

# Pharmacometabolomics-guided Pharmacogenomics in Precision Medicine

**Theodora Katsila, Biochemist BSc (Hons) ARCS MSc PhD  
Senior Research Scientist**



## LETTERS

## Pharmaco-metabonomic phenotyping and personalized drug treatment

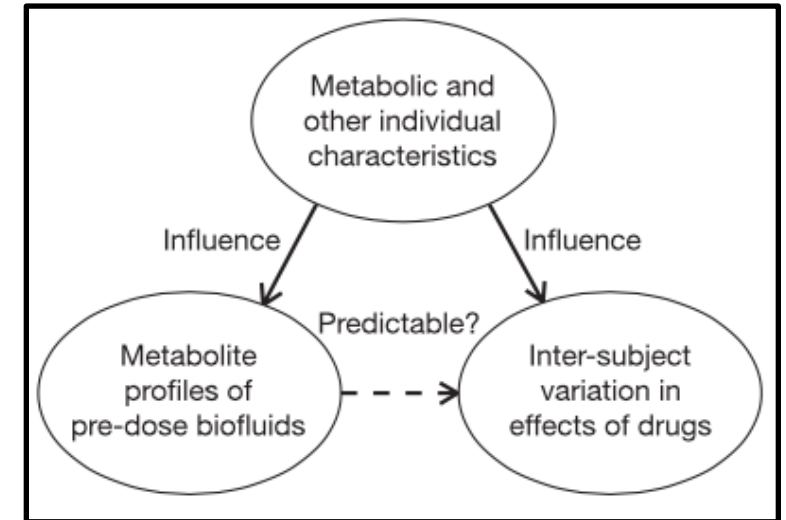
T. Andrew Clayton<sup>1</sup>, John C. Lindon<sup>1</sup>, Olivier Cloarec<sup>1</sup>, Henrik Antti<sup>2</sup>, Claude Charuel<sup>3</sup>, Gilles Hanton<sup>3</sup>, Jean-Pierre Provost<sup>3</sup>, Jean-Loïc Le Net<sup>3</sup>, David Baker<sup>4</sup>, Rosalind J. Walley<sup>5</sup>, Jeremy R. Everett<sup>5</sup> & Jeremy K. Nicholson<sup>1</sup>

### Pharmacometabonomic identification of a significant host-microbiome metabolic interaction affecting human drug metabolism

T. Andrew Clayton<sup>a</sup>, David Baker<sup>b</sup>, John C. Lindon<sup>a</sup>, Jeremy R. Everett<sup>c</sup>, and Jeremy K. Nicholson<sup>a,1</sup>

<sup>a</sup>Biomolecular Medicine, SORA Division, Faculty of Medicine, Sir Alexander Fleming Building, Imperial College London, South Kensington, London SW7 2AZ, United Kingdom; <sup>b</sup>Pfizer Inc., 50 Pequot Avenue, New London, CT 06320; and <sup>c</sup>Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ, United Kingdom

Communicated by Burton H. Singer, Princeton University, Princeton, NJ, April 29, 2009 (received for review December 8, 2008)



PNAS

PNAS

## Drugs, bugs, and personalized medicine: Pharmacometabonomics enters the ring

Ian D. Wilson<sup>1</sup>

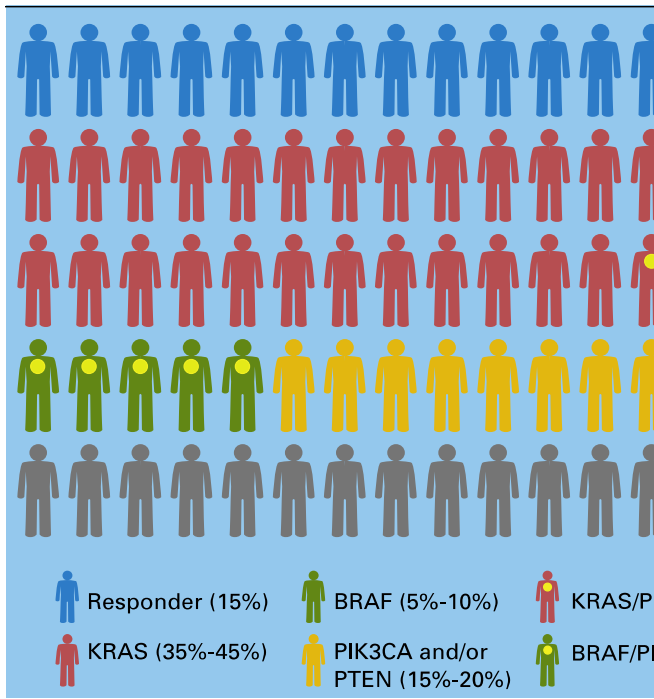
Department of Clinical Pharmacology, Drug Metabolism, and Pharmacokinetics, AstraZeneca, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, United Kingdom


