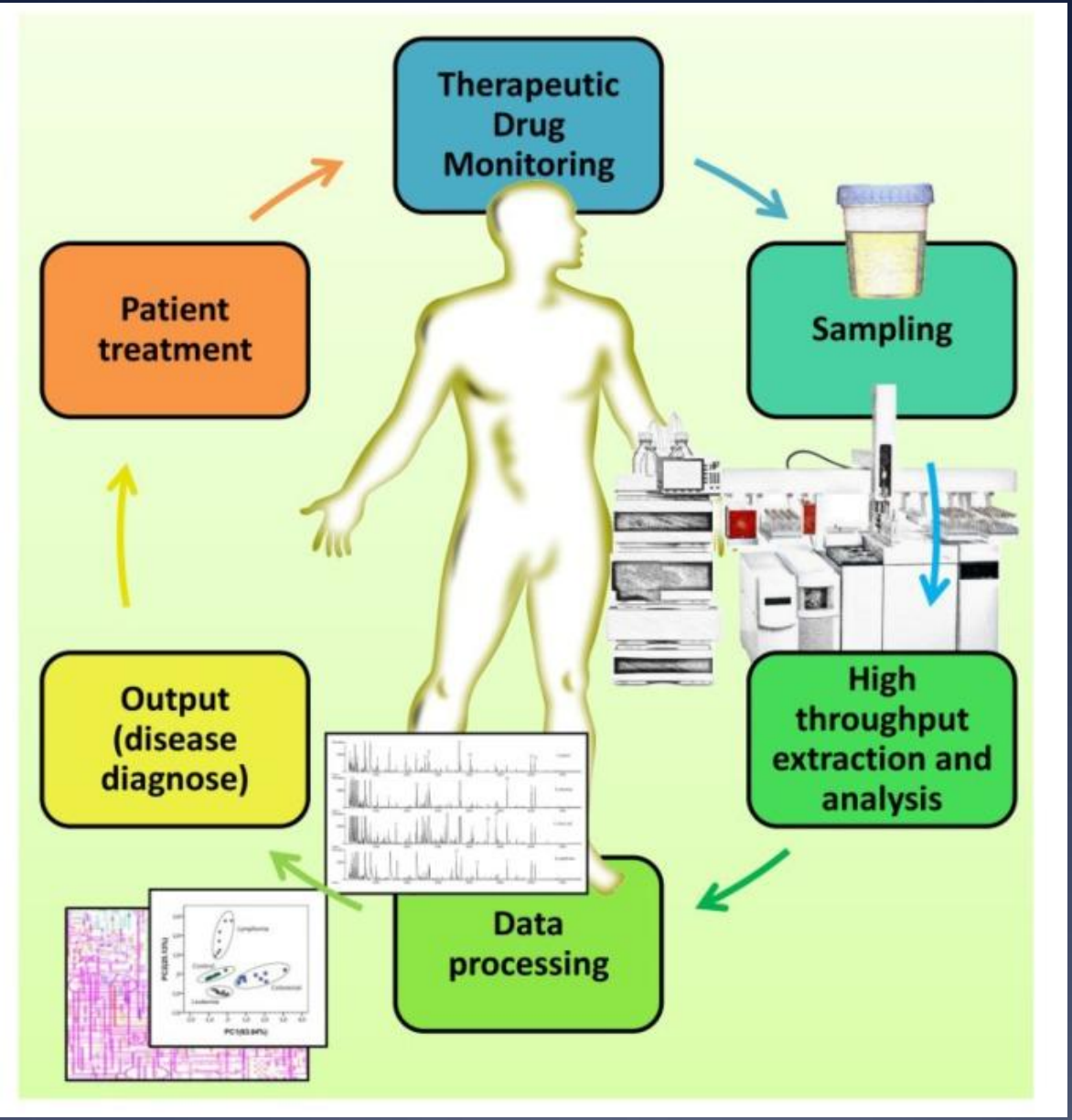
•Body fluids that are most proximal to a disease site can often provide a source of informative biomarkers; therefore, urine-based monitoring for bladder condition is the most attractive strategy among other biofluids-based methods.

Why do we measure the metabolome?



What is metabolomics?





Metabolites. Mar 2014; 4(1): 71–97.

APPLICATION OF METABOLOMICS IN URINE BIOLOGY RESEARCH

Techniques and Data Analysis of Metabolomics Data

- *Analytical techniques*
  - *NMR or MS?:* advantages and limitations
    - *NMR:* minimum sample requirement, quantitative ability, and safe metabolite identification that provides detailed information on structure
    - *MS:* sensitivity
  - *Targeted or nontargeted?:*

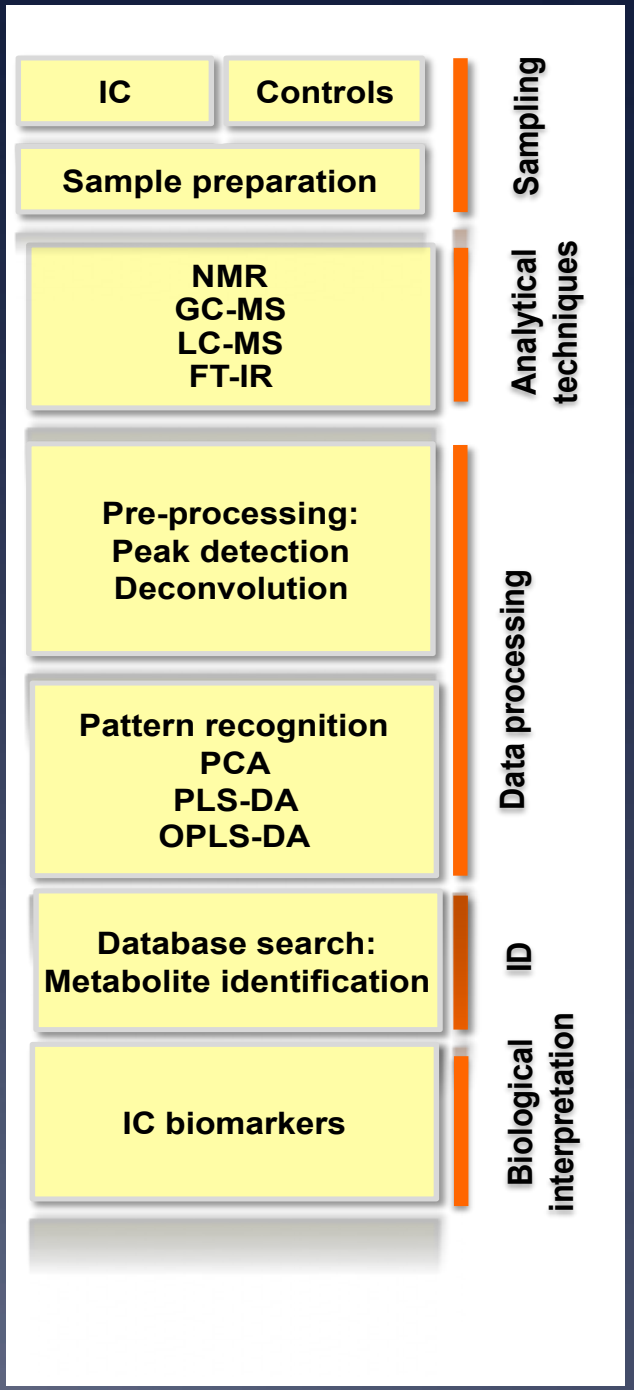
APPLICATION OF METABOLOMICS IN URINE BIOLOGY RESEARCH

•*Data processing and metabolite identification:*

•Databases: HMDB (http://www.hmdb.ca/), METLIN (http://metlin.scripps.edu/), Massbank (http://www.massbank.jp), PubChem (http://ncbi.nim.nih.gov/), KEGG (http://www.kegg.com/), MetaCyc, ChEBI, PDB, UniProt, and GenBank as well as to GeneCard IDs, GeneAtlas IDs and HGNC IDs

A workflow for metabolic profiling.

