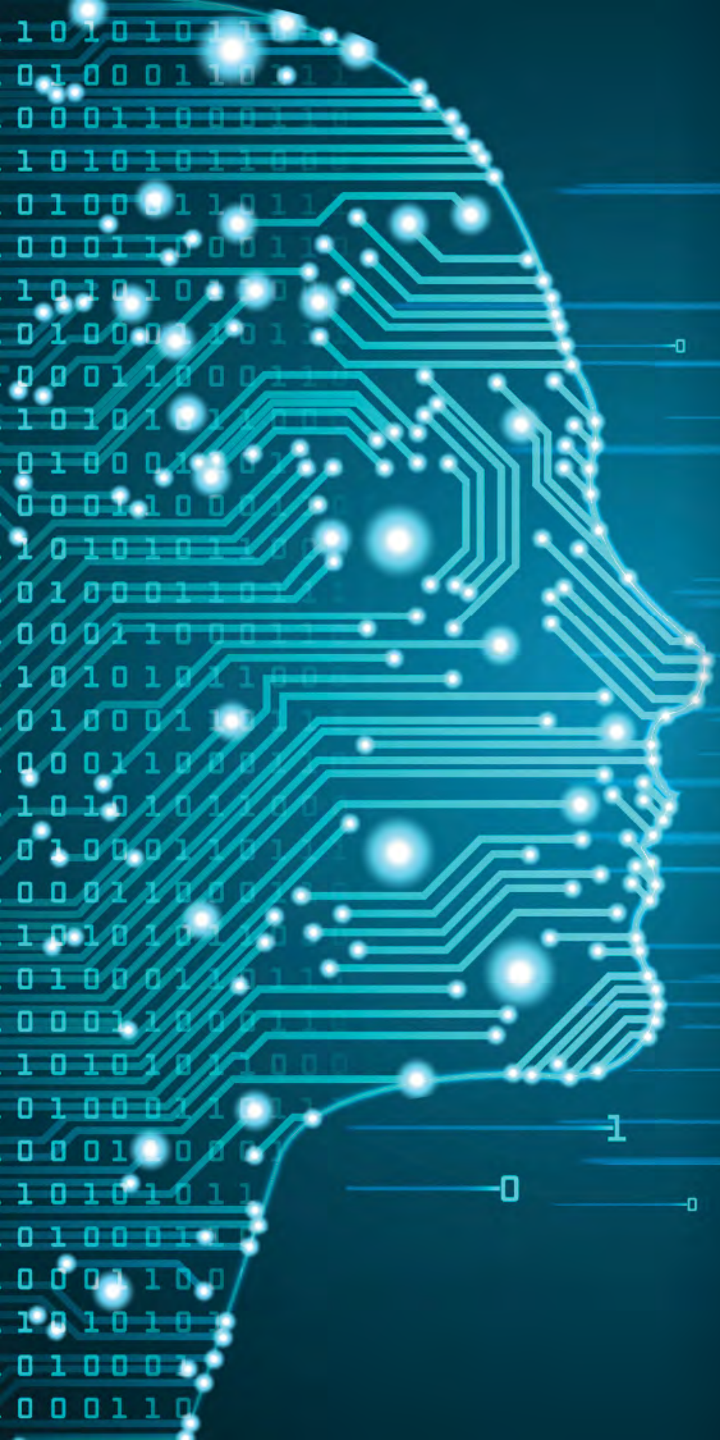
UHN Schroeder Arthritis Institute



AI is Not Enough

Explainable Biology for Improved Therapies

Krembil Relentless.

DATA SCIENCE DISCOVERY CENTRE for Chronic Diseases

Jurisicalab

DECODING ARTHRITIS TO BUILD A CURE

Artemis

The Hospital for Sick Children
in Toronto,
the Neonatal Intensive Care unit

- Monitoring premature infants' vital sign data using IBM InfoSphere Streams
- Each infant generates >1,200 points of data per second
- nearly 90 million points of data per day


TIME
Artificial Intelligence
The Future of Humankind
Artificial Intelligence
ARTIFICIAL INTELLIGENCE
CONSIDERING THE ETHICS
A PARLIAMENT MAGAZINE SPECIAL SUPPLEMENT
IEEE
Science
2018
BREAKTHROUGH of the YEAR
Science
ARTIFICIAL INTELLIGENCE
Science
AI
TRANSFORMS SCIENCE
Harvard Business Review
Meet Your New Employee
How to manage the man-machine collaboration
nature
LEARNING CURVE
nature
ALL SYSTEMS GO
nature
LESIONS LEARNT
D SRUPTION
Artificial intelligence
Forbes
ARTIFICIAL INTELLIGENCE GETS REAL
AI Magazine
INTELLIGENT ASSISTANTS
TOTAL DISRUPTION
The Sex Robots Are Coming
POPULAR SCIENCE
THE NEW ARTIFICIAL INTELLIGENCE
Discover
ARTIFICIAL INTELLIGENCE
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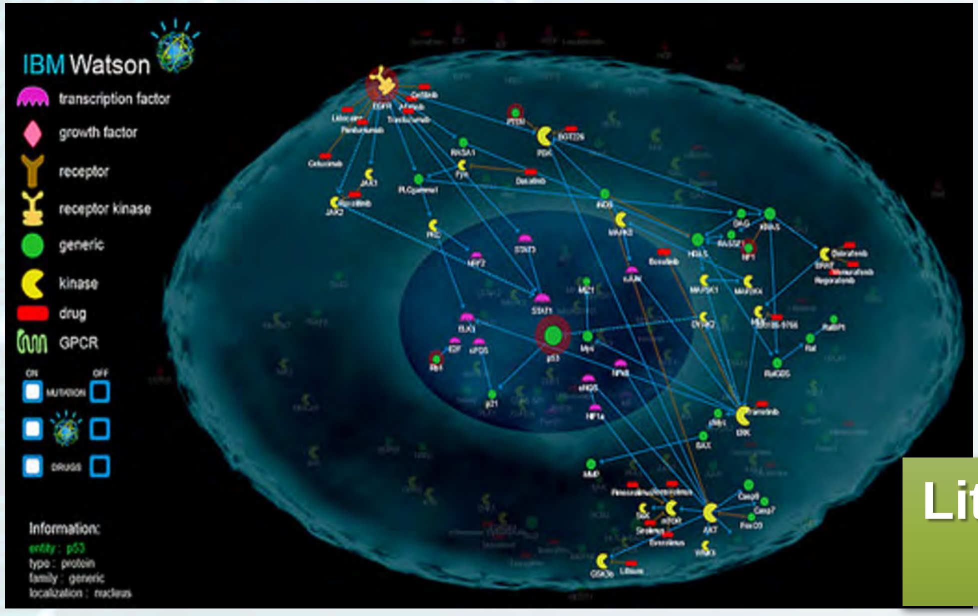
Hacking the Future of...
Beer!
Technology Review
The Artificial Intelligence Issue
CANADIAN Lawyer
AI
Artificial Intelligence will change the legal profession.
Forbes
AI: The Killer App for Your Business
TERADATA
TIME
2045
The Year Man Becomes Immortal
AI in HEALTHCARE
BUILDING THE FOUNDATION
PURESTORAGE
Professional Outsourcing
ARTIFICIAL INTELLIGENCE
THE COMING WAVE
WIRED
Artificial Intelligence is here. But it's nothing like we expected.
Think:Act
AI think, therefore AI am
D!gitalist Magazine
The Machine Learning Issue
EMPATHY MACHINE
SAP
The Economist
Artificial Intelligence
The promise and the peril
The Economist
AI-spy

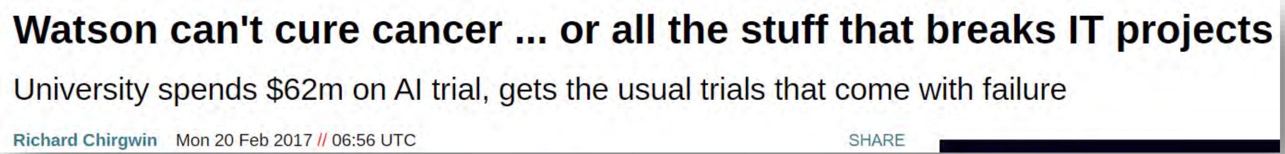
Technology vs Process Failure ?

MDA: IBM WATSON & CANCER

> **MD Anderson Taps IBM Watson to Power "Moon Shots" Mission Aimed at Ending Cancer, Starting with Leukemia**
> (Houston - 18 Oct 2013)



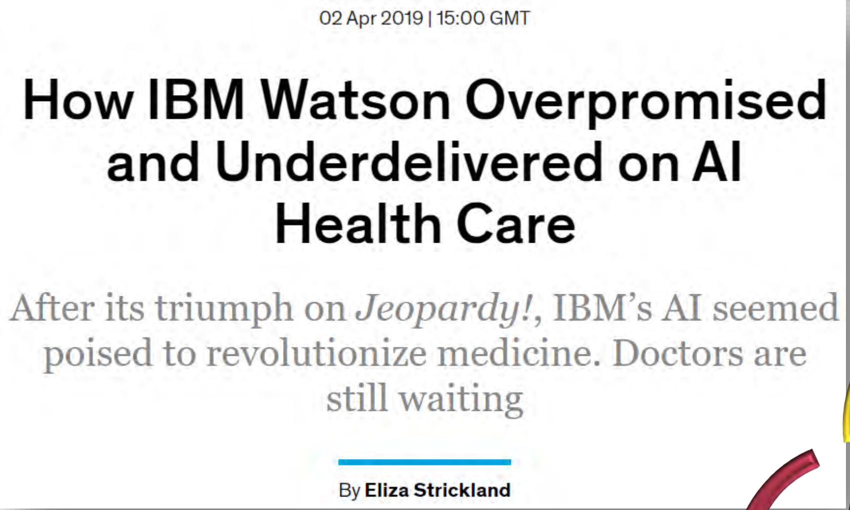
4 YEARS AND $62M LATER



Watson can't cure cancer ... or all the stuff that breaks IT projects

University spends $62m on AI trial, gets the usual trials that come with failure

Richard Chirgwin Mon 20 Feb 2017 // 06:56 UTC SHARE



02 Apr 2019 | 15:00 GMT

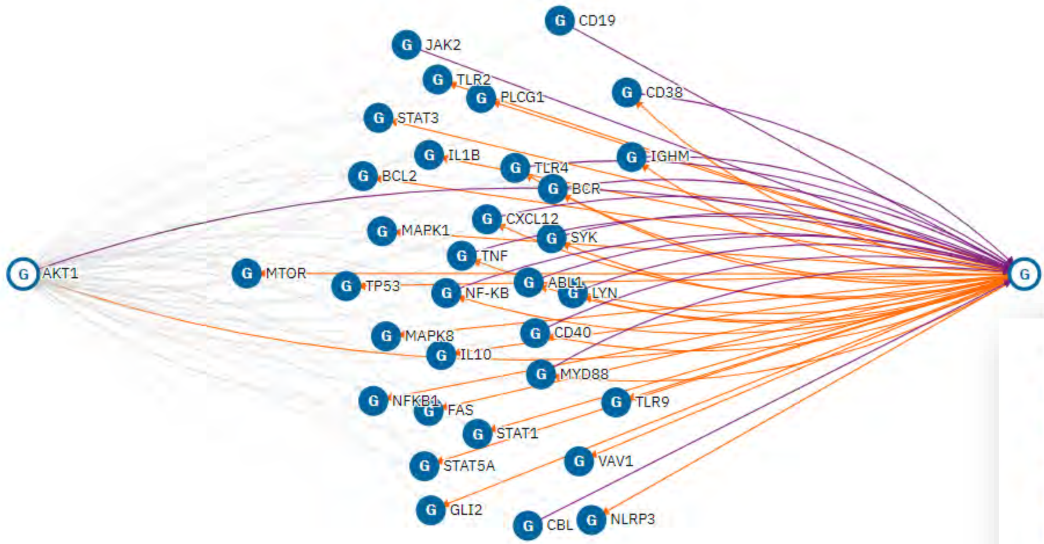
How IBM Watson Overpromised and Underdelivered on AI Health Care

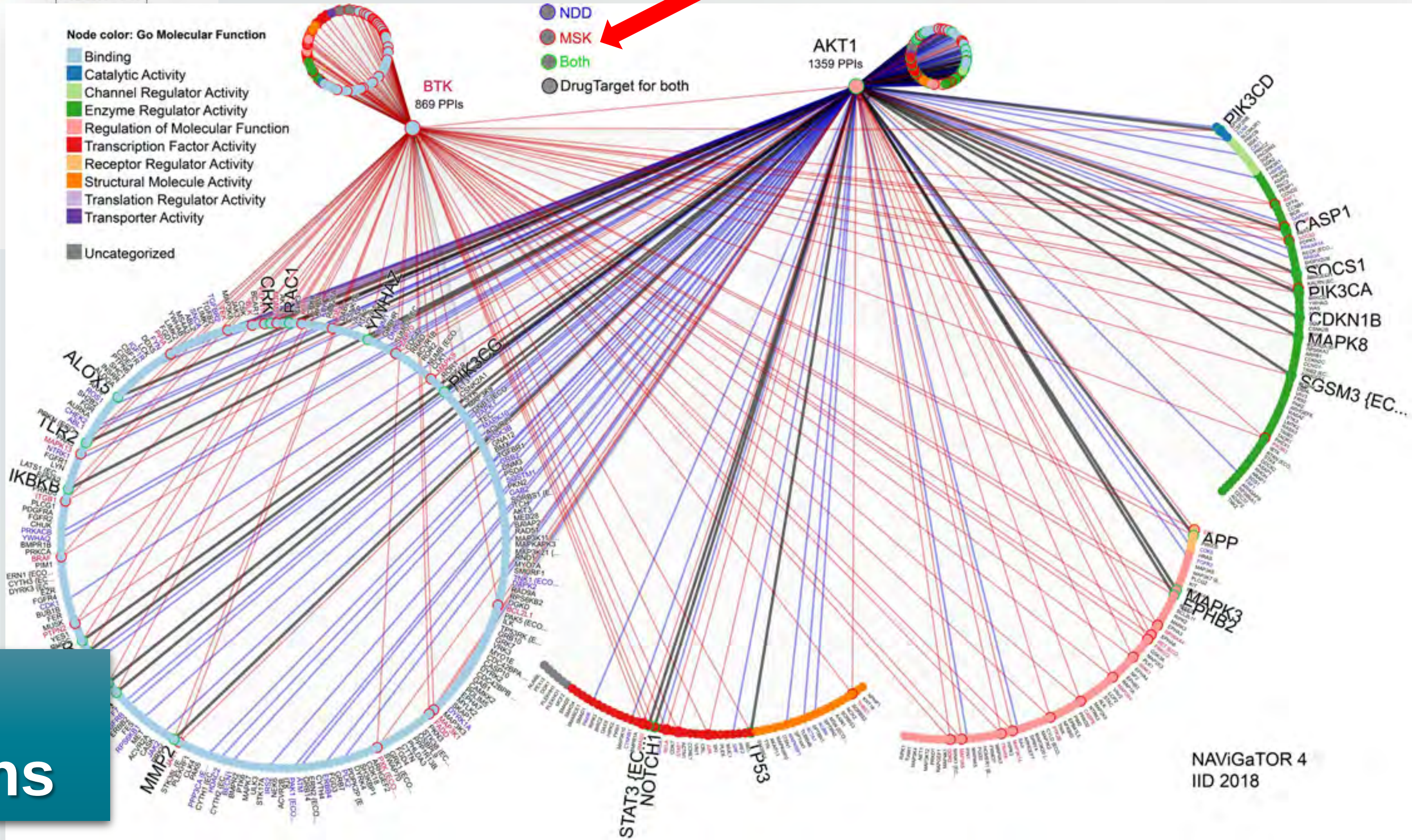
After its triumph on *Jeopardy!*, IBM's AI seemed poised to revolutionize medicine. Doctors are still waiting

By **Eliza Strickland**

Literature vs
Literature + Data + Predictions

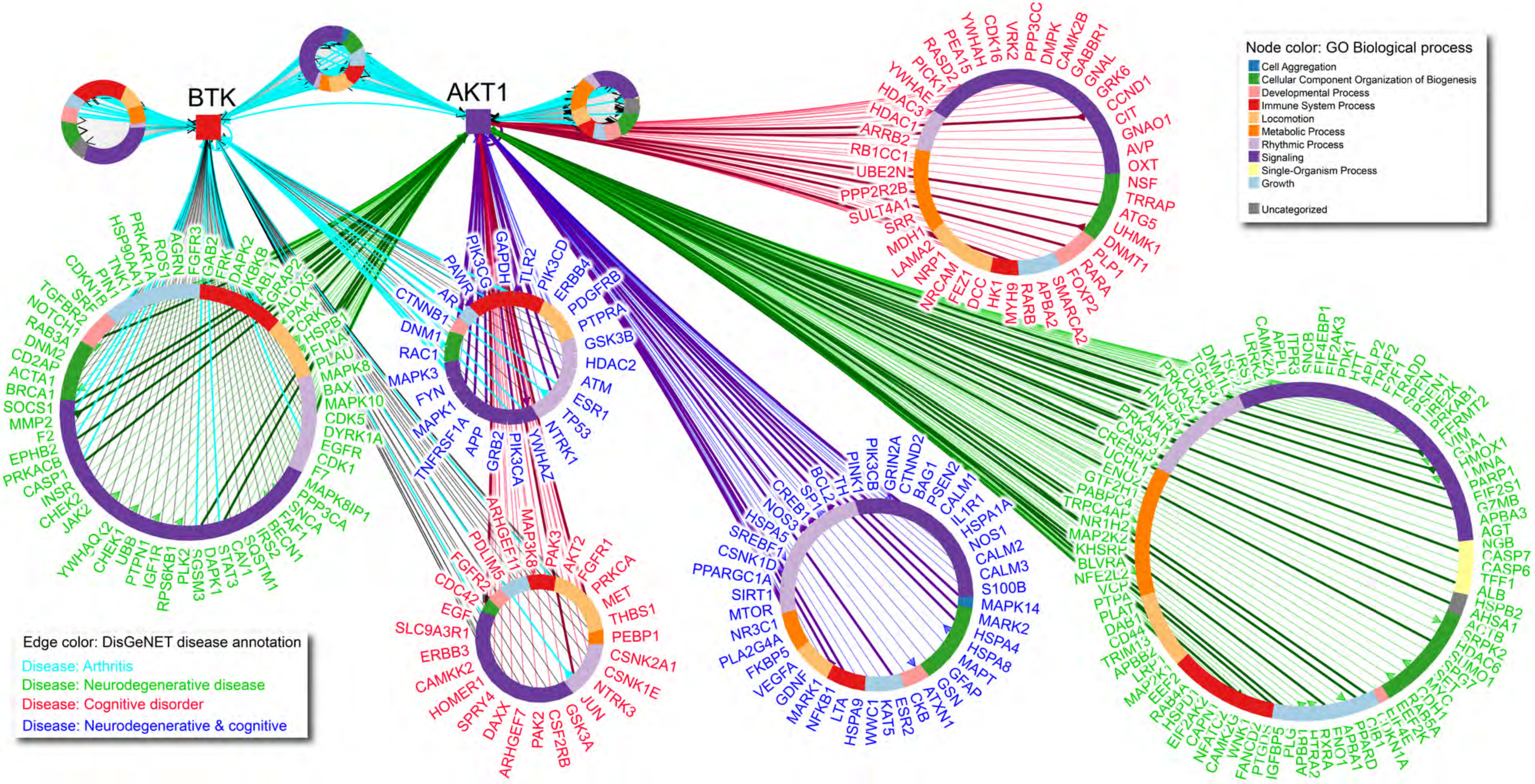
IBM WDD vs IID & NAViGaTOR





Literature vs
Literature + Data + Predictions

1,862 proteins connected by 2,324edges



Node color: GO Biological process
- 🟦 Cell Aggregation
- 🟩 Cellular Component Organization of Biogenesis
- 🟥 Developmental Process
- 🟥 Immune System Process
- 🟧 Locomotion
- 🟧 Metabolic Process
- 🟪 Rhythmic Process
- 🟪 Signaling
- 🟨 Single-Organism Process
- 🟦 Growth
- ⬛ Uncategorized

Edge color: DisGeNET disease annotation
- Disease: Arthritis
- Disease: Neurodegenerative disease
- Disease: Cognitive disorder
- Disease: Neurodegenerative & cognitive

Challenges in Data-Driven Medicine

- **Technical – ethical – legal**
- Heterogeneity – samples, assays, analysis
- **Biases** – data collection, confounding factors, ground truth, bad platforms
  - Unknowns – life style,(co-)treatments, missing data
  - **Fraud (75%)**, mistakes (<25%)
- **Statistical significance vs biological/clinical importance**
- AI/ML issues – transfer learning, drift of cohorts
  - performance on the cohort (accuracy) vs confidence in a single prediction
- Importance of **explanation & modeling**, not just classification

PNAS

Misconduct accounts for the majority of retracted scientific publications

Ferric C. Fang[a,b,1], R. Grant Steen[c,1], and Arturo Casadevall[d,1,2]

Departments of [a]Laboratory Medicine and [b]Microbiology, University of Washington School of Medicine, Seattle, WA 98195; [c]MediCC! Medical Communications Consultants, Chapel Hill, NC 27517; and [d]Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461

Edited by Thomas Shenk, Princeton University, Princeton, NJ, and approved September 6, 2012 (received for review July 18, 2012)

A detailed review of all 2,047 biomedical and life-science research articles indexed by PubMed as retracted on May 3, 2012 revealed

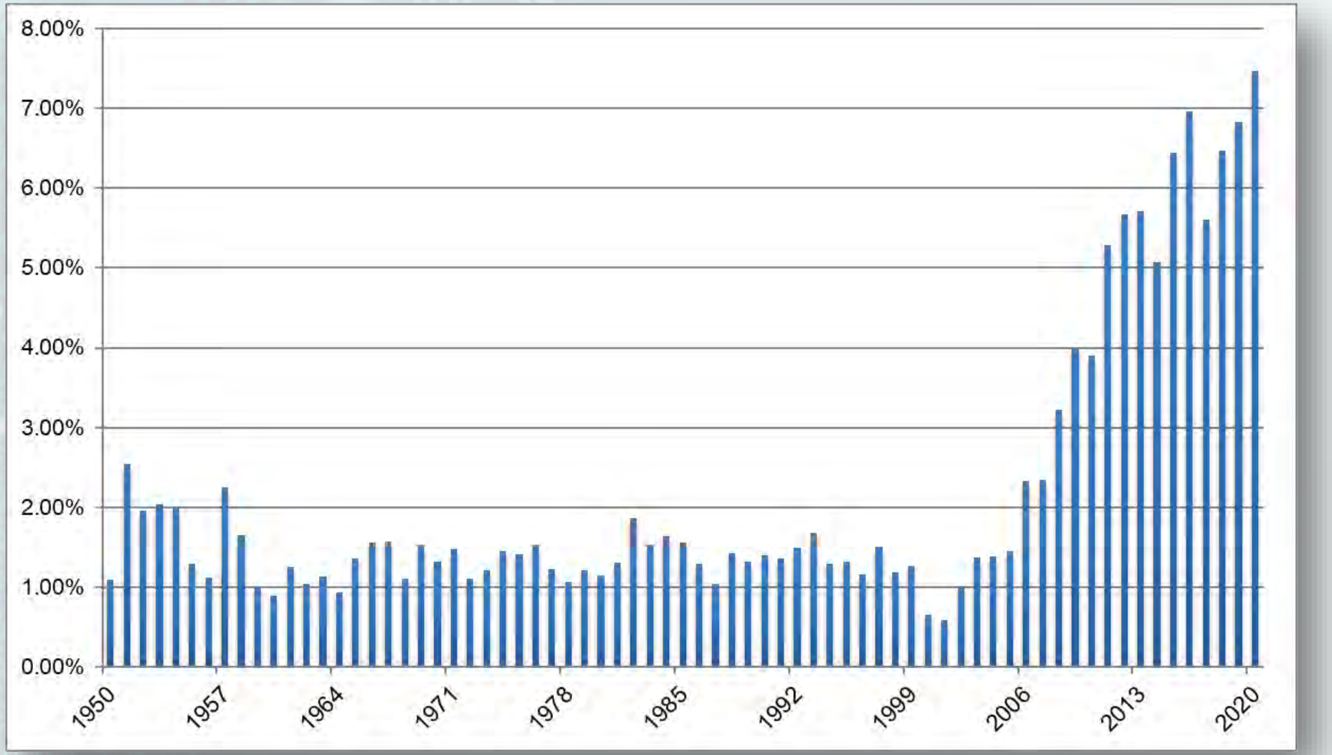
published by the authors of a manuscript in the *Journal of Cell Biology* stated that "In follow-up experiments . . . we have shown

AI: Algorithm – Data – System – Use

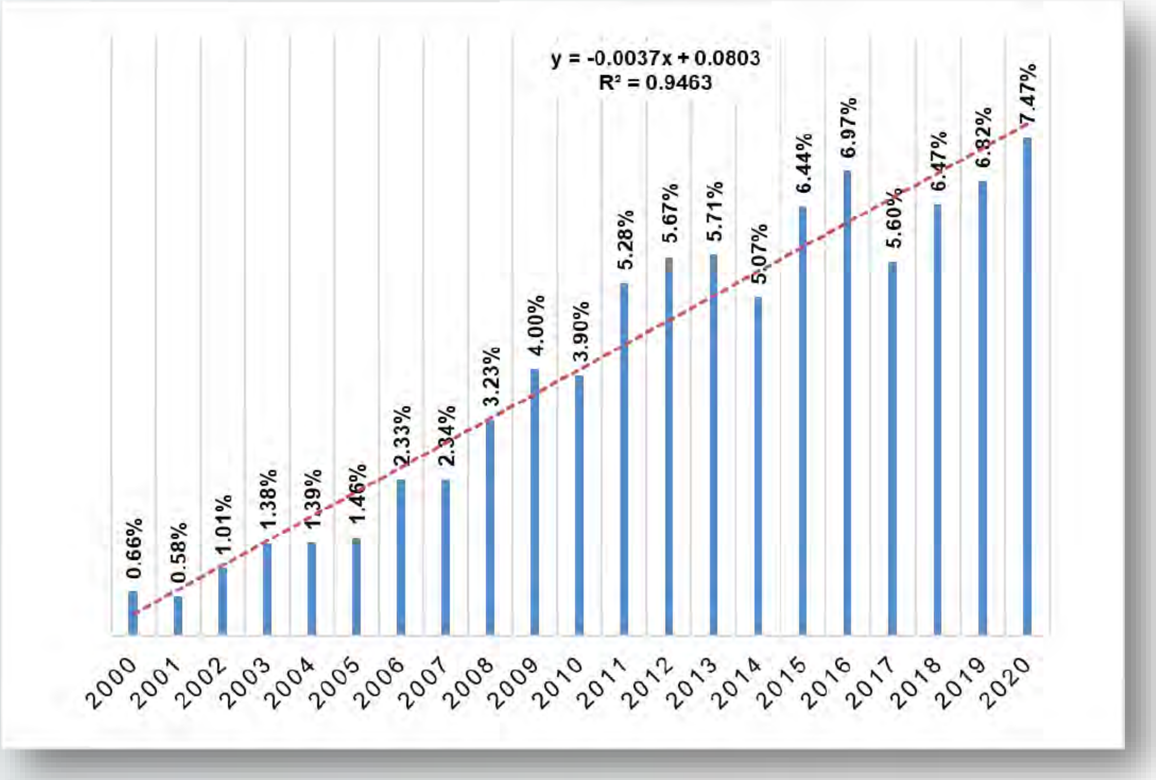
Data Quality


Medical-AI Systems and Applications:
Future Challenges and Research Directions

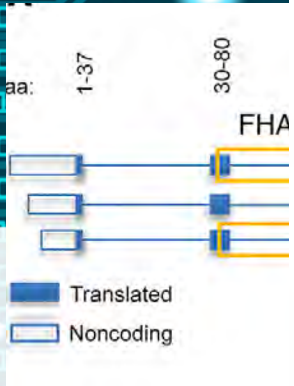
Andreas Holzinger[a,b,*], Matthias Dehmer[c,d],
Frank Emmert-Streib[e], Natalia Díaz-Rodríguez[j], Chris Biemann[1],
Igor Jurisica[f,g,h,i]

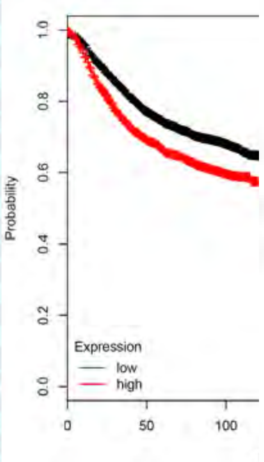


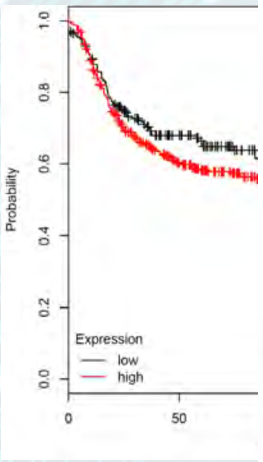
a)