**T**he development of personalized treatment regimens, optimized to the measured biological sta-

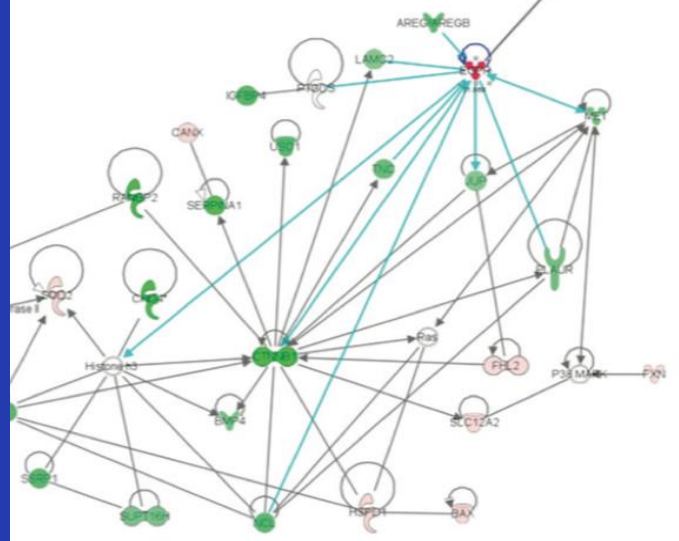
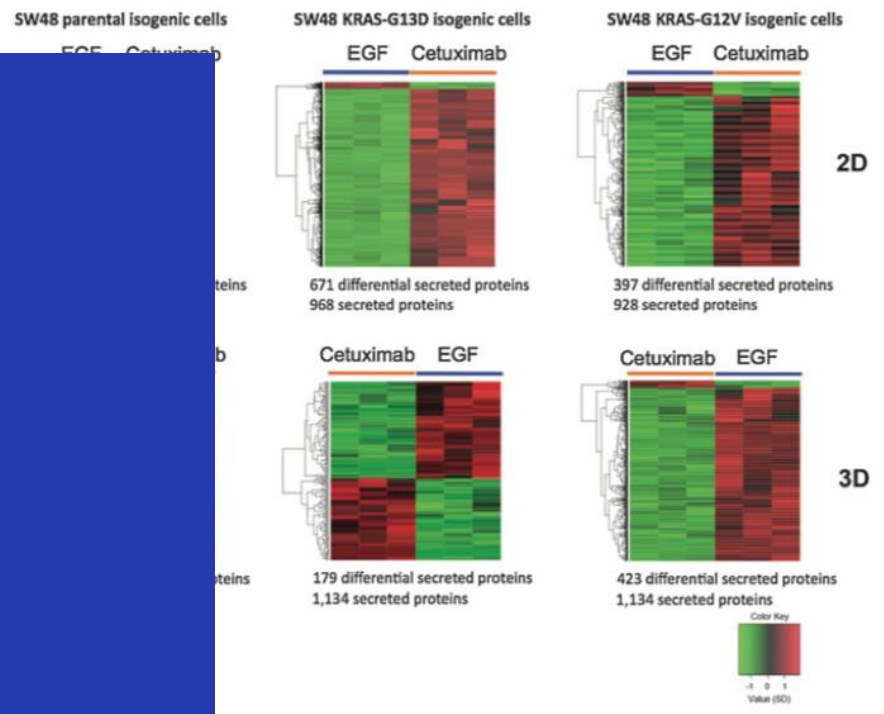
catenation of many physiological, chemical, genetic, and environmental influences.