LC-MS: Liquid chromatography-mass spectrometry; GC-MS: Gas chromatography-mass spectrometry; NMR: Nuclear magnetic resonance; PCA: Principal component analysis; OPLS-DA: Orthogonal partial least squares discriminant analysis; PLS-DA: Partial least squares discriminant analysis.



BUT…analytical challenges

Wide variations in the ionic strength, pH, and osmolarity, particularly under conditions of physiological stress, diet, medications, environmental conditions.

Review Article

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http://dx.doi.org/10.5213/inj.2014.18.3.106
pISSN 2093-4777 · eISSN 2093-6931

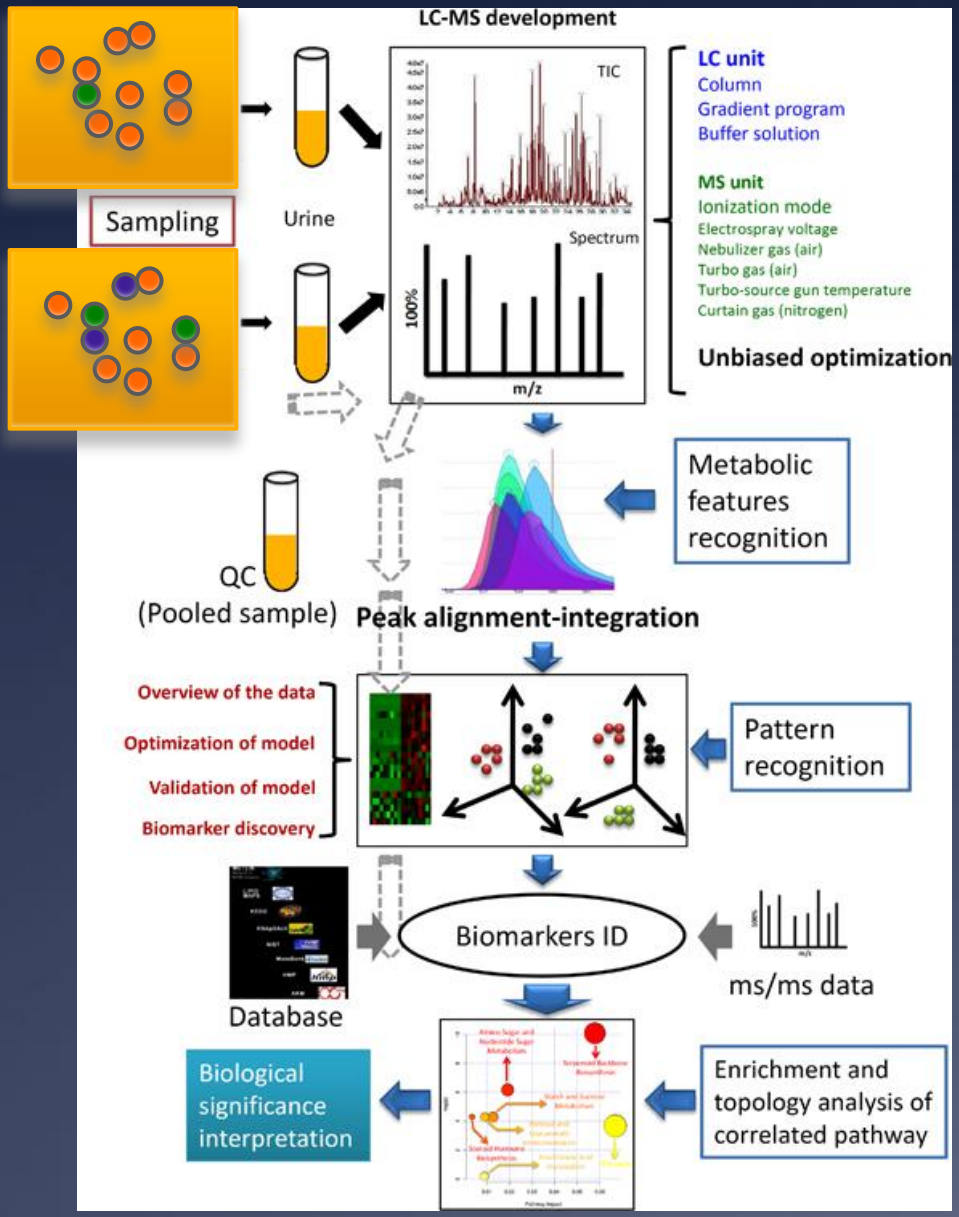
International Neurourology Journal
INJ

Metabolomics Insights Into Pathophysiological Mechanisms of Interstitial Cystitis

Oliver Fiehn[1,2], Jayoung Kim[3,4,5]

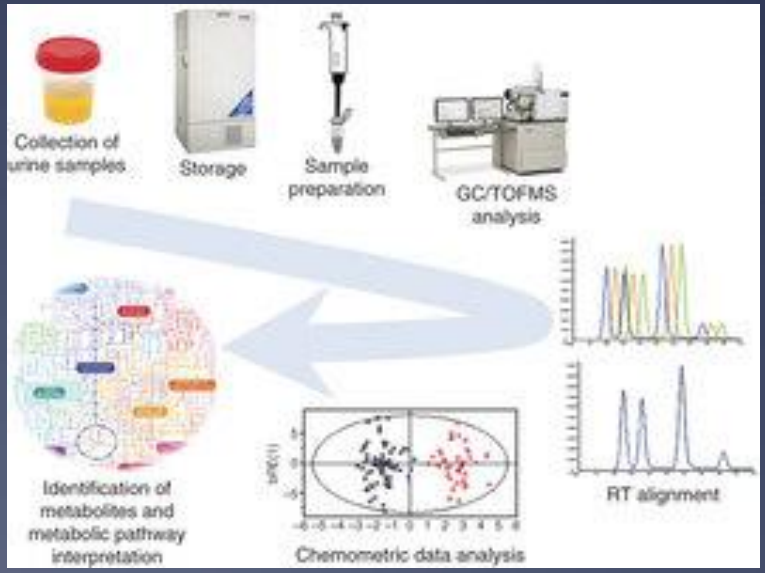
[1]West Coast Metabolomics Center, University of California, Davis, Davis, CA, USA;
[2]King Abdulaziz University, Jeddah, Saudi Arabia;
[3]Departments of Surgery and Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, CA;
[4]Department of Medicine, University of California, Los Angeles, Los Angeles, CA;
[5]The Urological Diseases Research Center, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

Interstitial cystitis (IC), also known as painful bladder syndrome or bladder pain syndrome, is a chronic lower urinary tract syndrome characterized by pelvic pain, urinary urgency, and increased urinary frequency in the absence of bacterial infection or



STUDY EXAMPLES:

How can we apply metabolomics analysis to understand of urine biology?



