Interstitial Cystitis-Associated Urinary Metabolites Identified by Mass-Spectrometry Based Metabolomics Analysis

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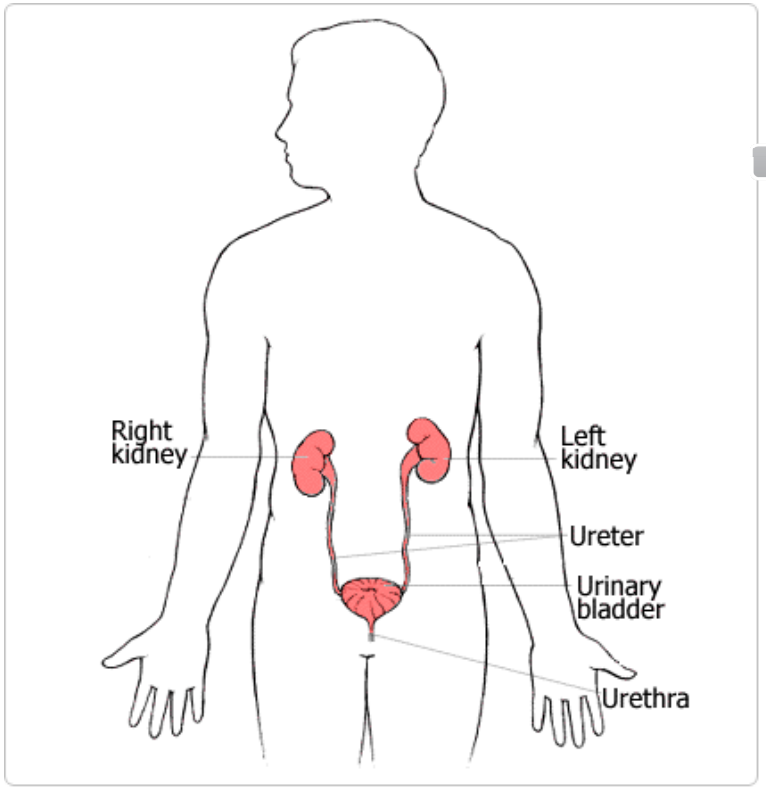
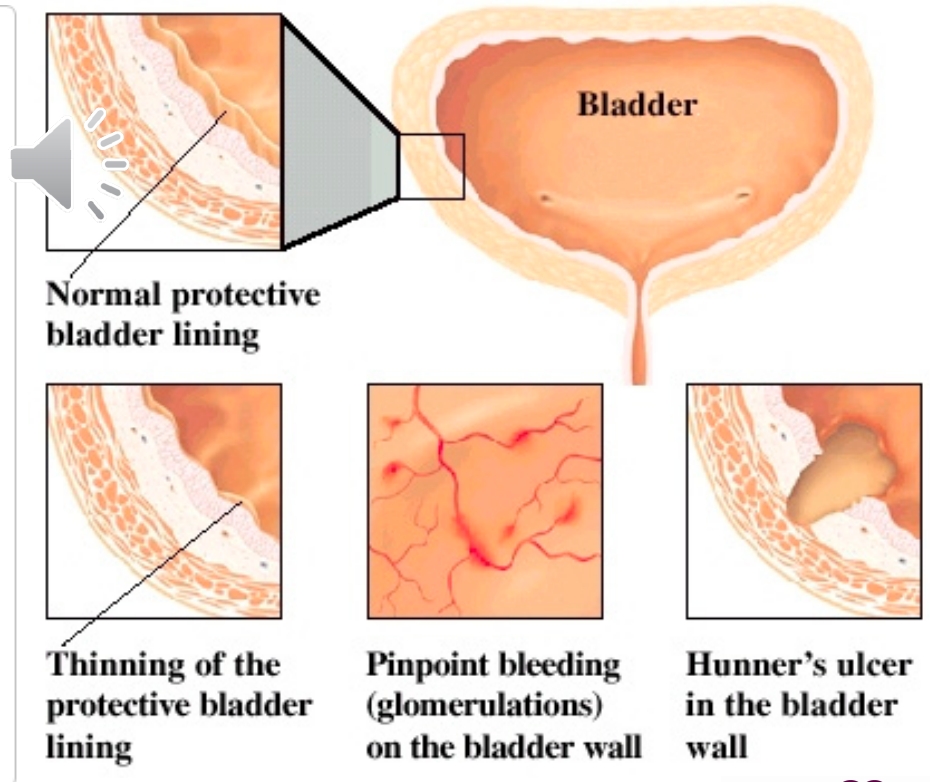
**Confidential* information included