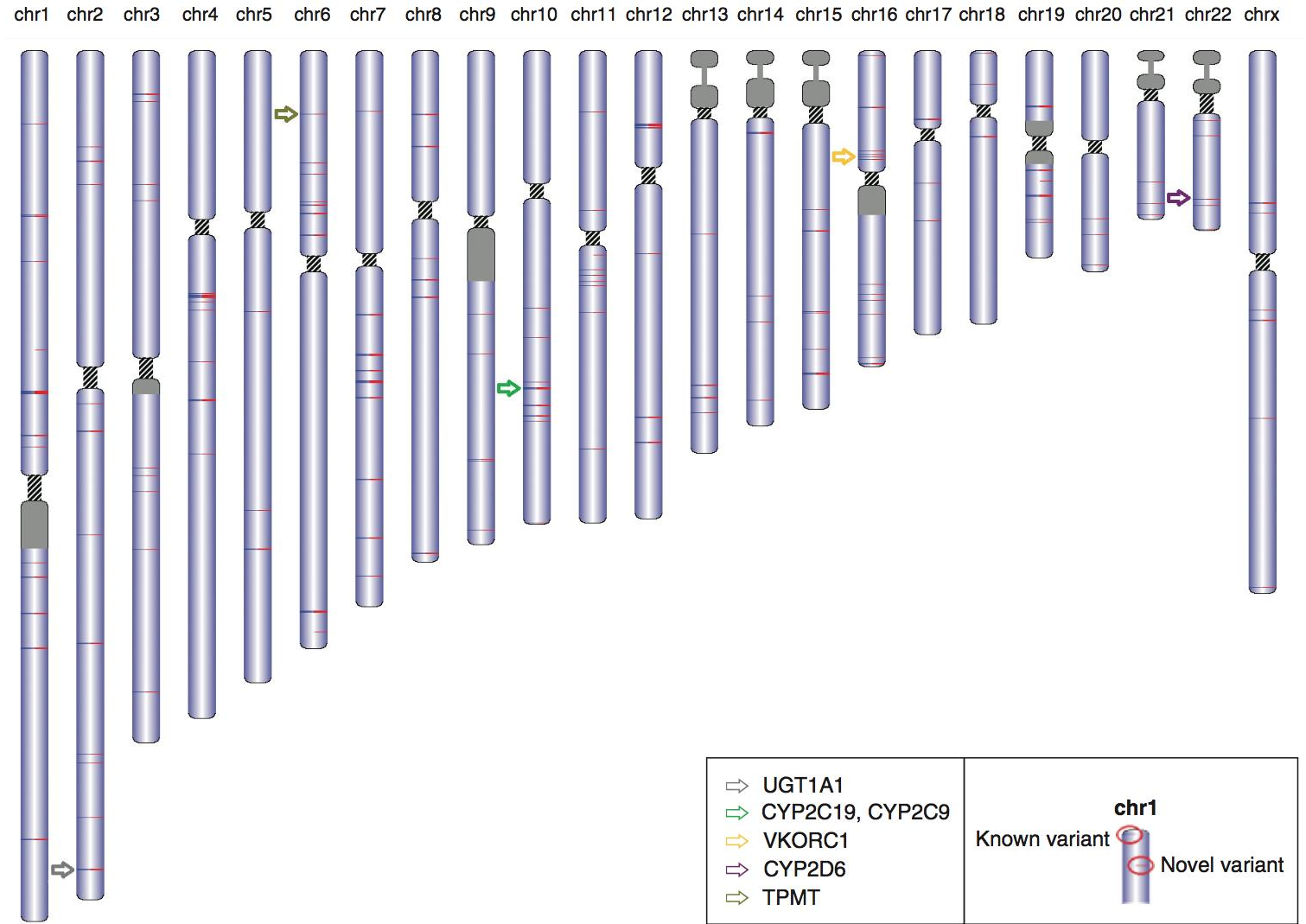
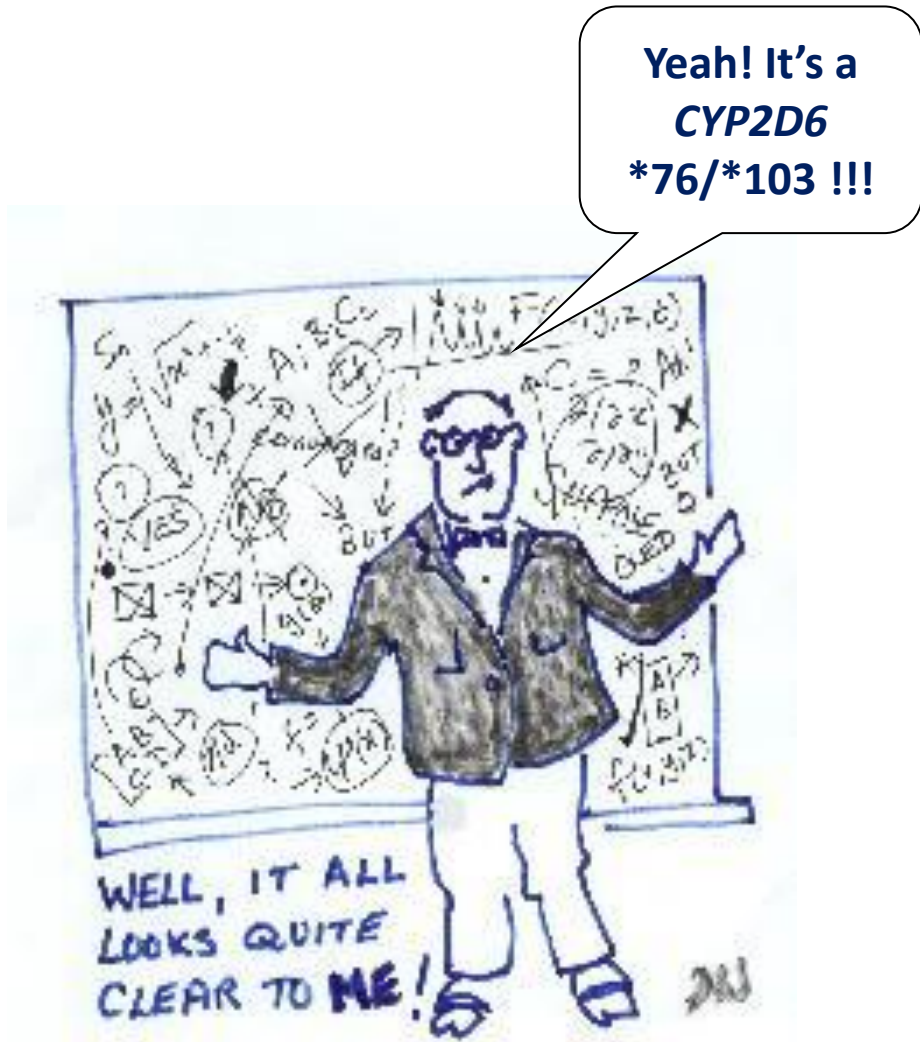
metabolic fate, liver damage, and pre-dose metabotype. The study in ref. 7 is important because it shows that pharma-

COMMENTARY



  
**KEEP CALM AND ANALYZE YOUR GENOME**







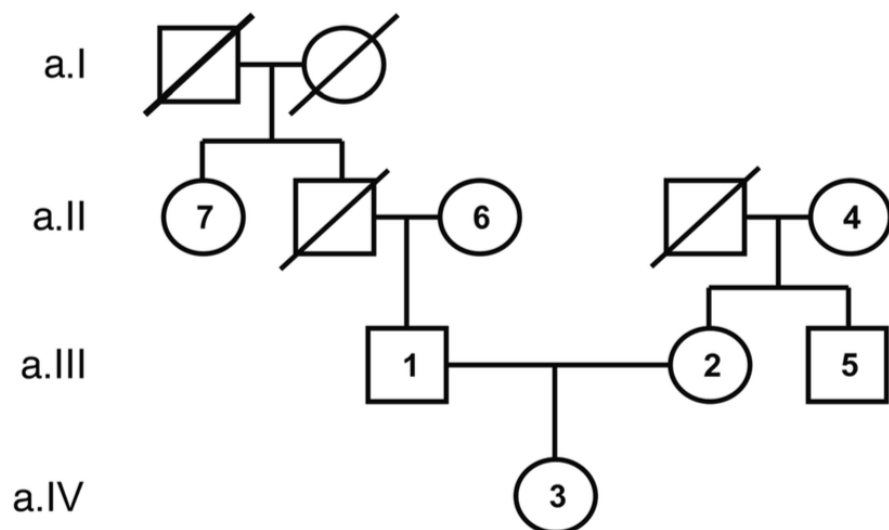
Review

## Pharmacometabolomics-aided Pharmacogenomics in Autoimmune Disease



Theodora Katsila \*, Evangelia Konstantinou, Ioanna Lavda, Harilaos Malakis, Ioanna Papantoni, Lamprini Skondra, George P. Patrinos

University of Patras, School of Health Sciences, Department of Pharmacy, University Campus, Rion, Patras, Greece