Nature Protocols ***6, 1483–1499 (2011)***

Journal of proteome research

Article

pubs.acs.org/jpr

Urinary Metabolite Profiling Combined with Computational Analysis Predicts Interstitial Cystitis-Associated Candidate Biomarkers

He Wen,[†,○] Tack Lee,[‡,○] Sungyong You,[§] Soo-Hwan Park,[‡] Hosuk Song,[‡] Karyn S. Eilber,[∥] Jennifer T. Anger,[∥] Michael R. Freeman,[§,⊥,#] Sunghyurk Park,*[,†] and Jayoung Kim*[,∥,⊥,#]

[†]Seoul National University, Seoul 151-724, Korea

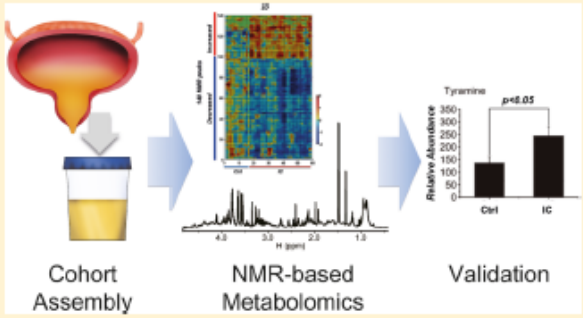
[‡]Inha University Hospital, Incheon 400-103, Korea

[§]Division of Cancer Biology and Therapeutics, Departments of Surgery, Medicine, and Biomedical Sciences, [∥]Division of Urology, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California 90048, United States

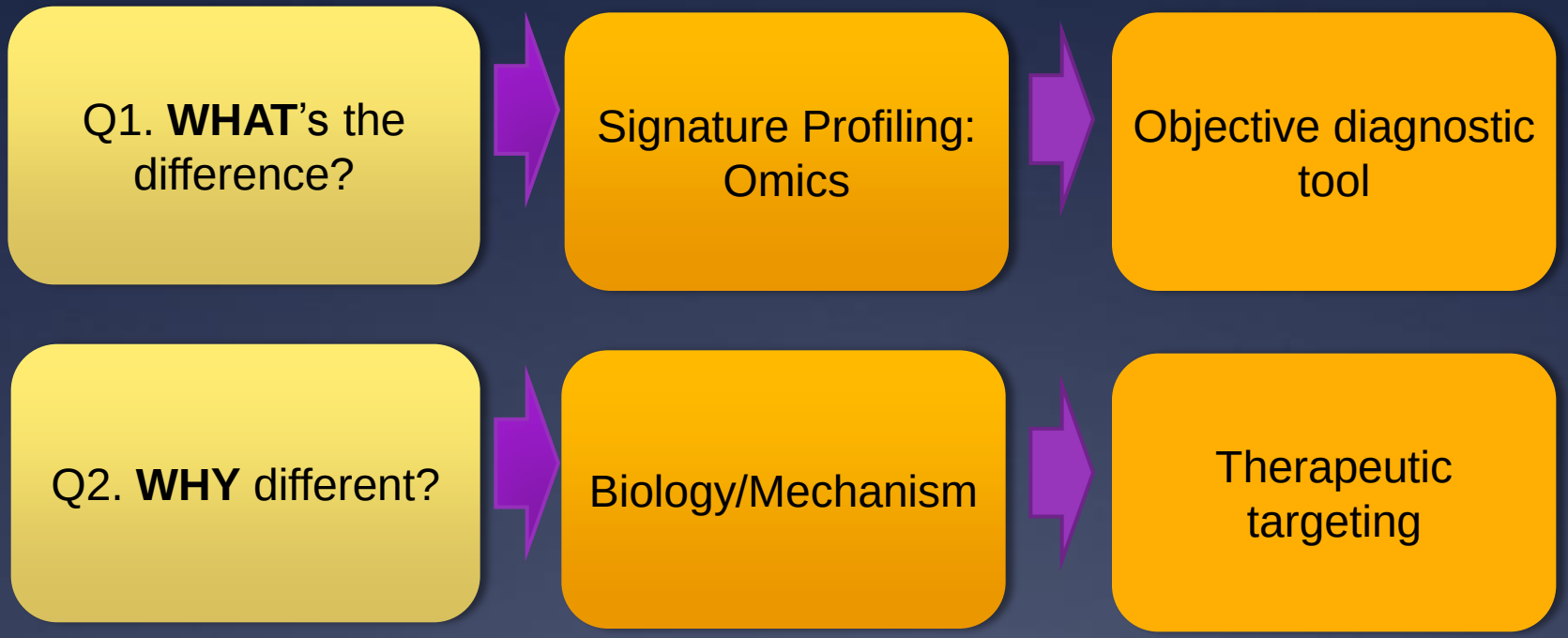
[⊥]Department of Medicine, University of California Los Angeles, Los Angeles, California 90095, United States

[#]The Urological Diseases Research Center, Boston Children's Hospital, Departments of Surgery and Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts 02115, United States

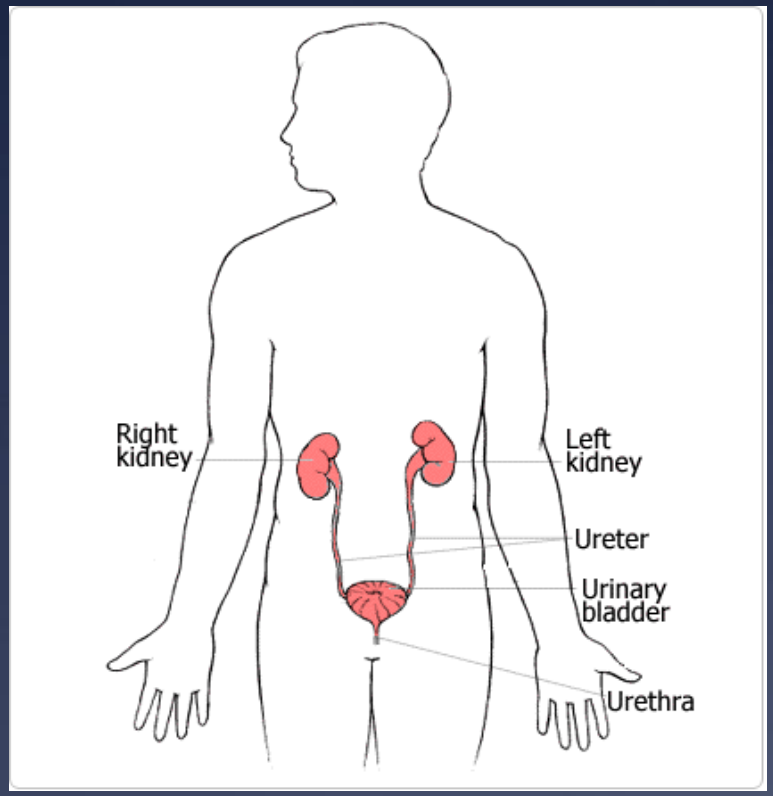
ABSTRACT: Interstitial cystitis/painful bladder syndrome (IC) is a chronic syndrome of unknown etiology that presents with bladder pain, urinary frequency, and urgency. The lack of specific biomarkers and a poor understanding of underlying molecular mechanisms present challenges for disease diagnosis and therapy. The goals of this study were to identify noninvasive biomarker candidates for IC from urine specimens and to potentially gain new insight into disease mechanisms using a nuclear magnetic resonance (NMR)-based global metabolomics analysis of urine from female IC patients and controls. Principal component analysis (PCA) suggested that the urinary metabolome of IC and controls was clearly different, with 140 NMR peaks significantly altered in IC patients (FDR < 0.05) compared to that in controls. On the basis of strong correlation scores, eight metabolite peaks were nominated as the strongest signature of IC. Among those signals that were higher in the IC group, three peaks were annotated as