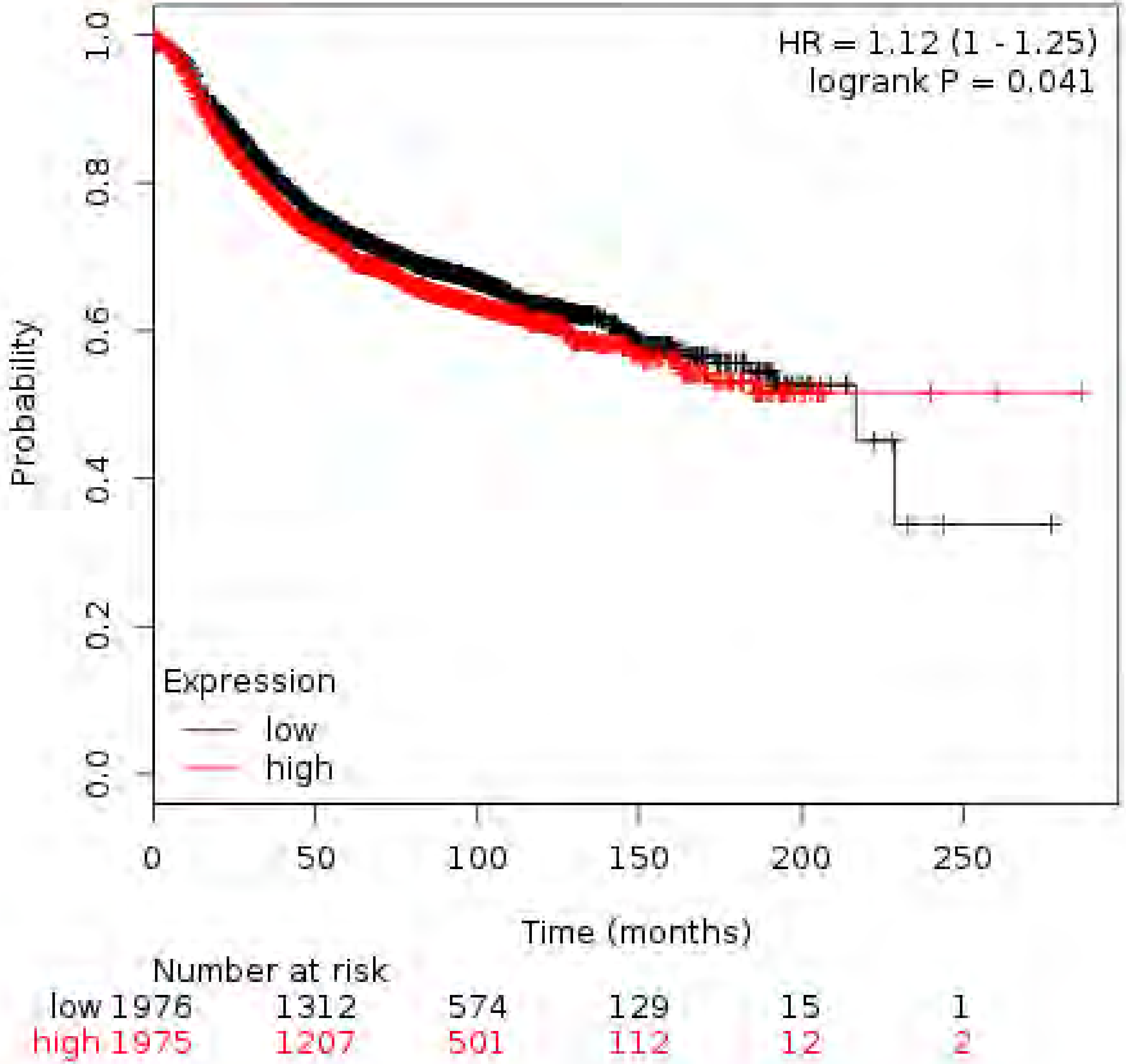


b)







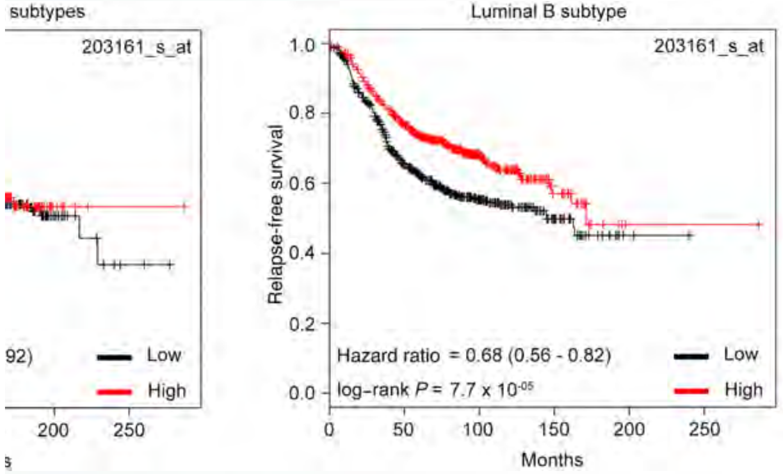


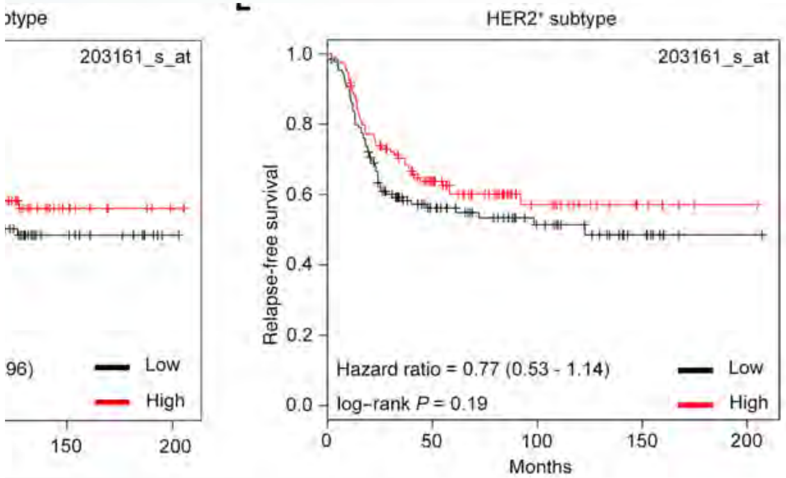
JCI The Journal of Clinical Investigation

Ubiquitin ligase RNF8 suppresses Notch signaling to regulate mammary development and tumorigenesis

Li Li, … , Anne Hakem, Razq Hakem

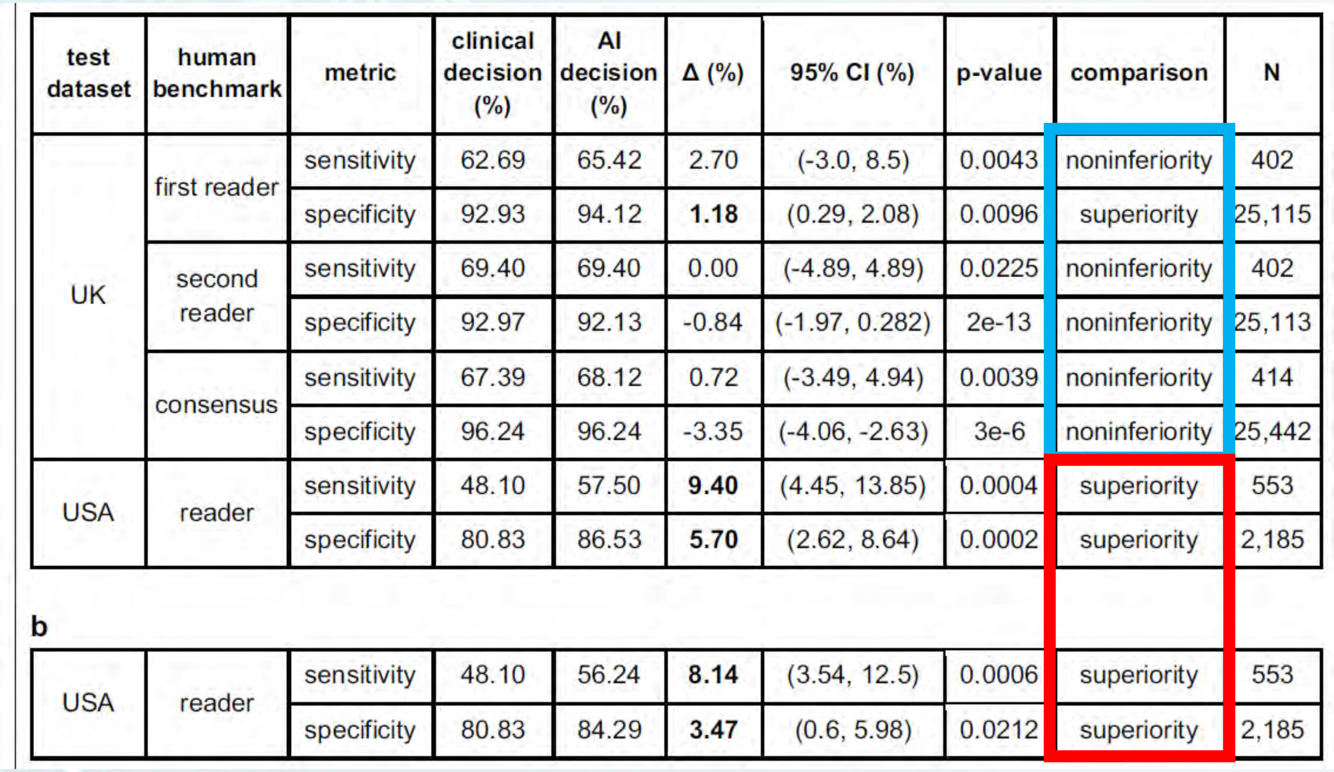
J Clin Invest. 2018. https://doi.org/10.1172/JCI120401.





AI & our Goals ?

- Expertise, process, standards!



test dataset	human benchmark	metric	clinical decision (%)	AI decision (%)	Δ (%)	95% CI (%)	p-value	comparison	N
UK	first reader	sensitivity	62.69	65.42	2.70	(-3.0, 8.5)	0.0043	noninferiority	402
		specificity	92.93	94.12	**1.18**	(0.29, 2.08)	0.0096	superiority	25,115
	second reader	sensitivity	69.40	69.40	0.00	(-4.89, 4.89)	0.0225	noninferiority	402
		specificity	92.97	92.13	-0.84	(-1.97, 0.282)	2e-13	noninferiority	25,113
	consensus	sensitivity	67.39	68.12	0.72	(-3.49, 4.94)	0.0039	noninferiority	414
		specificity	96.24	96.24	-3.35	(-4.06, -2.63)	3e-6	noninferiority	25,442
USA	reader	sensitivity	48.10	57.50	**9.40**	(4.45, 13.85)	0.0004	superiority	553
		specificity	80.83	86.53	**5.70**	(2.62, 8.64)	0.0002	superiority	2,185

b

USA	reader	sensitivity	48.10	56.24	**8.14**	(3.54, 12.5)	0.0006	superiority	553
		specificity	80.83	84.29	**3.47**	(0.6, 5.98)	0.0212	superiority	2,185

nature
International weekly journal of science

International evaluation of an AI system for breast cancer screening

https://doi.org/10.1038/s41586-019-1799-6

Received: 27 July 2019

Accepted: 5 November 2019

Published online: 1 January 2020

Scott Mayer McKinney[1,14*], Marcin Sieniek[1,14], Varun Godbole[1,14], Jonathan Godwin[2,14], Natasha Antropova[2], Hutan Ashrafian[3,4], Trevor Back[2], Mary Chesus[2], Greg C. Corrado[1], Ara Darzi[3,4,5], Mozziyar Etemadi[6], Florencia Garcia-Vicente[6], Fiona J. Gilbert[7], Mark Halling-Brown[8], Demis Hassabis[2], Sunny Jansen[9], Alan Karthikesalingam[10], Christopher J. Kelly[10], Dominic King[10], Joseph R. Ledsam[2], David Melnick[6], Hormuz Mostofi[1], Lily Peng[1], Joshua Jay Reicher[11], Bernardino Romera-Paredes[2], Richard Sidebottom[12,13], Mustafa Suleyman[2], Daniel Tse[1*], Kenneth C. Young[8], Jeffrey De Fauw[2,15] & Shravya Shetty[1,15*]

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Integrative Computational Biology


European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04382-9

ORIGINAL ARTICLE

Why imaging data alone is not enough: AI-based integration of imaging, omics, and clinical data

Andreas Holzinger[1] · Benjamin Haibe-Kains[2,3] · Igor Jurisica[3,4,5]

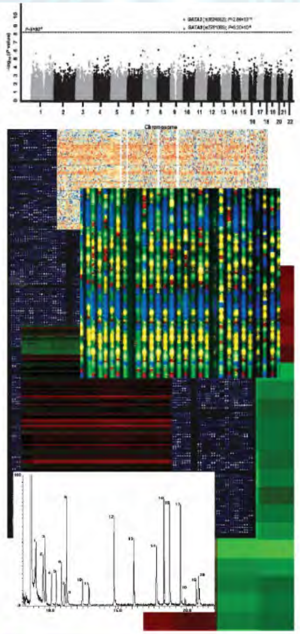
1 Biobank

2 HTP platforms

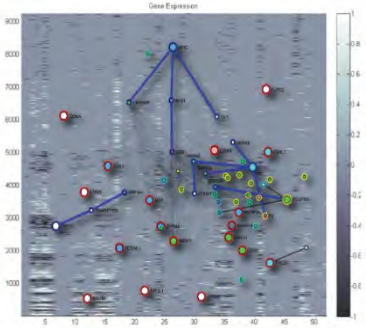
3 Data portals Integration, Analytics

4 Models

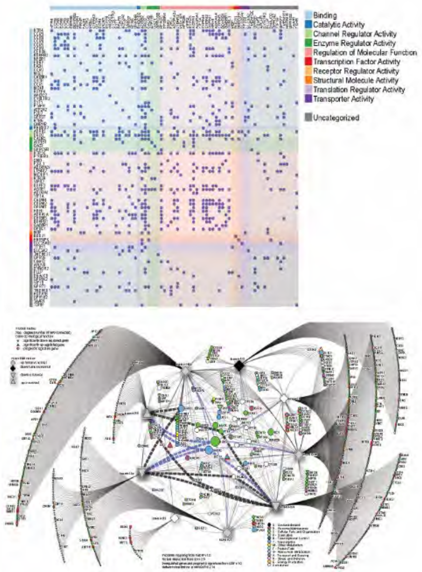
5 Precision treatments Improved outcomes



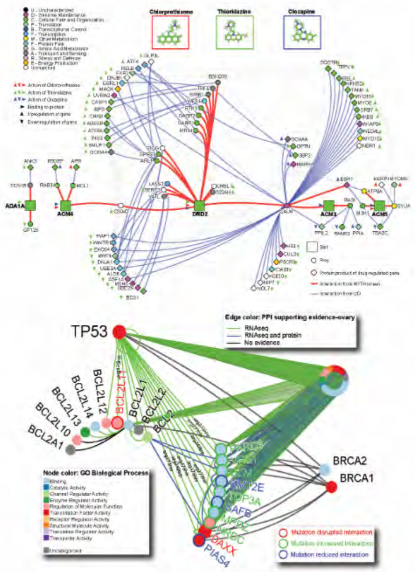
Omics profiles across genome, proteome, metabolome can be analyzed separately or combined to find differentially expressed entities



Network relationships link relevant entities within each data layer and identify better biomarkers

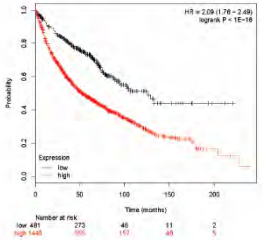


Layers of annotated networks; annotated with tissue, disease, network properties can further characterize potential biomarkers



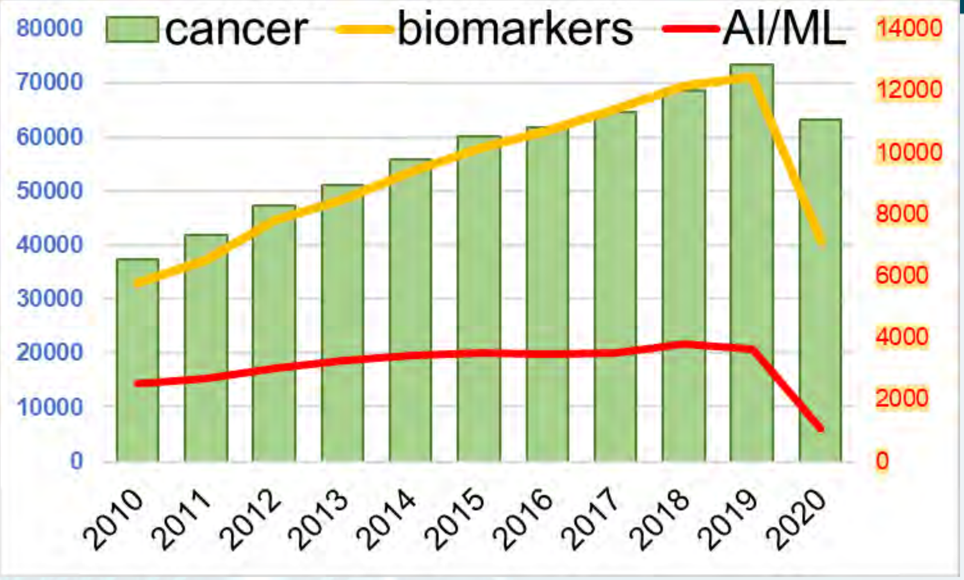
Discovered relationships across data layers identify combined biomarkers, drug mechanism of action and create explainable disease models

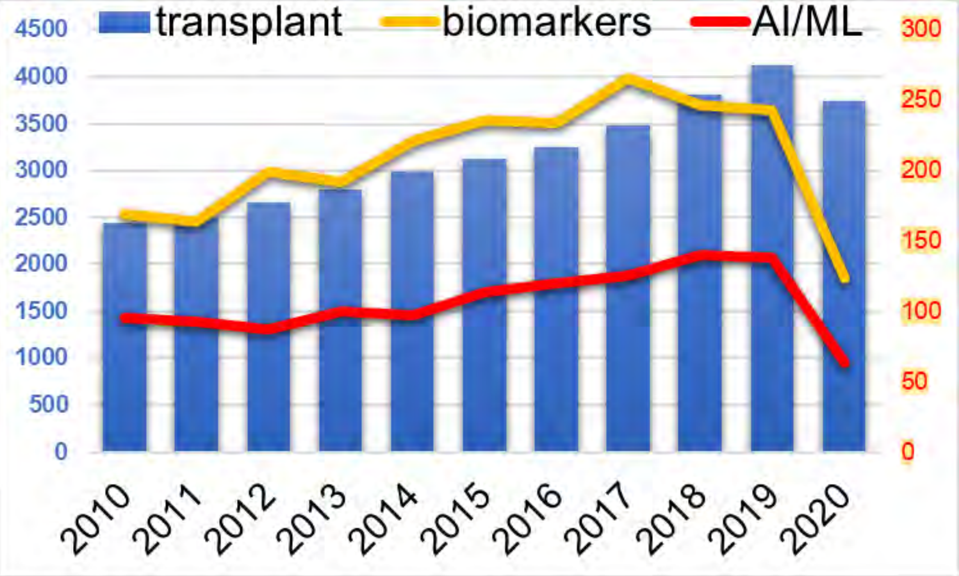
Combined biomarkers identify clinically-relevant patient subgroups

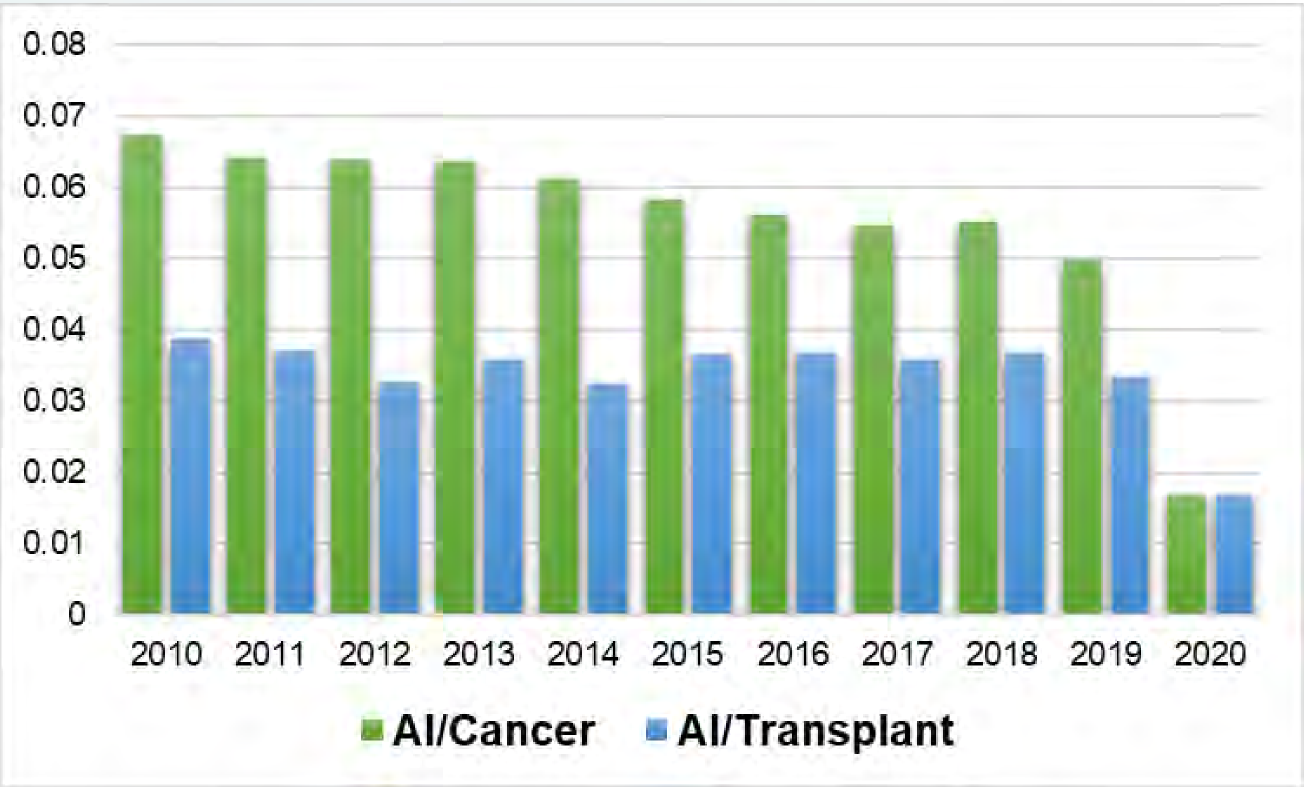


Treatment tailored to patient subgroups results in improved patient outcomes

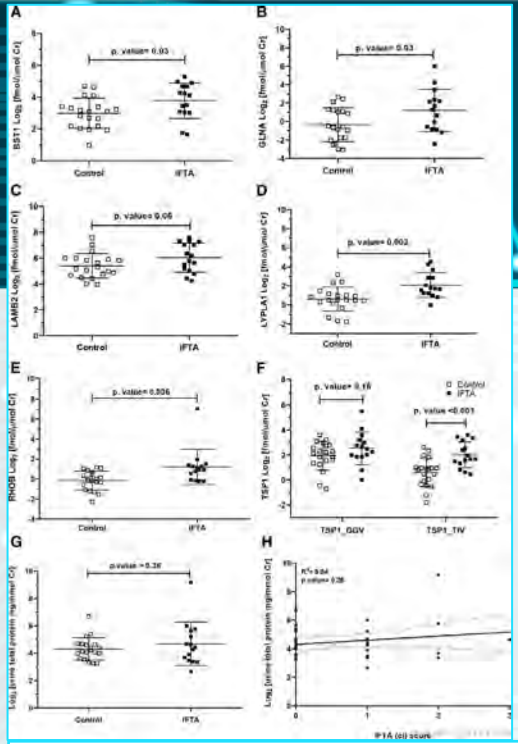
AI & Biomarkers in Precision Medicine





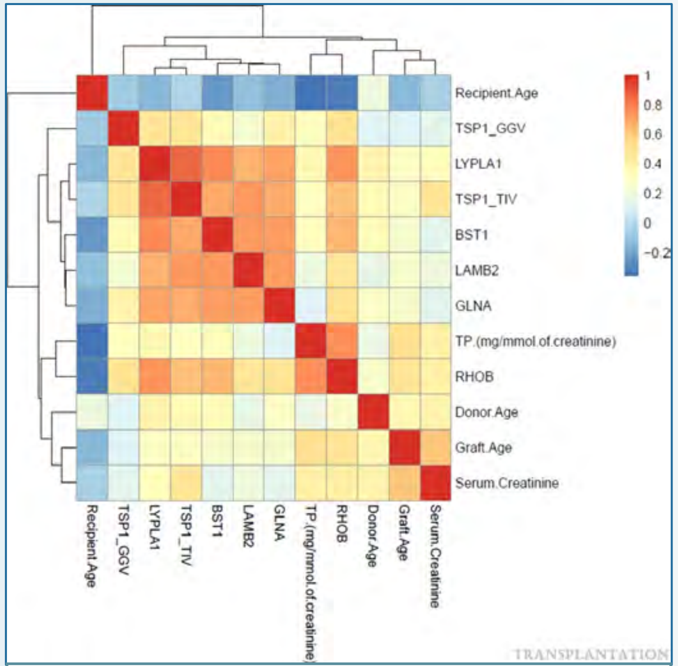


Predicting & Modeling Kidney Fibrosis

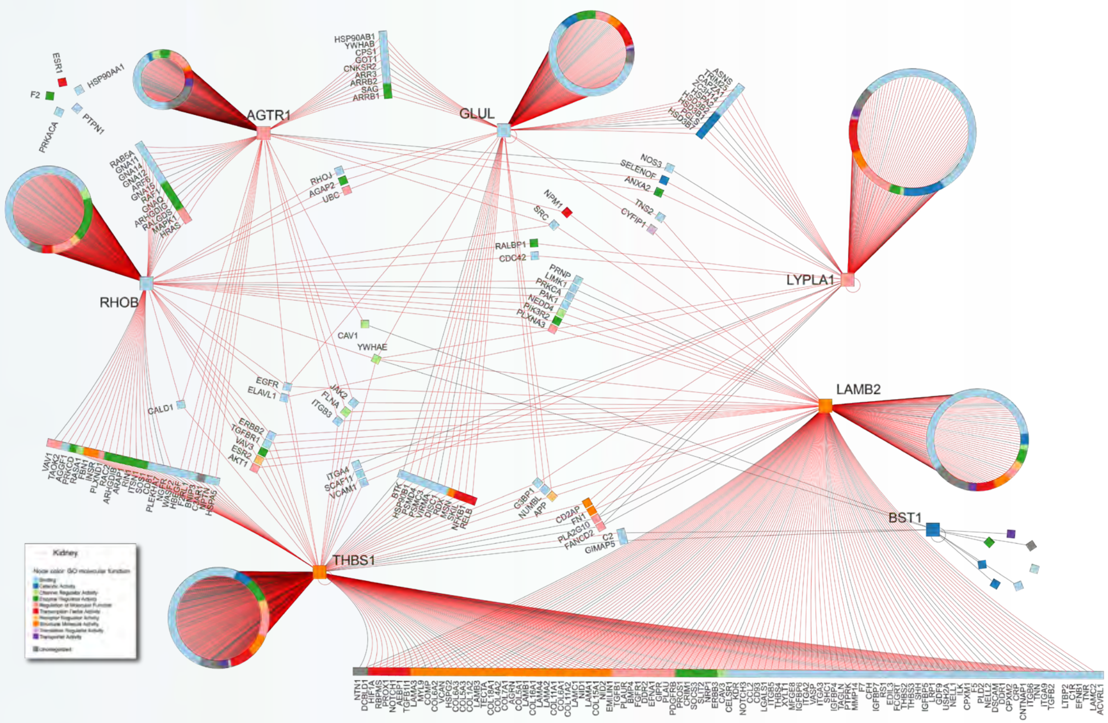


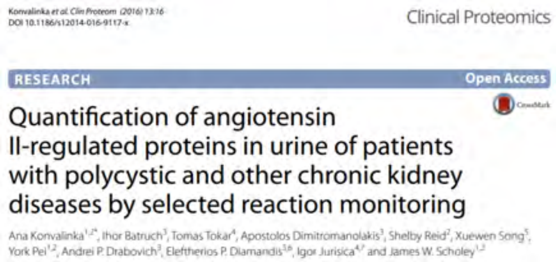
Urine excretion rates of AngII signature proteins is increased in patients with IFTA (interstitial fibrosis/tubular atrophy)

AngII, Angiotensin II
BST1, bone marrow stromal cell antigen 1
GLNA, glutamine synthetase
LAMB2, laminin subunit beta-2
LYPLA1, lysophospholipase I
RHOB, ras homolog family member B
TSP1, thrombospondin-I