>variantId	chromosome	varType	1	2	3	4	5	6	7	symbol	impact
913940	chr2	snp	0	1	1	0	0	0	0	<i>SLC9A4</i>	MISSENSE
922428	chr2	snp	0	1	1	0	0	0	0	<i>NCK2</i>	MISSENSE
1115916	chr2	snp	0	1	1	0	0	0	0	<i>HOXD12</i>	MISSENSE
2250049	chr4	snp	0	1	1	0	0	0	0	<i>KIAA1109</i>	MISSENSE
2250061	chr4	sub	0	1	1	NN	0	0	0	<i>KIAA1109</i>	MISSENSE
3096020	chr6	snp	NN	1	1N	NN	NN	NN	0N	<i>HLA-DRB5</i>	MISSENSE
7113250	chr17	snp	0	1	1	0	0	0	0	<i>HOXB6</i>	MISSENSE

## **HLA class II high-resolution genotyping in Greek children with celiac disease and impact on disease susceptibility**

Maro Krini<sup>1</sup>, Giorgos Chouliaras<sup>1</sup>, Maria Kanariou<sup>2</sup>, Ioanna Varela<sup>2</sup>, Kleopatra Spanou<sup>2</sup>, Joanna Panayiotou<sup>1</sup>, Eleftheria Roma<sup>1</sup> and Nikki Constantinidou<sup>2</sup>

## HLA genotyping in pediatric celiac disease patients

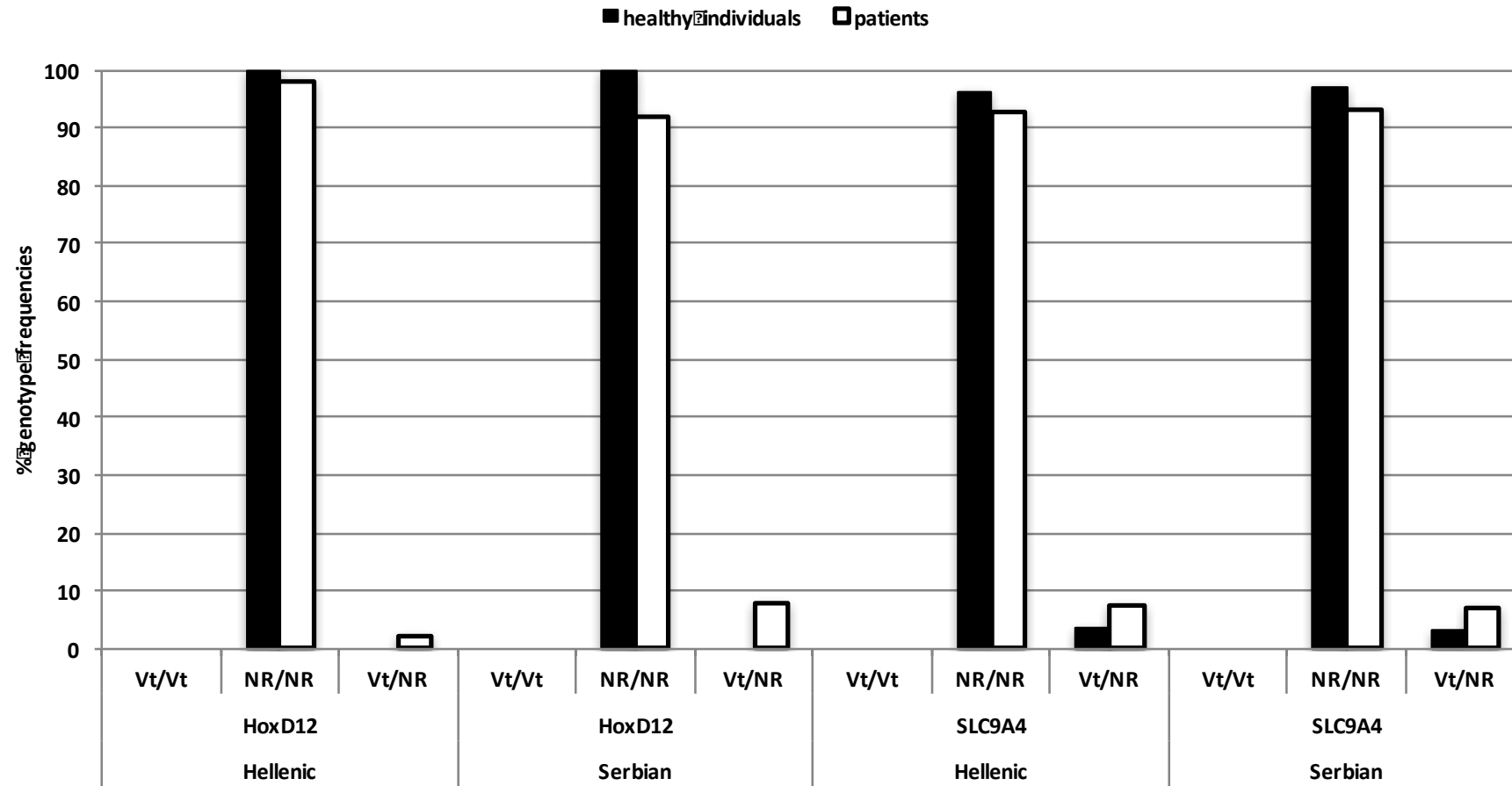
Biljana Stanković<sup>1</sup>, Nedeljko Radlović<sup>2</sup>, Zoran Leković<sup>2</sup>, Dragana Ristić<sup>2</sup>, Vladimir Radlović<sup>2</sup>, Gordana Nikčević<sup>1</sup>, Nikola Kotur<sup>1</sup>, Ksenija Vučićević<sup>3</sup>, Tatjana Kostić<sup>1</sup>, Sonja Pavlović<sup>1</sup>, Branka Zukić<sup>1</sup>

<sup>1</sup>Laboratory for Molecular Biomedicine, Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia.