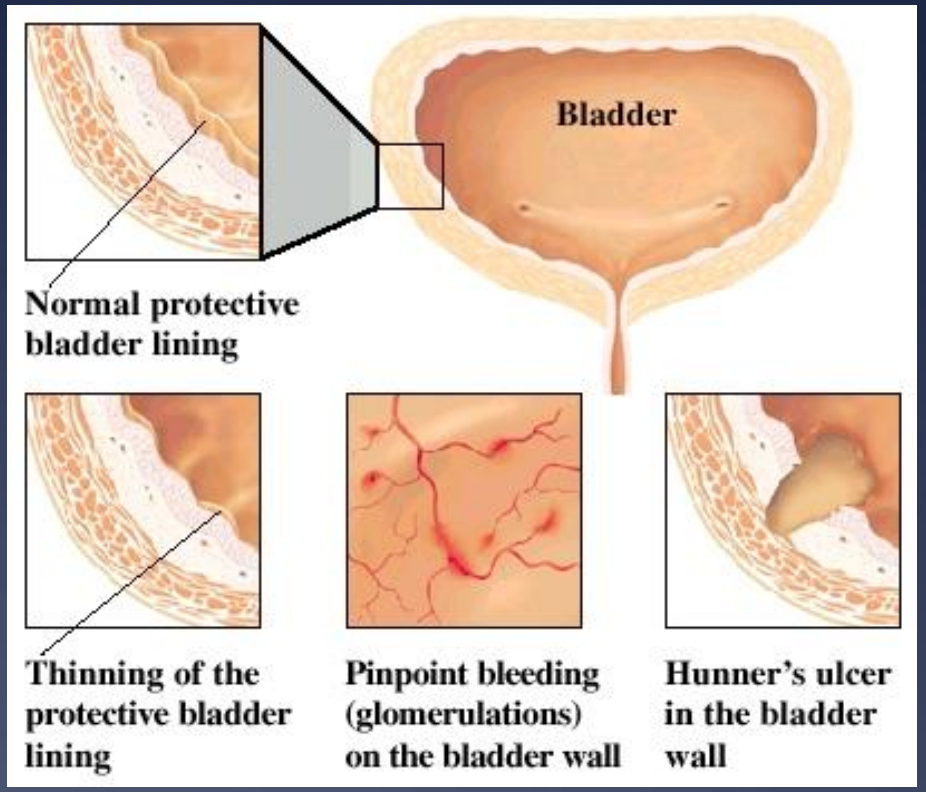


Omics Approaches



Urinary Metabolite Profiling Combined with Computational Analysis Suggest Interstitial Cystitis-Associated Candidate Biomarkers





Cedars-Sinai Medical Center

Interstitial Cystitis

- A chronic syndrome of unknown etiology
- Very common bladder disease among old generation (more than one out of 77 people in USA)
- Affects quality of life, productivity and work performance—Public health burden
- Elmiron, the first FDA-approved oral drug for IC, shows unfavorable side effects
- Need for new medication for IC
- Need for objective and clinically relevant indicators

IC-Associated Mechanistic Signaling Network 1:

The Frizzled 8-Associated Antiproliferative Factor Enhances p53 Stability Through USP2a and MDM2

FEBS Letters 581 (2007) 3795–3799

p53 mediates interstitial cystitis antiproliferative factor (APF)-induced growth inhibition of human urothelial cells

Jayoung Kim[a,b], Susan K. Keay[c], Jordan D. Dimitrakov[a,b], Michael R. Freeman[a,b,*]

[a] *The Urological Diseases Research Center, Children's Hospital Boston, Boston, MA 02115, USA*
[b] *Departments of Surgery, Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115, USA*
[c] *Division of Infectious Diseases, Department of Medicine, The University of Maryland School of Medicine and VA Medical Center, Baltimore, MD 21201, USA*

Received 6 February 2007; accepted 21 June 2007

Heparin-binding epidermal growth factor-like growth factor functionally antagonizes interstitial cystitis antiproliferative factor via mitogen-activated protein kinase pathway activation

BJUI
BJU INTERNATIONAL

Jayoung Kim*†, Susan K. Keay‡ and Michael R. Freeman*†

*The Urological Diseases Research Center, Children's Hospital Boston, †Departments of Surgery and Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, and ‡Division of Infectious Diseases, Department of Medicine, the University of Maryland School of Medicine and VA Medical Center, Baltimore, MD, USA

Accepted for publication 10 July 2008

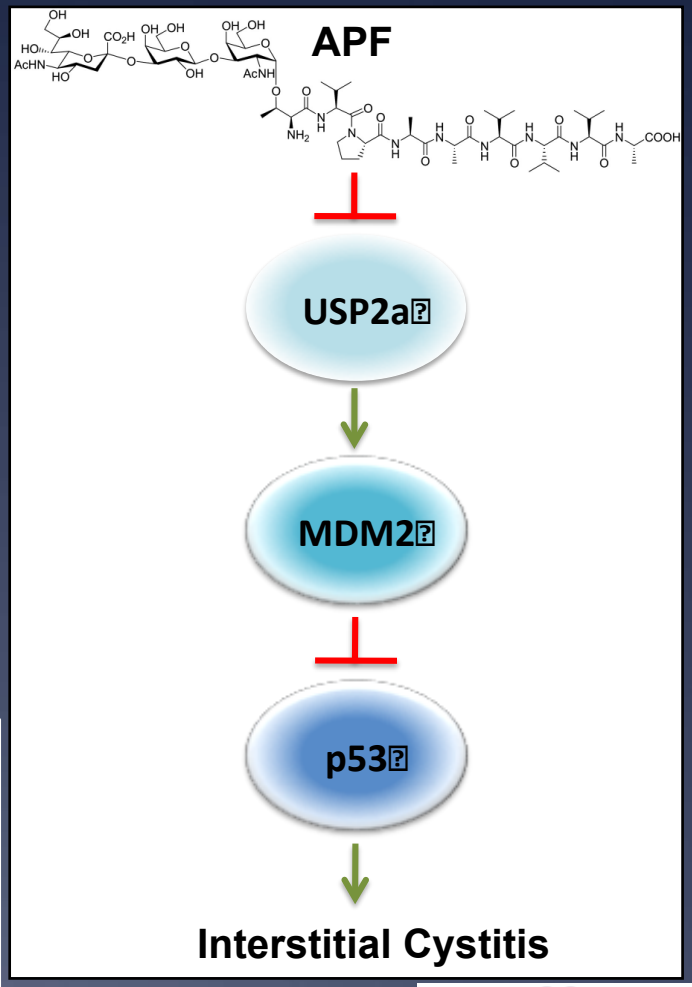
OPEN ACCESS Freely available online

PLOS | ONE

A Synthetic Form of Frizzled 8-Associated Antiproliferative Factor Enhances p53 Stability through USP2a and MDM2

Jayoung Kim[1,2,3]*, Susan K. Keay[4], Sungyong You[1], Massimo Loda[5,6,7], Michael R. Freeman[1,2,3]

1 Division of Cancer Biology and Therapeutics, Departments of Surgery and Biomedical Sciences, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, California, United States of America, **2** The Urological Diseases Research Center, Children's Hospital Boston, Boston, Massachusetts, United States of America, **3** Departments of Surgery and Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts, United States of America, **4** Division of Infectious Diseases, Department of Medicine, the University of Maryland School of Medicine and VA Maryland Health Care Center, Baltimore, Maryland, United States of America, **5** Department of Medical Oncology, Harvard Medical School, Boston, Massachusetts, United States of America, **6** Center for Molecular Oncologic Pathology, Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, United States of America, **7** Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States of America