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





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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

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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,*]

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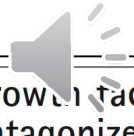

BJUI
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Heparin-binding epidermal growth factor-like growth factor functionally antagonizes interstitial cystitis antiproliferative factor via mitogen-activated protein kinase pathway activation

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*

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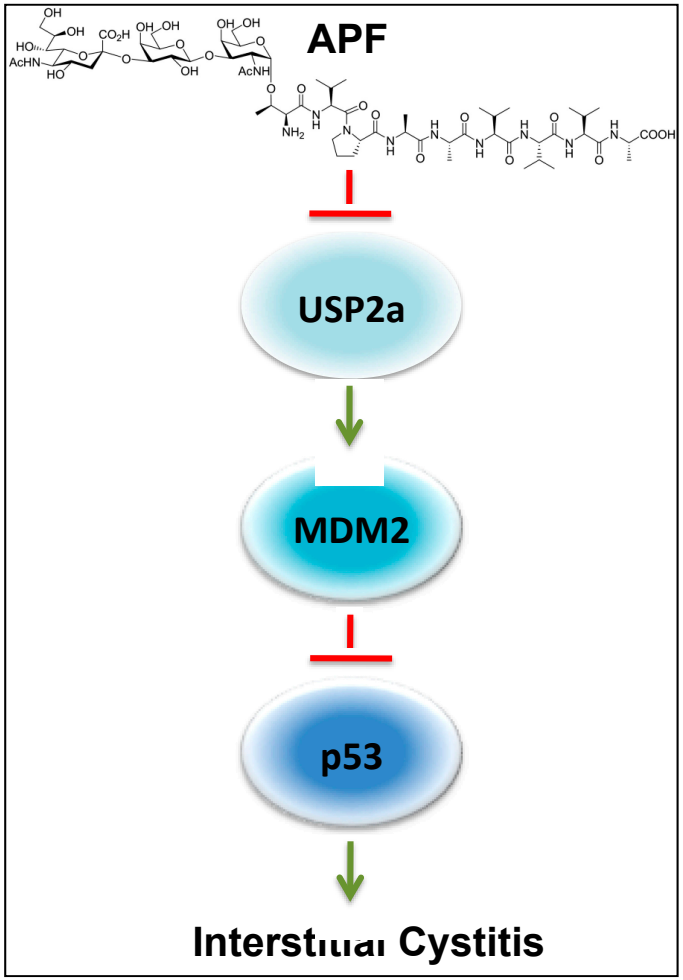
PLOS | ONE