Positive correlation among all urine excretion rates of AngII-regulated proteins




Konvalinka et al. Clin Proteom (2016) 13:16
DOI 10.1186/s12014-016-9117-x

Clinical Proteomics

RESEARCH Open Access

Quantification of angiotensin II-regulated proteins in urine of patients with polycystic and other chronic kidney diseases by selected reaction monitoring

Ana Konvalinka[1,2*], Ihor Batruch[3], Tomas Tokar[4], Apostolos Dimitromanolakis[3], Shelby Reid[2], Xuewen Song[5], York Pei[1,2], Andrei P. Drabovich[3], Eleftherios P. Diamandis[3,6], Igor Jurisica[4,7] and James W. Scholey[1,2]


Determination of an Angiotensin II-regulated Proteome in Primary Human Kidney Cells by Stable Isotope Labeling of Amino Acids in Cell Culture (SILAC)

Received for publication, May 14, 2013, and in revised form, June 21, 2013 Published, JBC Papers in Press, July 11, 2013, DOI 10.1074/jbc.M113.485326

Ana Konvalinka, Joyce Zhou, Apostolos Dimitromanolakis, Andrei P. Drabovich, Fei Fang, Susan Gurley, Thomas Coffman, Rohan John, Shao-Ling Zhang, Eleftherios P. Diamandis, and James W. Scholey

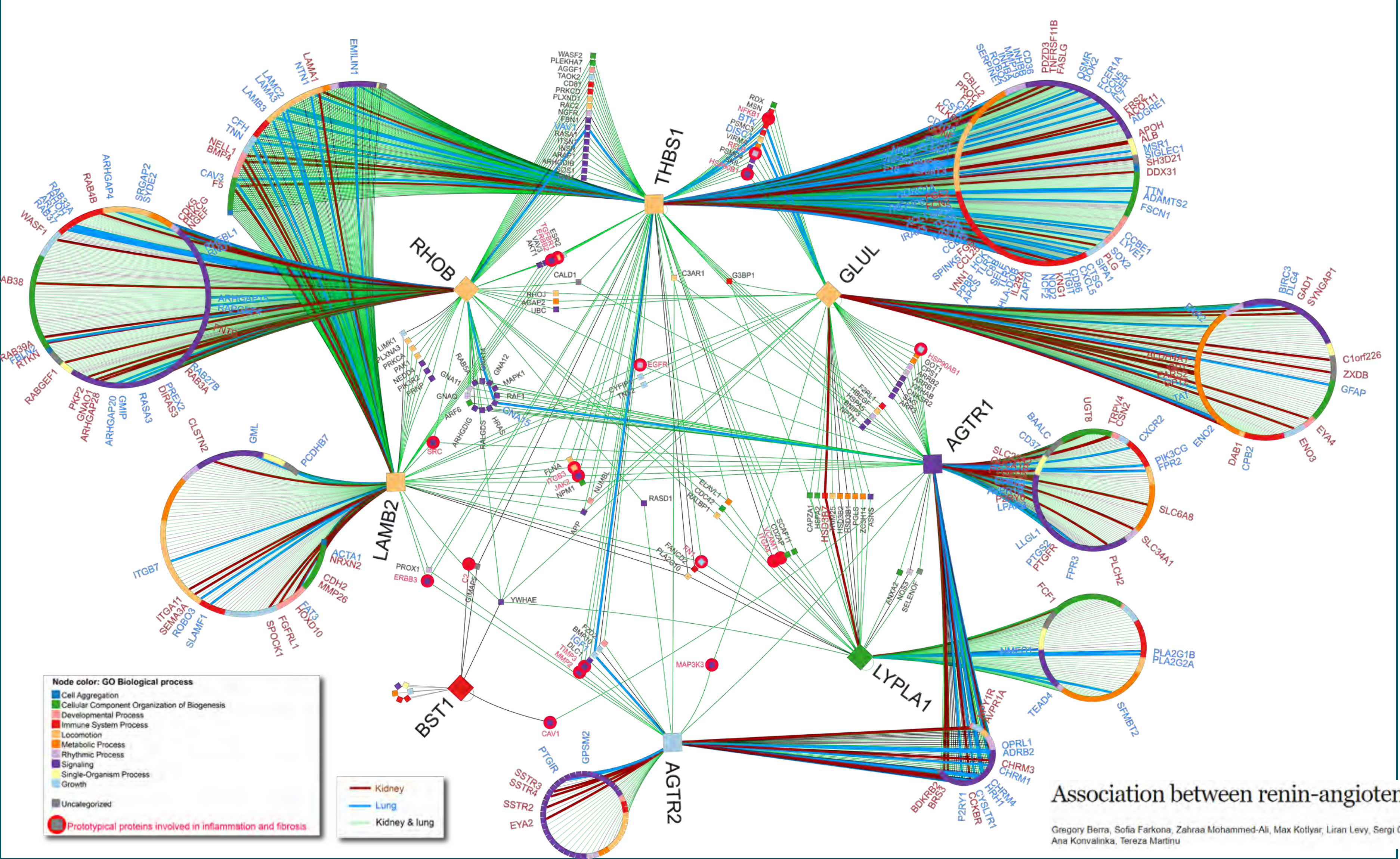
From the Institute of Medical Sciences, University of Toronto, Toronto, Ontario M5S 1A8, Canada, the Division of Nephrology, Department of Medicine, University Health Network, University of Toronto, Toronto, Ontario M5G 2C4, Canada, the Department of Pathology and Laboratory Medicine, University of Toronto, Toronto, Ontario M5G 2C4, Canada, the Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario M5G 1W7, Canada, the **Division of Nephrology, Department of Medicine, Duke University and Durham Veterans Affairs Medical Centers, Durham, North Carolina 27710, and the Faculty of Medicine, Hôtel-Dieu Hôpital, University of Montreal, Montreal, Quebec H2W 1T8, Canada

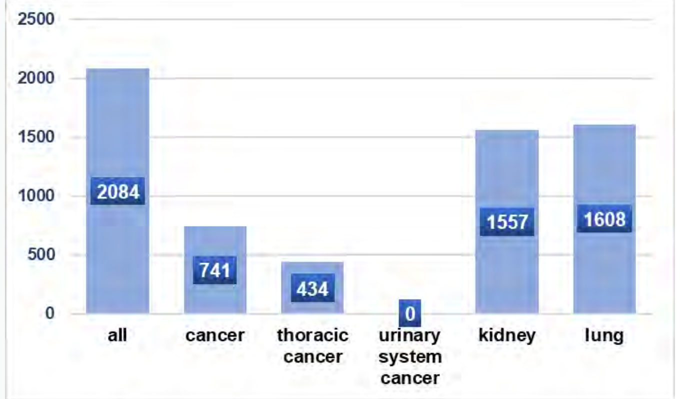

Original Basic Science—General

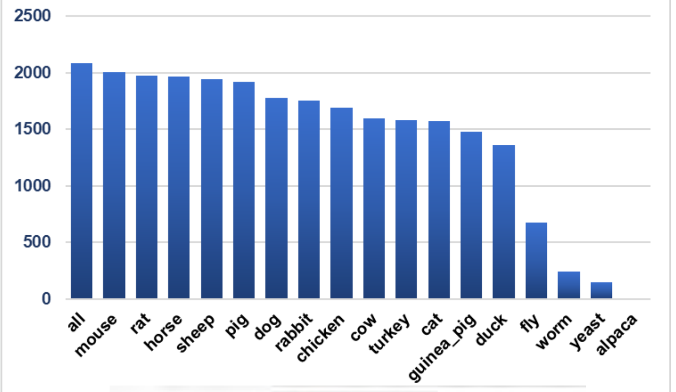
Urine Angiotensin II Signature Proteins as Markers of Fibrosis in Kidney Transplant Recipients

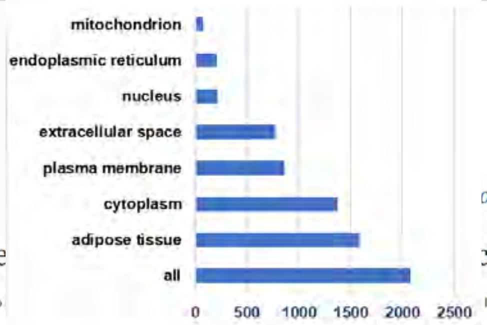
Zahraa Mohammed-Ali, PhD,[1] Tomas Tokar, PhD,[2] Ihor Batruch, MSc,[3] Shelby Reid, MSc,[4] Alexandre Tavares-Brum, BSc,[5] Paul Yip, PhD, FCACB,[1] Héloïse Cardinal, MD, PhD, FRCPC,[5] Marie-Josée Hébert, MD, PhD, FRCPC,[5] Yanhong Li, PhD,[1] S. Joseph Kim, MD, PhD, FRCPC,[1,6] Igor Jurisica, PhD,[2,7] Rohan John, MD,[8] and Ana Konvalinka, MD, PhD, FRCPC[1,6]

Translating from Kidney to Lung







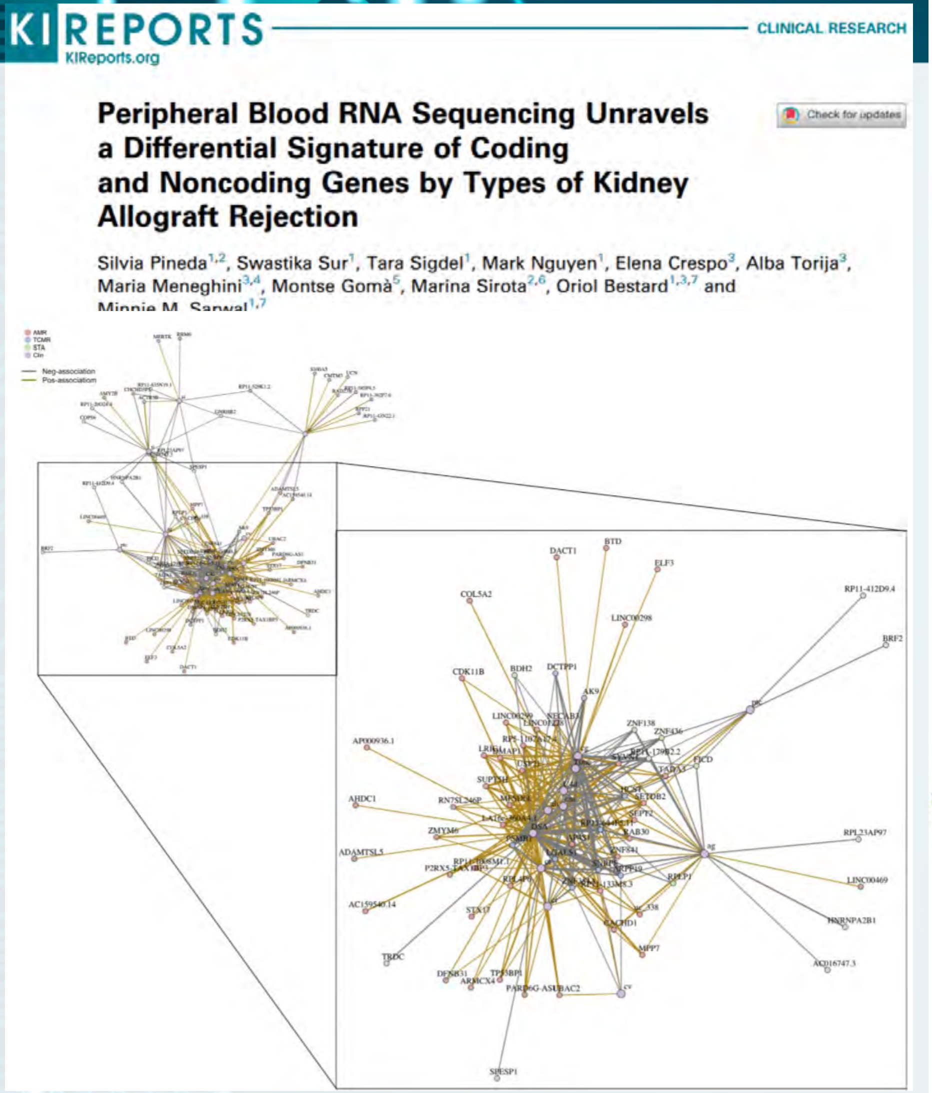


ournal

Association between renin-angiotensin syste ction

Gregory Berra, Sofia Farkona, Zahraa Mohammed-Ali, Max Kotlyar, Liran Levy, Sergi Clotet-Freixas, Phillip Igor Jurisica, Ana Konvalinka, Tereza Martinu

Linking to Other Studies



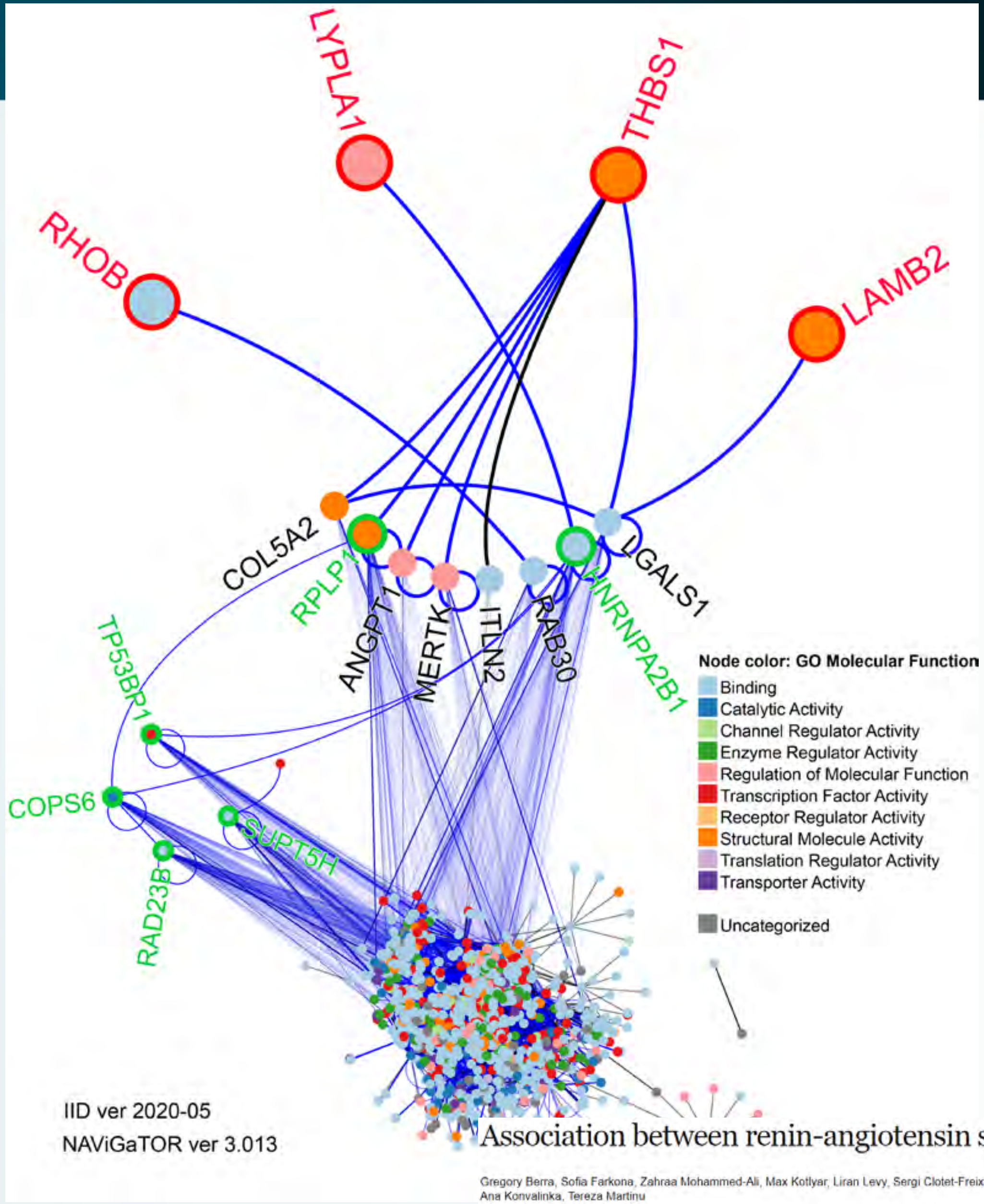
KI REPORTS
KIReports.org

CLINICAL RESEARCH

Check for updates

Peripheral Blood RNA Sequencing Unravels a Differential Signature of Coding and Noncoding Genes by Types of Kidney Allograft Rejection

Silvia Pineda[1,2], Swastika Sur[1], Tara Sigdel[1], Mark Nguyen[1], Elena Crespo[3], Alba Torija[3], Maria Meneghini[3,4], Montse Gomà[5], Marina Sirota[2,6], Oriol Bestard[1,3,7] and Minnie M. Sarwal[1,7]



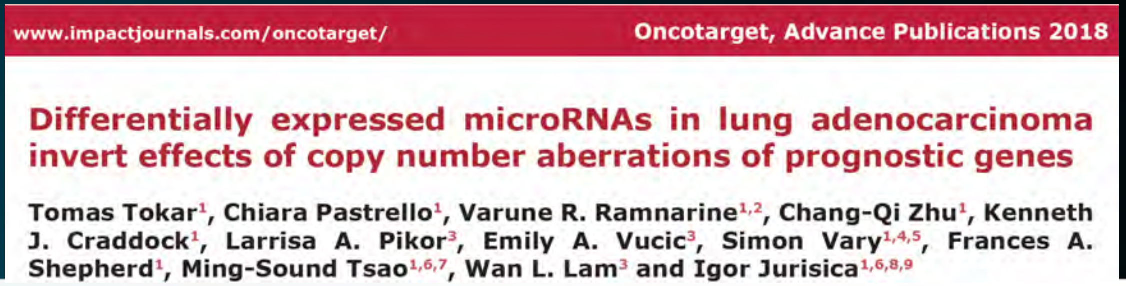
EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Association between renin-angiotensin system and chronic lung allograft dysfunction

Gregory Berra, Sofia Farkona, Zahraa Mohammed-Ali, Max Kotlyar, Liran Levy, Sergi Clotet-Freixas, Phillip Ly, Benjamin Renaud-Picard, Guan Zehong, Tina Daigneault, Allen Duong, Ihor Batruch, Igor Jurisica, Ana Konvalinka, Tereza Martinu

Paradoxes

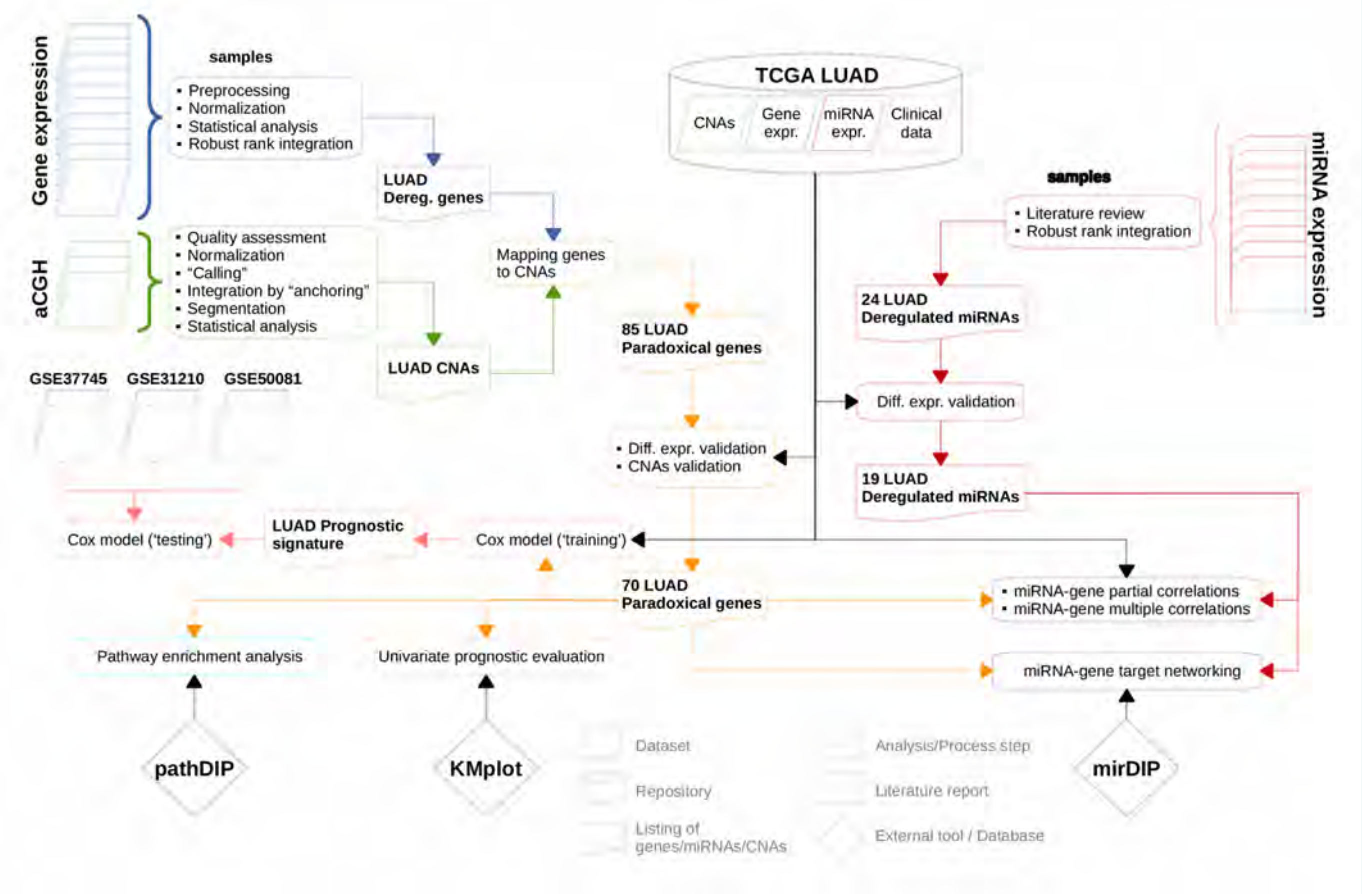
1,062 LUAD RNA samples
241 normal lung samples
63 LUAD aCGH samples
→ 85 paradoxical genes

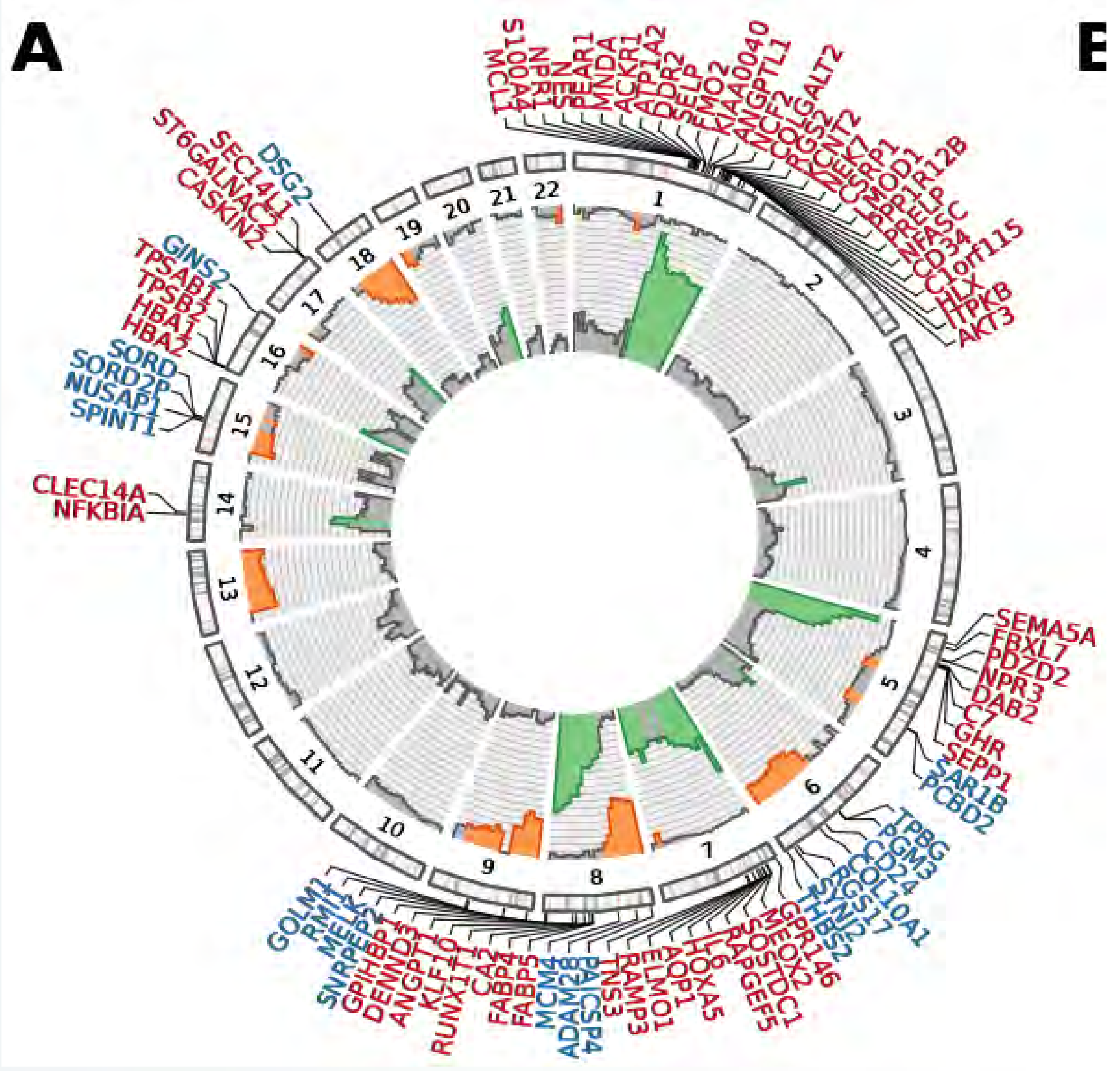


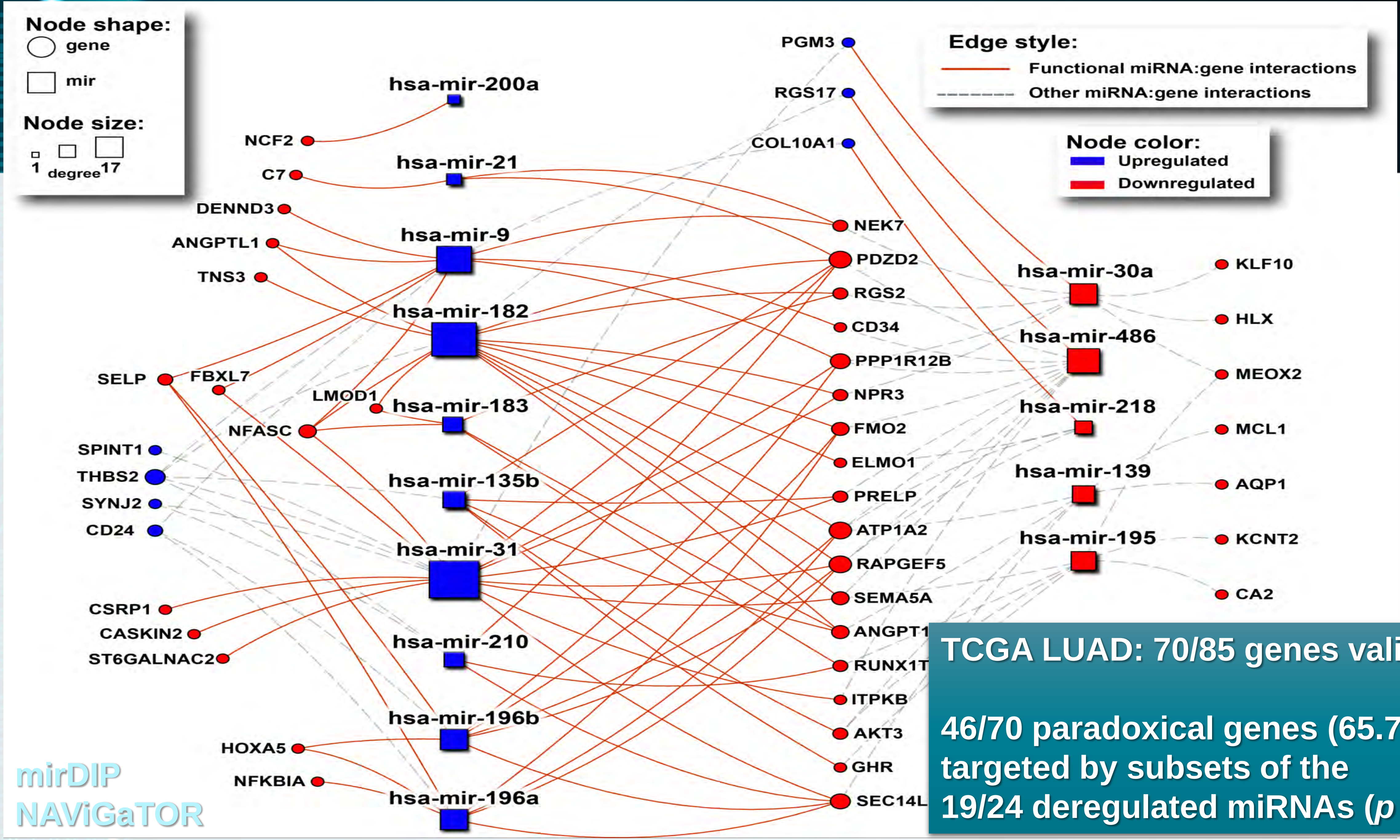
www.impactjournals.com/oncotarget/ Oncotarget, Advance Publications 2018

