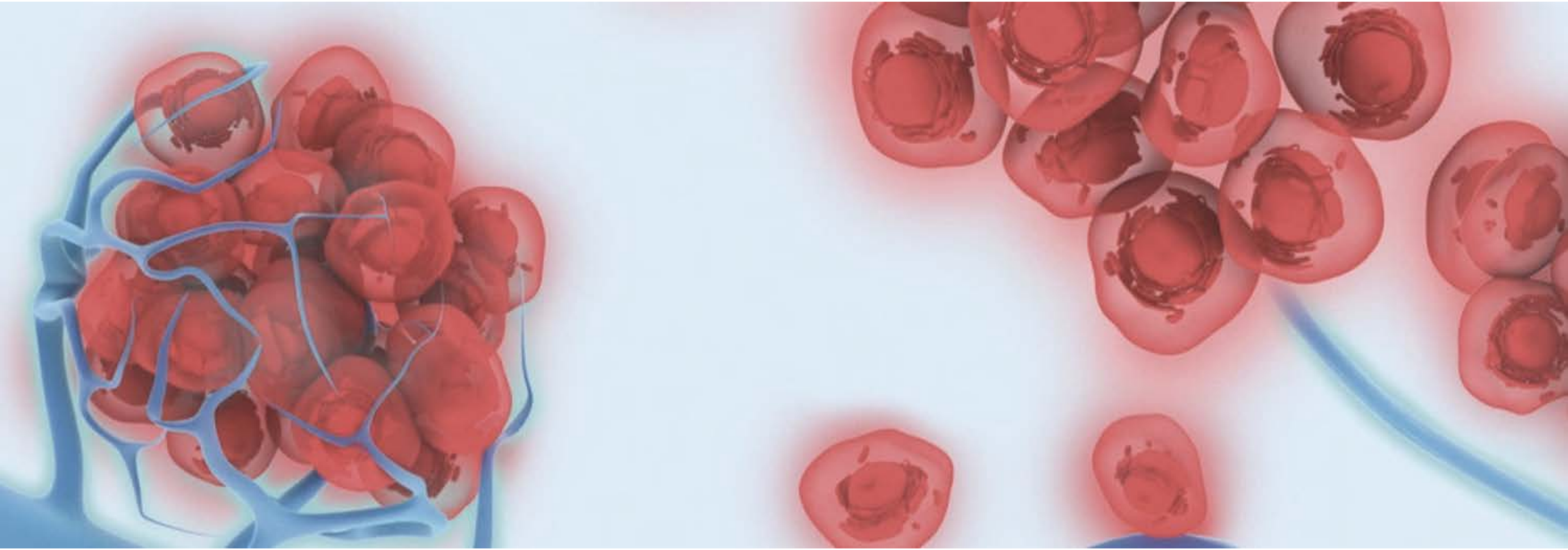


Transcriptomics, Proteomics and Metabolic Changes in Post-Natal Mouse Heart analyzed with Ingenuity Pathway Analysis (IPA) and OmicSoft

Jean-Noël Billaud, Ph.D. Senior Principal Scientist, QIAGEN Bioinformatics

Legal disclaimer

Agenda

- QIAGEN Sample to Insight
- Processing and uploading the transcriptome, proteome and metabolome datasets
- Biological analysis of the transcriptome, proteome and metabolome of post-natal mouse cardiomyocytes
- Understand the biological results in larger context
- Conclusions

Objectives: What is happening in post-natal mouse heart

- **What transcriptional program underpins the development of heart post-natally?**
  - Which transcription regulators are predicted to be activated or inhibited?
  - What are the significant biological processes connected to these transcription regulators?

- **What hypotheses could be generated then validated in the lab?**
  - Are they master regulators driving some of the post-natal mouse heart?
  - Are they therapeutically targetable or usable in biomarker application?

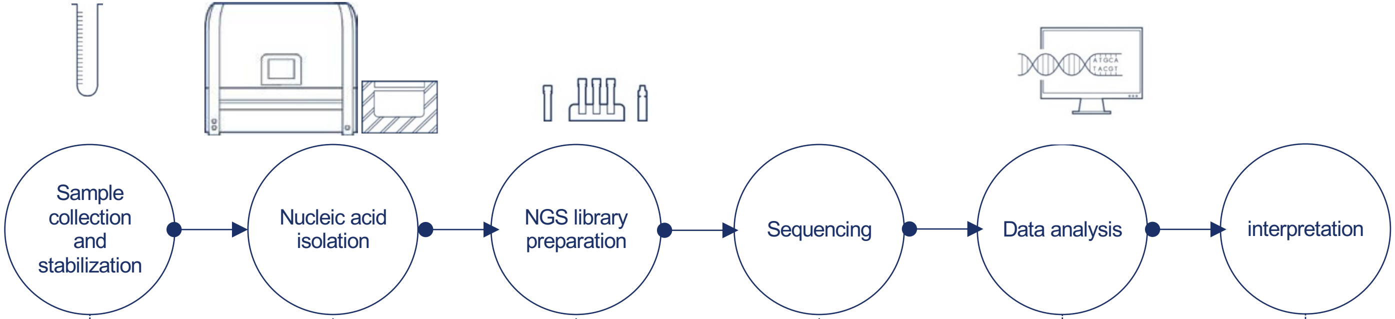
- **Can we identify tissue-specific splicing variants of interest?**
  - Are there splicing variants enriched in heart tissues?
  - What are their functions?
  - Can we identify a splicing variant for biomarker application?

- **What biological information can we get by comparing our analysis to >52,000 datasets**?
  - Is there a common pattern in other biological processes?
  - Can we identify common players?

- **Can we establish connection between two genes in heart development?**
  - What important genes are connected in heart development?
  - What correlation exist between these genes?

QIAGEN Sample to Insight

Sample to Insight solutions



Sample collection and stabilization

Nucleic acid isolation

NGS library preparation

Sequencing

Data analysis

interpretation

- PAXgene® systems

- QIAcube Connect®
- QIAsymphony®
- EZ1® Advanced XL

- QIAamp® Kits
- RNeasy® Kits
- miRNeasy Kits
- exoRNeasy Kits

- QIAseq RNA
- QIAseq DNA

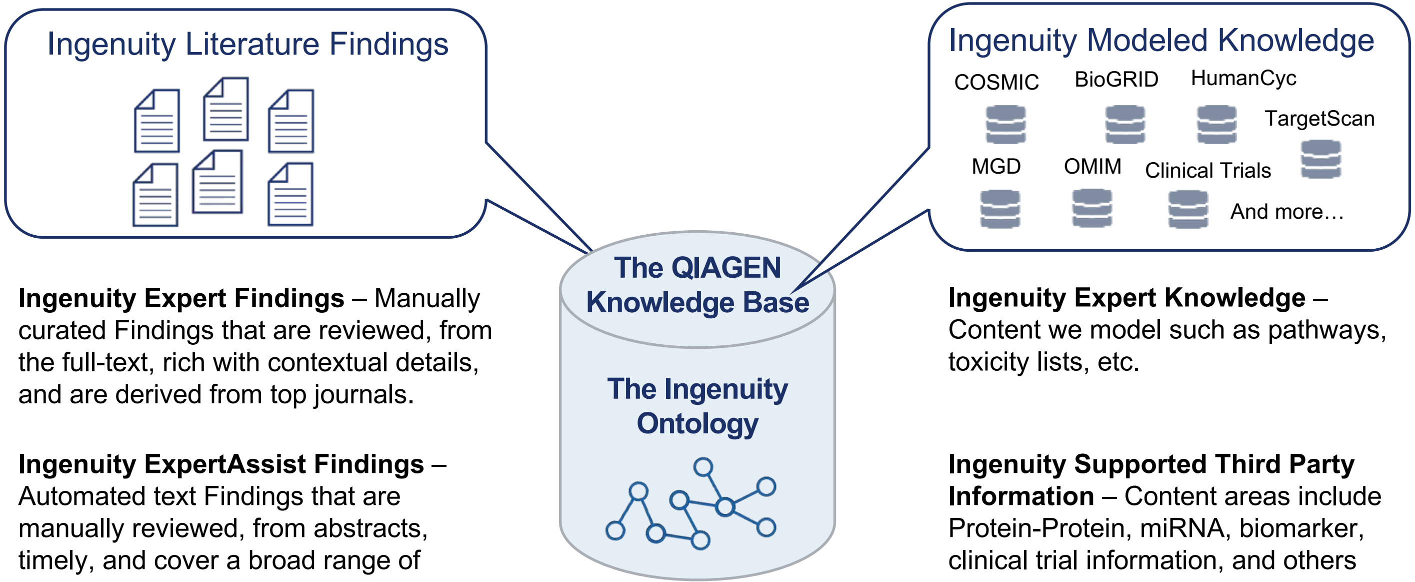
Illumina & Thermo Fisher sequencers

- OmicSoft Array Suite
- CLC Genomics Workbench
- QIAGEN Microbial Genomics Module
- CLC Main Workbench
- CLC Genome Finishing Module

- Ingenuity® Pathway Analysis
- Ingenuity Variant Analysis
- HGMD®
- OmicSoft Land Explorer
- OmicSoft DiseaseLand
- OmicSoft OncoLand
- OmicSoft GeneticsLand

The foundation for all of QIAGEN Bioinformatics products

A massive, manually curated Knowledge Base



Ingenuity Literature Findings

Ingenuity Modeled Knowledge

COSMIC
BioGRID
HumanCyc
TargetScan
MGD
OMIM
Clinical Trials
And more…

The QIAGEN Knowledge Base

The Ingenuity Ontology

Ingenuity Expert Findings – Manually curated Findings that are reviewed, from the full-text, rich with contextual details, and are derived from top journals.

Ingenuity ExpertAssist Findings – Automated text Findings that are manually reviewed, from abstracts, timely, and cover a broad range of publications. These comprise a small percentage of IPA's findings.