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

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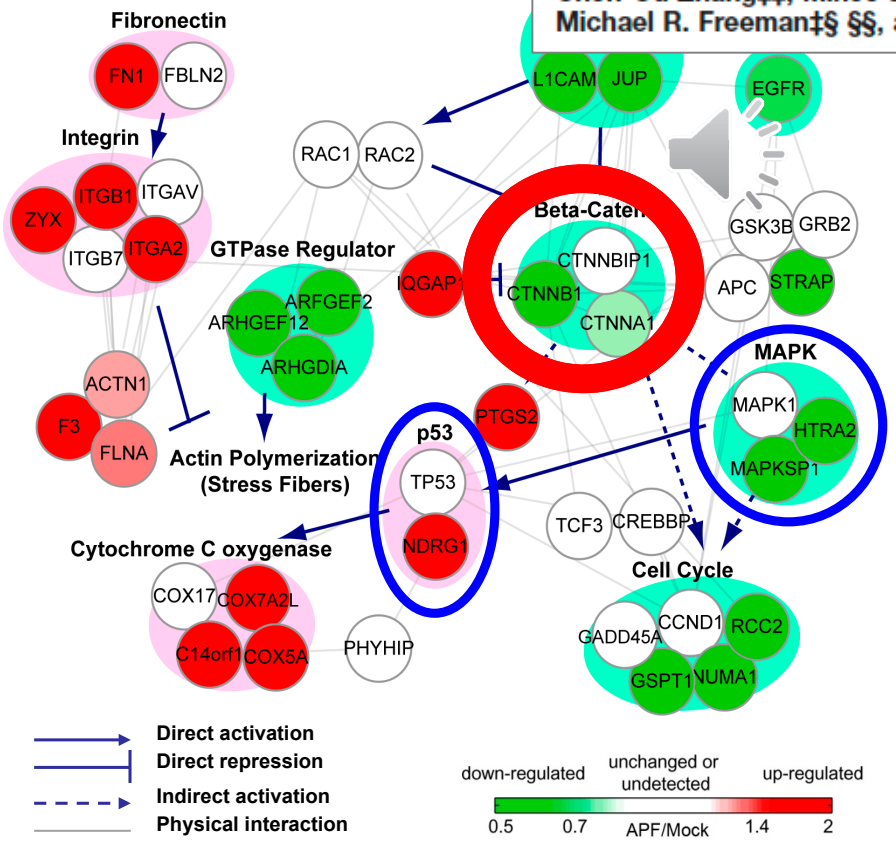
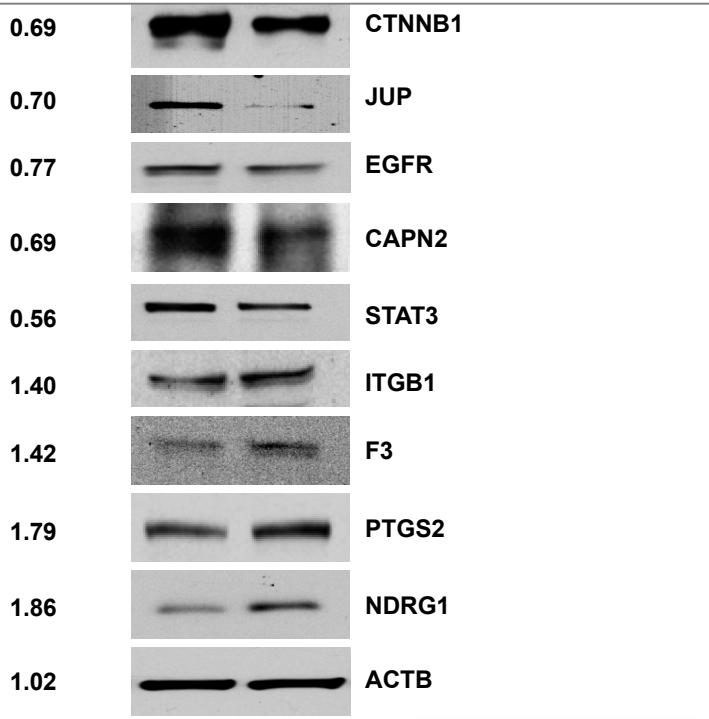
Quantitative Proteomics Identifies a β-Catenin Network as an Element of the Signaling Response to Frizzled-8 Protein-Related Antiproliferative Factor*