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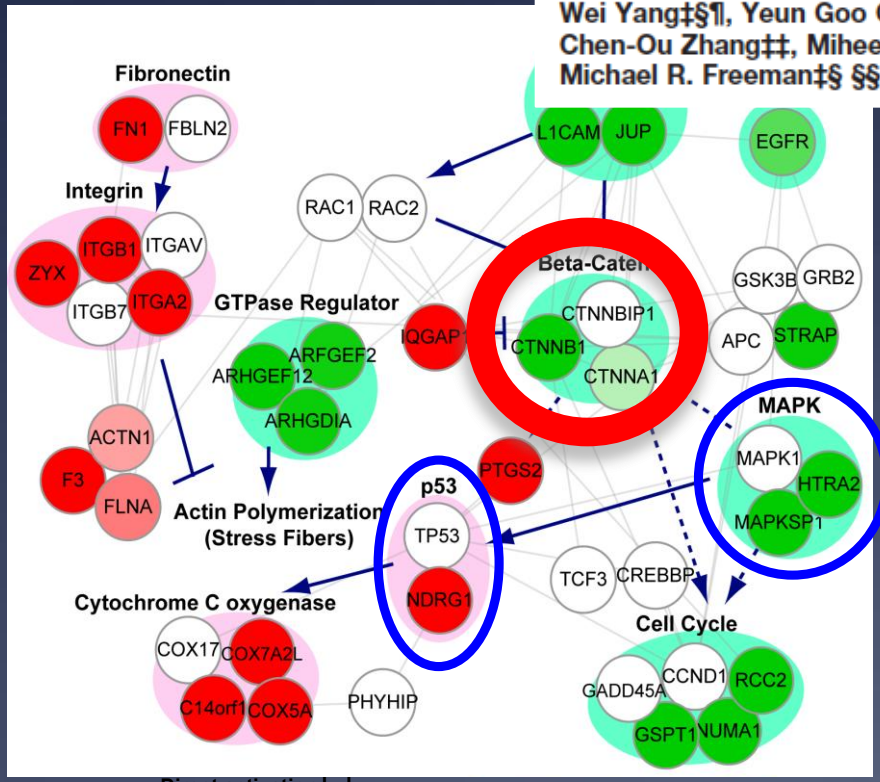
IC-Associated Mechanistic Signaling Network 2:

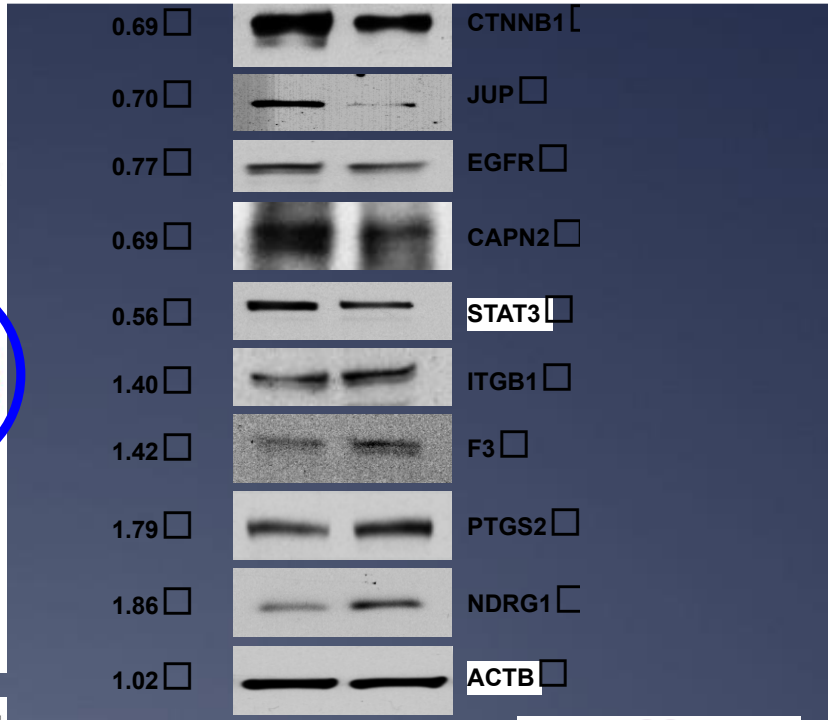
MOLECULAR & CELLULAR PROTEOMICS

Research

Quantitative Proteomics Identifies a β-Catenin Network as an Element of the Signaling Response to Frizzled-8 Protein-Related Antiproliferative Factor*

Wei Yang‡§¶, Yeun Goo Chung‡, Yongsoo Kim‖, Taek-Kyun Kim‖, Susan K. Keay**, Chen-Ou Zhang‡‡, Mihee Ji‡, Daehee Hwang‖, Kwang Pyo Kim§§, Hanno Steen¶ ¶¶, Michael R. Freeman‡§ §§, and Jayoung Kim‡§‖‖





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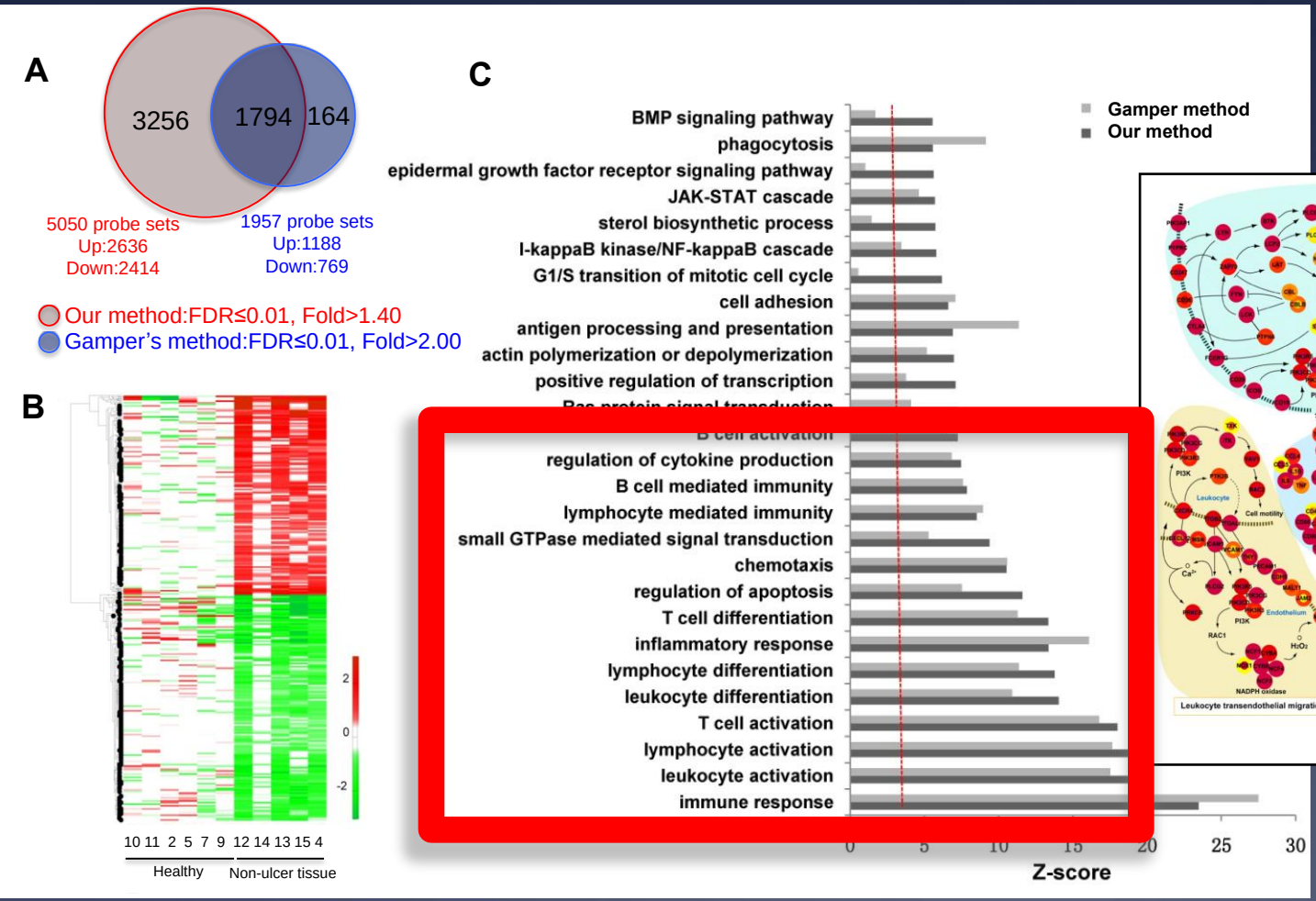
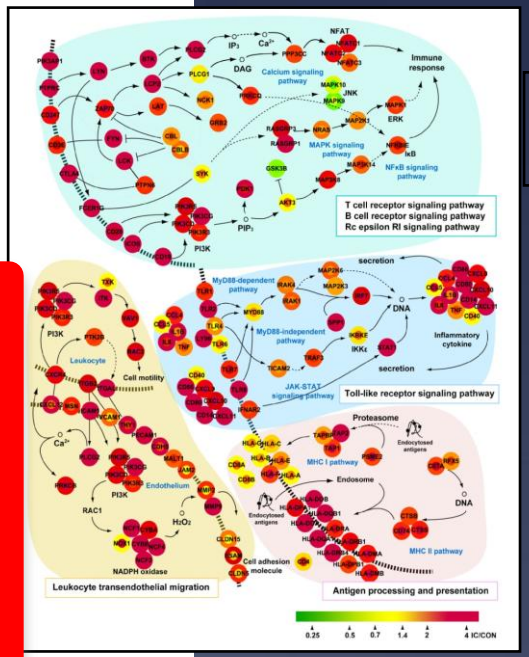
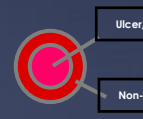
IC-Associated Mechanistic Signaling Network 3:

Integration Analysis of Quantitative Proteomics and Transcriptomics Data Identifies Potential Targets of Frizzled-8 Protein-related Antiproliferative Factor *In Vivo*







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'OMICS' Approaches to Understand Intersitital Cystitis

More 'OMICS' Profiles using the **Cutting-Edge Technology** are needed

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Integration analysis of quantitative proteomics and transcriptomics data identifies potential targets of frizzled-8 protein-related antiproliferative factor *in vivo*

Wei Yang[1,2,3], Yongsoo Kim[4], Taek-Kyun Kim[4], Susan K. Keay[5], Kwang Pyo Kim[6], Hanno Steen[3,7], Michael R. Freeman[1,2,6,8], Daehee Hwang[4] and Jayoung Kim[1,2,8]

Review Article

Int Neurourol J 2012;16:159-168
http://dx.doi.org/10.5213/inj.2012.16.4.159
pISSN 2093-4777 · eISSN 2093-6931

International Neurourology Journal
INJ

'Omics' Approaches to Understanding Interstitial Cystitis/Painful Bladder Syndrome/Bladder Pain Syndrome

Sungyong You[1], Wei Yang[1], Jennifer T. Anger[2], Michael R. Freeman[1,3,4], Jayoung Kim[1,3,4]

[1]Division of Cancer Biology and Therapeutics, Departments of Surgery and Biomedical Sciences, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA;
[2]Department of Surgery, Cedars-Sinai Medical Center, Center for Women's Continence and Pelvic Health at Cedars-Sinai, Los Angeles, CA;
[3]The Urological Diseases Research Center, Boston Children's Hospital, Boston, MA;
[4]Departments of Surgery and Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, USA

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Urinary Metabolite Profiling Combined with Computational Analysis

The goals of this study are to identify non-invasive biomarker candidates for IC and to gain new insight into disease mechanisms suggesting objective, clinically relevant indicators of the disease that might be employed clinically.

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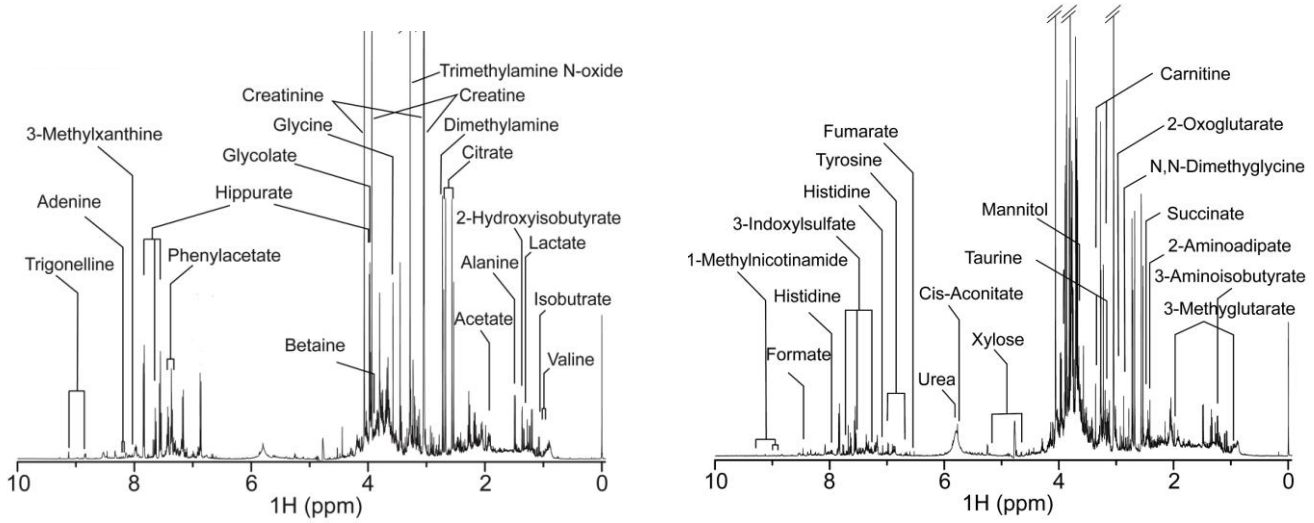
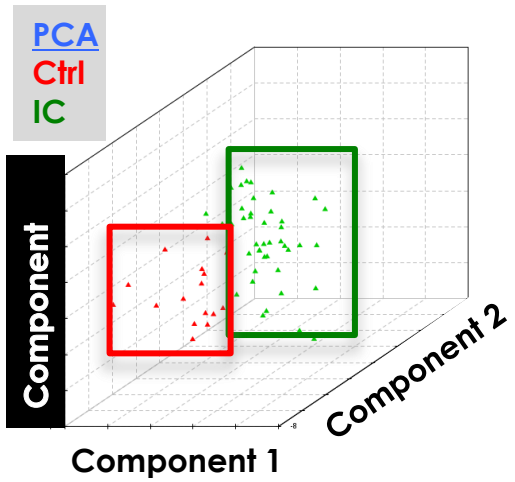
Representative ^{1}H Nuclear Magnetic Resonance (NMR) spectra of urine from IC and matched controls