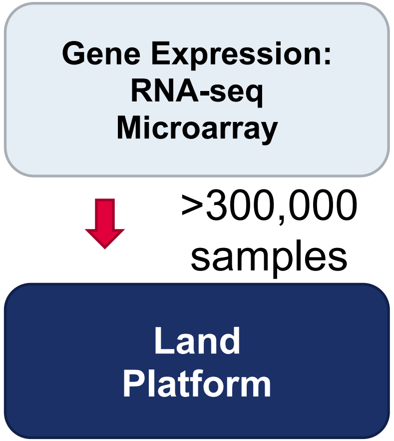
Ingenuity Expert Knowledge – Content we model such as pathways, toxicity lists, etc.

Ingenuity Supported Third Party Information – Content areas include Protein-Protein, miRNA, biomarker, clinical trial information, and others

INGENUITY
PATHWAY ANALYSIS

>52,000 comparison datasets from OmicSoft Lands in IPA

OmicSoft Lands, expression data in IPA



Gene Expression:
RNA-seq
Microarray

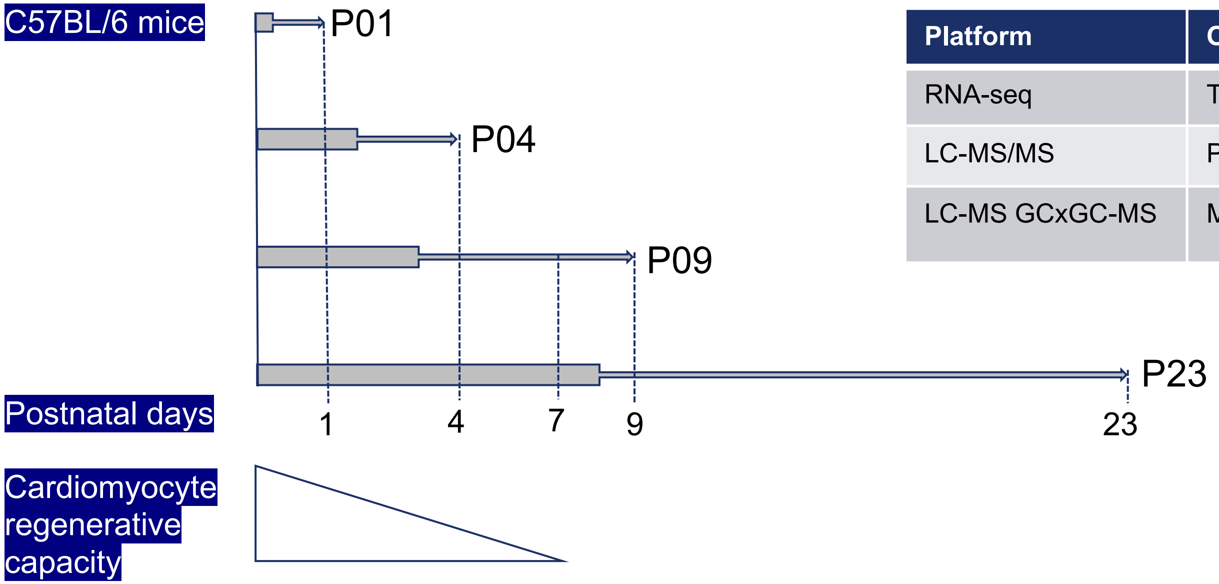
>300,000
samples

Land
Platform

RNAseq data analyzed using QIAGEN bioinformatics

Experimental design for the multiomics analysis of postnatal mouse hearts.

Two separate sets of mouse ventricular tissue samples collected on postnatal day 1 (P01), P04, P09, and P23 were used.



Platform	Omics
RNA-seq	Transcriptomics
LC-MS/MS	Proteomics
LC-MS GCxGC-MS	Metabolomics

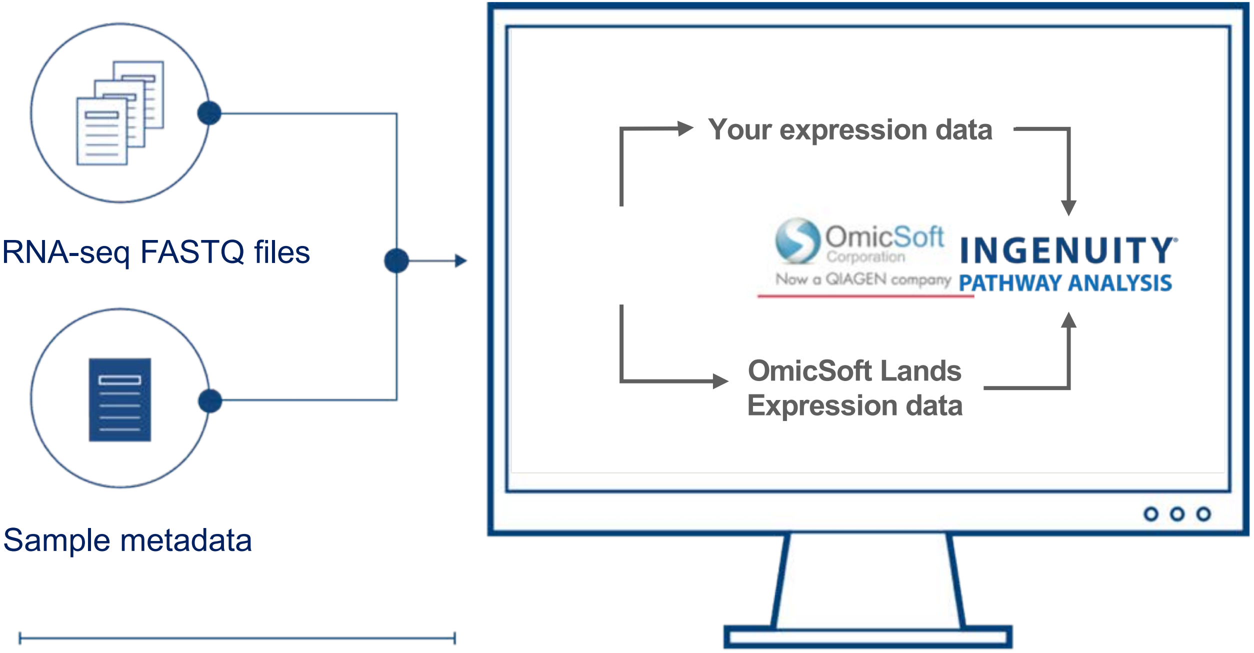
Talman V. et al. (2018) Molecular Atlas of Postnatal Mouse Heart Development. J Am Heart Assoc. PMID: 30371266, GSE119530

Transcriptomics, Proteomics, Metabolic Changes in Postnatal Mouse Heart

- ✓ Explore the underlying transcriptional programs (Upstream Analysis)
- ✓ Generate hypotheses to validate in the lab (Causal Network)
- ✓ Identify tissue-enriched splicing variant and its expression pattern (IsoProfiler)
- ✓ Compare our analysis to pre-computed datasets (Analysis Match – OmicSoft Lands)
- ✓ Visualize the connections of important genes in heart development (OmicSoft)

Integration Array Studio

Ingenuity Pathway Analysis (IPA) - FASTQ to insight



RNA-seq FASTQ files

Sample metadata

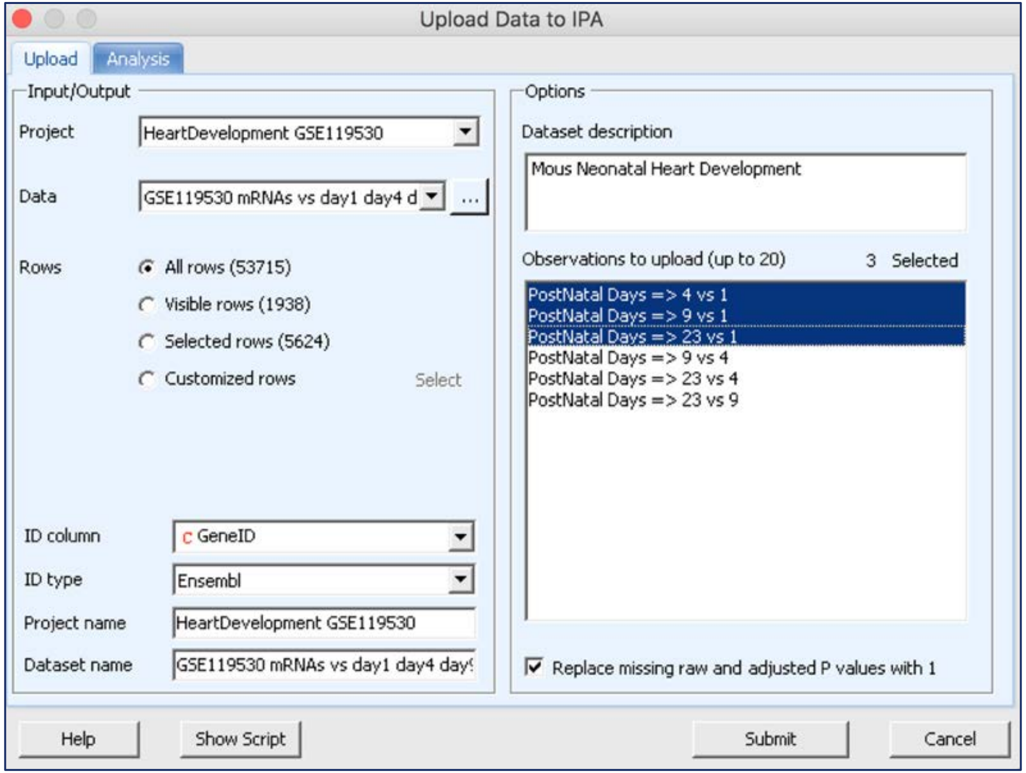
IMPORT

Your expression data

OmicSoft Lands Expression data

Upload dataset to IPA

OS-IPA integration: Analyzed dataset in AS is sent to IPA via Plugin



Upload Data to IPA

Input/Output

Project: HeartDevelopment GSE119530

Data: GSE119530 mRNAs vs day1 day4 d

Rows:
- ● All rows (53715)
- ○ Visible rows (1938)
- ○ Selected rows (5624)
- ○ Customized rows

ID column: c GeneID

ID type: Ensembl

Project name: HeartDevelopment GSE119530

Dataset name: GSE119530 mRNAs vs day1 day4 day!