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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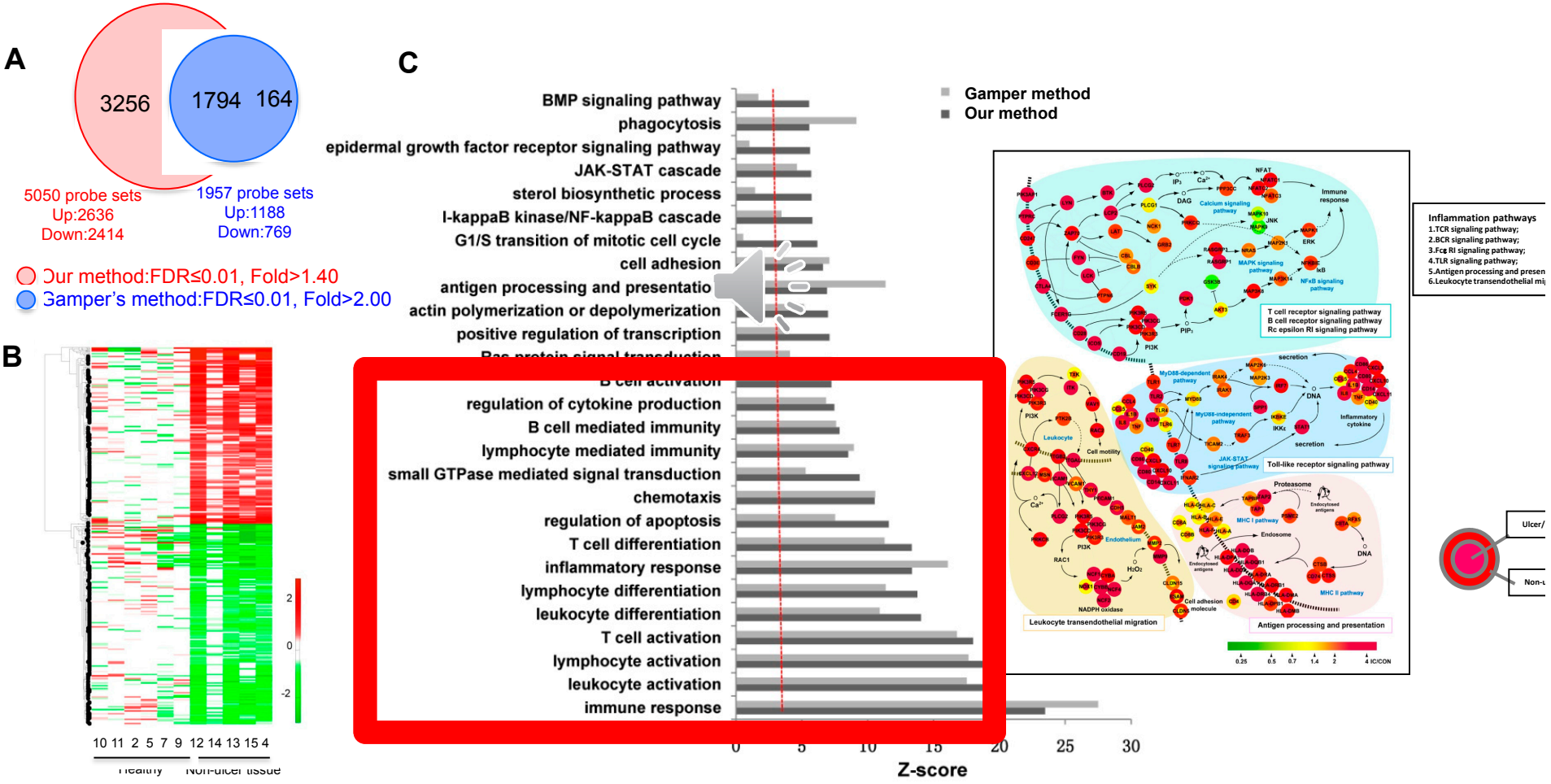
IC-Associated Mechanistic Signaling Network 3:

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

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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]