Differentially expressed microRNAs in lung adenocarcinoma invert effects of copy number aberrations of prognostic genes

Tomas Tokar[1], Chiara Pastrello[1], Varune R. Ramnarine[1,2], Chang-Qi Zhu[1], Kenneth J. Craddock[1], Larrisa A. Pikor[3], Emily A. Vucic[3], Simon Vary[1,4,5], Frances A. Shepherd[1], Ming-Sound Tsao[1,6,7], Wan L. Lam[3] and Igor Jurisica[1,6,8,9]







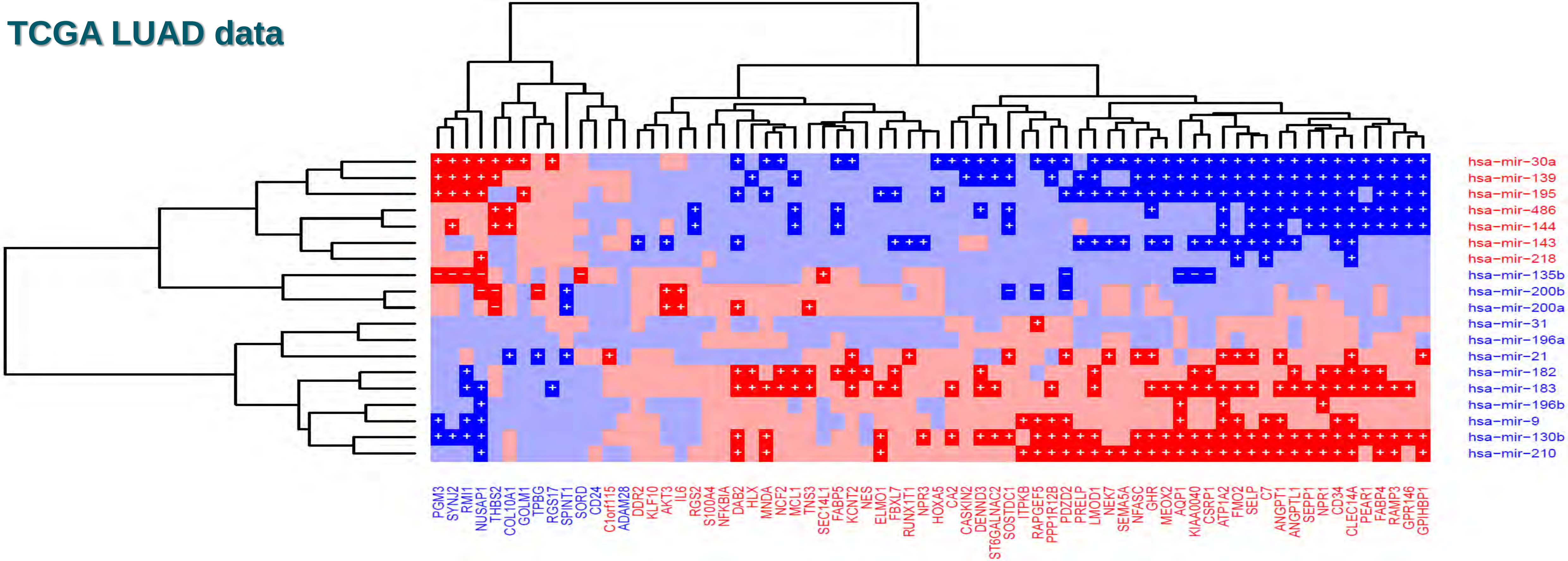
mirDIP
NAViGaTOR

TCGA LUAD: 70/85 genes validated

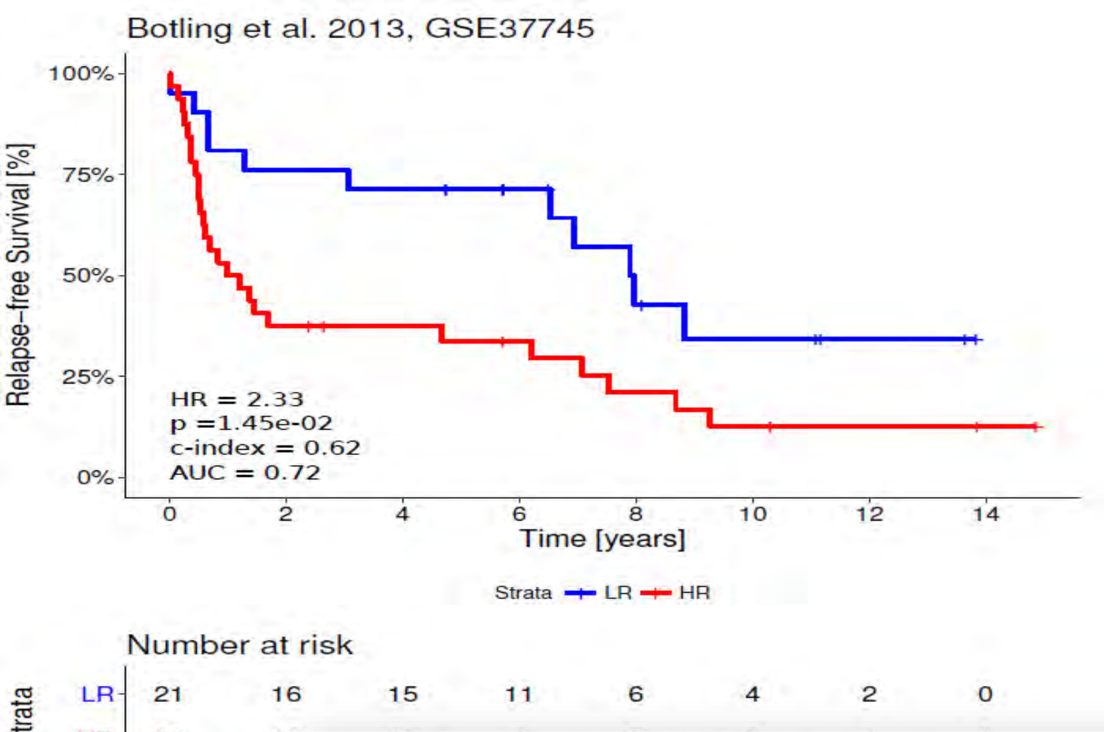
46/70 paradoxical genes (65.7%) are targeted by subsets of the 19/24 deregulated miRNAs ($p = 4.8E-3$)
]

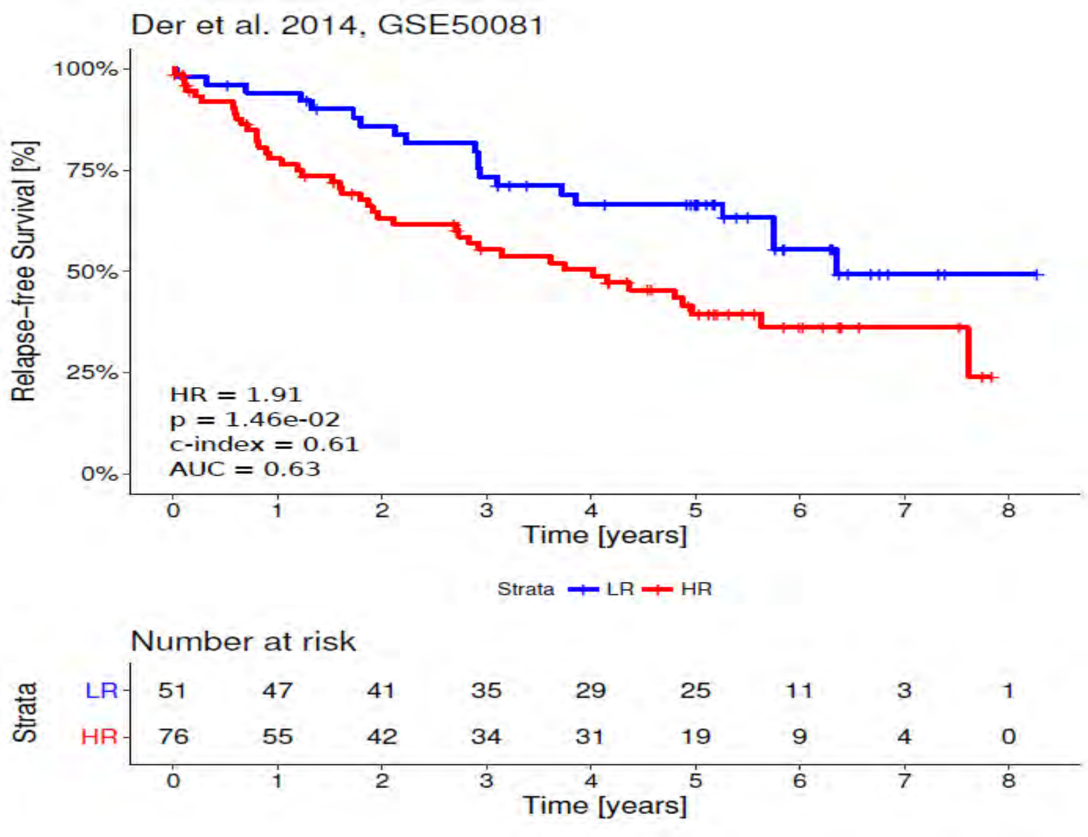
darker shade	significant correlations, $p < 0.05$
+	causal explanation
-	significant correlation, non-causal

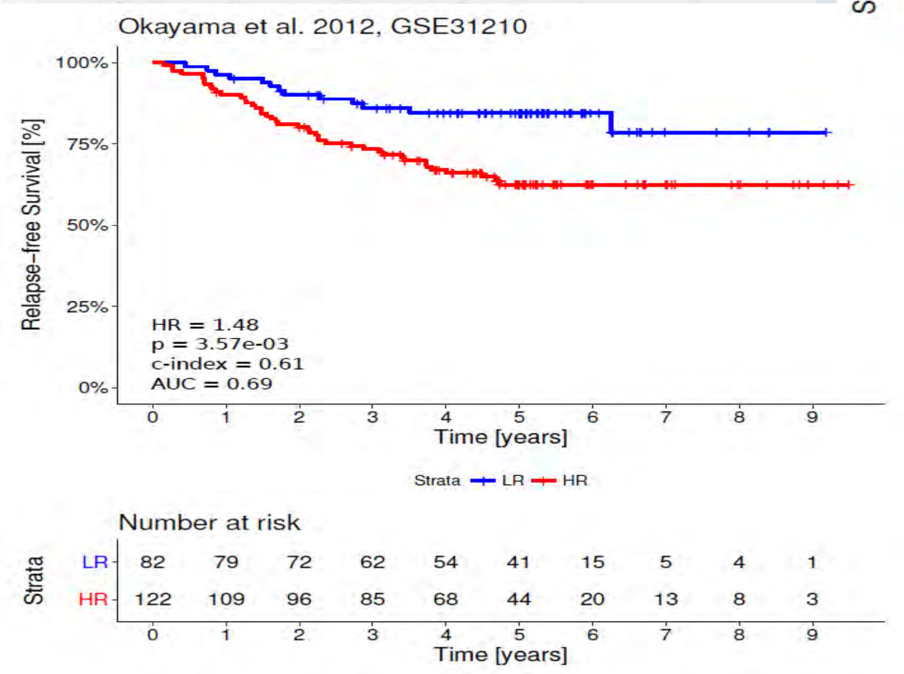
TCGA LUAD data



369 co-expressed miRNA:gene pairs (27% of all miRNA:gene combinations),
362 (98.1%) of which are explanatory



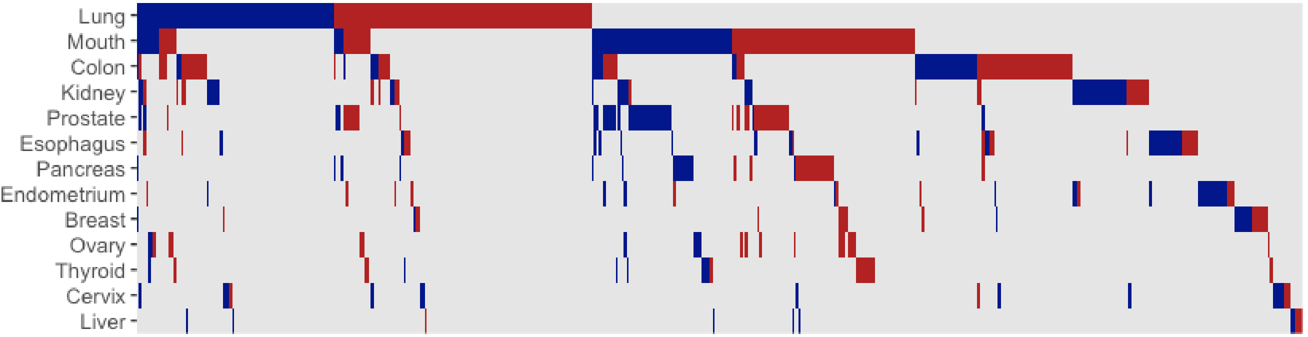




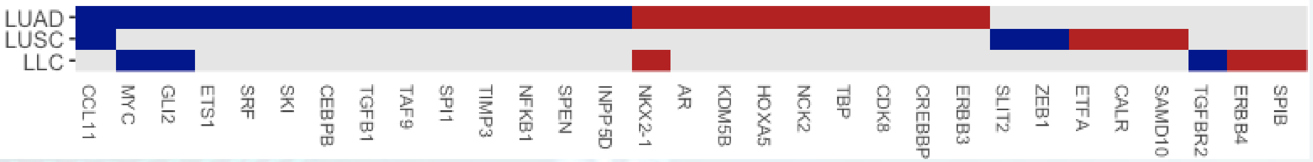
41/70 genes (**58.6%**) significantly associated with survival (*FDR < 0.05*)

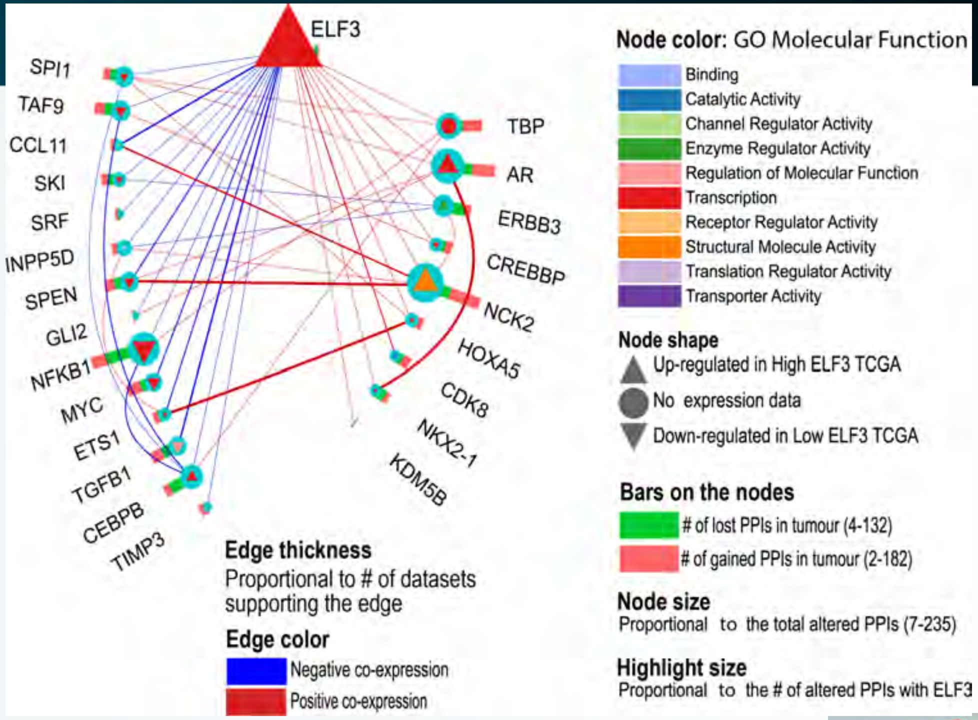
Tissue-Specific Network Remodeling

Pan-tissue analysis of ELF3 PPI networks disrupted in cancer



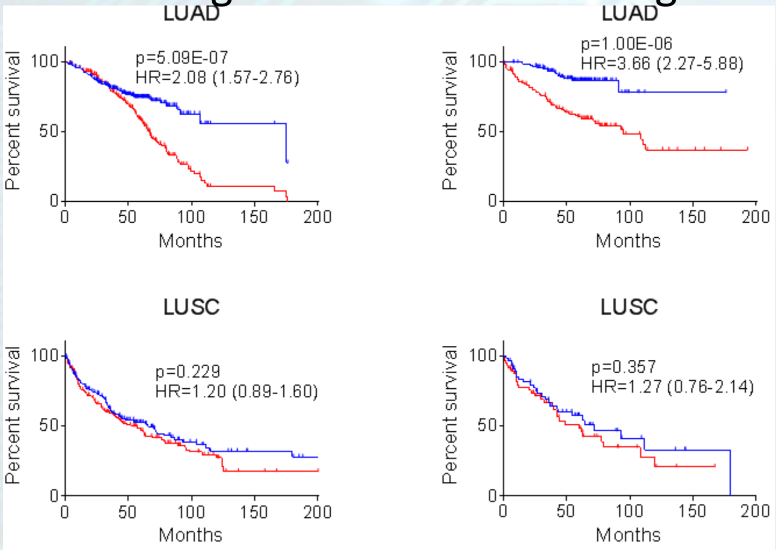
Analysis of ELF3 PPI networks disrupted in non-small cell lung cancer subtypes

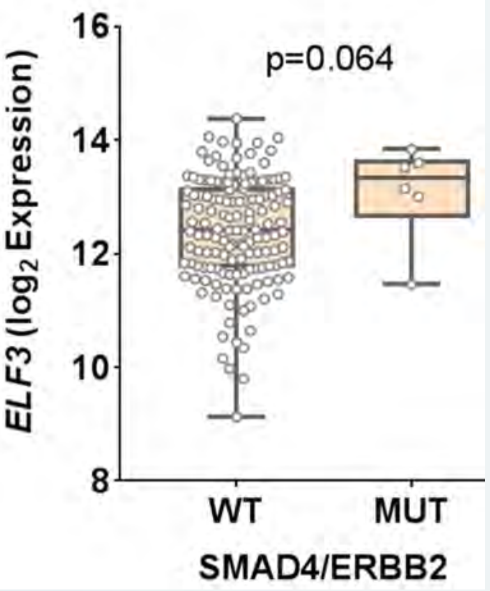




All stages

Stage I





Epithelial Tumour Suppressor ELF3 is a Lineage-Specific Amplified Oncogene in Lung Adenocarcinoma

Katey SS Enfield[1], Erin A Marshall[1], Christine Anderson[1], Kevin W Ng[1], Sara Rahmati[2], Zhaolin Xu[3], Megan Fuller[1], Katy Milne[4], Daniel Lu[1], Rocky Shi[1], David A Rowbotham[1], Daiana D Becker-Santos[1], Fraser Johnson[1], John C English[5], Calum E MacAulay[1], Stephen Lam[1], William W Lockwood[1], Raj Chari[6], Aly Karsan[1], Igor Jurisica[2], Wan L Lam[1]

Integrating Networks

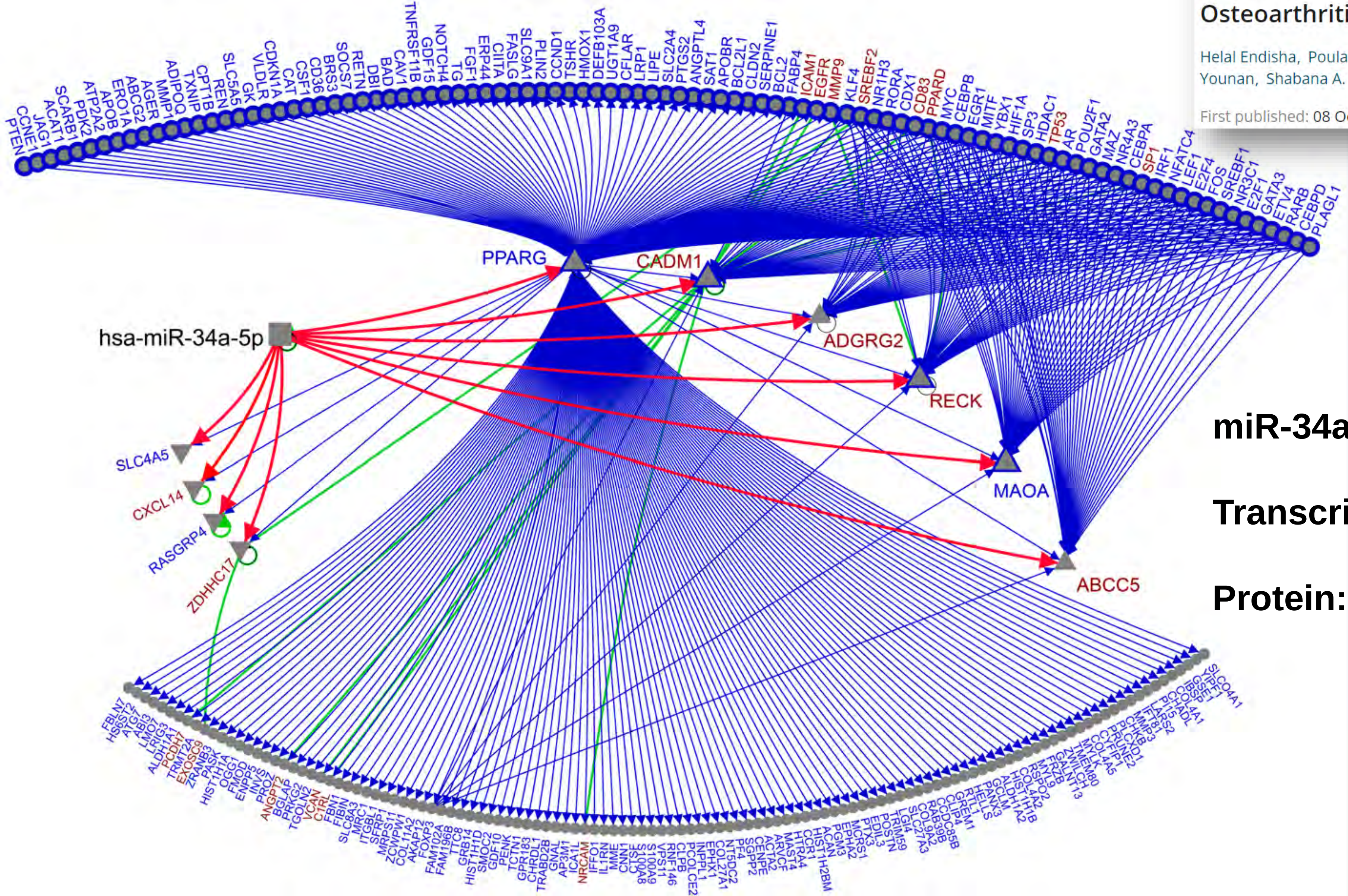
Arthritis & Rheumatology
AN OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF RHEUMATOLOGY
American College of Rheumatology
Empowering Rheumatology Professionals

FULL LENGTH | Open Access

MicroRNA-34a-5p Promotes Joint Destruction during Osteoarthritis

Helal Endisha, Poulami Datta, Anirudh Sharma, Sayaka Nakamura, Evgeny Rossomacha, Carolen Younan, Shabana A. Ali, Ghazaleh Tavallaee, Starlee Lively, Pratibha Potla ... See all authors

First published: 08 October 2020 | https://doi.org/10.1002/art.41552

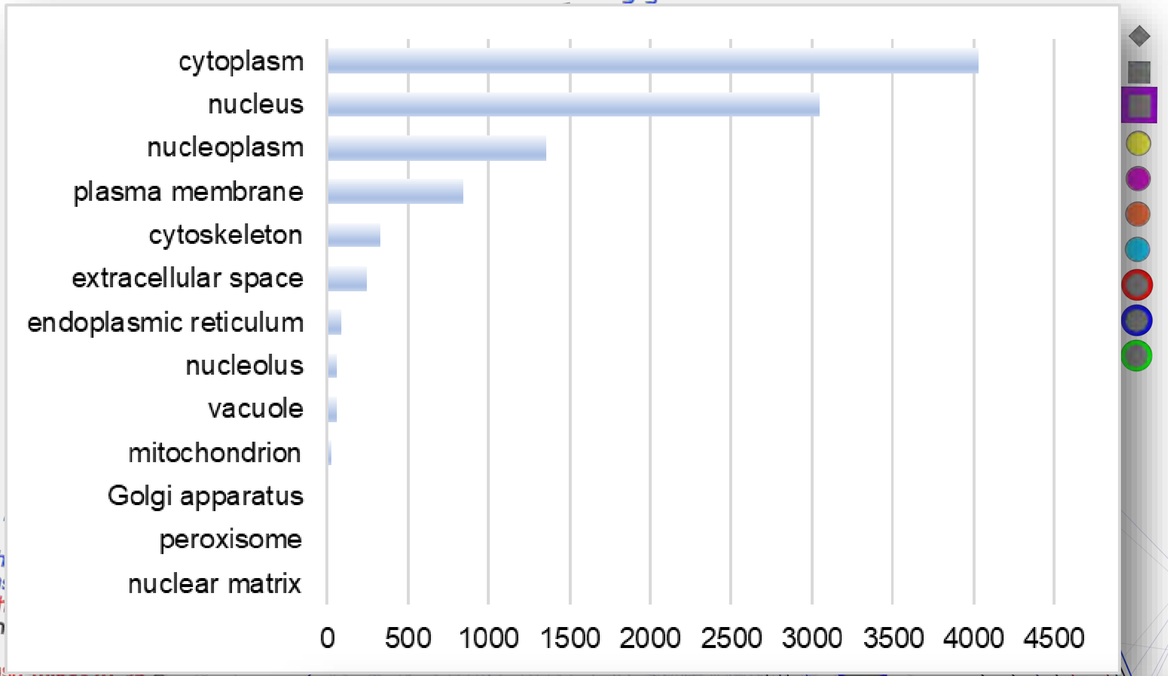


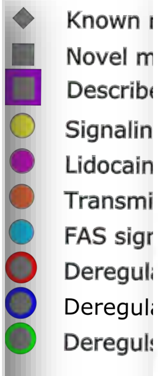
miR-34a-5p:target interactions

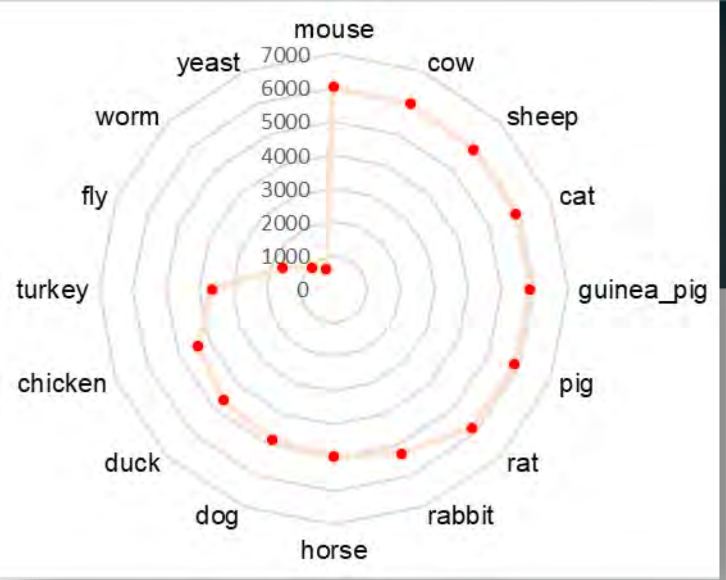
Transcription factor:target interactions

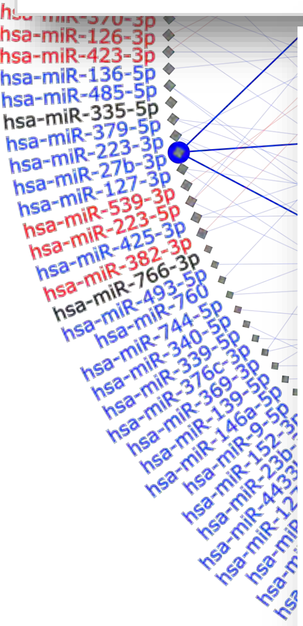
Protein:protein interactions

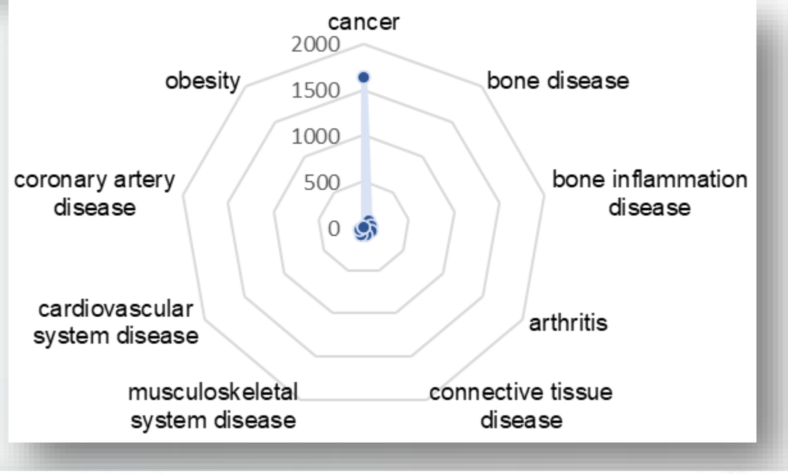
multiple












Osteoarthritis and Cartilage

Sequencing identifies a distinct signature of circulating microRNAs in early radiographic knee osteoarthritis