Options

Dataset description: Mous Neonatal Heart Development

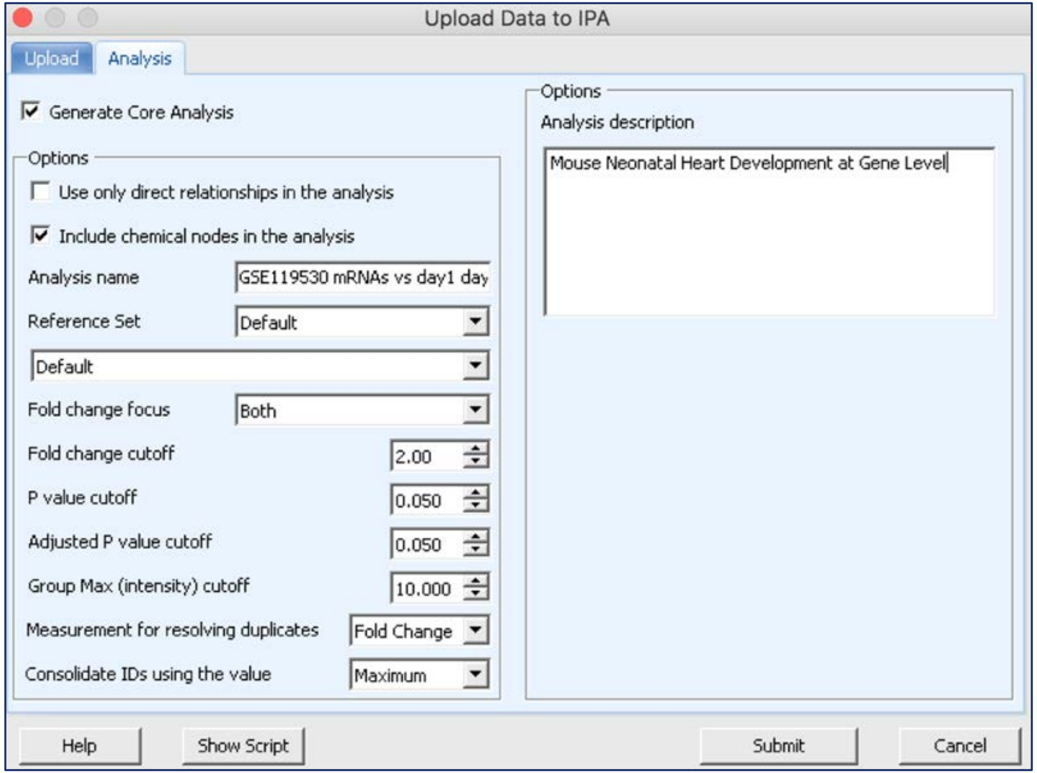
Observations to upload (up to 20) 3 Selected

- PostNatal Days => 4 vs 1
- PostNatal Days => 9 vs 1
- PostNatal Days => 23 vs 1
- PostNatal Days => 9 vs 4
- PostNatal Days => 23 vs 4
- PostNatal Days => 23 vs 9

☑ Replace missing raw and adjusted P values with 1

Auto-submit IPA core analysis from Array Studio dataset

The dataset will be automatically analyzed in IPA with the supplied cutoffs



☑ Generate Core Analysis

Options

☐ Use only direct relationships in the analysis

☑ Include chemical nodes in the analysis

Analysis name: GSE119530 mRNAs vs day1 day

Reference Set: Default

Default

Fold change focus: Both

Fold change cutoff: 2.00

P value cutoff: 0.050

Adjusted P value cutoff: 0.050

Group Max (intensity) cutoff: 10.000

Measurement for resolving duplicates: Fold Change

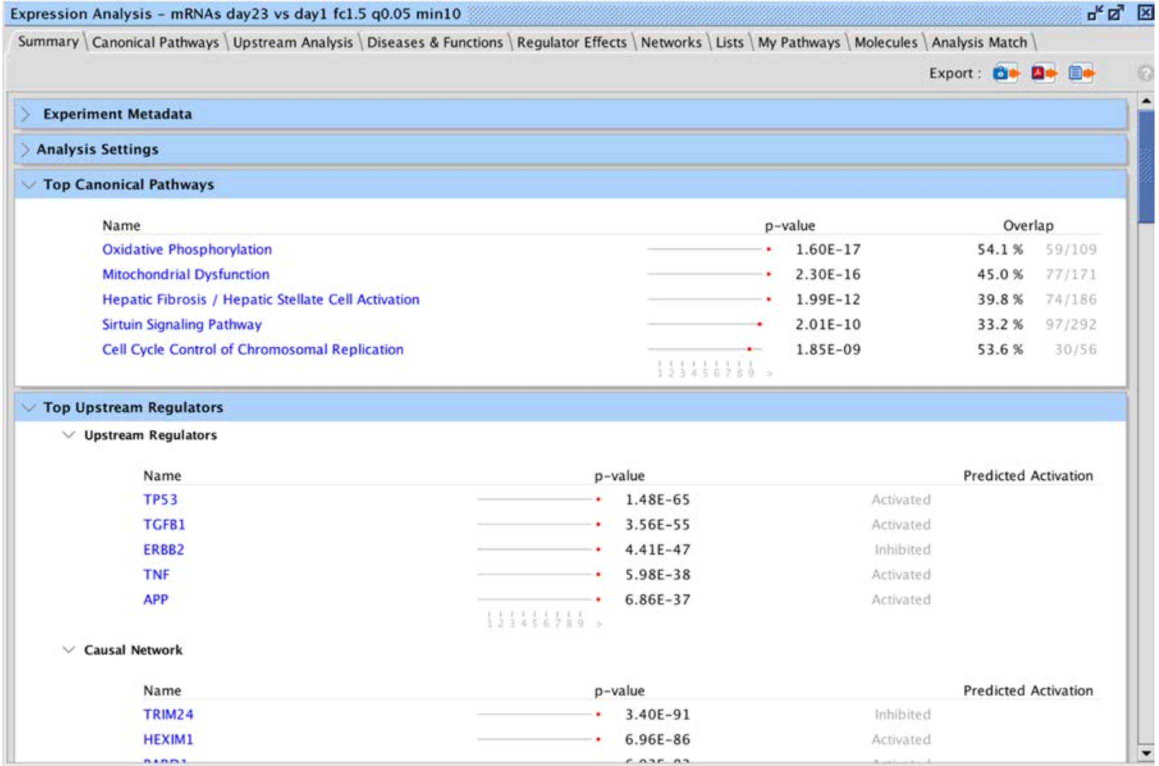
Consolidate IDs using the value: Maximum

Options

Analysis description: Mouse Neonatal Heart Development at Gene Level

Summary of the Core Analysis: mRNA day 23 vs day 1

Summary at the gene (GE) level, |fold change|>1.5, q<0.05, min counts >10 in day 23 or day 1



Expression Analysis - mRNAs day23 vs day1 fc1.5 q0.05 min10

Experiment Metadata

Analysis Settings

Top Canonical Pathways

Name	p-value	Overlap	
Oxidative Phosphorylation	1.60E-17	54.1 %	59/109
Mitochondrial Dysfunction	2.30E-16	45.0 %	77/171
Hepatic Fibrosis / Hepatic Stellate Cell Activation	1.99E-12	39.8 %	74/186
Sirtuin Signaling Pathway	2.01E-10	33.2 %	97/292
Cell Cycle Control of Chromosomal Replication	1.85E-09	53.6 %	30/56

Top Upstream Regulators

Upstream Regulators

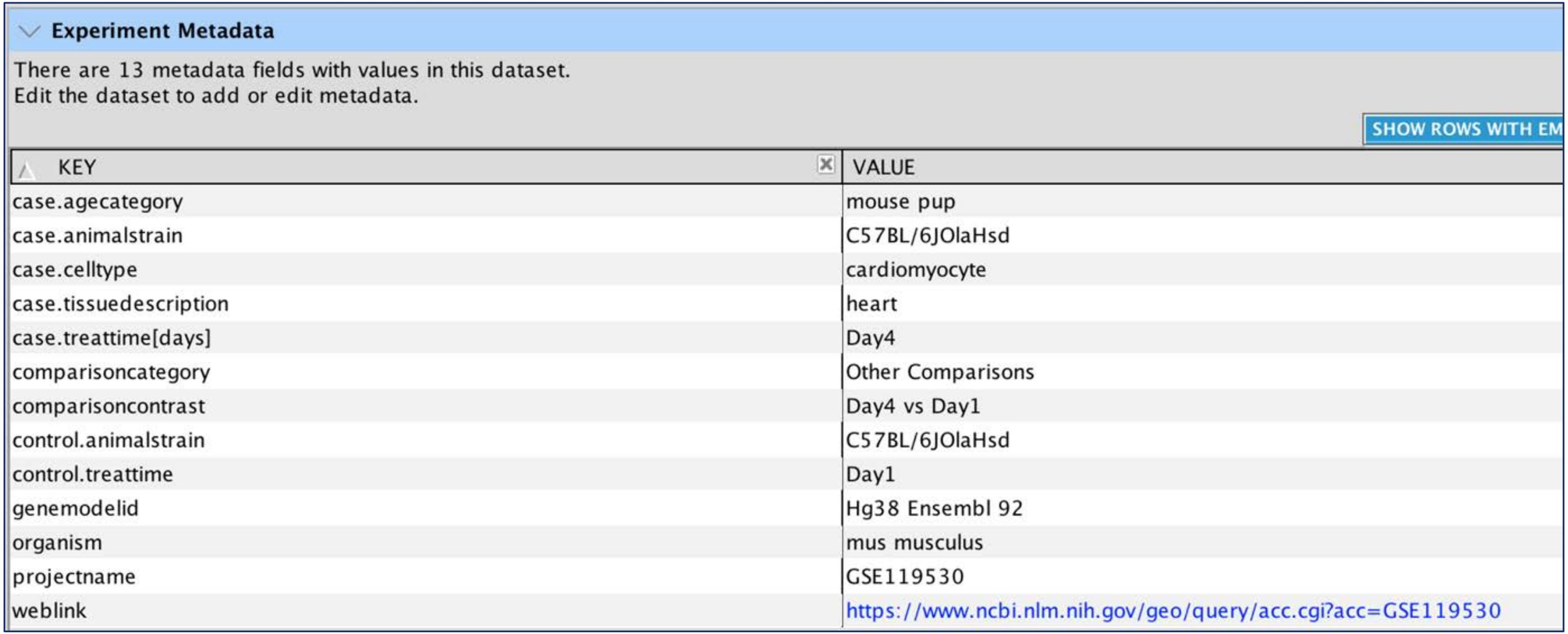
Name	p-value	Predicted Activation
TP53	1.48E-65	Activated
TGFB1	3.56E-55	Activated
ERBB2	4.41E-47	Inhibited
TNF	5.98E-38	Activated
APP	6.86E-37	Activated