<sup>2</sup>Department of Gastroenterology and Nutrition, University Children's Hospital, Medical Faculty, University of Belgrade, Belgrade, Serbia.

<sup>3</sup>Faculty of Medical Sciences, University of Kragujevac, Serbia

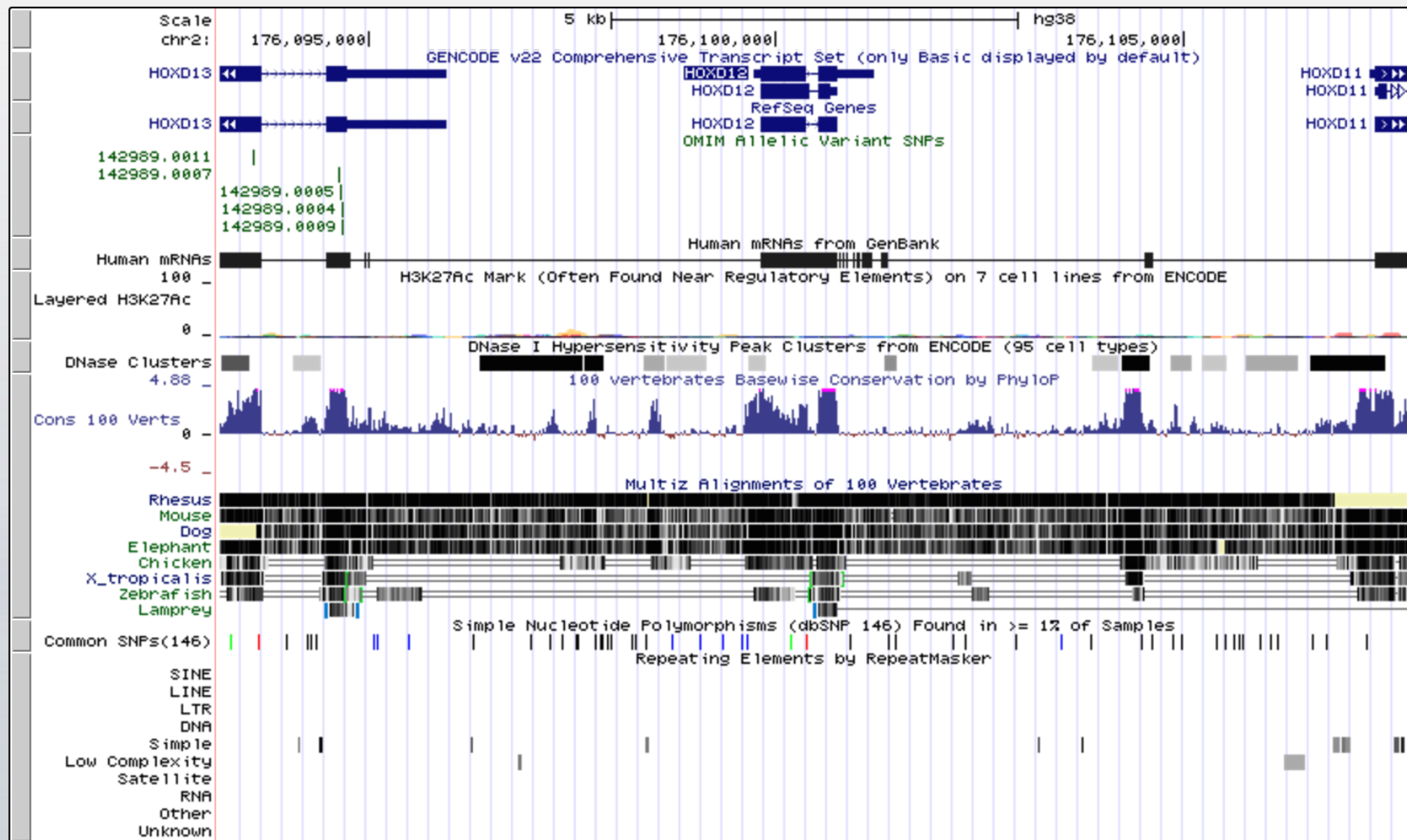
# Serbian and Hellenic Cohorts



# UCSC Genome Browser on Human Dec. 2013 (GRCh38/hg38) Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

chr2:176,093,162-176,107,761 14,600 bp.