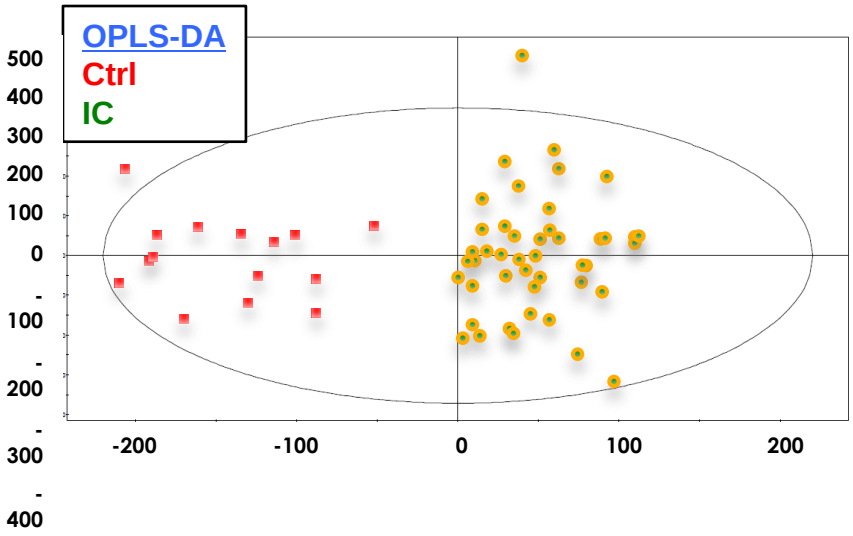


^{1}H-NMR Spectra Could Segregate IC Patients from Controls

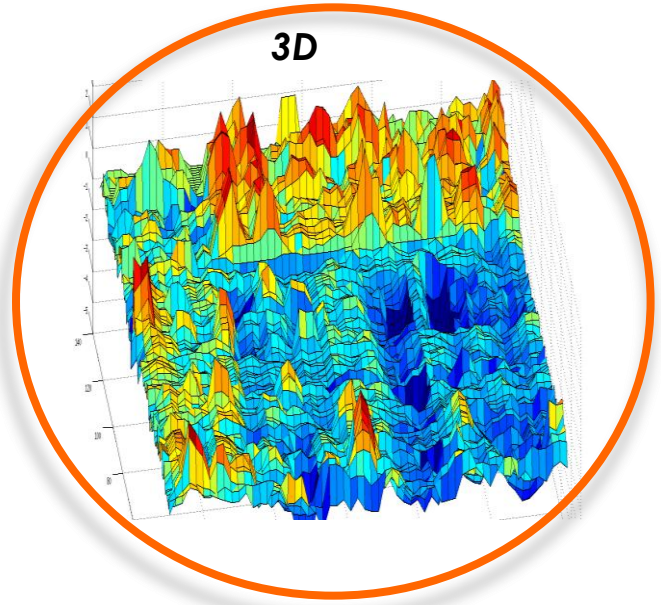
A

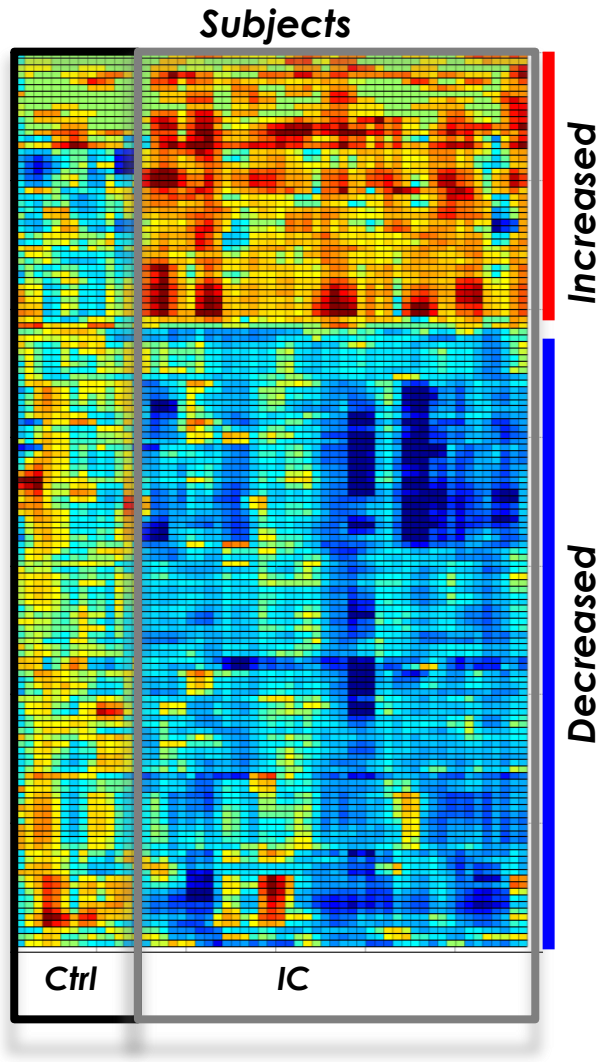


B



Identification of NMR Peaks Perturbed in Specimens from IC Patients





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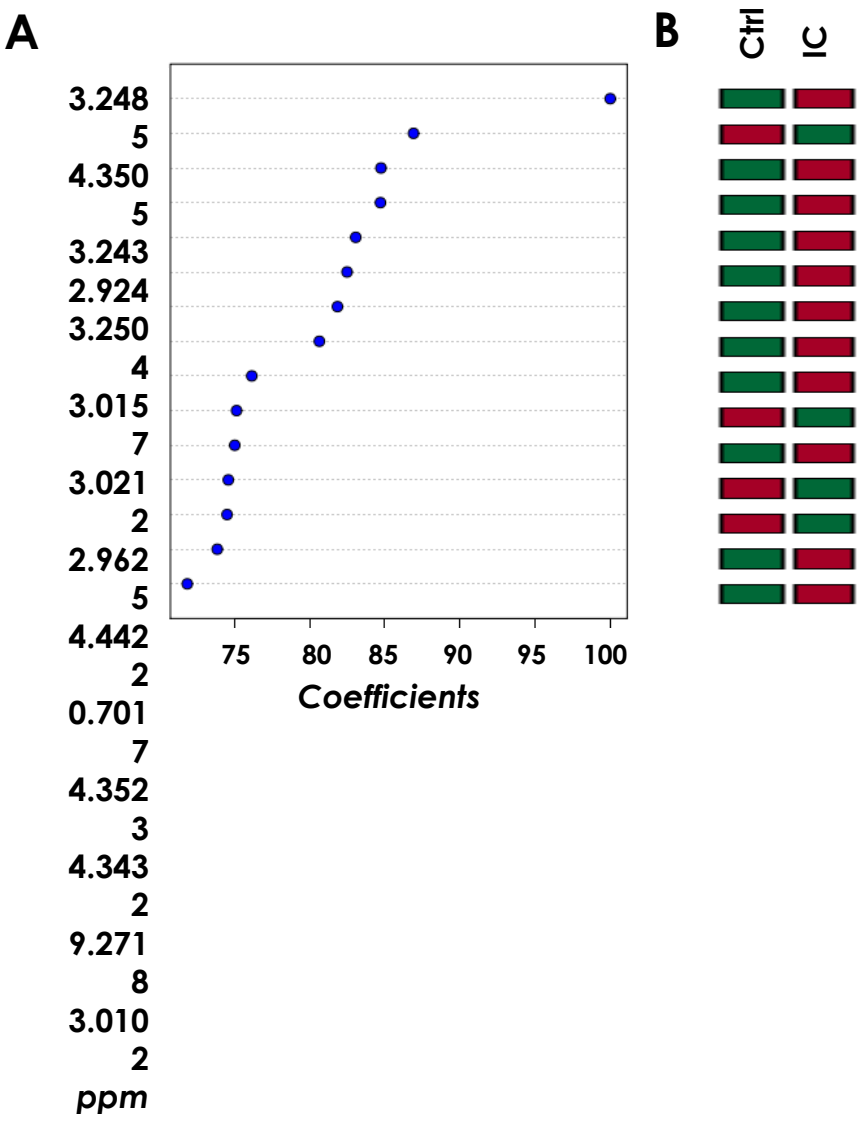
NMR Spectra Segregating IC from Controls

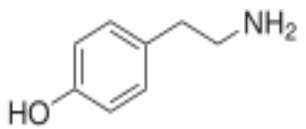


Upregulated metabolites that could be used to segregating IC patients from normal subjects