Causal Network

Name	p-value	Predicted Activation
TRIM24	3.40E-91	Inhibited
HEXIM1	6.96E-86	Activated

Core Analysis: day 23 vs day 1 (example)

Experiment Metadata

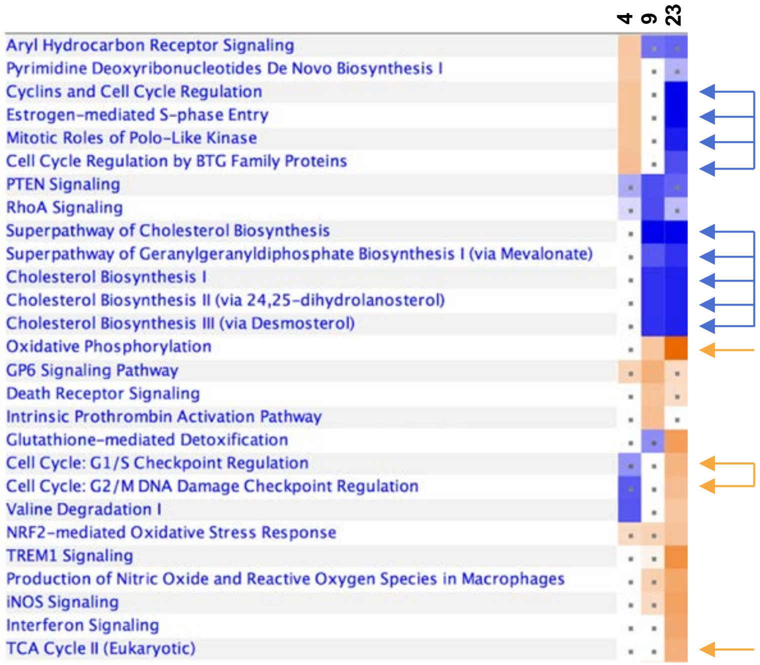


There are 13 metadata fields with values in this dataset.
Edit the dataset to add or edit metadata.

KEY	VALUE
case.agecategory	mouse pup
case.animalstrain	C57BL/6JOlaHsd
case.celltype	cardiomyocyte
case.tissuedescription	heart
case.treattime[days]	Day4
comparisoncategory	Other Comparisons
comparisoncontrast	Day4 vs Day1
control.animalstrain	C57BL/6JOlaHsd
control.treattime	Day1
genemodelid	Hg38 Ensembl 92
organism	mus musculus
projectname	GSE119530
weblink	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE119530

Transcriptomics changes in post-natal mouse heart

Canonical Pathways comparison indicate switch in energy metabolism and changes in cell cycle.



Aryl Hydrocarbon Receptor Signaling
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I
Cyclins and Cell Cycle Regulation
Estrogen-mediated S-phase Entry
Mitotic Roles of Polo-Like Kinase
Cell Cycle Regulation by BTG Family Proteins
PTEN Signaling
RhoA Signaling
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Cholesterol Biosynthesis I
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)
Cholesterol Biosynthesis III (via Desmosterol)
Oxidative Phosphorylation
GP6 Signaling Pathway
Death Receptor Signaling
Intrinsic Prothrombin Activation Pathway
Glutathione-mediated Detoxification
Cell Cycle: G1/S Checkpoint Regulation
Cell Cycle: G2/M DNA Damage Checkpoint Regulation
Valine Degradation I
NRF2-mediated Oxidative Stress Response
TREM1 Signaling
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages
iNOS Signaling
Interferon Signaling
TCA Cycle II (Eukaryotic)

Cell Cycle decreased

Cholesterol synthesis decreased

Oxidative phosphorylation increased

Cell cycle checkpoint increased

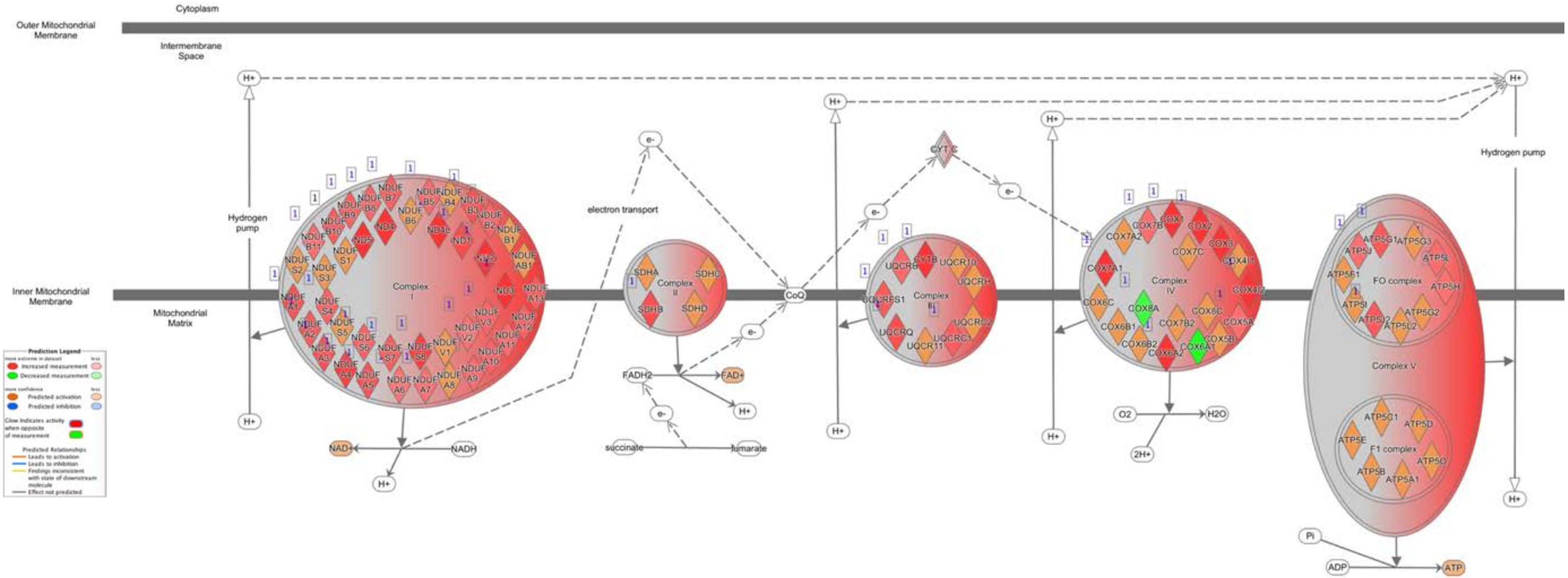
TCA cycle increased

Post-natal cardiomyocytes arrest their cell cycle progression and increase oxidative phosphorylation starting at day 9 after birth.

Transcriptomics, Proteomics and Metabolic Changes in Postnatal Mouse Heart analyzed with IPA and OmicSoft

Oxidative phosphorylation is predicted to be activated at day 9 and day 23

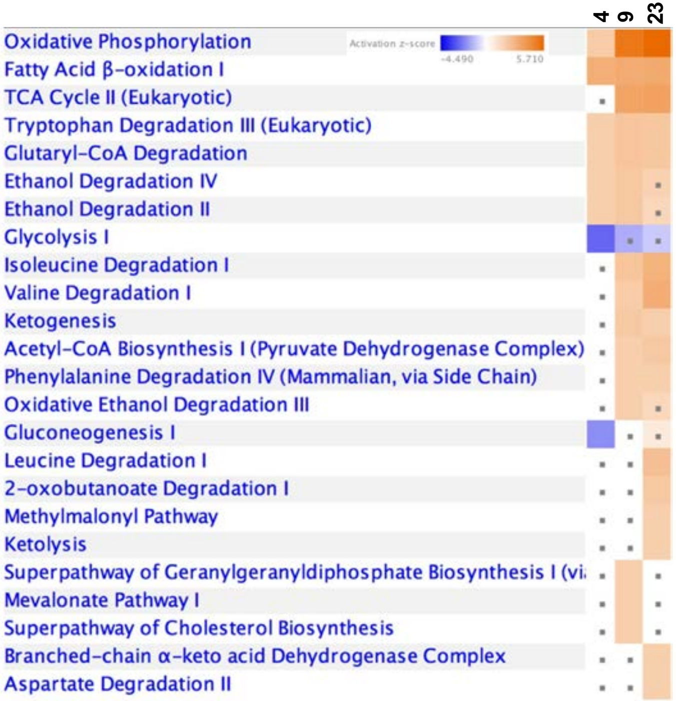
Comparison of transcriptomics analysis indicates that oxidative phosphorylation pathway is activated from day 9 on.



Post-natal mouse cardiomyocytes switch to oxidative phosphorylation for efficient ATP production starting at day 9 after birth.

Proteomics analysis shows energy switch in post-natal cardiomyocytes

Proteomics indicate major switch in energy metabolism and energy substrates after birth.