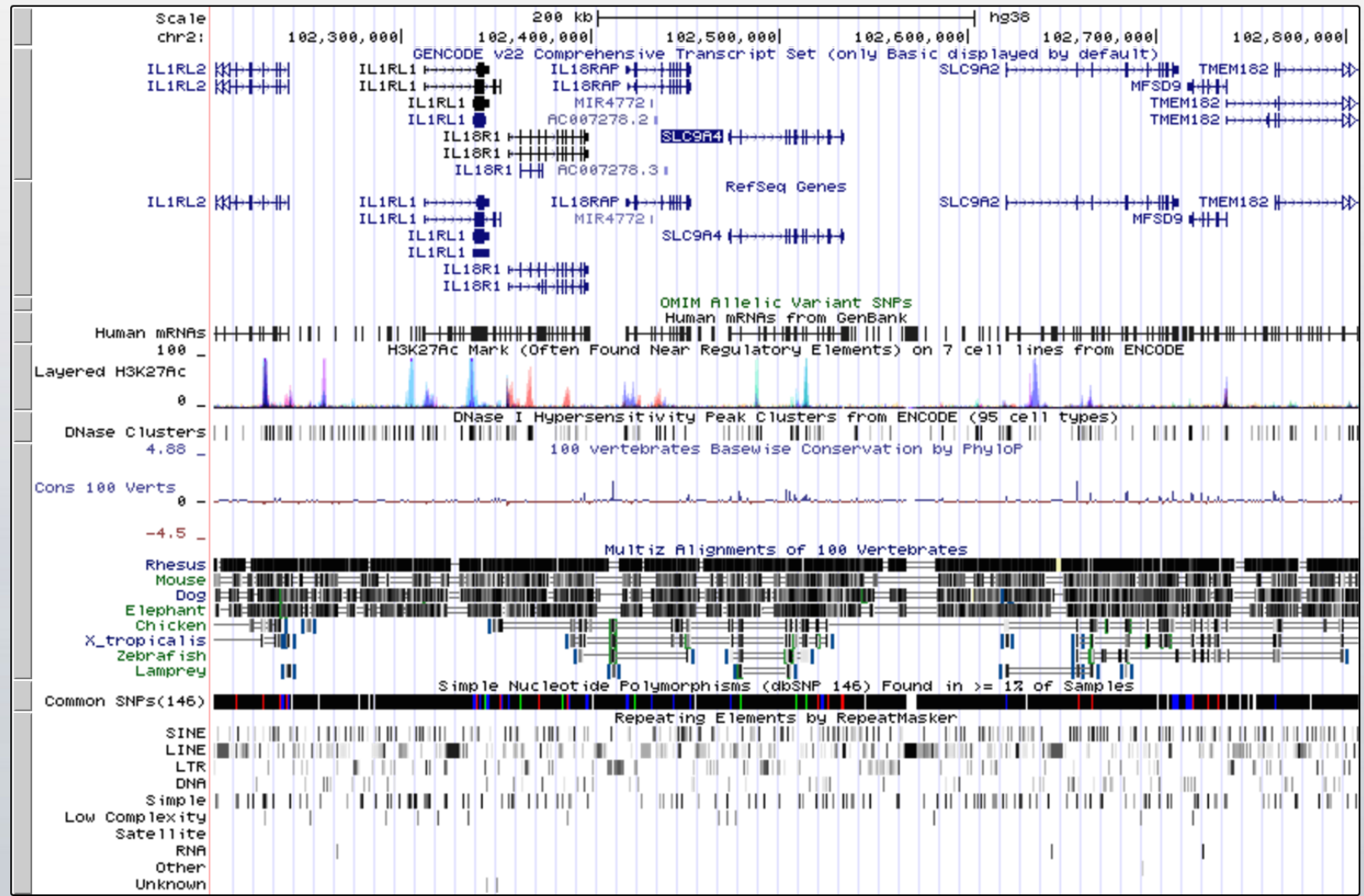




# UCSC Genome Browser on Human Dec. 2013 (GRCh38/hg38) Assembly

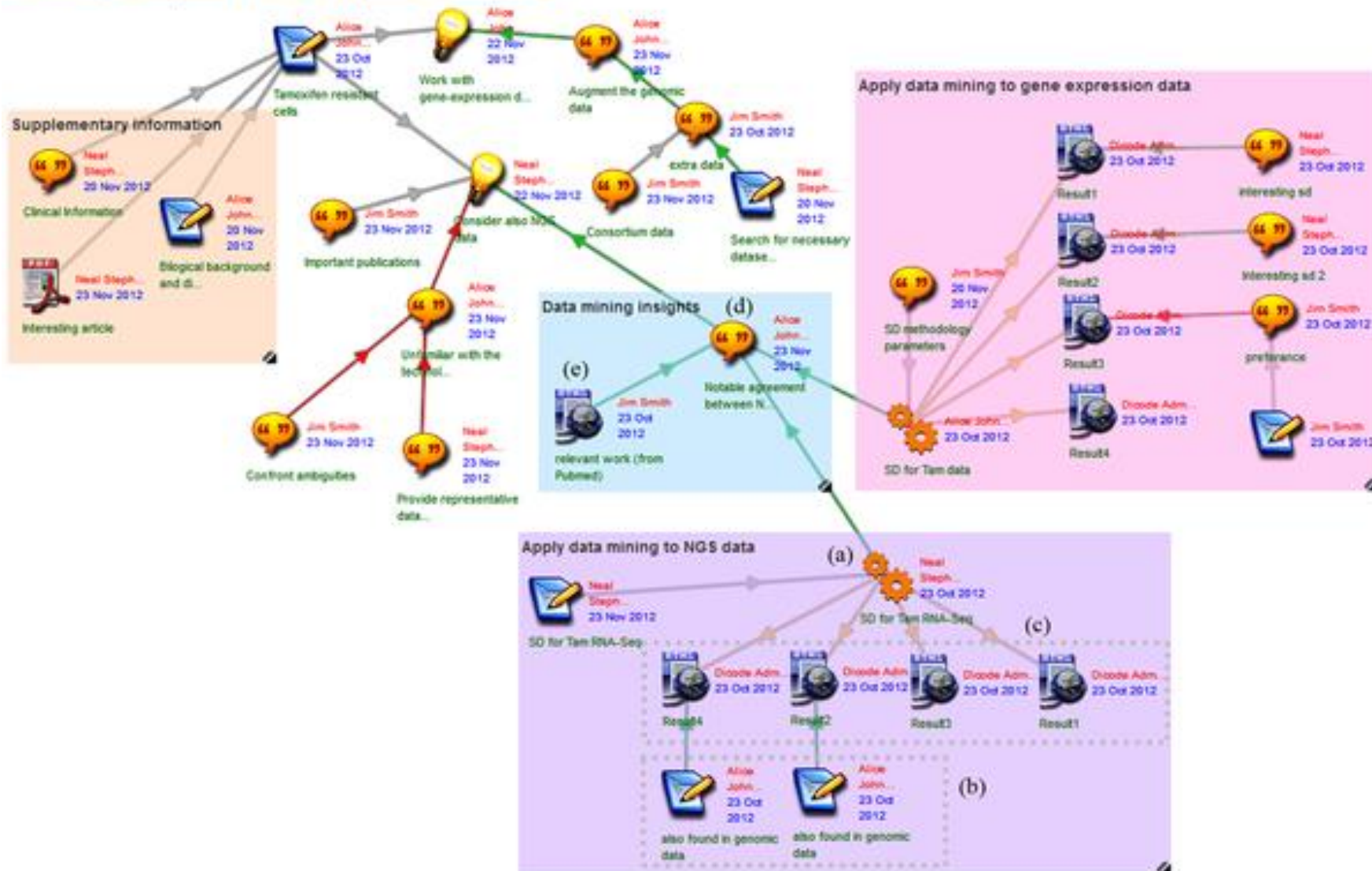
move <<< << < > >> >>> zoom in 1.5x 3x 10x base ZOOM out 1.5x 3x 10x 100x