S.A. Ali [† ‡], R. Gandhi [† §], P. Potla [†], S. Keshavarzi [†], O. Espin-Garcia [†], K. Shestopaloff [†], C. Pastrello [†], D. Bethune-Waddell [†], S. Lively [†], A.V. Perruccio [† § ||], Y.R. Rampersaud [† §], C. Veillette [† §], J.S. Rockel [†], I. Jurisica [† ††], C.T. Appleton [¶], M. Kapoor [† § # *]

Data Integration Portal

lung, ovarian, prostate, sarcoma, head&neck, liver,

OA, RA, NDD, fibrosis, kidney

	#Datasets	#Samples	#UPgenes Top1%	#DOWNgenesTop1%	#Genes
OA	87	11,609	130	183	13,193
Lung CA	30	6,270	51	625	16,658
Ovarian CA	87	839	123	115	9,942
Prostate CA	125	850	109	167	12,472
HN CA	291	1,437	90	78	9,110
Sarcoma	224	6,032	201	126	14,637
Liver CA	85	3,899	51	340	12,355

Results: 11

1

source : dc
sample : NCI_Lung_80_U133A
adjuvant_chemo : Yes
adjuvant_rt : Yes
age : 81
alt_sample_id : 226787
cause_of_death : null
data_subset_id1 : MI
data_subset_id2 : Train
dc_study_id : A80
dfs : null
differentiation : null
disease_specific_survival : null
dof : null
dor : null
dos : null
dss_status : null
egfr : null
histology : ADC
ihc_per : null

ihc_tumor_per : null
in_dc_study : 1
kras : null
laboratory_batch : 18
median_intensity_unnormalized : 192
n : null
n_stage : N1, ACCORDING TO AJCC CRITERIA
os : null
p_call_pct : 71
p53_mutation : null
patient_id : 79
pct_array_outlier : 2.643
pct_single_outlier : 0.703
race : Not Reported(98)
rand : null
ras : null
recu : No
sample_prep : snap frozen
sample_source : tumour

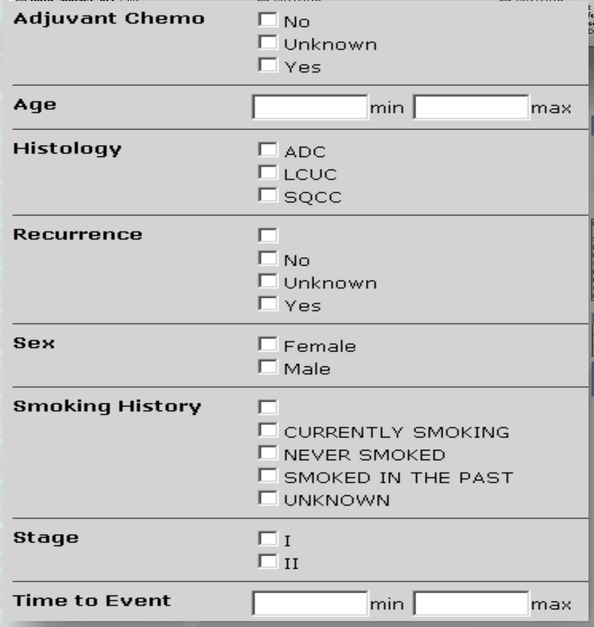
sex : Female
smoking_history : NEVER SMOKED
stage : null
study_id : A80
surgical_margins : ALL MARGINS PATHOLOGICALLY NEGATIVE
t_stage : T2, ACCORDING TO AJCC CRITERIA
time_to_event : 32.9
time_to_last_followup : 32.9
time_to_relapse :
vital_status : Alive
warning :

2

source : dc
sample : NCI_Lung_82_U133A
adjuvant_chemo : Yes
adjuvant_rt : Yes
age : 76
alt_sample_id : 222148
cause_of_death : null

ihc_tumor_per : null
in_dc_study : 1
kras : null
laboratory_batch : 18
median_intensity_unnormalized : 192
n : null
n_stage : N0, ACCORDING TO AJCC CRITERIA

sex : Female
smoking_history : NEVER SMOKED
stage : null
study_id : A82
surgical_margins : ALL MARGINS PATHOLOGICALLY NEGATIVE
t_stage : T1, ACCORDING TO AJCC CRITERIA



Adjuvant Chemo
☐ No
☐ Unknown
☐ Yes

Age min max

Histology
☐ ADC
☐ LCUC
☐ SQCC

Recurrence
☐
☐ No
☐ Unknown
☐ Yes

Sex
☐ Female
☐ Male

Smoking History
☐
☐ CURRENTLY SMOKING
☐ NEVER SMOKED
☐ SMOKED IN THE PAST
☐ UNKNOWN

Stage
☐ I
☐ II

Time to Event min max

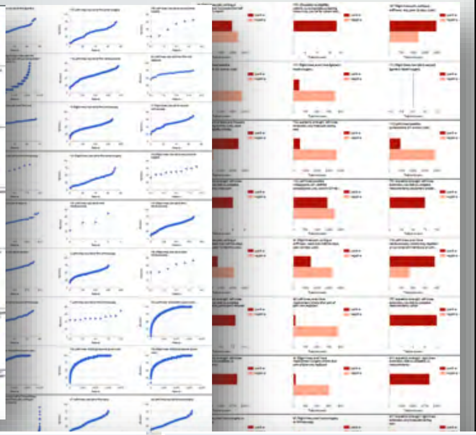
● Display (Clinical Info Only)

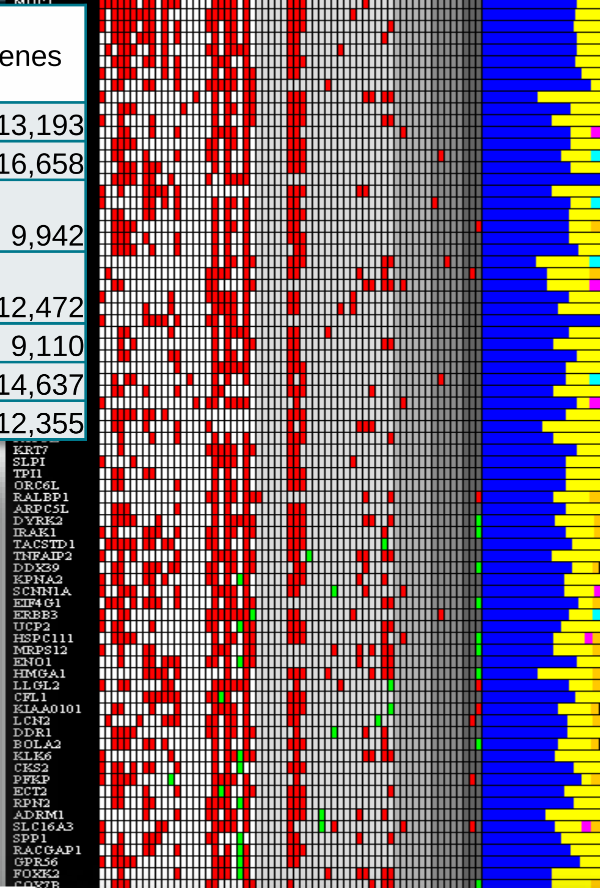
○ Download to file (Clinical Info + Gene Expression

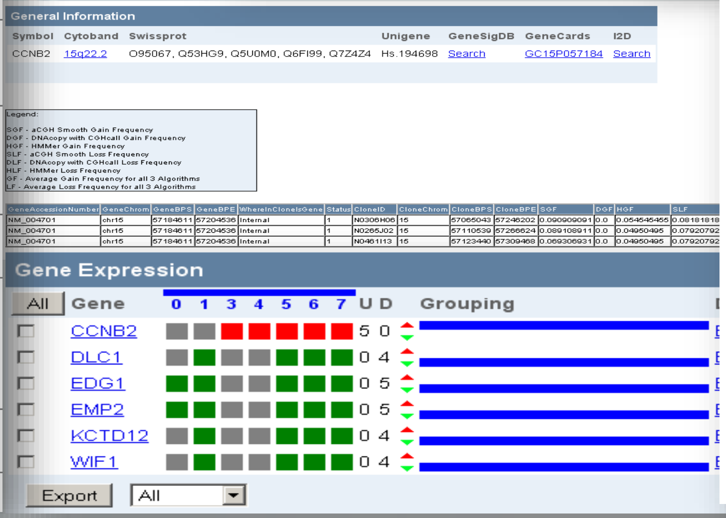
Gene Expression Search may take several minutes to complete

○ Download to GeneE file

[+] Dataset Info
[+] Demographic
[+] Joint
[+] Sample Type
[+] Time Line
[+] Diagnosis
[+] Biophysical
[+] Health Assessment Scores
[+] IDs
[+] Expression







General Information

Symbol	Cytoband	Swissprot	Unigene	GeneSigDB	GeneCards	I2D
CCNB2	15q22.2	O95067, Q53HG9, Q5U0M0, Q6FI99, Q7Z4Z4	Hs.194698	Search	GC15P057184	Search

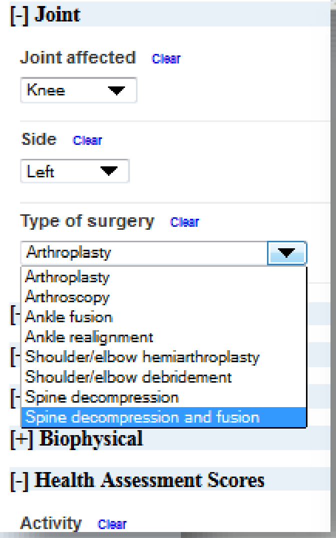
Legend:

SGF - aCGH Smooth Gain Frequency
DGF - DNAcopy with CGHcall Gain Frequency
HGF - HMMer Gain Frequency
SLF - aCGH Smooth Loss Frequency
DLF - DNAcopy with CGHcall Loss Frequency
HLF - HMMer Loss Frequency
GF - Average Gain Frequency for all 3 Algorithms
LF - Average Loss Frequency for all 3 Algorithms

GeneAccessionNumber	GeneChrom	GeneBPS	GeneBPE	WhereInCloneIsGene	Status	CloneID	CloneChrom	CloneBPS	CloneBPE	SGF	DGF	HGF	SLF
NM_004701	chr15	57184611	57204536	Internal	1	N0306H06	15	57065043	57246202	0.090909091	0.0	0.054545455	0.0818181
NM_004701	chr15	57184611	57204536	Internal	1	N0265J02	15	57110539	57266624	0.089108911	0.0	0.04950495	0.0792079
NM_004701	chr15	57184611	57204536	Internal	1	N0461I13	15	57123440	57309468	0.069306931	0.0	0.04950495	0.0792079

Gene Expression

All	Gene	0	1	3	4	5	6	7	U	D	Grouping
☐	CCNB2	■	■	🟥	🟥	🟥	🟥	🟥	5	0	
☐	DLC1	■	🟩	■	■	🟩	🟩	🟩	0	4	
☐	EDG1	🟩	🟩	■	■	🟩	🟩	🟩	0	5	
☐	EMP2	🟩	🟩	■	■	🟩	🟩	🟩	0	5	
☐	KCTD12	■	🟩	■	■	🟩	🟩	🟩	0	4	
☐	WIF1	■	🟩	■	■	🟩	🟩	🟩	0	4	



[-] Joint

Joint affected: Knee

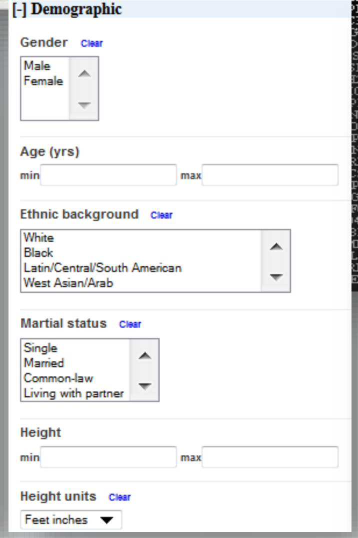
Side: Left

Type of surgery: Arthroplasty

[+] Biophysical

[-] Health Assessment Scores

Activity



[-] Demographic

Gender

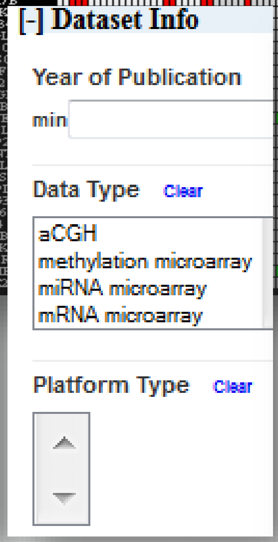
Age (yrs) min max

Ethnic background

Martial status

Height min max

Height units: Feet inches

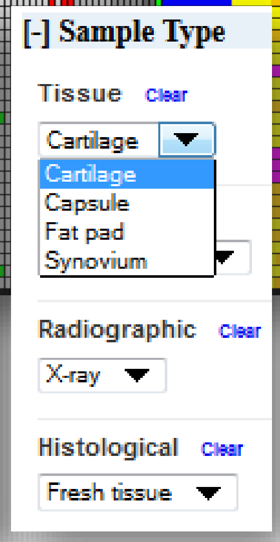


[-] Dataset Info

Year of Publication min

Data Type

Platform Type



[-] Sample Type

Tissue: Cartilage

Radiographic: X-ray

Histological: Fresh tissue

OsteoDIP

Osteoarthritis Data Integration Portal (OsteoDIP): A web-based gene and non-coding RNA expression database

Pastrello, C, Abovsky M, Lu R, Ahmed Z, Kotlyar M, Veillette V, Jurisica I.

Curation: 1204 papers

319 non patients

292 non HT

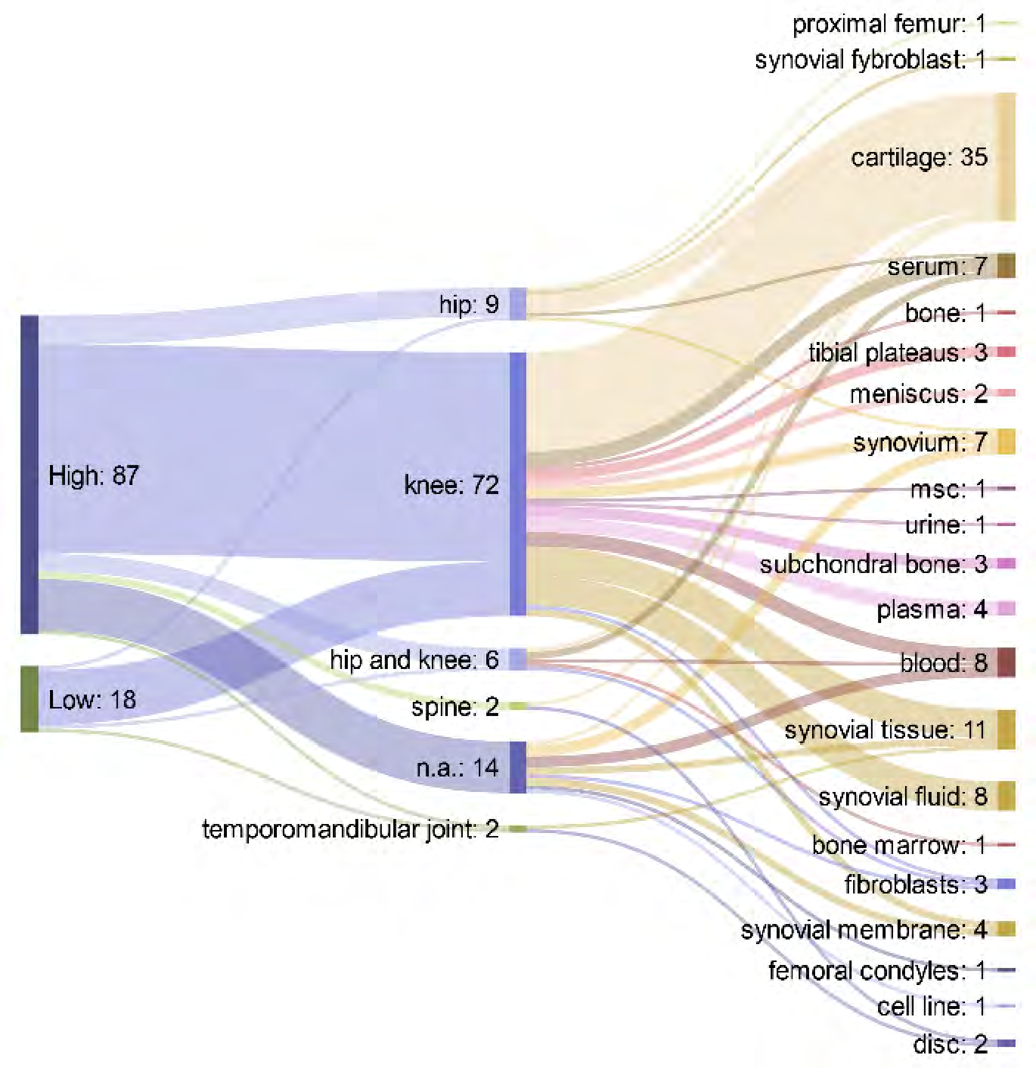
155 non OA

135 non available

128 non applicable

112 non original

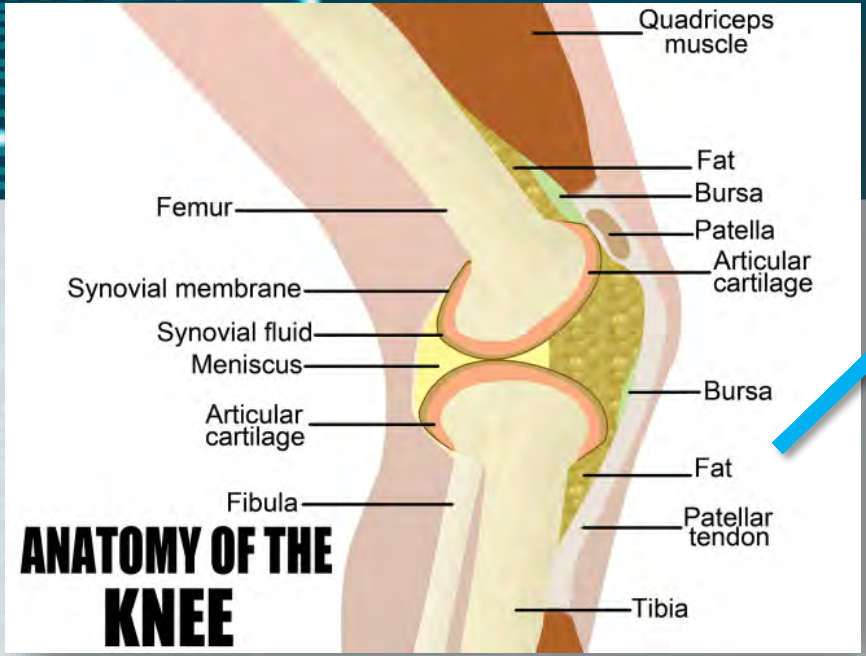
63 collected

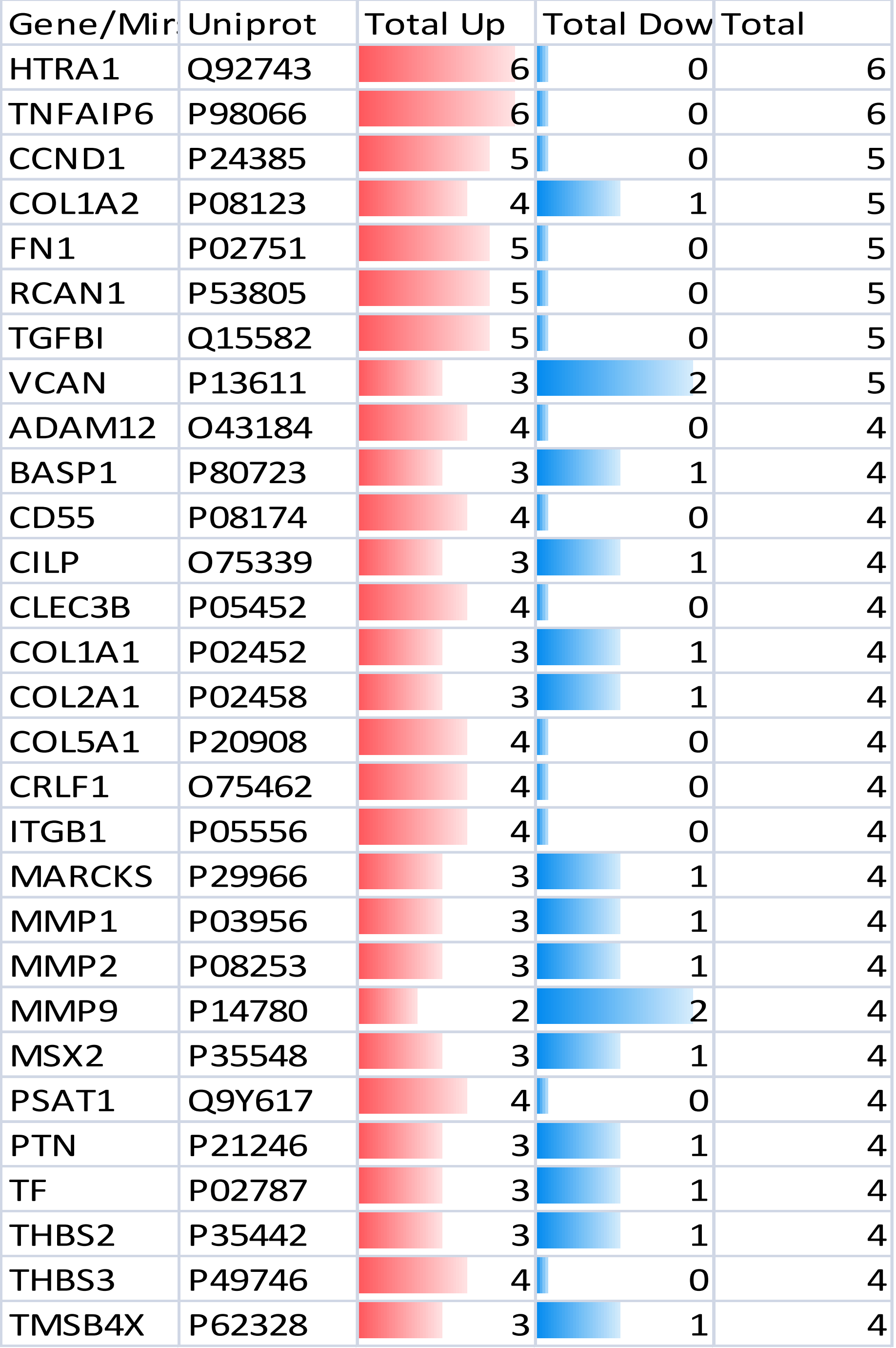


Deregulated in at least one study:

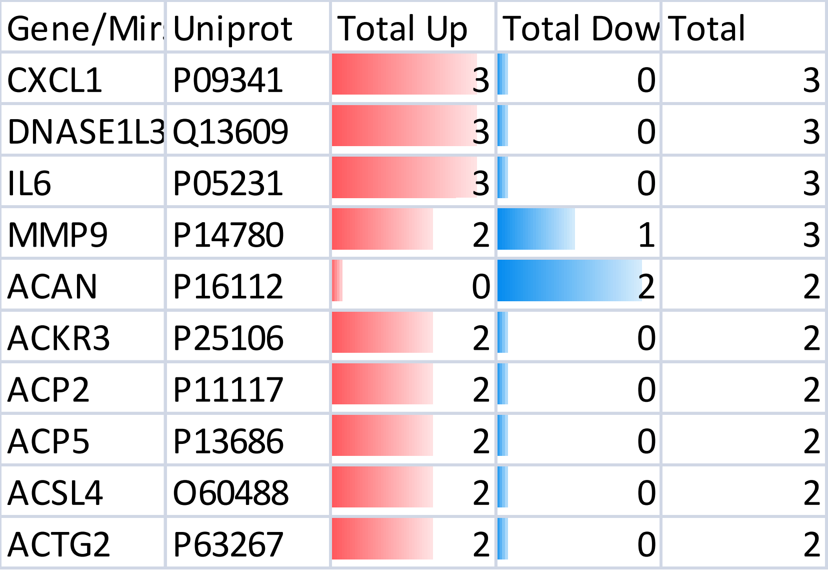
- 8,905 genes
- 402 lncRNAs
- 56 microRNAs
- 58 circRNAs

https://beyondthedish.wordpress.com/category/joint-treatments/





Gene/Mir	Uniprot	Total Up	Total Dow	Total
HTRA1	Q92743	6	0	6
TNFAIP6	P98066	6	0	6
CCND1	P24385	5	0	5
COL1A2	P08123	4	1	5
FN1	P02751	5	0	5
RCAN1	P53805	5	0	5
TGFBI	Q15582	5	0	5
VCAN	P13611	3	2	5
ADAM12	O43184	4	0	4
BASP1	P80723	3	1	4
CD55	P08174	4	0	4
CILP	O75339	3	1	4
CLEC3B	P05452	4	0	4
COL1A1	P02452	3	1	4
COL2A1	P02458	3	1	4
COL5A1	P20908	4	0	4
CRLF1	O75462	4	0	4
ITGB1	P05556	4	0	4
MARCKS	P29966	3	1	4
MMP1	P03956	3	1	4
MMP2	P08253	3	1	4
MMP9	P14780	2	2	4
MSX2	P35548	3	1	4
PSAT1	Q9Y617	4	0	4
PTN	P21246	3	1	4
TF	P02787	3	1	4
THBS2	P35442	3	1	4
THBS3	P49746	4	0	4
TMSB4X	P62328	3	1	4

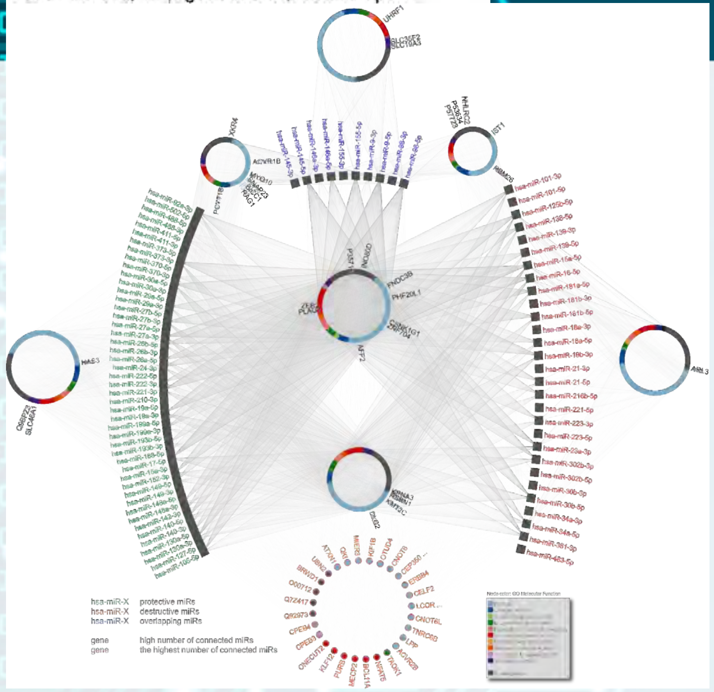


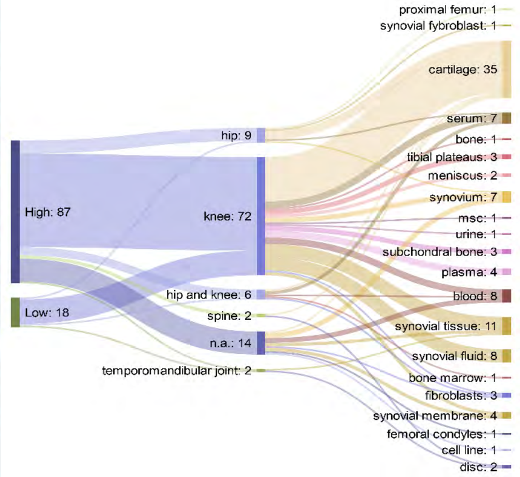
Gene/Mir	Uniprot	Total Up	Total Dow	Total
CXCL1	P09341	3	0	3
DNASE1L3	Q13609	3	0	3
IL6	P05231	3	0	3
MMP9	P14780	2	1	3
ACAN	P16112	0	2	2
ACKR3	P25106	2	0	2
ACP2	P11117	2	0	2
ACP5	P13686	2	0	2
ACSL4	O60488	2	0	2
ACTG2	P63267	2	0	2