Oxidative phosphorylation

Fatty acid β-oxidation

Production of ATP, CO2, NADH

Glycolysis decreased

Ketone metabolism

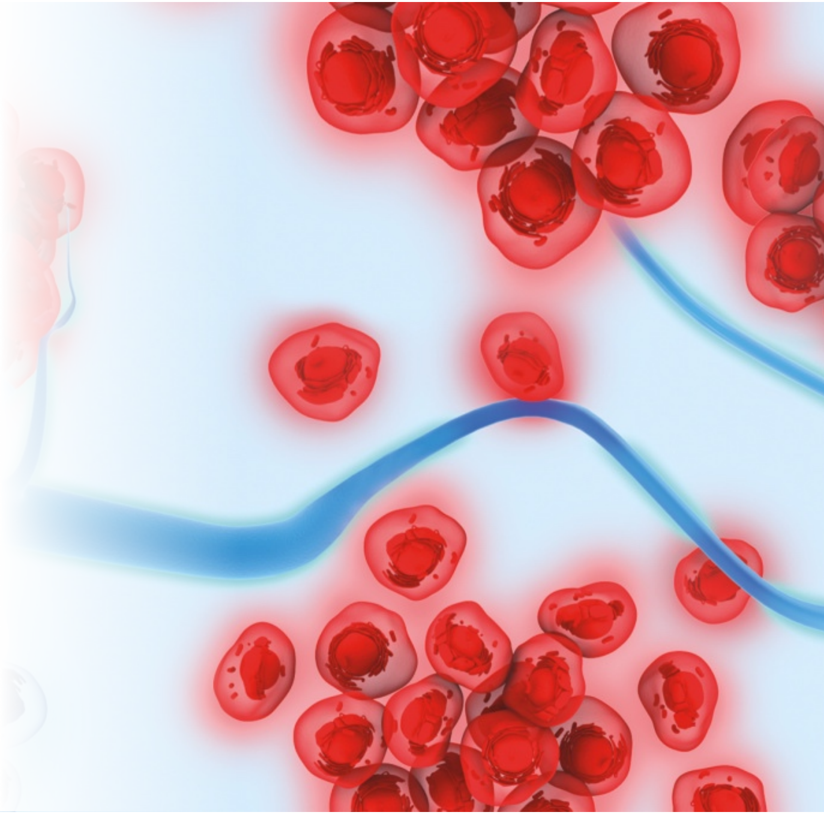
BCAA degradation

Post-natal mouse cardiomyocytes switch from glycolysis to oxidative phosphorylation, and increase fatty acid β-oxidation and branched-chain amino-acid degradation.

Transcriptomics, Proteomics and Metabolic Changes in Postnatal Mouse Heart analyzed with IPA and OmicSoft

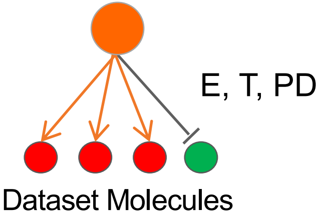
Explore the underlying transcriptional programs

Upstream Analysis



Network types in IPA

Upstream Regulator



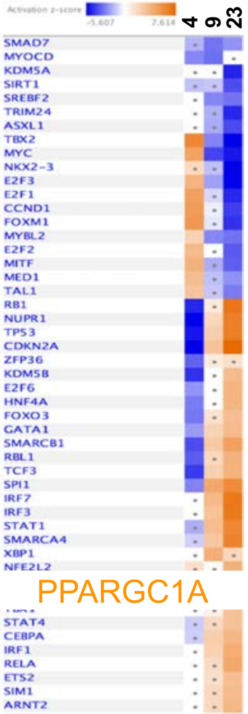
E, T, PD

Dataset Molecules

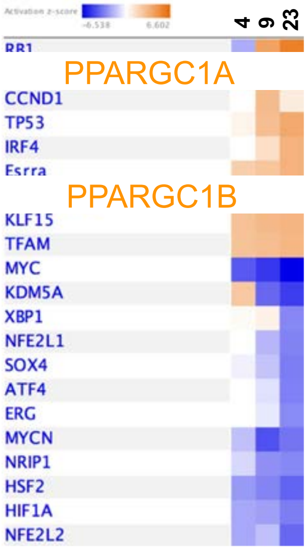
Multi-omics analysis indicate similar transcriptional drivers

Upstream Regulators Analysis of transcriptomics, proteomics and metabolomics show induction of fatty oxidation regulation by PPARG coactivators.

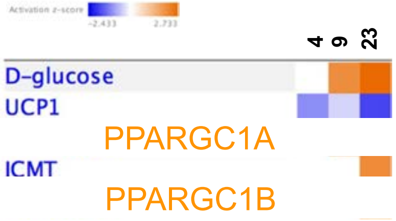
Transcriptomic



Proteomic



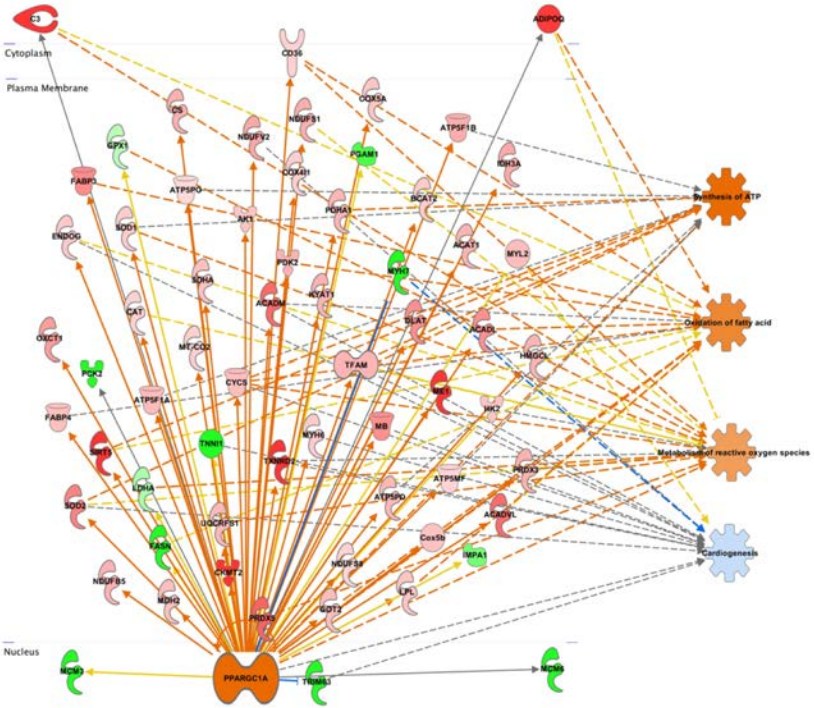
Metabolomic



Transcriptomics, Proteomics and Metabolic Changes in Postnatal Mouse Heart analyzed with IPA and OmicSoft

PPARGC1A is predicted to induce ATP synthesis

At day 23 post-birth, PPARGC1A is predicted to be activated and drives ATP synthesis and metabolism of ROS up through increase of fatty acid oxidation (transcriptomics).



PPARGC1A

Synthesis of ATP
p-value 8.01E-15

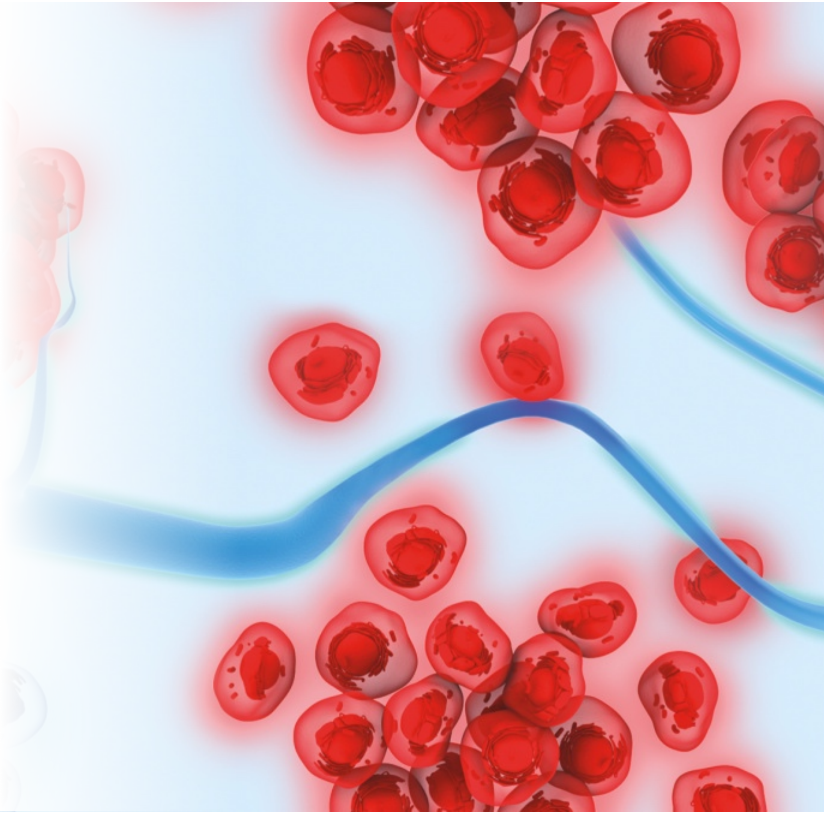
Oxidation of Fatty acid
p-value 4.61E-16