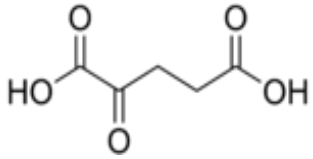
A

ppm	Assignment
3.2485	Tyramine
2.9606	n.a.
3.2504	n.a.
3.0212	2-oxoglutarate

B

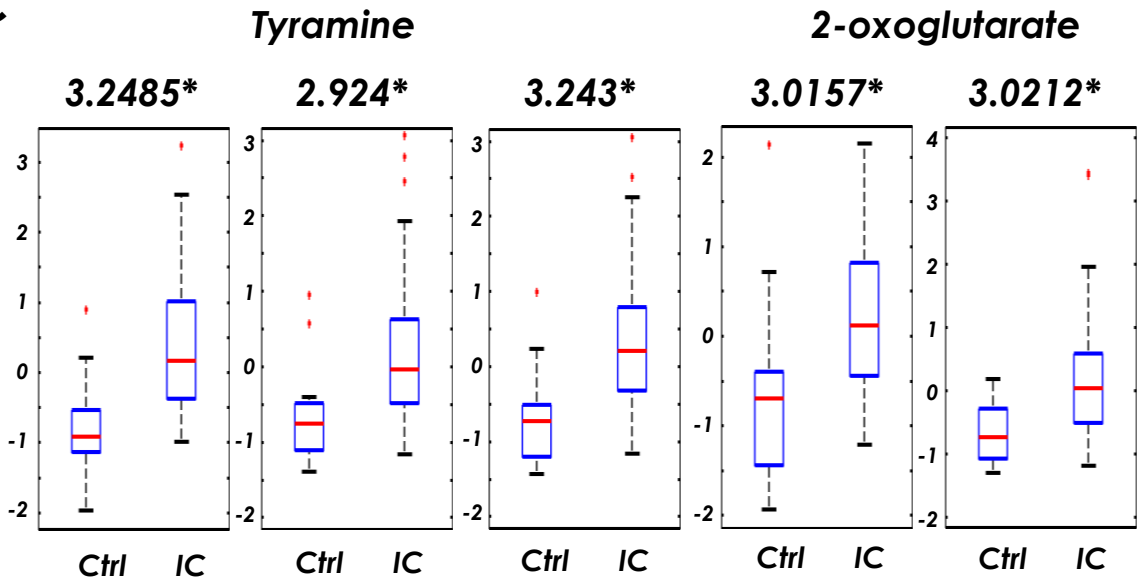


Tyramine



2-oxoglutarate

C



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Summary

- **Three IC-related signaling networks were suggested.**
  - In vitro culture system: USP2a-MDM2-p53 pathway
  - A quantitative proteomics analysis: β-catenin-COX2-PGE_2 pathway
  - Computational analysis of publicly available IC data sets: Chronic inflammation, immune responses

- In the recent metabolomics study, we identify **non-invasive classifiers** that can discriminate IC patients from controls. This finding can be the basis for one or more **prospective clinical trials** and thus has direct relevance to human health and patient care.

www.mappnetwork.org

United States
National Institute of
Diabetes & Digestive & Kidney Diseases
of the National Institutes of Health

Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain

A A A

About MAPP | Discovery Sites | Core Sites | Projects | Resources | MAPP Portal | Questionnaires

Welcome to the MAPP Research Network Home Page

MAPP research network

- MAPP News
- Epidemiological Studies
- Urological Phenotyping
- Non-Urological Phenotyping
- Neuroimaging / Neurobiology
- Biomarkers
- Organ Cross-Talk / Pain Pathways

Sponsor Links

Department of Health & Human Services (HHS)

A New Look at Urological Chronic Pelvic Pain ...

To help better understand the underlying causes of the two most prominent chronic urological pain syndromes—interstitial cystitis/painful bladder syndrome (IC/PBS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)—the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), has launched a new and novel research study.

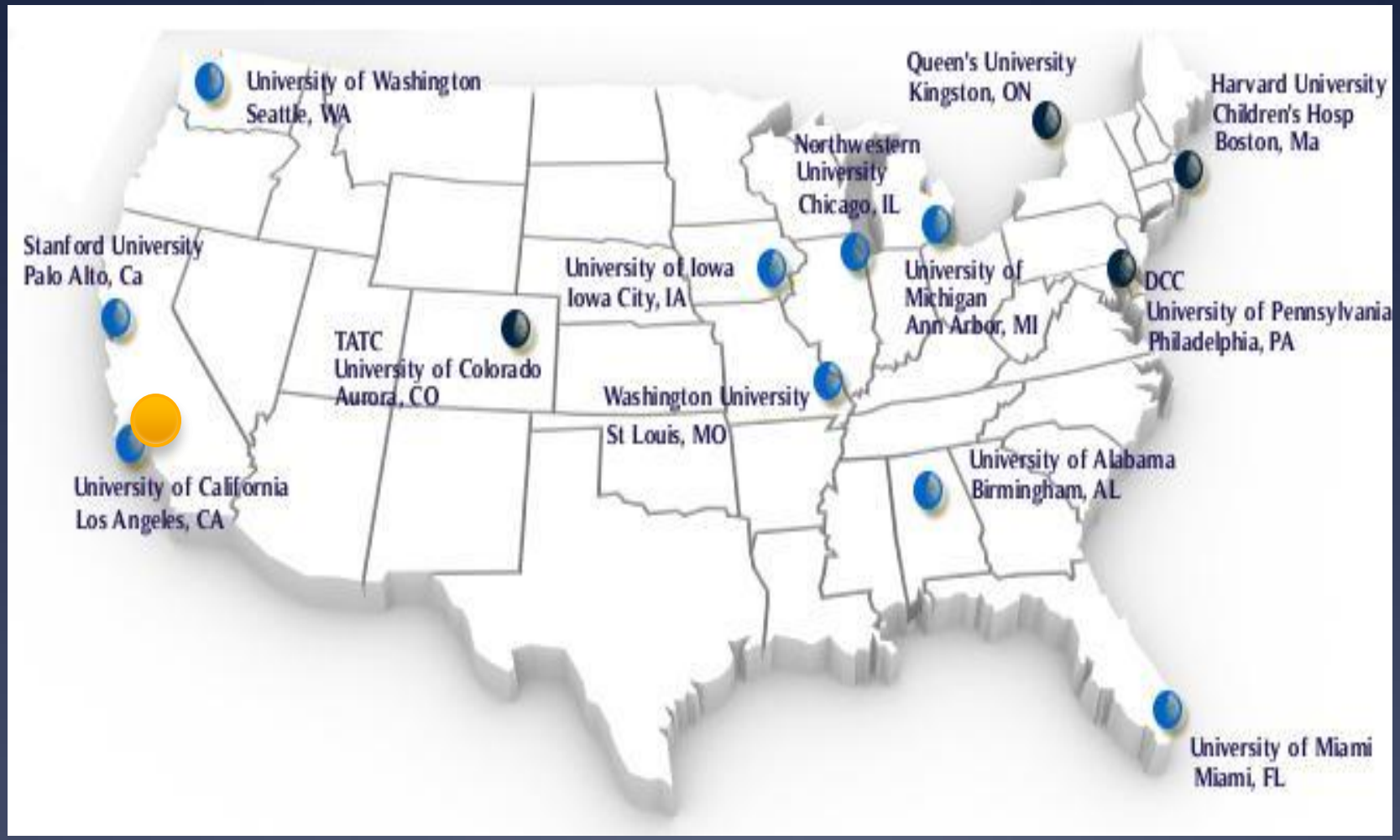
The NIDDK's Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network embraces a systemic—or whole-body—approach in the study of IC/PBS and CP/CPPS. In addition to moving beyond traditional bladder- and prostate-specific research directions, MAPP Network scientists are investigating potential relationships between these two urological syndromes and other chronic conditions that are sometimes seen in IC/PBS and CP/CPPS patients, such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome.

The multidisciplinary (i.e., scientists employing a variety of research approaches) MAPP Network includes researchers with clinical, epidemiological, and basic research expertise, all working collaboratively:

Chronic Pelvic Pain (MAPP) Research Network

Cooperative Agreement (U01) funded by NIDDK, NIH

MAPP Research Network Sites



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- U24 DK097154
- UCLA CTSI UL1TR000124
- Interstitial Cystitis Association (ICA) Pilot grant
- Fishbein Family IC Research Foundation
- New York Academy of Medicine
- Children's Hospital Boston Faculty Development
- J.K. is an IMAGINE NO IC Scholar, American Urological Association Foundation Research Scholar and an Eleanor and Miles Shore Scholar of Harvard Medical School.

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