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[2]Department of Surgery, Cedars-Sinai Medical Center, Center for Women’s Continence and Pelvic Health at Cedars-Sinai, Los Angeles, CA;
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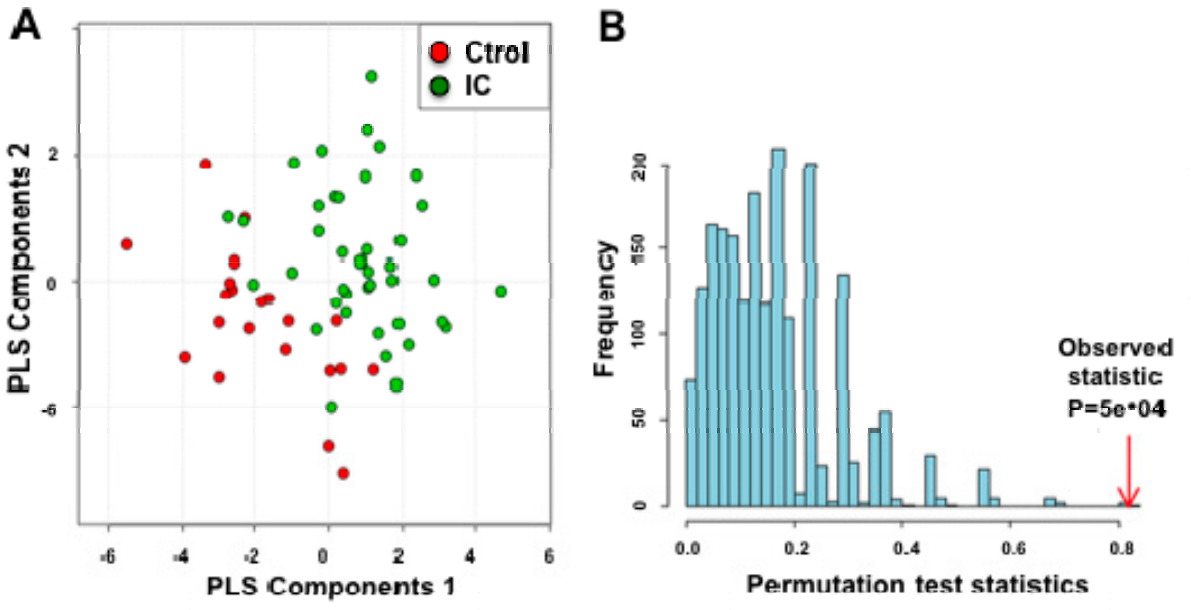

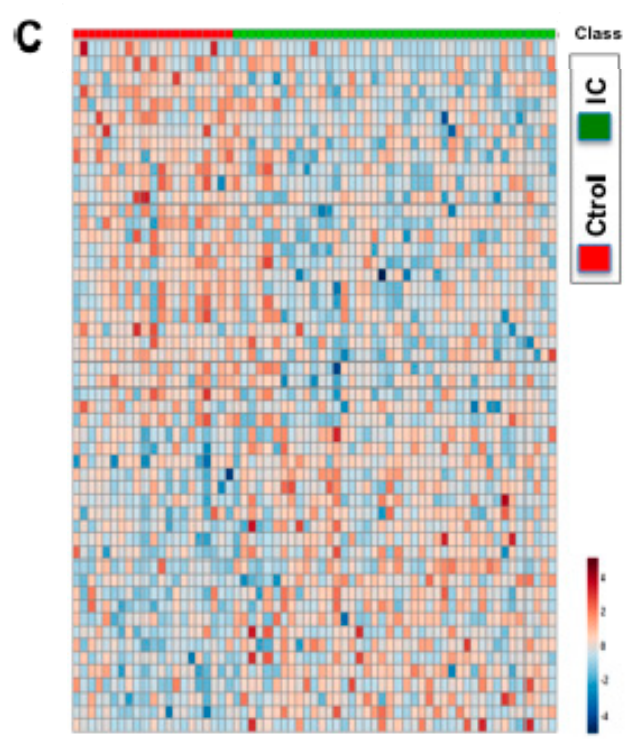

Differentiation of IC patients and healthy control groups using multivariate analysis