Metabolism of ROS
p-value 7.65E-12

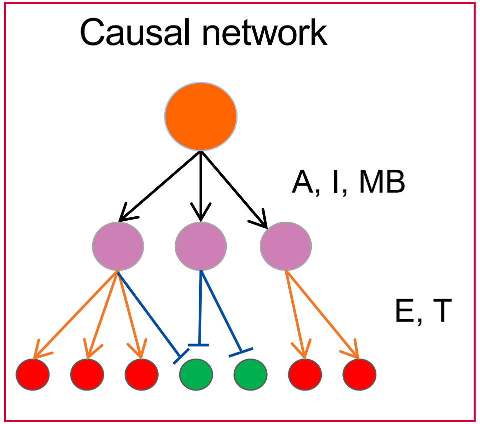
Cardiogenesis
P-value 4.03E-10

Generate hypotheses to validate in the lab

Causal Network

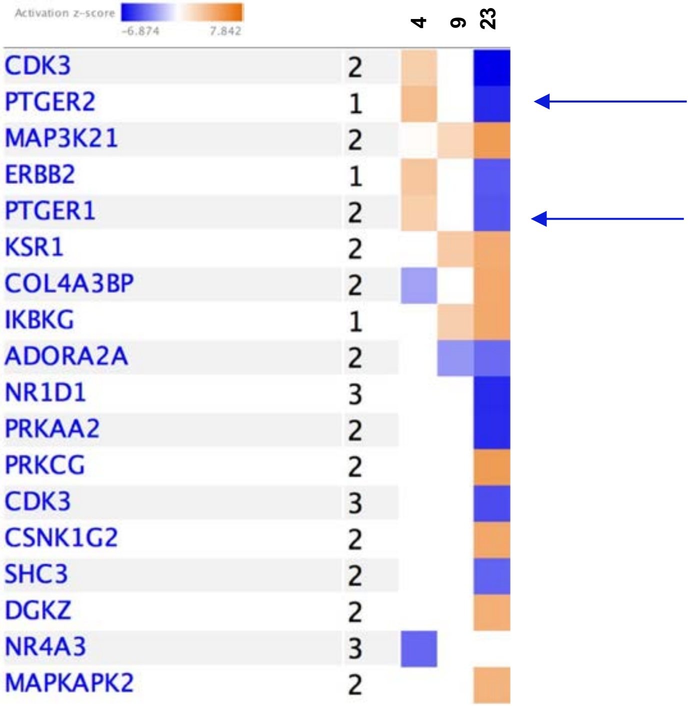


Network types in IPA



Causal Network Analysis of transcriptomics in post-natal mouse heart

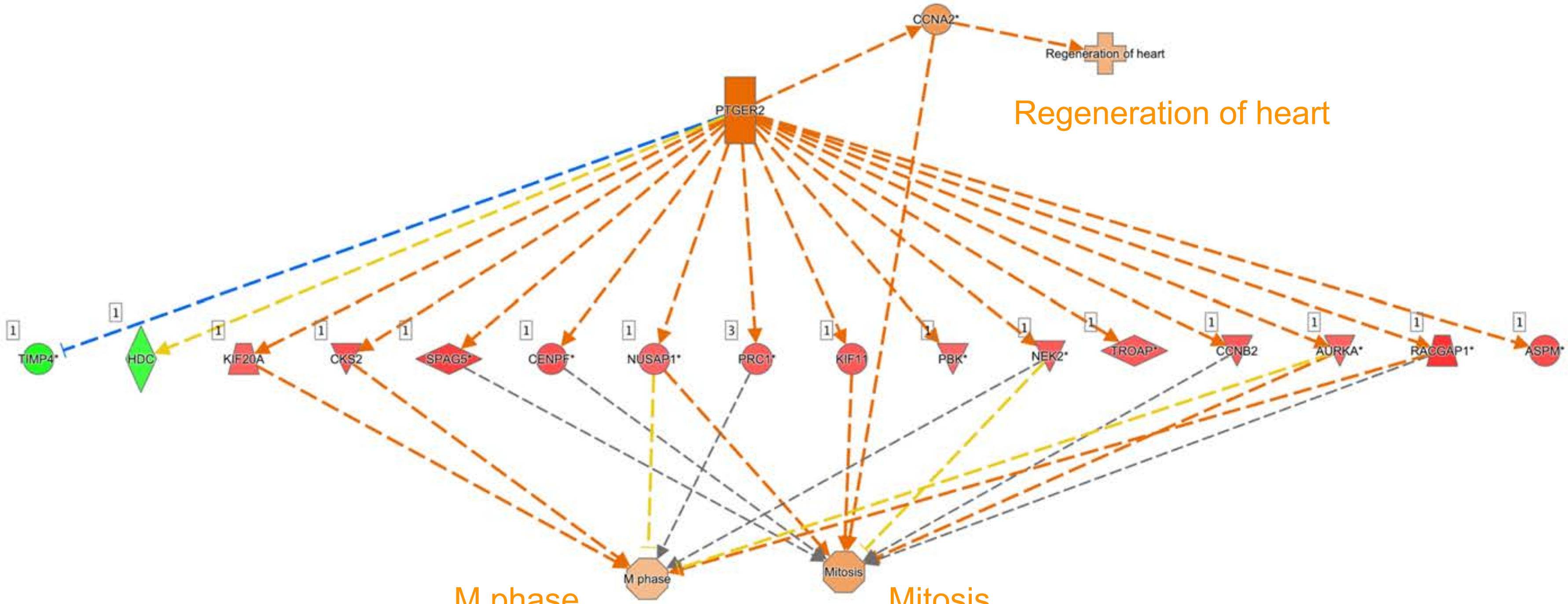
Comparison of Causal Network at day 4 and day 23, switch in usage of PTGER2 and PTGER1.



		4	9	23
CDK3	2	🟧		🟦
PTGER2	1	🟧		🟦
MAP3K21	2		🟧	🟧
ERBB2	1	🟧		🟦
PTGER1	2	🟧		🟦
KSR1	2		🟧	🟧
COL4A3BP	2	🟦		🟧
IKBKG	1		🟧	🟧
ADORA2A	2		🟦	🟦
NR1D1	3			🟦
PRKAA2	2			🟦
PRKCG	2			🟧
CDK3	3			🟦
CSNK1G2	2			🟧
SHC3	2			🟦
DGKZ	2			🟧
NR4A3	3	🟦		
MAPKAPK2	2			🟧

Regeneration of heart is predicted to be increased at day 4 post-birth

PTGER2 is predicted to be activated and may promote the regeneration of heart at day 4 post-birth.



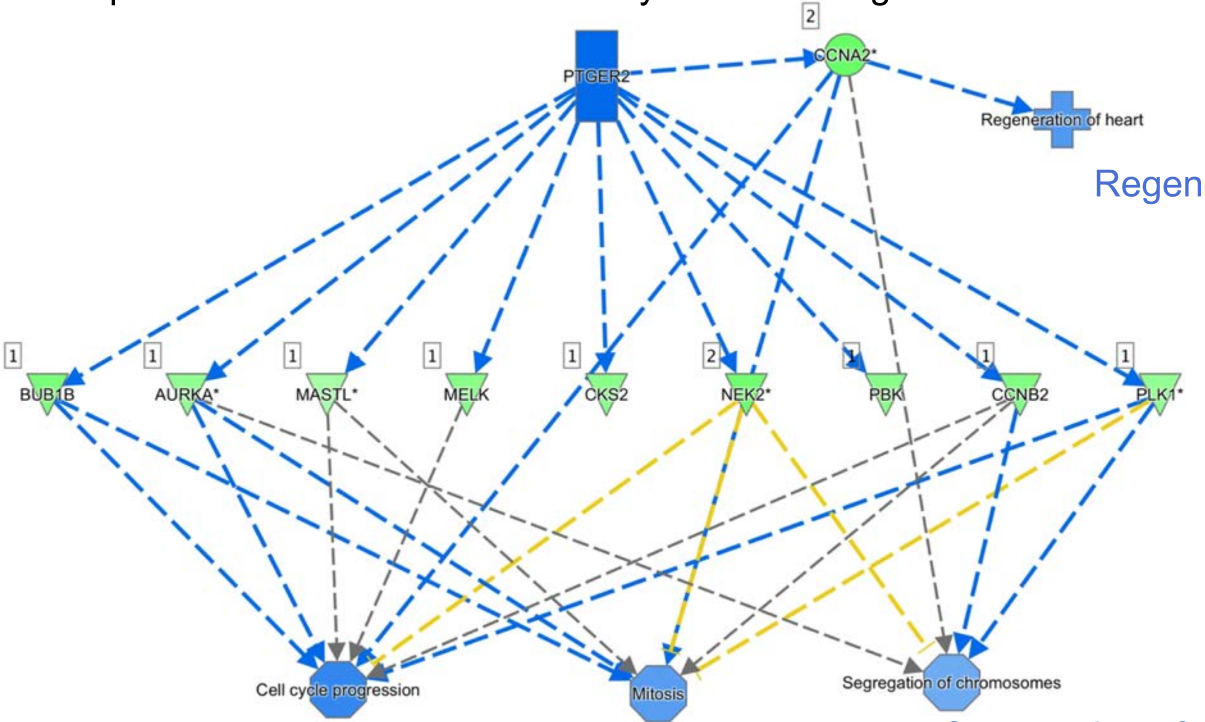
Regeneration of heart

M phase
P-value 2.96E-10

Mitosis
P-value 1.97E-10

Regeneration of heart is predicted to be decreased at day 23 post-birth

PTGER2 is predicted to be inhibited and may inhibit the regeneration of heart at day 23 post- birth.