chr2:102,200,288-102,806,987 606,700 bp.



# Application of SubGroup Discovery service to NGS data, Assessment of Results, and Insights

Active Workspace: Comparative NGS vs Gene Expression Tamoxifen data



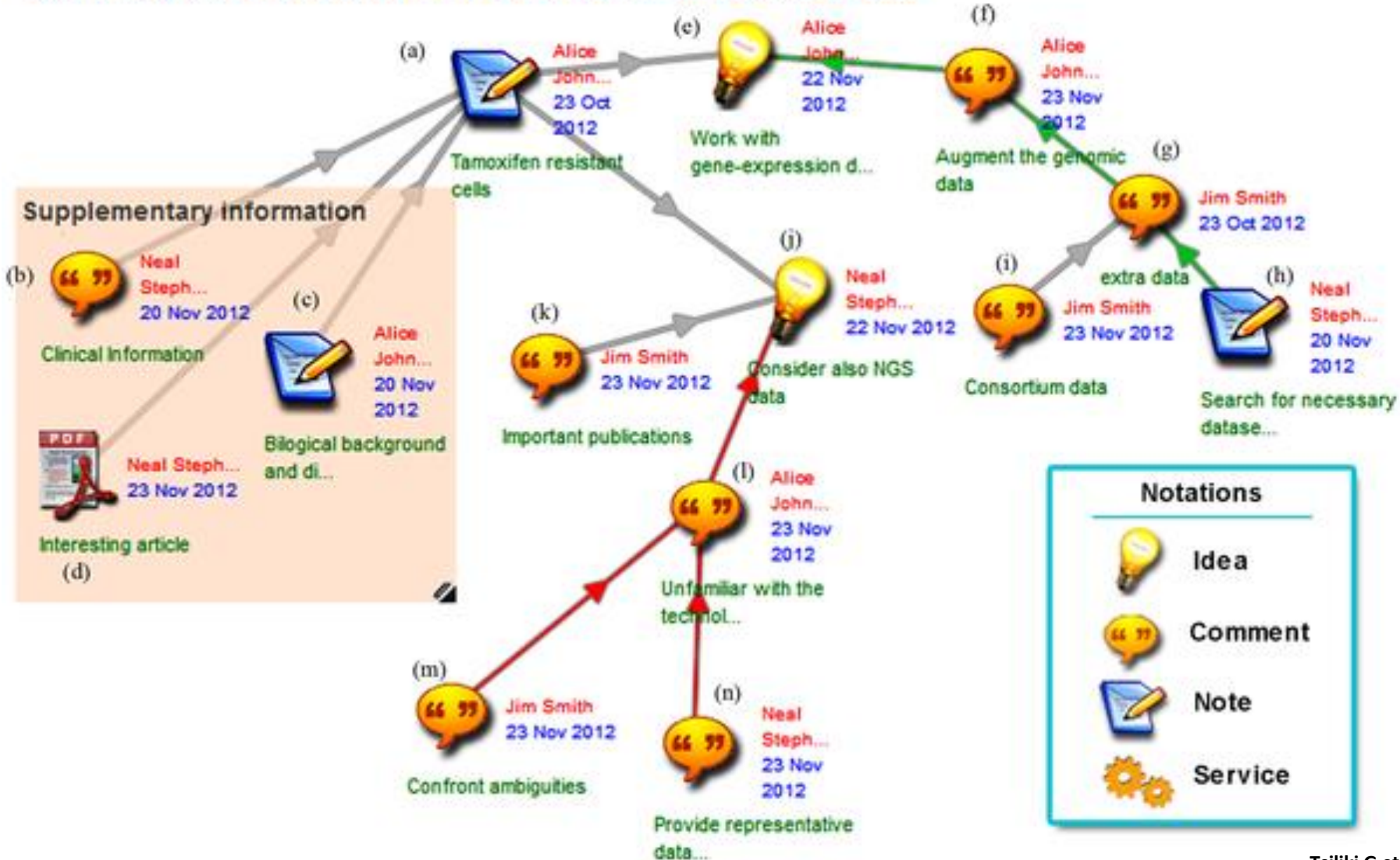
# Input Data for the Biomedical Research Assimilator Context