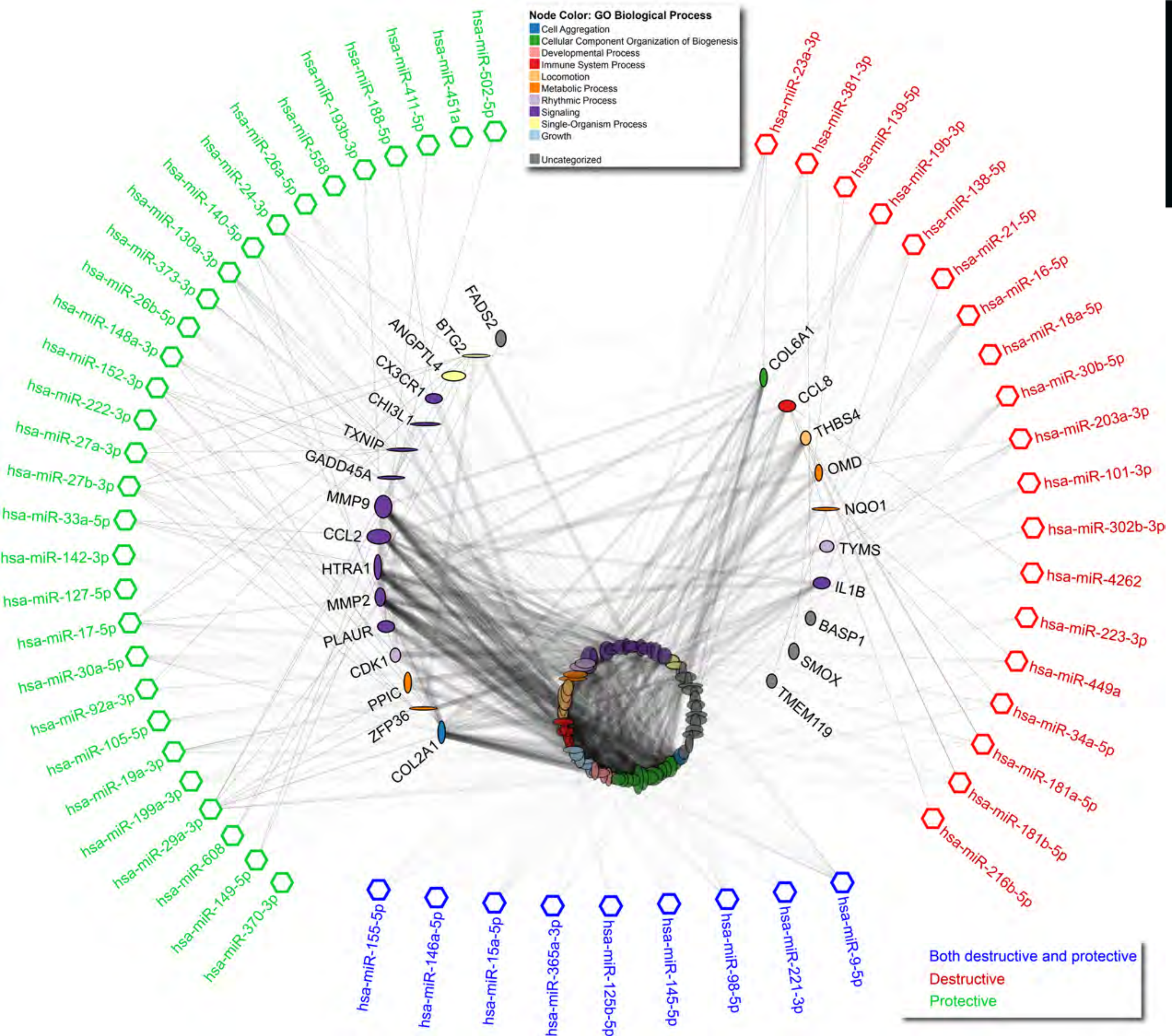
JCI insight

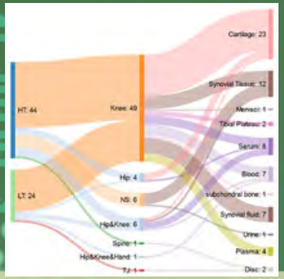
The complex landscape of microRNAs in articular cartilage: biology, pathology, and therapeutic targets

Helal Endisha, … , Igor Jurisica, Mohit Kapoor

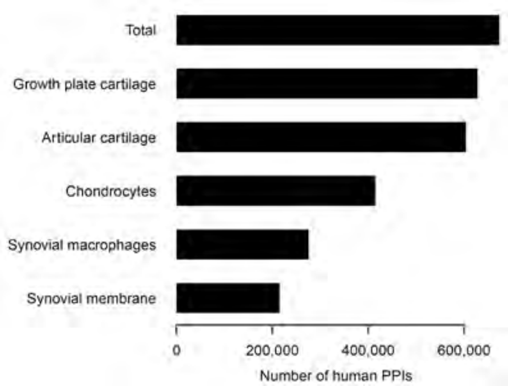


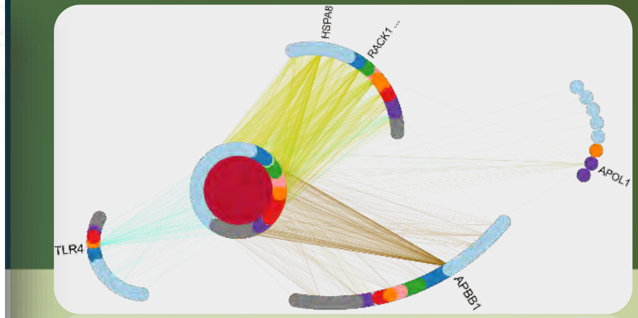


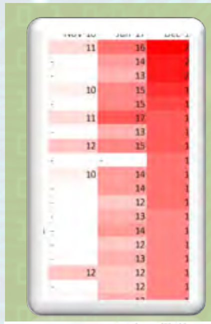


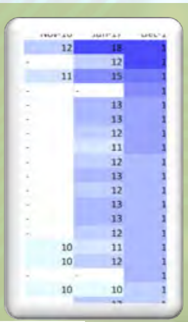


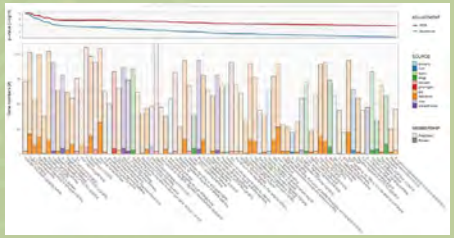
osteoarthritis initiative
a knee health study

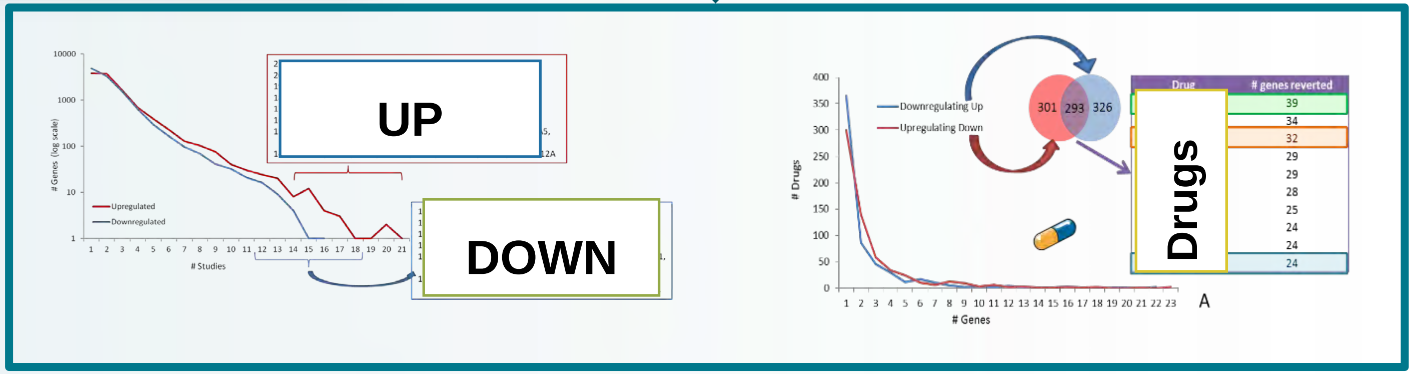








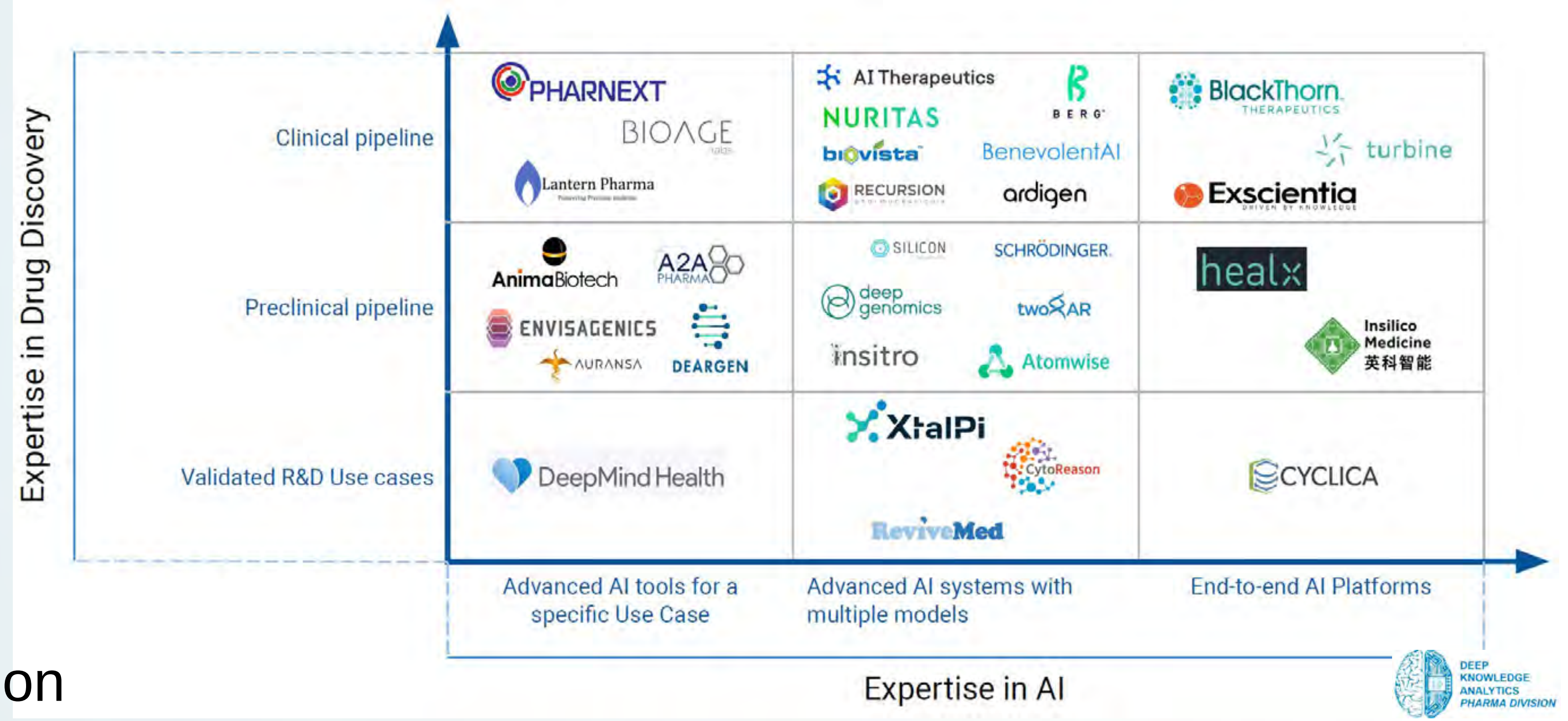




Dexamethasome (hormone)
Progesterone (hormone)
Estradiol (hormone)
Trichlostatin A (HDAC inhibitor)
JQ1 compound (BET inhibitor)

AI in Drug Discovery Pipeline

- > Diagnostics
- > Biomarker discovery
- > Drug repurposing
- > Drug target discovery
- > Drug development
- > Testing
- > Clinical trial
- > Drug delivery optimization



	Advanced AI tools for a specific Use Case	Advanced AI systems with multiple models	End-to-end AI Platforms
Clinical pipeline	PHARNEXT BIOAGE Lantern Pharma	AI Therapeutics BERG NURITAS biovista BenevolentAI RECURSION ardigen	BlackThorn THERAPEUTICS turbine Exscientia
Preclinical pipeline	AnimaBiotech A2A PHARMA ENVISAGENICS AURANSA DEARGEN	SILICON SCHRÖDINGER deep genomics twoXAR insitro Atomwise	healx Insilico Medicine 英科智能
Validated R&D Use cases	DeepMind Health	XtalPi CytoReason ReviveMed	CYCLICA

Target Discovery
Lead Discovery
Lead Optimization
Pre-Clinical
Phase I
Phase II
Phase III
FDA

OpenPandemics – COVID-19

Dr. Stefano Forli
Principal Investigator
Scripps Research

- > **Rapid deployment**
- > **300 days – 100K volunteers**

world community grid

POWERED BY BOINC

300,000,000 simulations

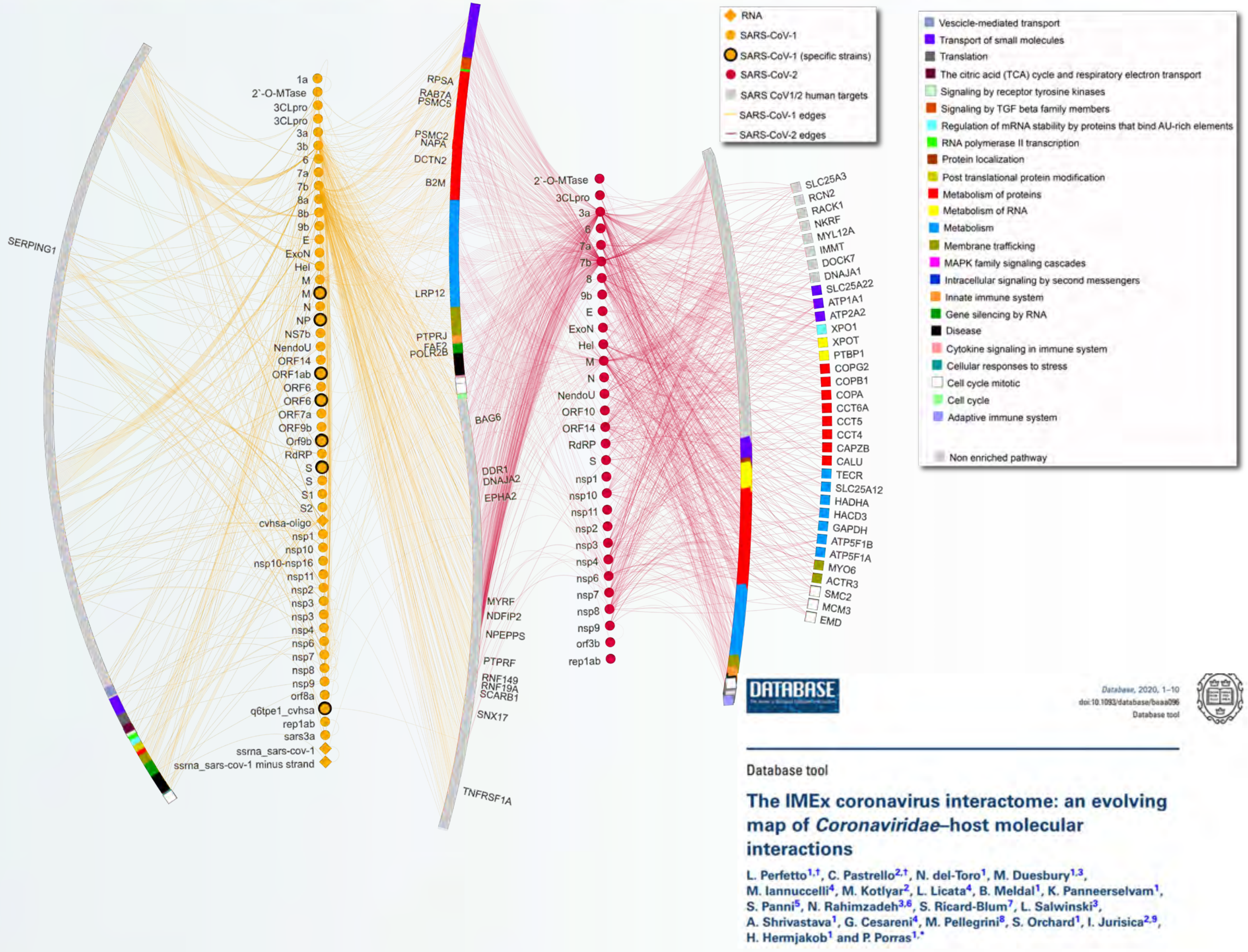
20,000 compounds screened

70 promising compounds

25 compounds in lab testing

Limitations of AI Speedup

- Grünenthal Thalidomide (Contergan)
  - “As a result of the thalidomide scandal, the Health Law in West Germany was strengthened and new requirements for pharmaceutical testing were created; the Federal Ministry of Health was established in 1962.” https://en.wikipedia.org/wiki/Grunenthal



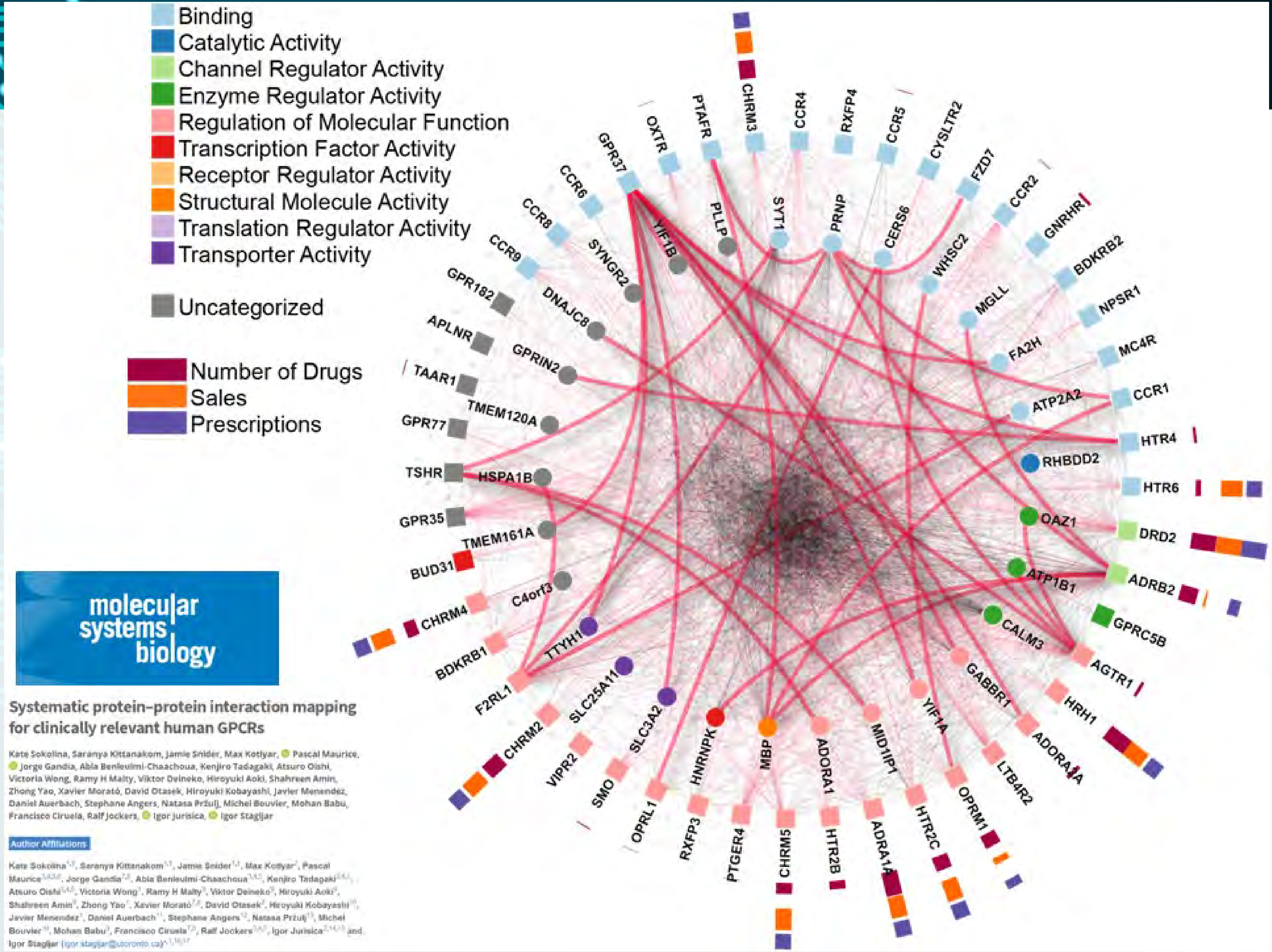
Database, 2020, 1–10
doi:10.1093/database/baaa096
Database tool

Database tool

The IMEx coronavirus interactome: an evolving map of *Coronaviridae*–host molecular interactions

L. Perfetto[1,†], C. Pastrello[2,†], N. del-Toro[1], M. Duesbury[1,3], M. Iannuccelli[4], M. Kotlyar[2], L. Licata[4], B. Meldal[1], K. Panneerselvam[1], S. Panni[5], N. Rahimzadeh[3,6], S. Ricard-Blum[7], L. Salwinski[3], A. Shrivastava[1], G. Cesareni[4], M. Pellegrini[8], S. Orchard[1], I. Jurisica[2,9], H. Hermjakob[1] and P. Porras[1,*]

MoA of Antipsychotic Drugs



molecular systems biology

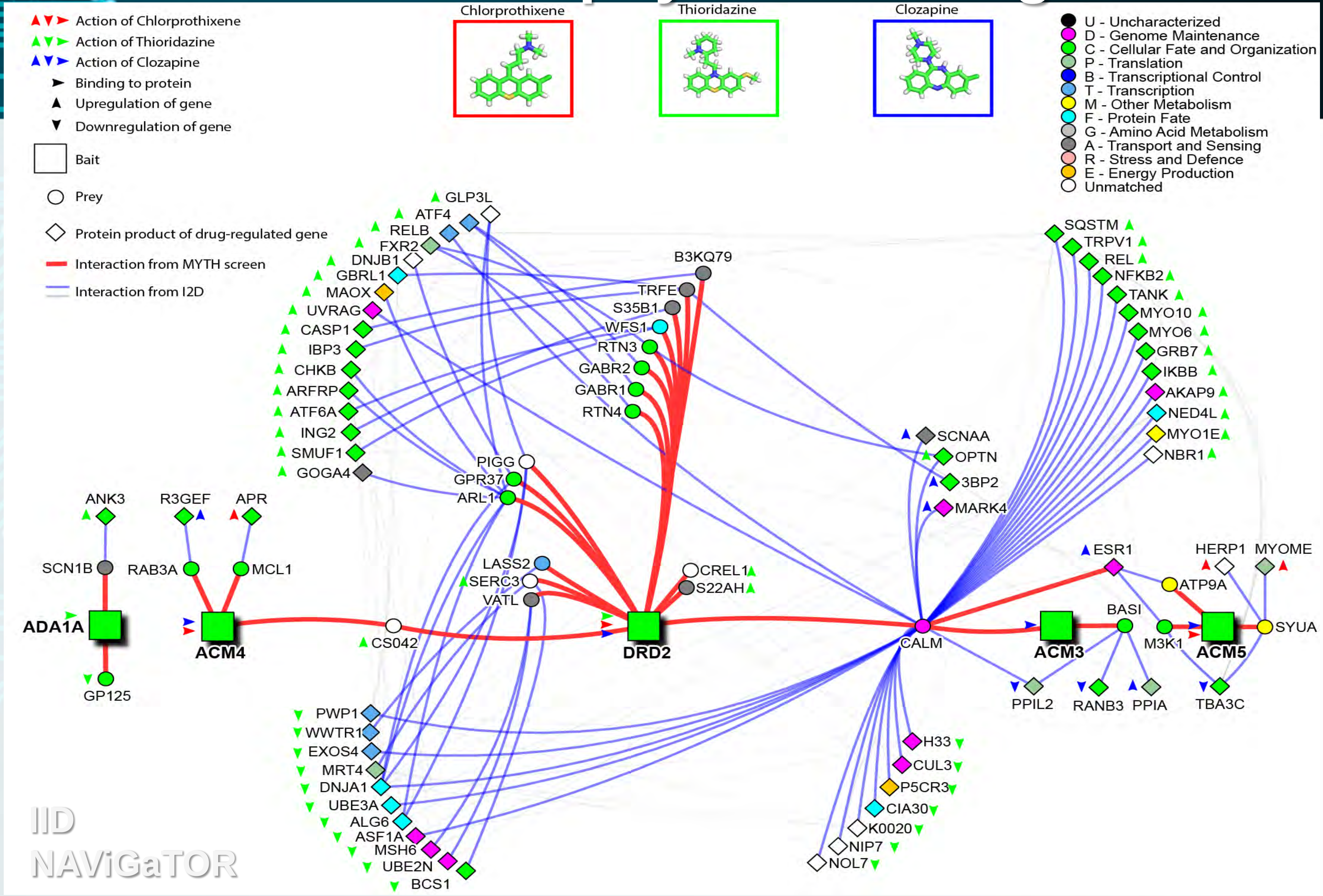
Systematic protein–protein interaction mapping for clinically relevant human GPCRs

Kate Sokolina, Saranya Kittanakom, Jamie Snider, Max Kotlyar, Pascal Maurice, Jorge Gandia, Abla Benleulmi-Chaachoua, Kenjiro Tadagaki, Atsuro Oishi, Victoria Wong, Ramy H Malty, Viktor Deineko, Hiroyuki Aoki, Shahreen Amin, Zhong Yao, Xavier Morató, David Otasek, Hiroyuki Kobayashi, Javier Menendez, Daniel Auerbach, Stephane Angers, Natasa Pržulj, Michel Bouvier, Mohan Babu, Francisco Ciruela, Ralf Jockers, Igor Jurisica, Igor Stagljar

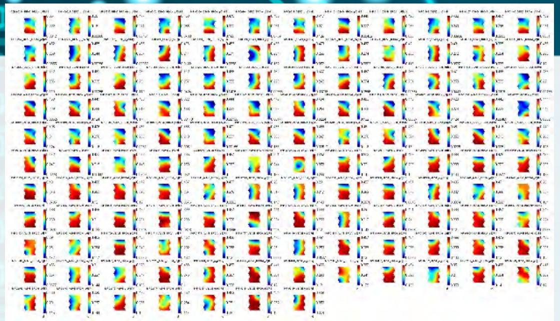
Author Affiliations

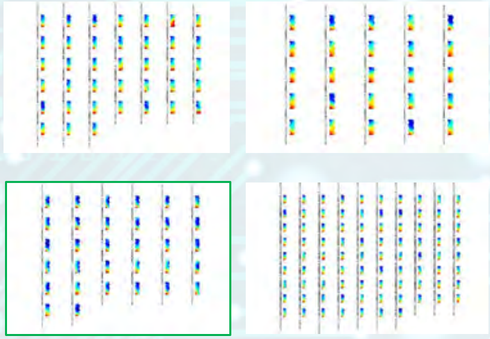
Kate Sokolina[1,2], Saranya Kittanakorn[1,2], Jamie Snider[1,2], Max Kotlyar[2], Pascal Maurice[3,4,5,6], Jorge Gandia[7,8], Abla Benleulmi-Chaachoua[3,4,5], Kenjiro Tadagaki[3,4,5], Atsuro Oishi[3,4,5], Victoria Wong[1], Ramy H Malty[9], Viktor Deineko[9], Hiroyuki Aoki[9], Shahreen Amin[9], Zhong Yao[1], Xavier Morató[7,8], David Otasek[2], Hiroyuki Kobayashi[10], Javier Menendez[1], Daniel Auerbach[11], Stephane Angers[12], Natasa Pržulj[13], Michel Bouvier[10], Mohan Babu[9], Francisco Ciruela[7,8], Ralf Jockers[3,4,5], Igor Jurisica[2,14,15] and Igor Stagljar (igor.stagljar@utoronto.ca)[*,1,16,17]