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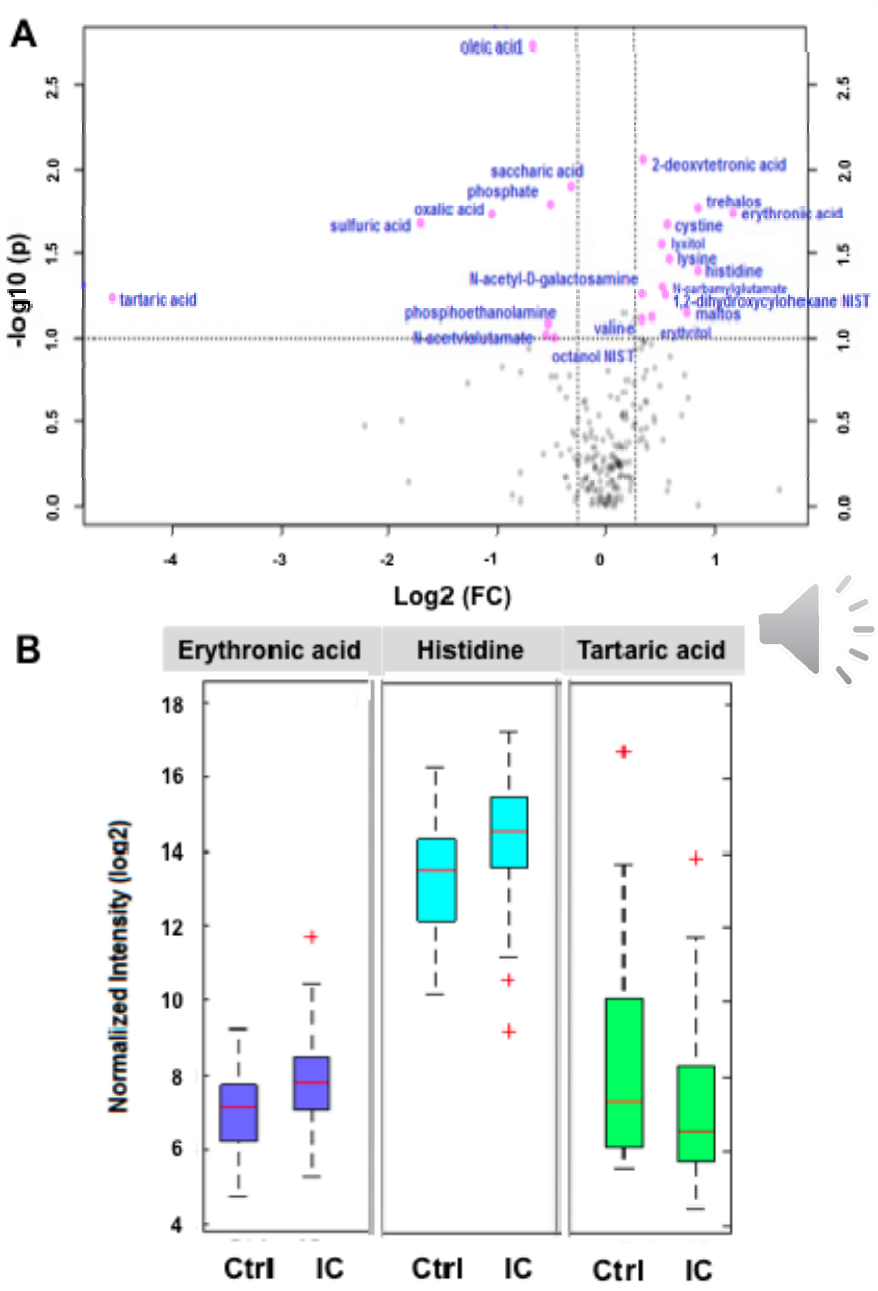

A volcano plot showing differentially expressed metabolites in IC patients.