Regeneration of heart

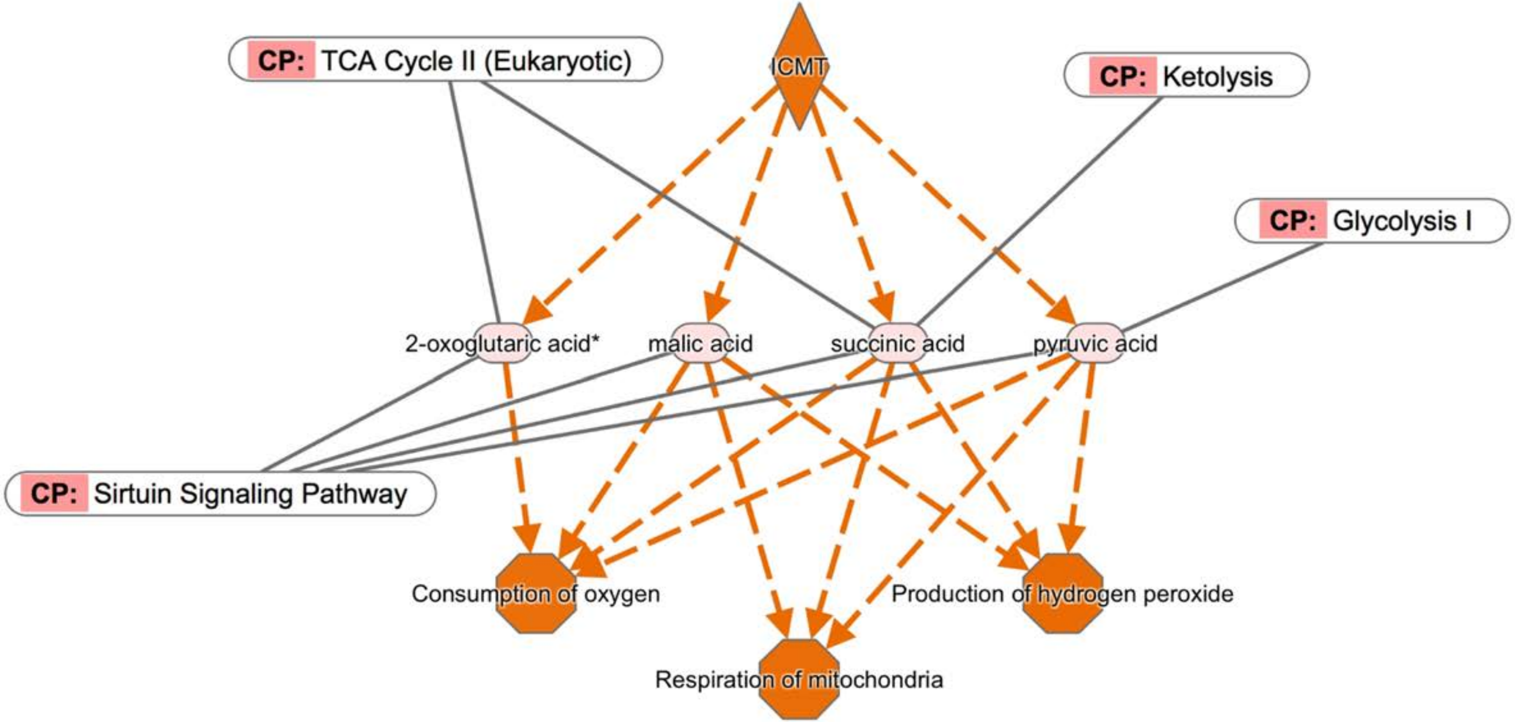
Cell cycle progression
p-value 2.33E-08

Mitosis
p-value 2.33E-08

Segregation of chromosomes
p-value 2.33E-08

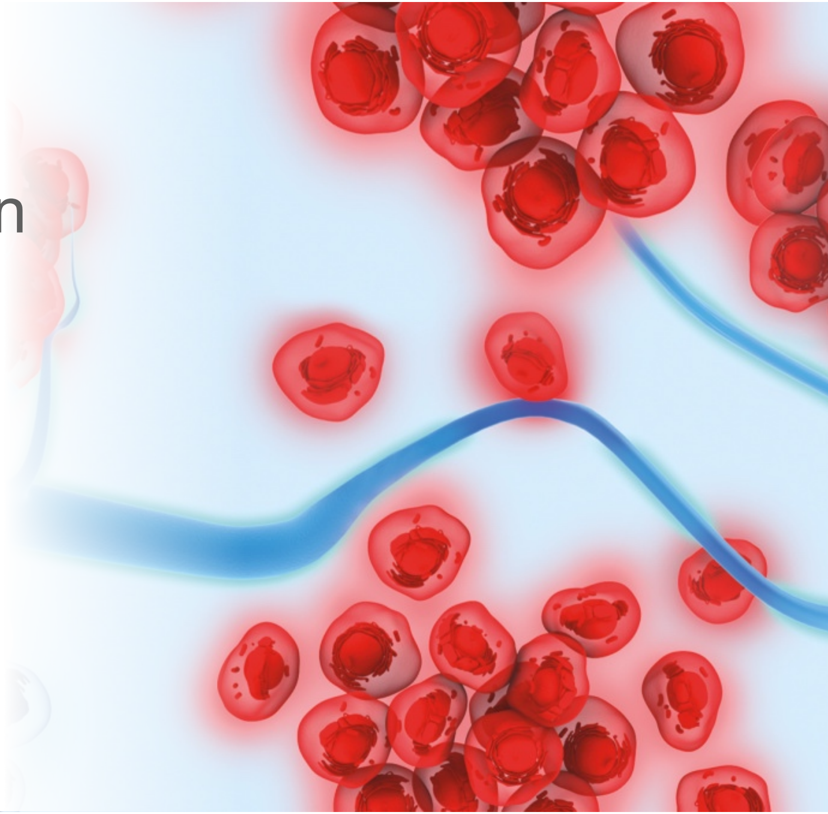
Regulator Effects predicts ICMT as a player in post-natal mouse heart

Comparison of metabolomics analysis shows that ICMT (Isoprenylcysteine carboxyl methyltransferase) is predicted to increase O2 consumption and oxidative phosphorylation at day 23 in post-natal mouse heart.



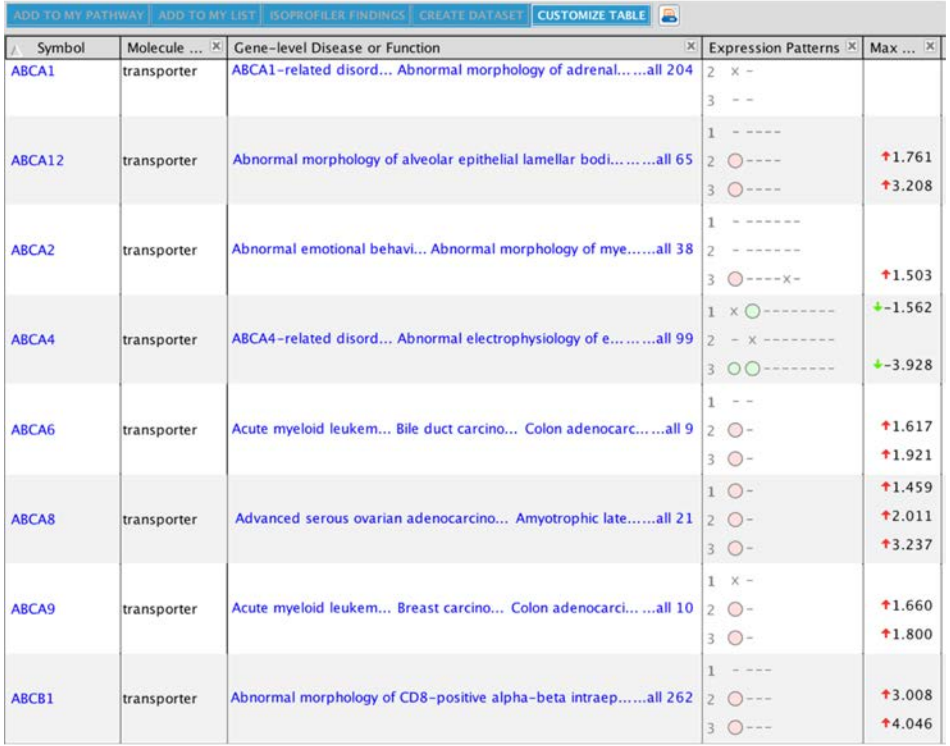
Identify tissue-enriched splicing variant and its expression pattern

IsoProfiler



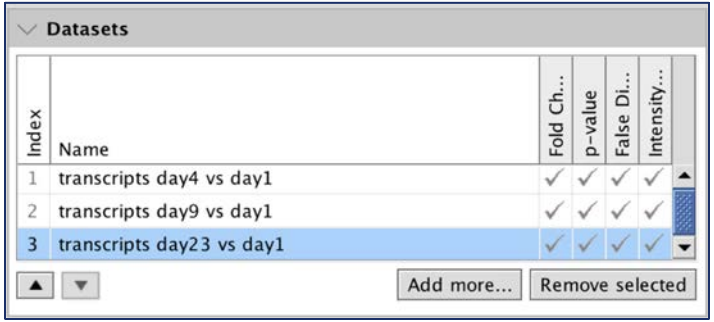
Isoforms differentially expressed observed in post-natal mouse heart

At q<0.05, 2256, 2965 and 6639 differentially expressed isoforms are found at day 4, day 9 and day 23 post-birth, respectively.



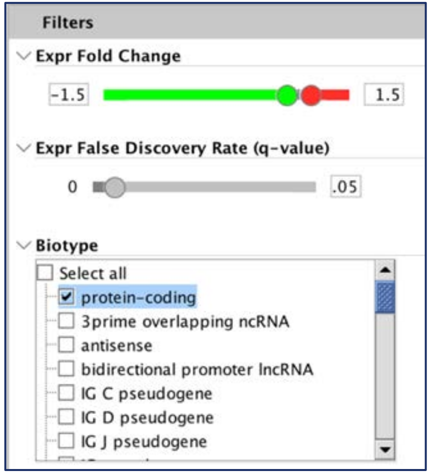
Symbol	Molecule ...	Gene-level Disease or Function	Expression Patterns	Max ...
ABCA1	transporter	ABCA1-related disord... Abnormal morphology of adrenal... ...all 204	2 x - 3 - -	
ABCA12	transporter	Abnormal morphology of alveolar epithelial lamellar bodi... ... ...all 65	1 - - - - - 2 ○- - - - 3 ○- - - -	↑1.761 ↑3.208
ABCA2	transporter	Abnormal emotional behavi... Abnormal morphology of mye... ...all 38	1 - - - - - - - 2 - - - - - - - 3 ○- - - - x -	↑1.503
ABCA4	transporter	ABCA4-related disord... Abnormal electrophysiology of e... ... ...all 99	1 x ○- - - - - - - - 2 - x - - - - - - - - 3 ○○- - - - - - - -	↓-1.562 ↓-3.928
ABCA6	transporter	Acute myeloid leukem... Bile duct carcino... Colon adenocarc... ...all 9	1 - - 2 ○- 3 ○-	↑1.617 ↑1.921
ABCA8	transporter	Advanced serous ovarian adenocarcino... Amyotrophic late... ...all 21	1 ○- 2 ○- 3 ○-	↑1.459 ↑2.011 ↑3.237
ABCA9	transporter	Acute myeloid leukem... Breast carcino... Colon adenocarci... ...all 10	1 x - 2 ○- 3 ○-	↑1.660 ↑1.800
ABCB1	transporter	Abnormal morphology of CD8-positive alpha-beta intraep... ...all 262	1 - - - - 2 ○- - - 3 ○- - -	↑3.008 ↑4.046