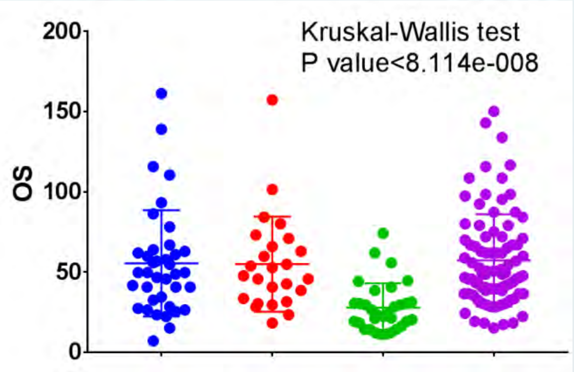
MoA of Antipsychotic Drugs

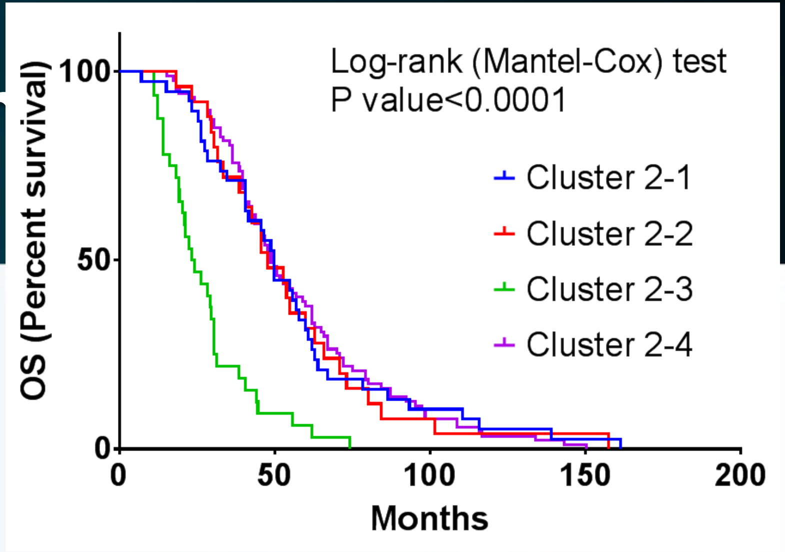


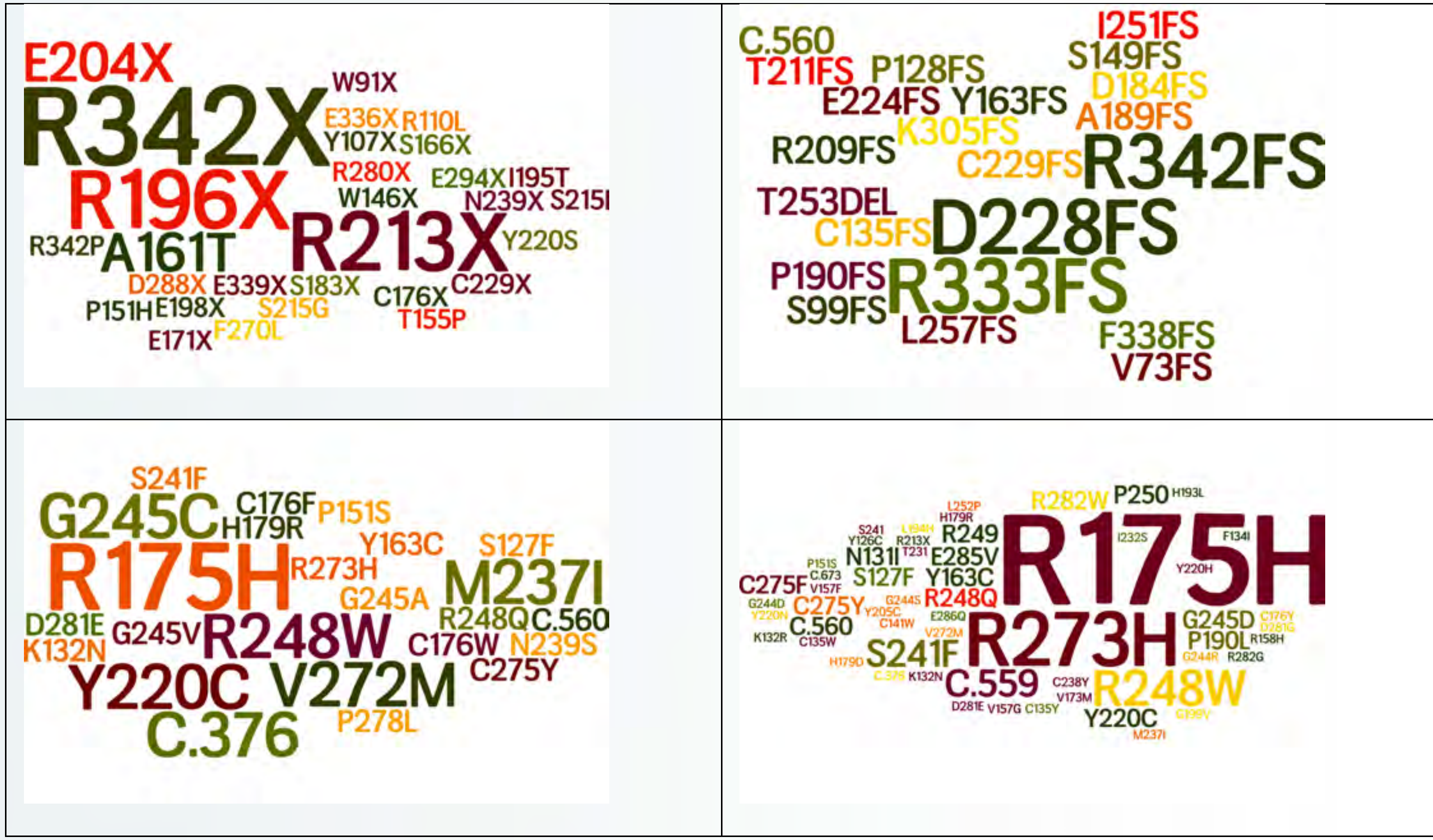
Pattern Discovery – an









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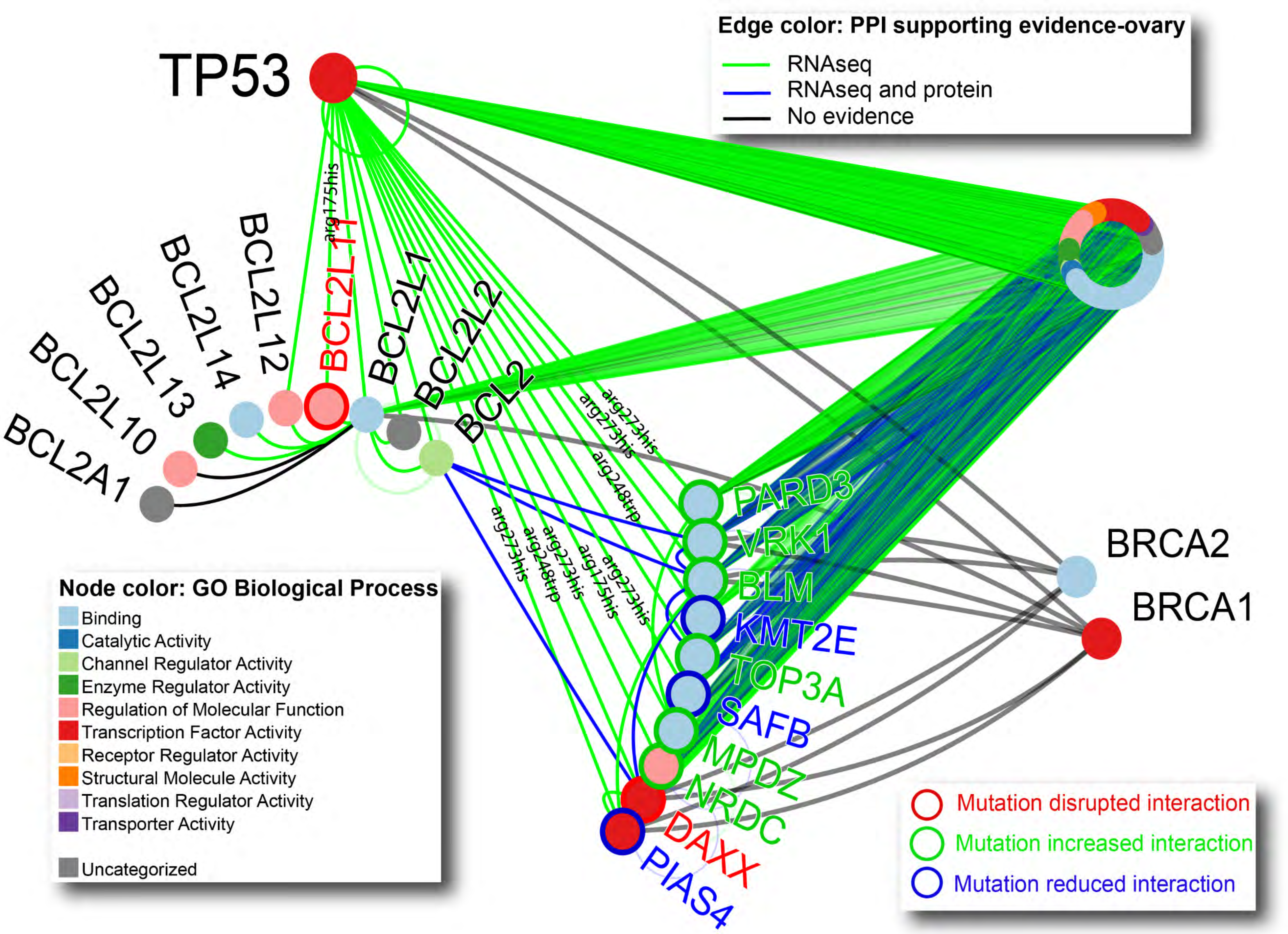
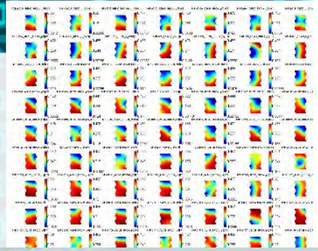
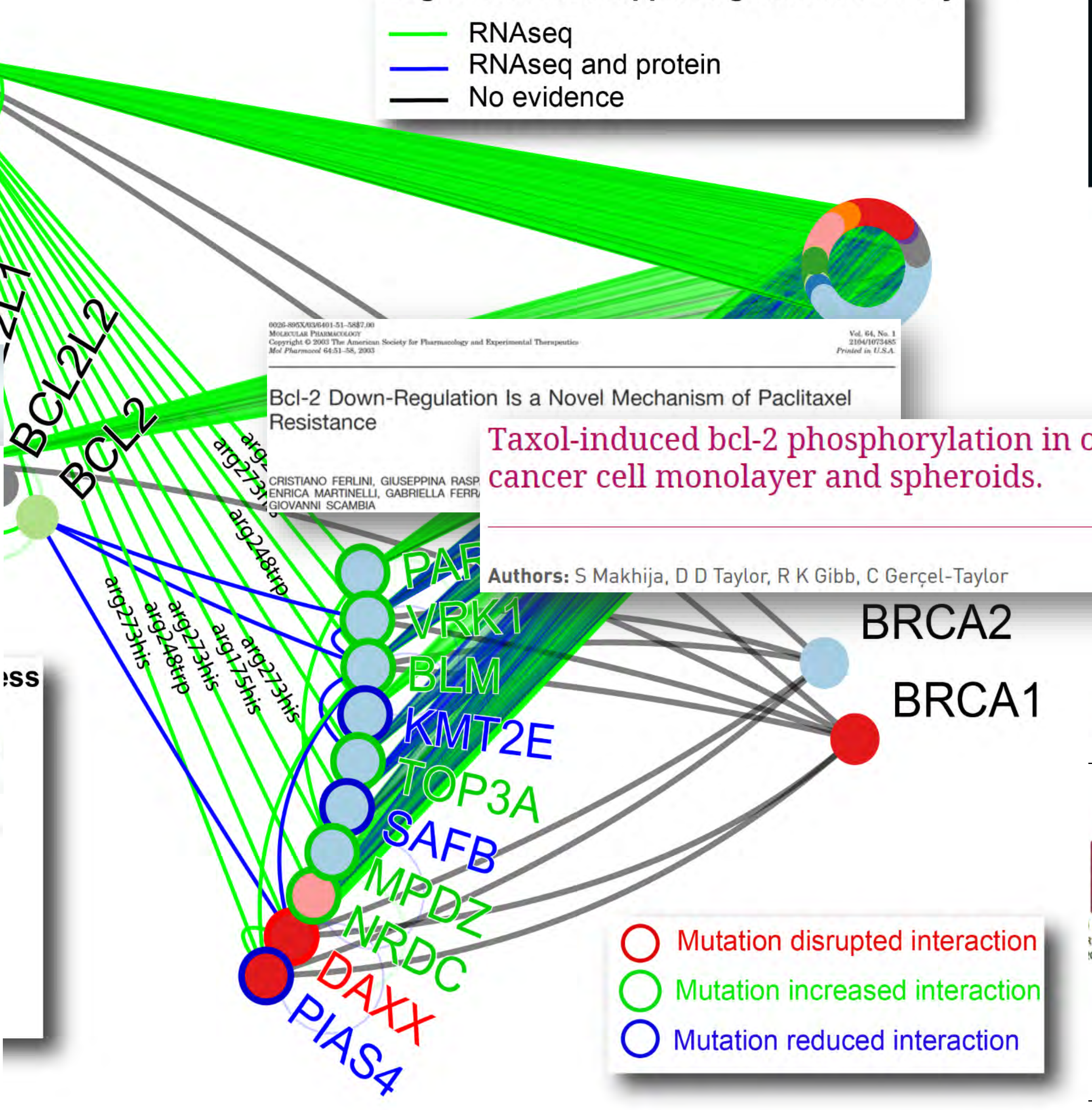

Edge color: PPI supporting evidence-ovary
RNAseq
RNAseq and protein
No evidence
TP53
BCL2L11
BCL2L12
BCL2L14
BCL2L13
BCL2L10
BCL2A1
BCL2L1
BCL2L2
BCL2
arg175his
arg273his
arg273his
arg248trp
arg273his
arg248trp
arg273his
arg175his
arg273his
PARD3
VRK1
BLM
KMT2E
TOP3A
SAFB
MPDZ
NRDC
DAXX
PIAS4
BRCA2
BRCA1
Node color: GO Biological Process
Binding
Catalytic Activity
Channel Regulator Activity
Enzyme Regulator Activity
Regulation of Molecular Function
Transcription Factor Activity
Receptor Regulator Activity
Structural Molecule Activity
Translation Regulator Activity
Transporter Activity
Uncategorized
Mutation disrupted interaction
Mutation increased interaction
Mutation reduced interaction


FS
H
C176Y
R158H





Edge color: PPI supporting evidence-ovary

🟩	RNAseq
🟦	RNAseq and protein
⬛	No evidence

○	Mutation disrupted interaction
○	Mutation increased interaction
○	Mutation reduced interaction

0026-895X/03/6401-51–58$7.00
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Mol Pharmacol 64:51–58, 2003

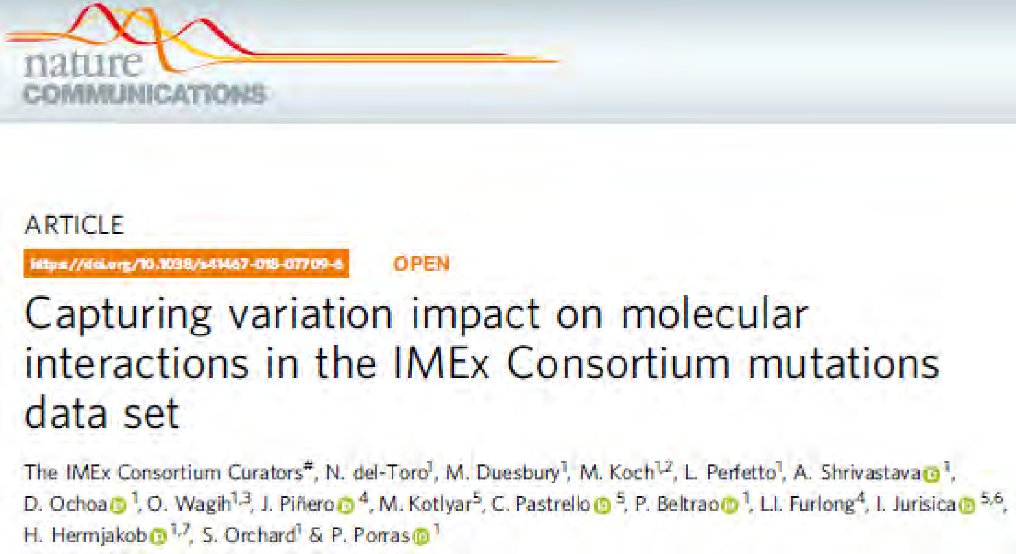
Vol. 64, No. 1
2104/1073485
Printed in U.S.A.

Bcl-2 Down-Regulation Is a Novel Mechanism of Paclitaxel Resistance

CRISTIANO FERLINI, GIUSEPPINA RASP
ENRICA MARTINELLI, GABRIELLA FERRA
GIOVANNI SCAMBIA

Taxol-induced bcl-2 phosphorylation in ovarian cancer cell monolayer and spheroids.

Authors: S Makhija, D D Taylor, R K Gibb, C Gerçel-Taylor



nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-018-07709-6 OPEN

Capturing variation impact on molecular interactions in the IMEx Consortium mutations data set

The IMEx Consortium Curators#, N. del-Toro[1], M. Duesbury[1], M. Koch[1,2], L. Perfetto[1], A. Shrivastava[1], D. Ochoa[1], O. Wagih[1,3], J. Piñero[4], M. Kotlyar[5], C. Pastrello[5], P. Beltrao[1], L.I. Furlong[4], I. Jurisica[5,6], H. Hermjakob[1,7], S. Orchard[1] & P. Porras[1]

Enzyme Regulator Activity

Original Article

INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

***TP53* mutations in high grade serous ovarian cancer and impact on clinical outcomes: a comparison of next generation sequencing and bioinformatics analyses**

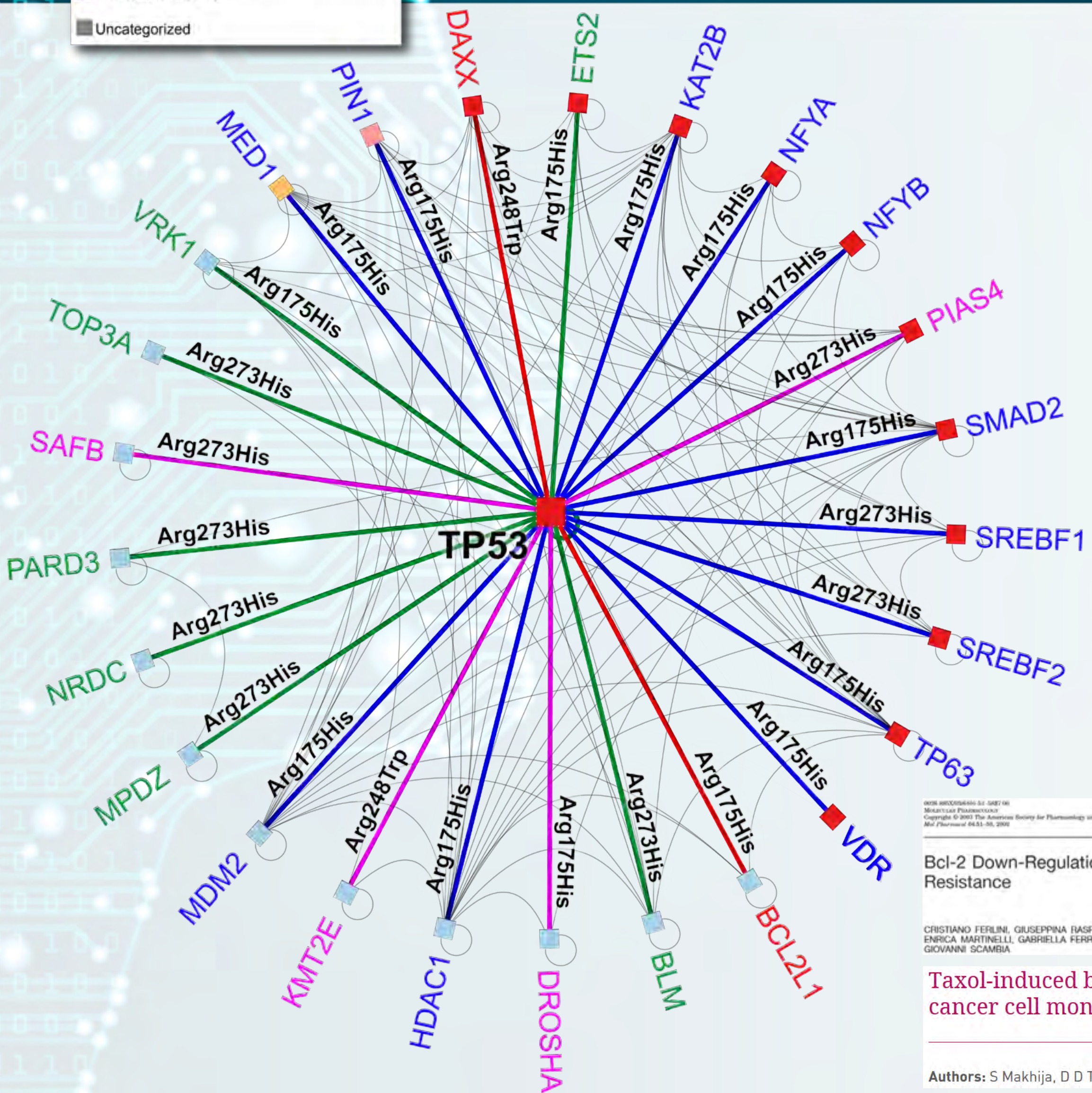
Victoria Mandilaras,[1] Swati Garg,[2] Michael Cabanero,[3] Qian Tan,[1] Chiara Pastrello,[4] Julia Burnier,[1] Katherine Karakasis,[1] Lisa Wang,[1] Neesha C Dhani,[1] Marcus O Butler,[1] Philippe L Bedard,[1] Lillian L Siu,[1] Blaise Clarke,[3] Patricia Ann Shaw,[3] Tracy Stockley,[2] Igor Jurisica,[4,5,6] Amit M Oza,[1] Stephanie Lheureux[1]

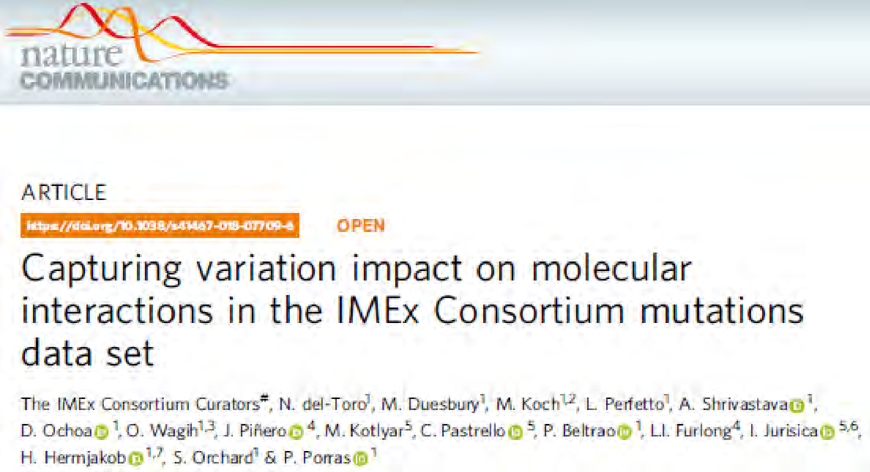
PPIs & Mutation

Node color: GO Molecular Function
- Binding
- Catalytic Activity
- Channel Regulator Activity
- Enzyme Regulator Activity
- Regulation of Molecular Function
- Transcription Factor Activity
- Receptor Regulator Activity
- Structural Molecule Activity
- Translation Regulator Activity
- Transporter Activity

- Uncategorized

Mutation affected interaction
Mutation increased interaction
Mutation decreasing interaction
Mutation disrupted interaction




nature COMMUNICATIONS

ARTICLE

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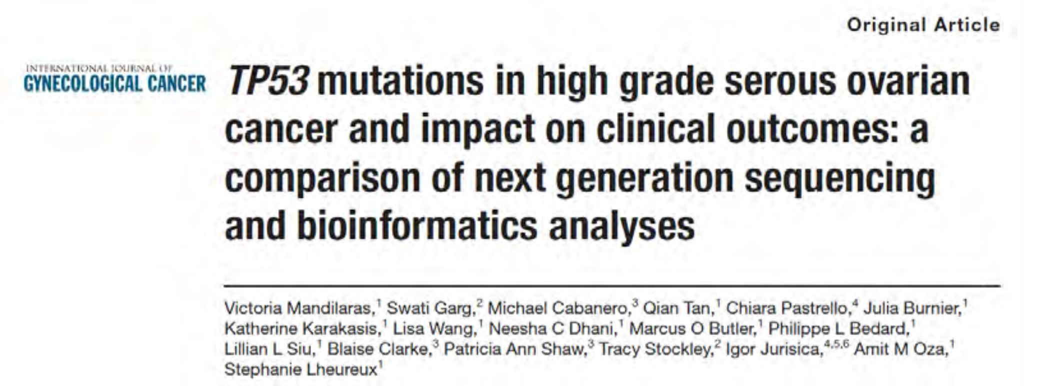
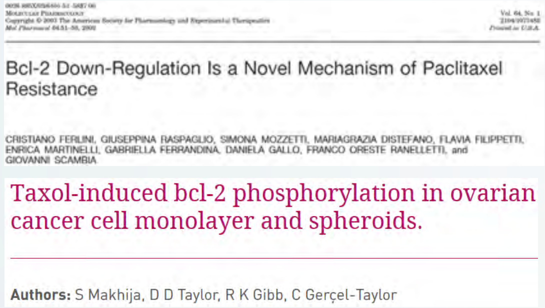

INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

Original Article

TP53 **mutations in high grade serous ovarian cancer and impact on clinical outcomes: a comparison of next generation sequencing and bioinformatics analyses**

Victoria Mandilaras,[1] Swati Garg,[2] Michael Cabanero,[3] Qian Tan,[1] Chiara Pastrello,[4] Julia Burnier,[1] Katherine Karakasis,[1] Lisa Wang,[1] Neesha C Dhani,[1] Marcus O Butler,[1] Philippe L Bedard,[1] Lillian L Siu,[1] Blaise Clarke,[3] Patricia Ann Shaw,[3] Tracy Stockley,[2] Igor Jurisica,[4,5,6] Amit M Oza,[1] Stephanie Lheureux[1]


MOLECULAR PHARMACOLOGY
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Mol Pharmacol 64:51–58, 2003

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Bcl-2 Down-Regulation Is a Novel Mechanism of Paclitaxel Resistance

CRISTIANO FERLINI, GIUSEPPINA RASPAGLIO, SIMONA MOZZETTI, MARIAGRAZIA DISTEFANO, FLAVIA FILIPPETTI, ENRICA MARTINELLI, GABRIELLA FERRANDINA, DANIELA GALLO, FRANCO ORESTE RANELLETTI, and GIOVANNI SCAMBIA

Taxol-induced bcl-2 phosphorylation in ovarian cancer cell monolayer and spheroids.