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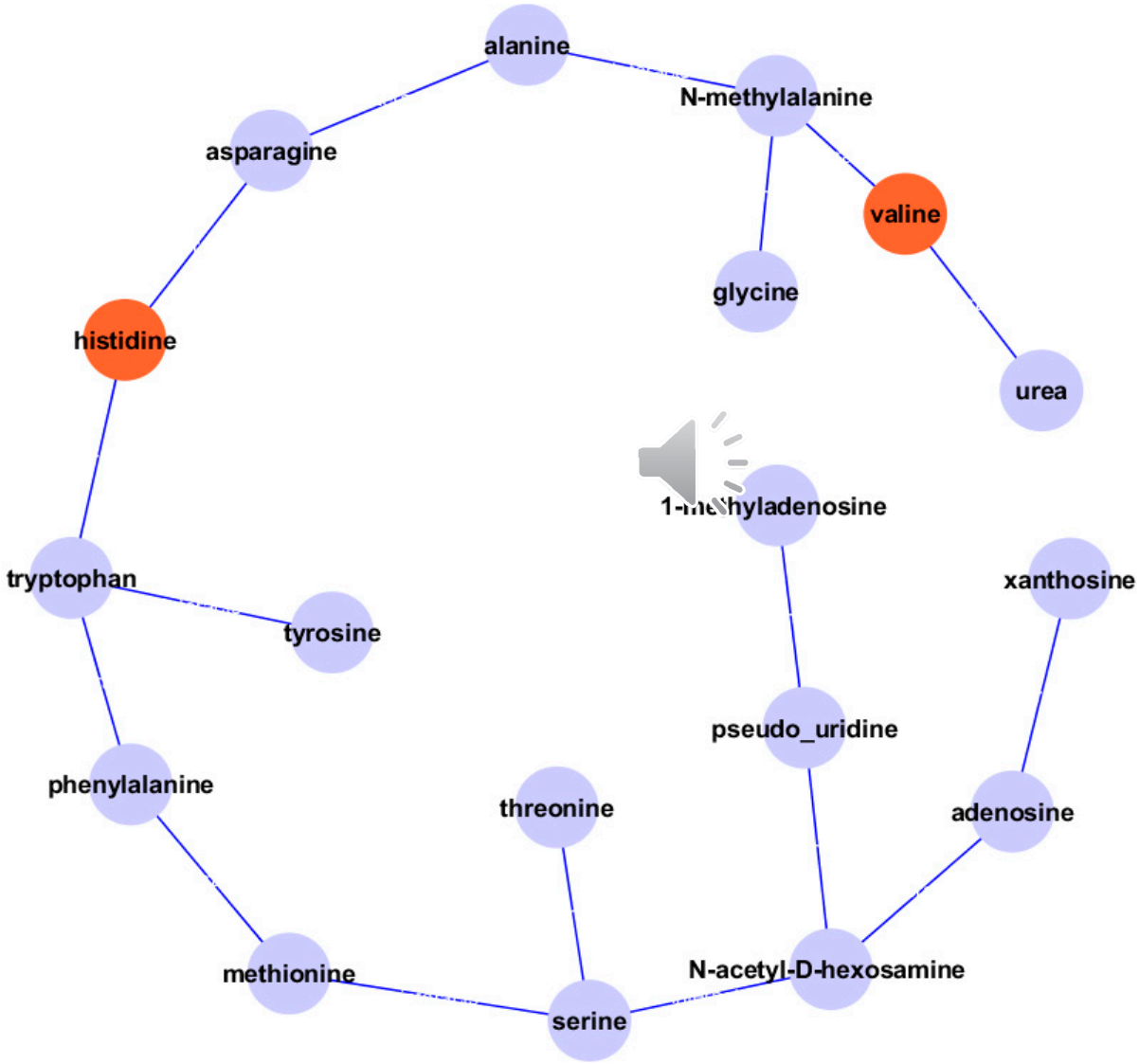
Network modeling derived from IC-associated metabolites