Data type & description	Databases (web available)	Data in numbers
<b>Genomics/Transcriptomics data: Normalized or raw data</b>	Gene Expression Omnibus	86 datasets, 7,607 samples (~500 Kb per sample, ~32 Mb per dataset)
	ArrayExpress	987 experiments; 69,483 samples
	Stanford Microarray Database	508 experiments
<b>Phenotypic data: Supplementary clinical or phenotypic data available</b>	As above	2 files on average per dataset (~10 Kb per dataset)
<b>Molecular Pathways: Data from known and established molecular networks</b>	Kyoto Encyclopedia of Genes and Genomics (KEGG)	416 pathway maps (153,758 total)
	Reactome	3,931,211 data entries
<b>Annotation data: Reference databases for biomedical &amp; genomic information</b>	Gene Ontology (GO)	~30,000 terms, ~50,000 relationships
	National Center of Biotechnology Information	26,473 annotated coding regions (RefSeq), 129,493 homo sapiens entries (Unigene), ~127 billion bases (GenBank), >21 million citations for biomedical literature (PubMed)

doi:10.1371/journal.pone.0108600.t001

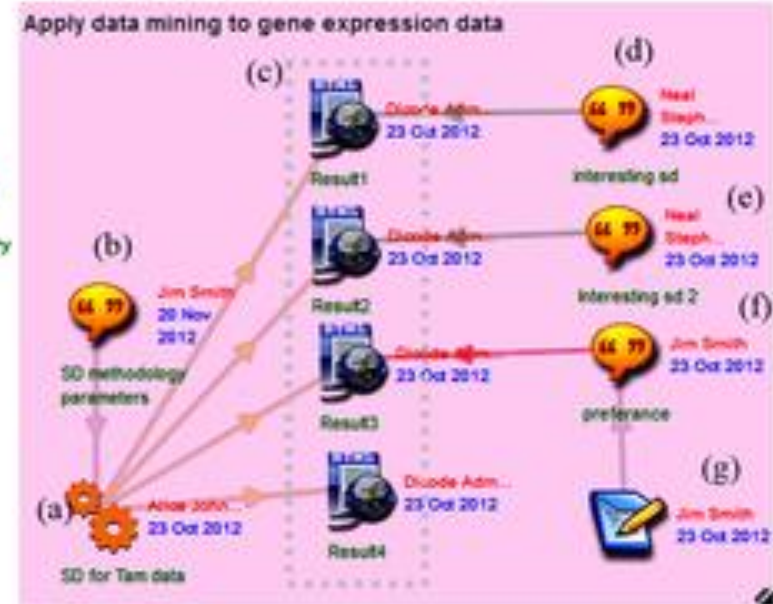
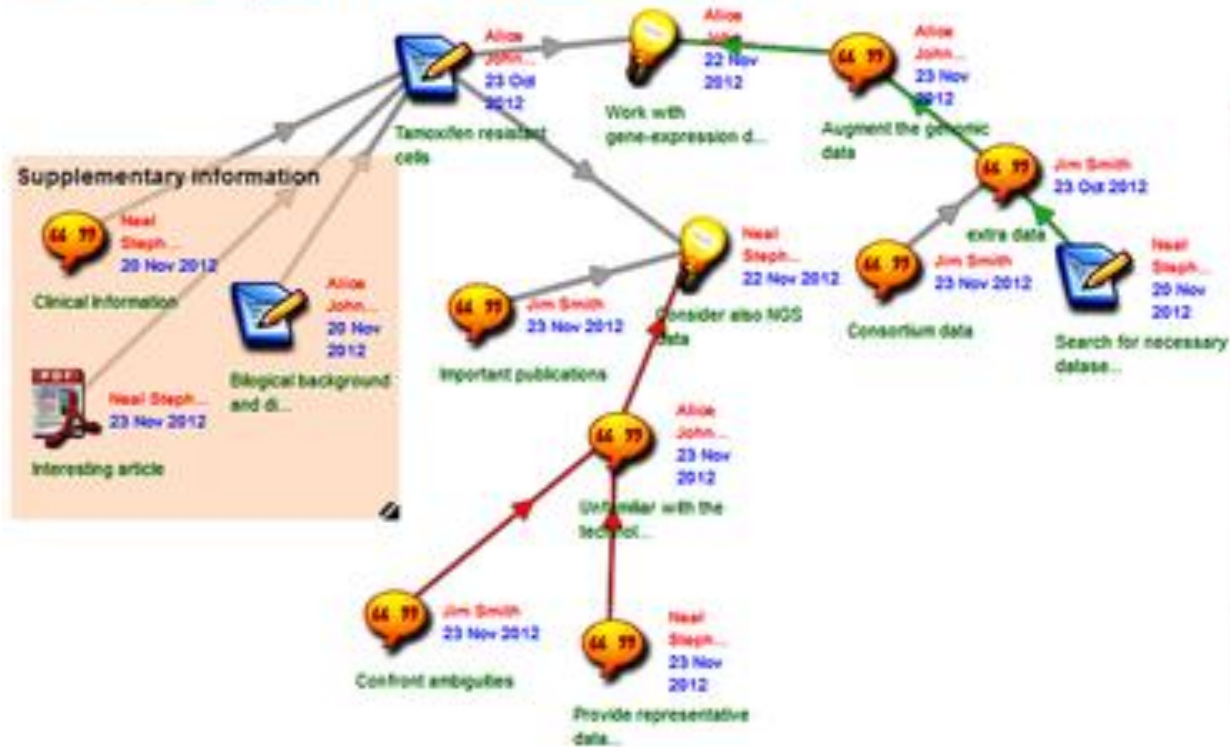
# A Collaboration Workspace for estimating the dominance of Tamoxifen-resistant cells to Global Gene Expression

Active Workspace: Comparative NGS vs Gene Expression Tamoxifen data



# Application of SubGroup Discovery service to Gene Expression Data Assessment of Results

Active Workspace: Comparative NGS vs Gene Expression Tamoxifen data



**Can we delineate inter-individual variability towards differential diagnosis?**

**Can we highlight the disease mechanisms in question to assist disease management?**

**What are the host–microbiome interactions?**

**Do post-dose drug metabolism and safety relate to pre-dose metabotypes and how?**



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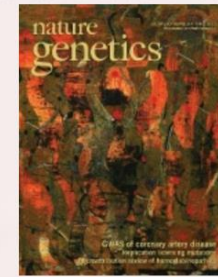
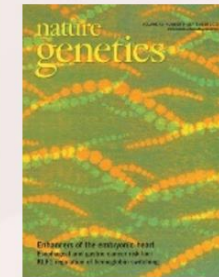


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