Authors: S Makhija, D D Taylor, R K Gibb, C Gerçel-Taylor


Perspective

nature COMMUNICATIONS

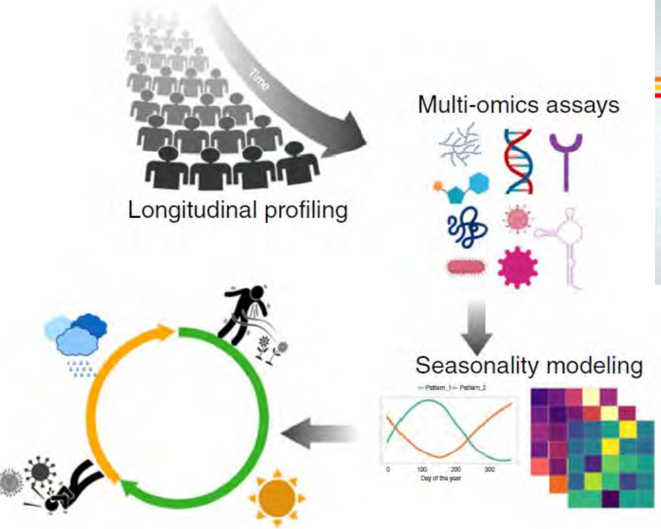
Towards a unified open access dataset of molecular interactions

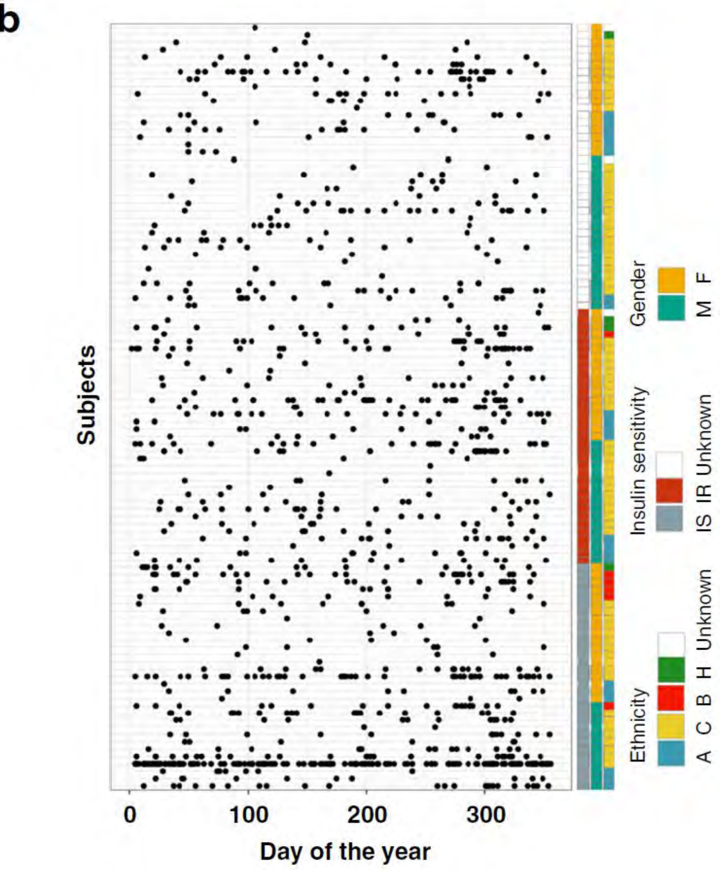
Pablo Porras[1], Elisabet Barrera[1], Alan Bridge[2], Noemi del-Toro[1], Gianni Cesareni[3,4], Margaret Duesbury[1,5], Henning Hermjakob[1], Marta Iannuccelli[3], Igor Jurisica[6,7,8], Luana Licata[3], Ruth, C. Lovering[9], David J. Lynn[10,11], Birgit Meldal[1], Bindu Nanduri[12], Kalpana Paneerselvam[1], Simona Panni[13], Matteo Pellegrini[14], Livia Perfetto[1], Negin Rahimzadeh[5], Prashansa Ratan[5], Sylvie Ricard-Blum[15], Lukasz Salwinski[5], Gautam Shirodkar[5], Anjalia Shrivastava[1,16], *Sandra Orchard[1]

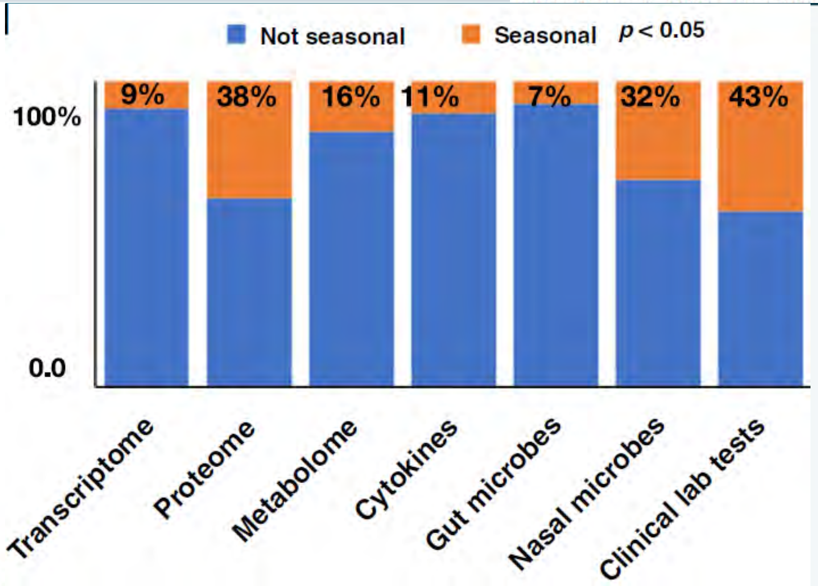
nature COMMUNICATIONS

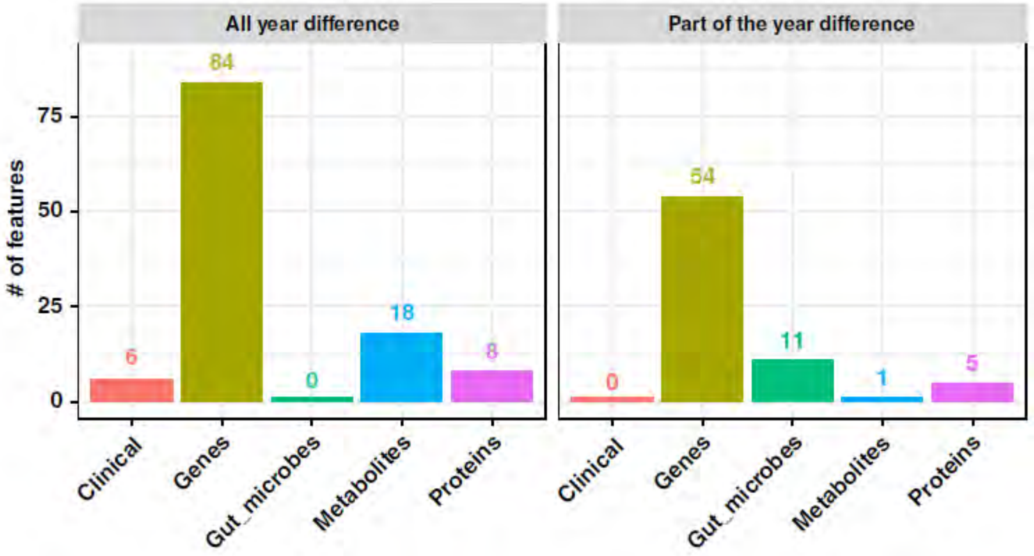
Deep longitudinal multiomics profiling reveals two biological seasonal patterns in California

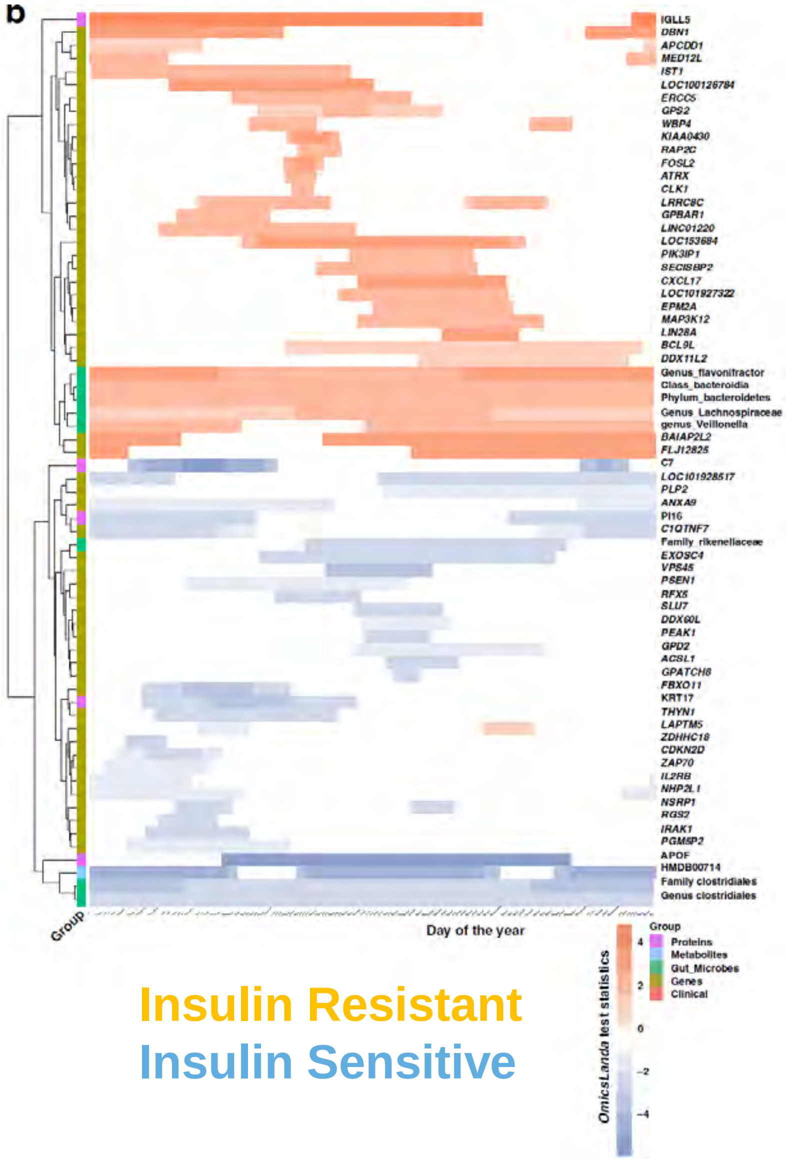
M. Reza Sailani[1,5], Ahmed A. Metwally[1,5], Wenyu Zhou[1], Sophia Miryam Schüssler-Fiorenza Rose[1], Sara Ahadi[1], Kevin Contrepois[1], Tejaswini Mishra[1], Martin Jinye Zhang[2], Łukasz Kidziński[3], Theodore J. Chu[4] & Michael P. Snyder[1✉]







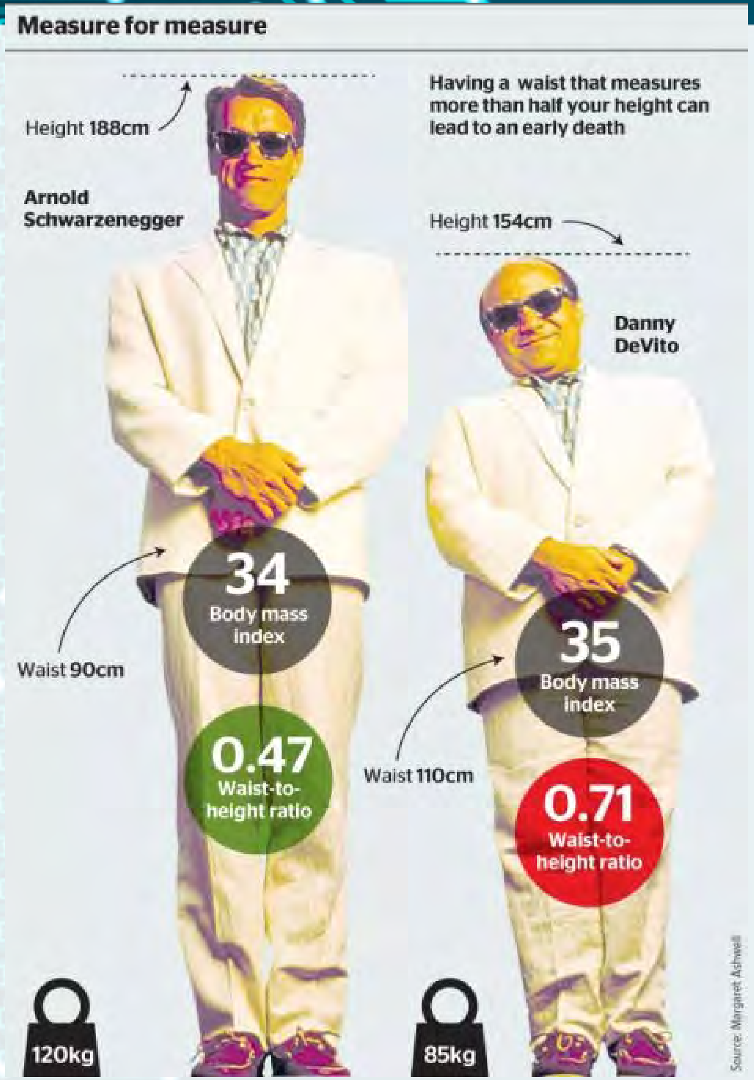




Insulin Resistant

Insulin Sensitive

BMI – Measurements … and Causality



http://www.thetimes.co.uk/tto/health/news/article3764026.ece

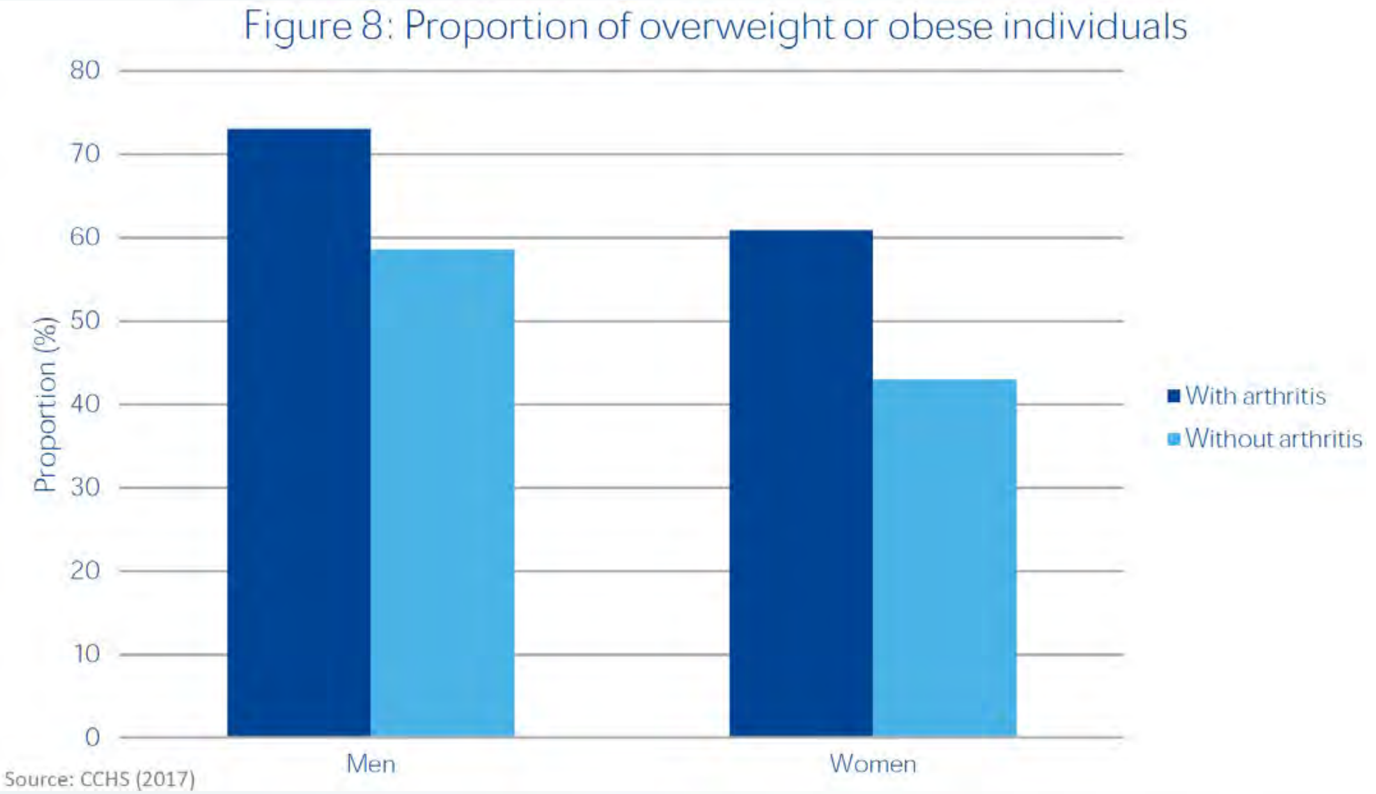


Figure 8: Proportion of overweight or obese individuals

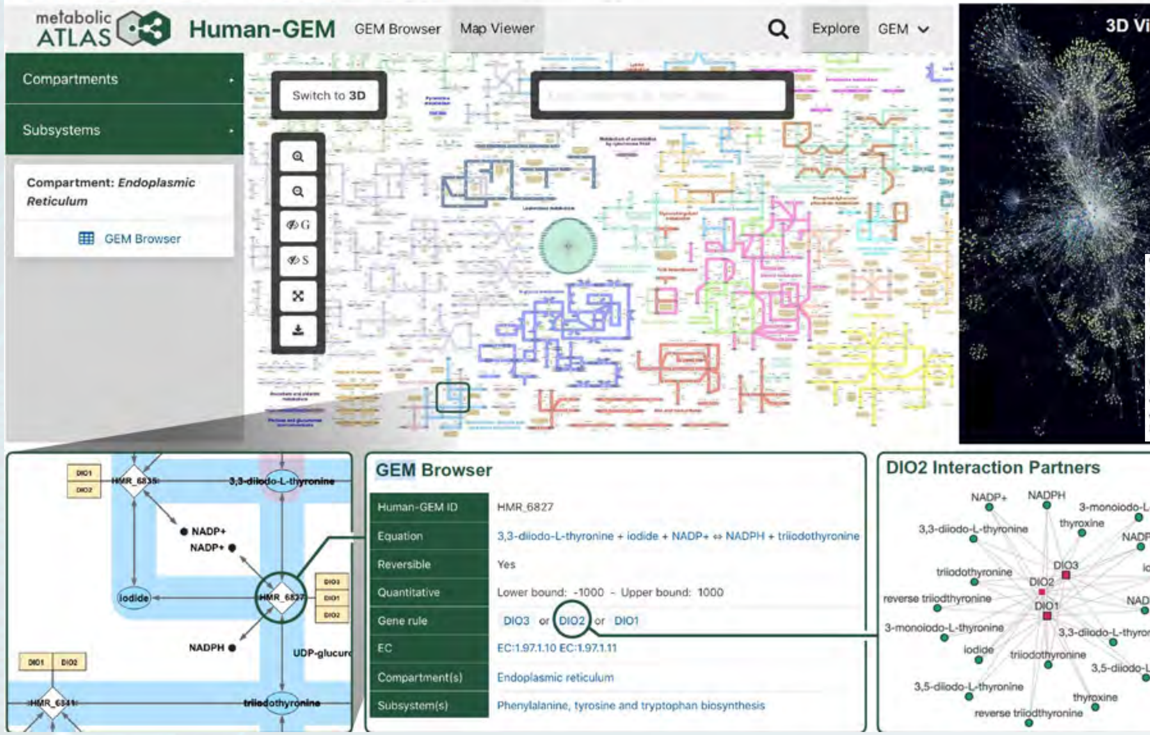
Source: CCHS (2017)

National Status of Arthritis in Canada Report ACREU
Arthritis Society: August 2019

Comprehensive & Systematic

An atlas of human metabolism

Jonathan L. Robinson[1,2]*, Pınar Kocabaş[1,2]*, Hao Wang[1,3,4]*, Pierre-Etienne Cholley[4]*, Daniel Cook[1], Avlant Nilsson[1], Mihail Anton[4], Raphael Ferreira[1], Iván Domenzain[1,2], Virinchi Billa[1], Angelo Limeta[1], Alex Hedin[1], Johan Gustafsson[1,2], Eduard J. Kerkhoven[1], L. Thomas Svensson[4], Bernhard O. Palsson[5,6,7], Adil Mardinoglu[8,9], Lena Hansson[4,10], Mathias Uhlén[5,8,11], Jens Nielsen[1,2,5,12]†



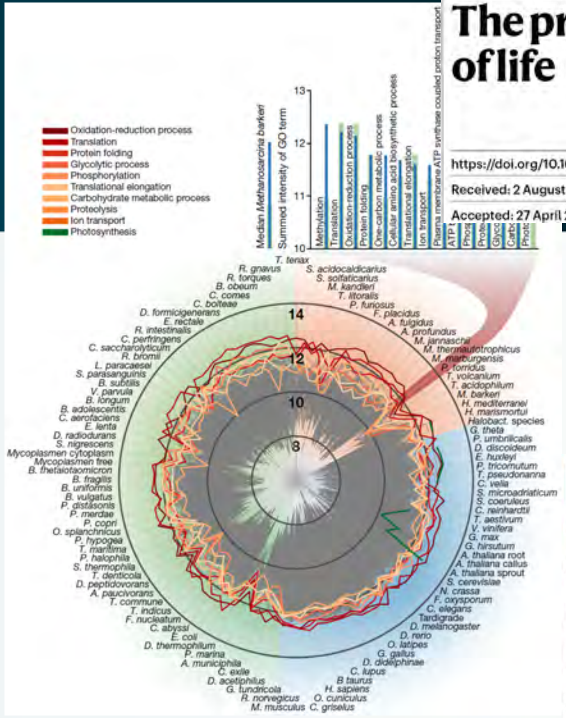
GEM Browser

Human-GEM ID	HMR_6827
Equation	3,3-diiodo-L-thyronine + iodide + NADP+ ⇔ NADPH + triiodothyronine
Reversible	Yes
Quantitative	Lower bound: -1000 - Upper bound: 1000
Gene rule	DIO3 or DIO2 or DIO1
EC	EC:1.97.1.10 EC:1.97.1.11
Compartment(s)	Endoplasmic reticulum
Subsystem(s)	Phenylalanine, tyrosine and tryptophan biosynthesis

The proteome landscape of the kingdoms of life

https://doi.org/10.1038/s41586-020-2402-x
Received: 2 August 2019
Accepted: 27 April 2020

Johannes B. Müller[1,7], Philipp E. Geyer[1,2,7], Ana R. Colaço[3], Peter V. Treit[1], Maximilian T. Strauss[1,2], Mario Oroshi[1], Sophia Doll[1,2], Sebastian Virreira Winter[1,2], Jakob M. Bader[1], Niklas Köhler[4], Fabian Theis[3,5], Alberto Santos[3,6] & Matthias Mann[1,3]✉

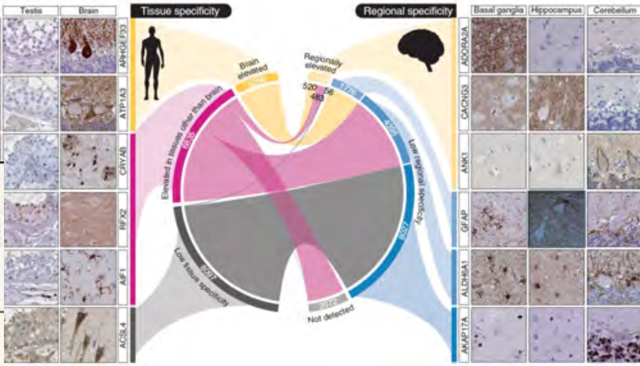


RESEARCH ARTICLE SUMMARY

INTEGRATIVE OMICS

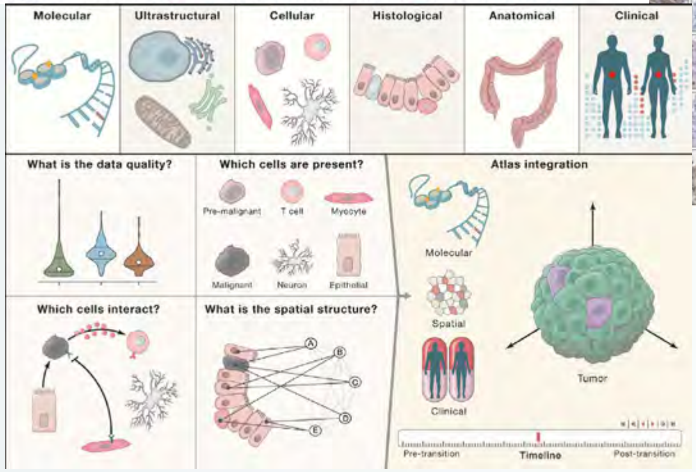
An atlas of the protein-coding genes in the human, pig, and mouse brain

Evelina Sjöstedt, Wen Zhong, Linn Fagerberg, Max Karlsson, Nicholas Mitsios, Csaba Adori, Per Oksvold, Fredrik Edfors, Agnieszka Limiszewska, Feria Hikmet, Jinrong Huang, Yutao Du, Lin Lin, Zhanying Dong, Ling Yang, Xin Liu, Hui Jiang, Xun Xu, Jian Wang, Huanming Yang, Lars Bolund, Adil Mardinoglu, Cheng Zhang, Kalle von Feilitzen, Cecilia Lindskog, Fredrik Pontén, Yonglun Luo, Tomas Hökfelt, Mathias Uhlén*†, Jan Mulder*†



The Human Tumor Atlas Network: Charting Tumor Transitions across Space and Time at Single-Cell Resolution

Orit Rozenblatt-Rosen,[1,35] Aviv Regev,[1,2,3,35,36,*] Philipp Oberdoerffer,[4,35] Tal Nawy,[5,35] Anna Hupalowska,[1] Jennifer E. Rood,[1] Orr Ashenberg,[1] Ethan Cerami,[6] Robert J. Coffey,[7] Emek Demir,[8] Li Ding,[9] Edward D. Esplin,[10] James M. Ford,[10,11] Jeremy Goecks,[12] Sharmistha Ghosh,[13] Joe W. Gray,[14] Justin Guinney,[15,16] Sean E. Hanlon,[17] Shannon K. Hughes,[4] E. Shelley Hwang,[18,19] Christine A. Iacobuzio-Donahue,[20] Judit Jané-Valbuena,[1]



Precision Medicine

- Systematically profile and characterize the “X” spectrum of diseases
- Data availability, quality, annotation
  - Standard protocols for sample collection/profiling
  - Detailed clinical information
  - Curated databases with relationships
- Explainable models
  - Increase trust, improve robustness
  - Proper train-test-validate workflow
  - Identify (sub)-cohorts, biomarkers, “missing” data, treatments

Characterize

Prevent

Detect

Treat

Repair

… from data to models to insights & treatments

Collaborations & Funding

UHN Schroeder Arthritis Institute


HELP CONQUER CANCER

Powered by IBM

world community grid
technology solving problems

University Health Network

Member name: Testname Points: 4242

Progress: 65%

Arthritis: Kapoor, Chandran, Gladman, Rahman, Haroon, Veillette, Inman, Rampersaud, Marshall, Keating, Eder, Passalent, …

Neuro: Sandmo, Filipcik, Cente, Hanes, Poschmann, Schulze, Tator, Kalia, Tartaglia, Paus, …

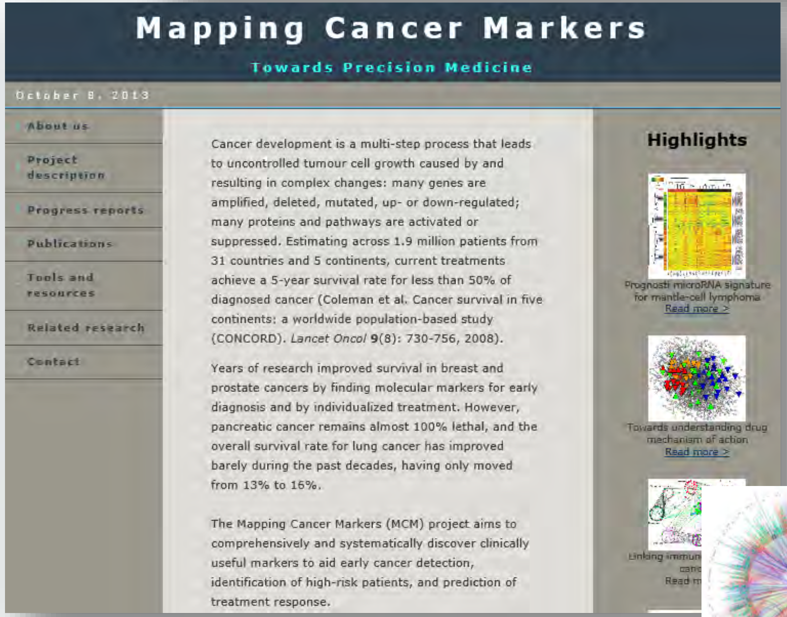
Cancer: Shepherd, Sound-Tsao, Lam, Singh, Kamel-Reid, Reis, Oza, Hedley, Mes-Masson, Jurisicova, Kaur, Kislinger, Rogatto, Dick, Minden, Salmena, Mego, …

Immunology: Lapointe, Winer, Tsai, Marques, …

Transplant: Konvalinka, Keshavjee, Martinu, …

Ph. Activity: Jurisicova, Cameron, Kotsopoulos, ...

Other: Stagljar, Maestro, Mills, Ricard-Blum, Hermjakob, Orchard, Tyers, Porras Millan, McCulloch, Glogauer, Rigoutsos, Holzinger, Gunning, DeTitta, Luft, Snell, …


Mapping Cancer Markers

Towards Precision Medicine

October 8, 2013

- About us
- Project description
- Progress reports
- Publications
- Tools and resources
- Related research
- Contact

Cancer development is a multi-step process that leads to uncontrolled tumour cell growth caused by and resulting in complex changes: many genes are amplified, deleted, mutated, up- or down-regulated; many proteins and pathways are activated or suppressed. Estimating across 1.9 million patients from 31 countries and 5 continents, current treatments achieve a 5-year survival rate for less than 50% of diagnosed cancer (Coleman et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* **9**(8): 730-756, 2008).

Years of research improved survival in breast and prostate cancers by finding molecular markers for early diagnosis and by individualized treatment. However, pancreatic cancer remains almost 100% lethal, and the overall survival rate for lung cancer has improved barely during the past decades, having only moved from 13% to 16%.

The Mapping Cancer Markers (MCM) project aims to comprehensively and systematically discover clinically useful markers to aid early cancer detection, identification of high-risk patients, and prediction of treatment response.

Highlights

Prognosti microRNA signature for mantle-cell lymphoma
Read more >

Towards understanding drug mechanism of action
Read more >

Ontario

Canada Foundation for Innovation
Fondation canadienne pour l'innovation

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

neuron
Network of European Funding for Neuroscience Research

NSERC CRSNG

MEDICINE by DESIGN

Canada Research Chairs

IMEx

KREMBIL FOUNDATION

Buchan Foundation

Toronto General & Western Hospital Foundation UHN

Campaign to Cure Arthritis
Mobility for Life.

DECODING ARTHRITIS
TO BUILD A CURE

Ride
Team Ian 2016

lenovo FOR THOSE WHO DO.

world community grid
technology solving problems

Powered by IBM technology

http://www.cs.utoronto.ca/~juris

Jurisicalab