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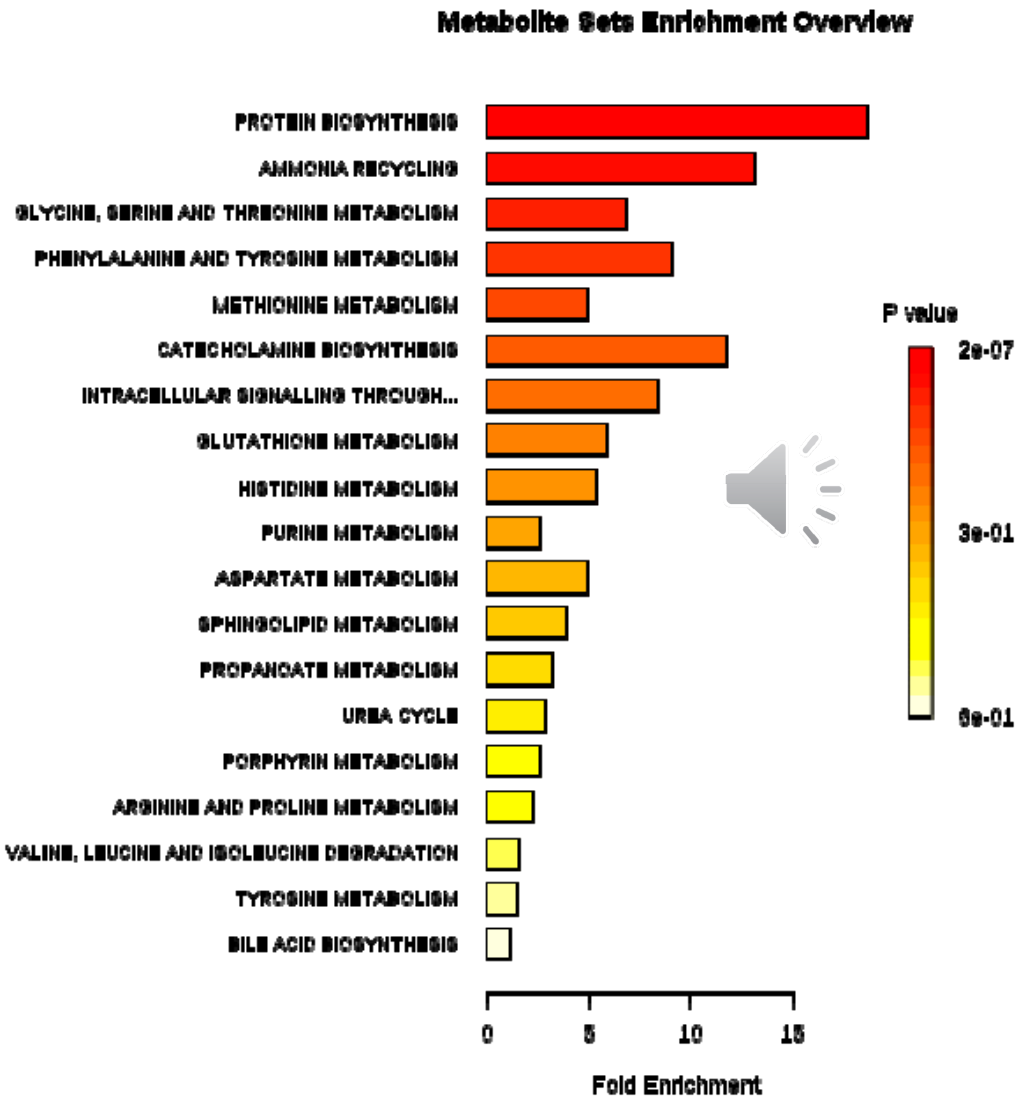
Differential network in IC is identified with multilevel local graphical model



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