IsoProfiler to filter transcripts from post-natal mouse cardiomyocytes



Datasets

Index	Name	Fold Ch...	p-value	False Di...	Intensity...
1	transcripts day4 vs day1	✓	✓	✓	✓
2	transcripts day9 vs day1	✓	✓	✓	✓
3	transcripts day23 vs day1	✓	✓	✓	✓



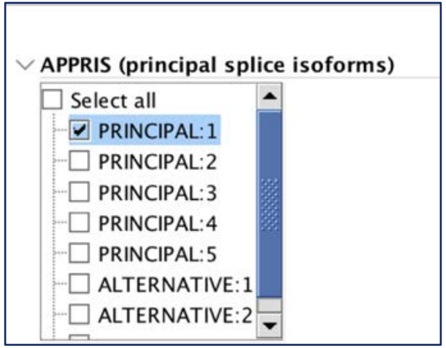
Filters

Expr Fold Change: -1.5 to 1.5

Expr False Discovery Rate (q-value): 0 to .05

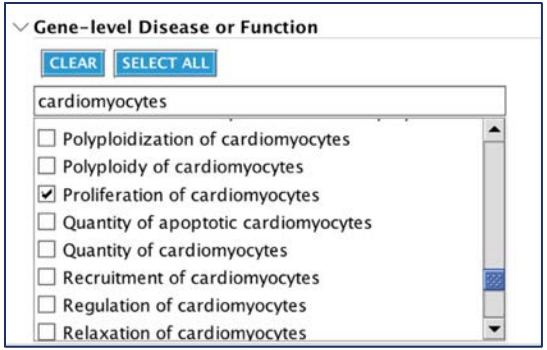
Biotype

- ☐ Select all
- ☑ protein-coding
- ☐ 3prime overlapping ncRNA
- ☐ antisense
- ☐ bidirectional promoter lncRNA
- ☐ IG C pseudogene
- ☐ IG D pseudogene
- ☐ IG J pseudogene



APPRIS (principal splice isoforms)

- ☐ Select all
- ☑ PRINCIPAL:1
- ☐ PRINCIPAL:2
- ☐ PRINCIPAL:3
- ☐ PRINCIPAL:4
- ☐ PRINCIPAL:5
- ☐ ALTERNATIVE:1
- ☐ ALTERNATIVE:2



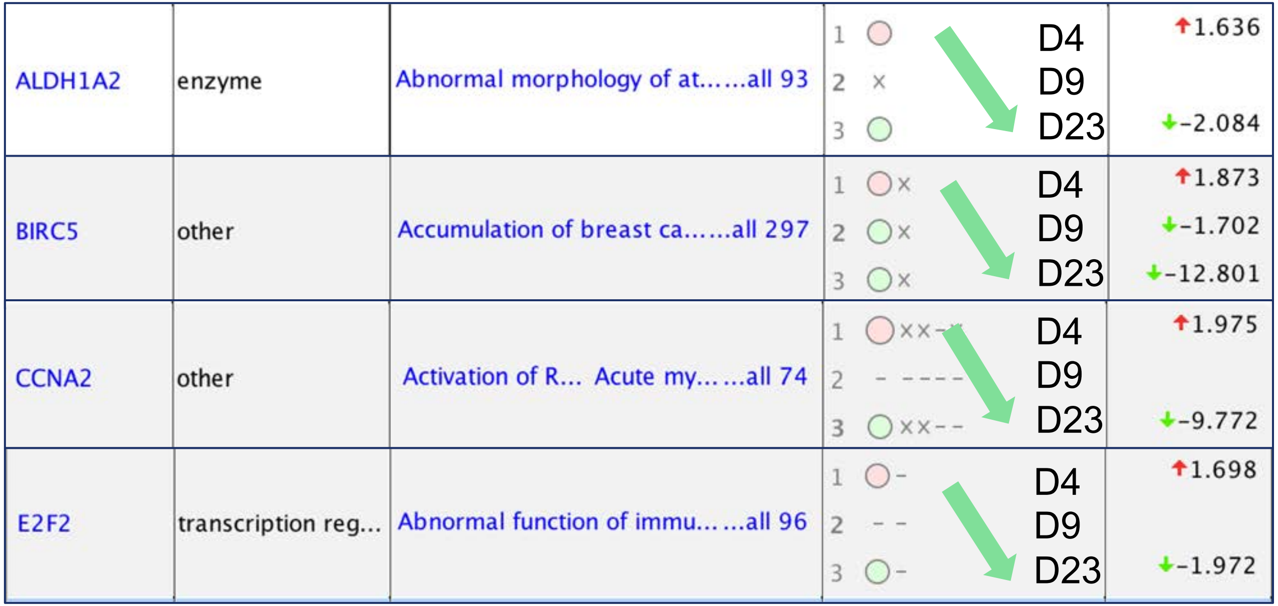
Gene-level Disease or Function

cardiomyocytes

- ☐ Polyploidization of cardiomyocytes
- ☐ Polyploidy of cardiomyocytes
- ☑ Proliferation of cardiomyocytes
- ☐ Quantity of apoptotic cardiomyocytes
- ☐ Quantity of cardiomyocytes
- ☐ Recruitment of cardiomyocytes
- ☐ Regulation of cardiomyocytes
- ☐ Relaxation of cardiomyocytes

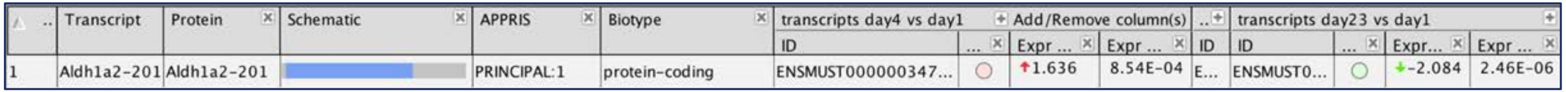
Isoforms involved in proliferation of cardiomyocytes

Principal isoforms of 4 genes of 21 after filtering are inversely regulated at day 4 and day 23 post-birth.



ALDH1A2	enzyme	Abnormal morphology of at... ...all 93	1 ○ 2 × 3 ○	D4 D9 D23	↑1.636 ↓-2.084
BIRC5	other	Accumulation of breast ca... ...all 297	1 ○× 2 ○× 3 ○×	D4 D9 D23	↑1.873 ↓-1.702 ↓-12.801
CCNA2	other	Activation of R... Acute my... ...all 74	1 ○××- 2 - ---- 3 ○××--	D4 D9 D23	↑1.975 ↓-9.772
E2F2	transcription reg...	Abnormal function of immu... ...all 96	1 ○- 2 - - 3 ○-	D4 D9 D23	↑1.698 ↓-1.972

Four isoforms are differentially expressed between day 4 and day 23

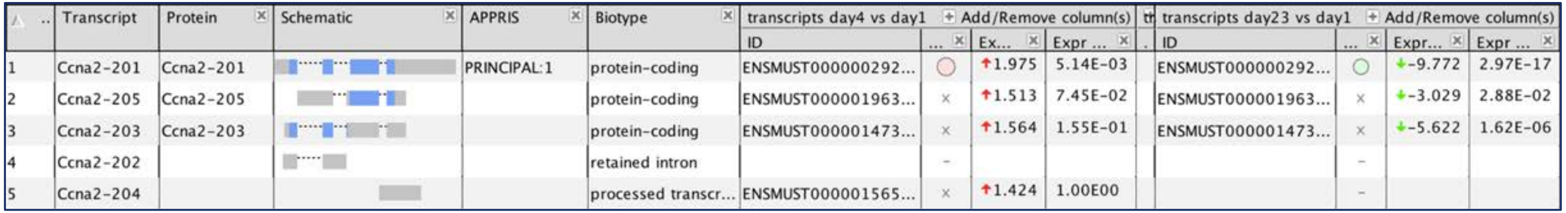


..	Transcript	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1		Add/Remove column(s)		..	transcripts day23 vs day1			
						ID	...	Expr ...	Expr ...	ID	ID	...	Expr...	Expr ...
1	Aldh1a2-201	Aldh1a2-201		PRINCIPAL:1	protein-coding	ENSMUST000000347...	○	↑1.636	8.54E-04	E...	ENSMUST0...	○	↓-2.084	2.46E-06

ALDH1A2 (retinoic acid producing enzyme) is necessary during the epicardial development.

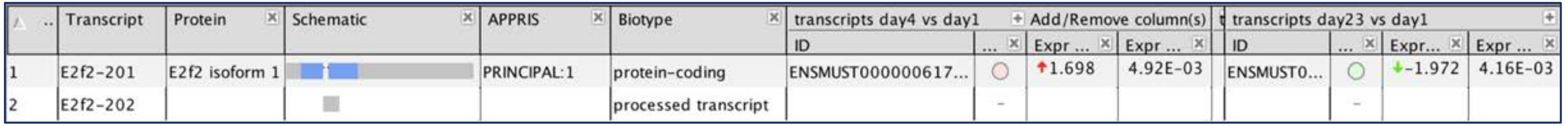
O...	Transcript	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1				transcripts day9 vs day1		Add/Remove column(s)		transcripts day23 vs day1			
						ID	...	Ex...	Expr ...	ID	...	Expr ...	Expr False ...	ID	...	Expr ...	Expr ...
1	Birc5-201	Birc5 isoform 1		PRINCIPAL:1	protein-coding	ENSMUST00...	○	↑1.873	2.33E-05	ENSMUST000...	○	↓-1.702	9.22E-04	ENSMUST0...	○	2.99E-28	2.89E-26
2	Birc5-202	Birc5 isoform 3			protein-coding	ENSMUST00...	×	↑2.071	1.88E-05	ENSMUST000...	×	↓-1.348	2.72E-01	ENSMUST0...	×	1.17E-11	3.82E-10

BIRC5 controls cardiomyocytes number in heart development, its overexpression promotes cell cycle progression. Its downregulation contributes to cell cycle arrest during postnatal cardiac development in a mouse model.



..	Transcript	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1		Add/Remove column(s)		tr	transcripts day23 vs day1		Add/Remove column(s)	
						ID	...	Ex...	Expr ...	.	ID	...	Expr...	Expr ...
1	Ccna2-201	Ccna2-201		PRINCIPAL:1	protein-coding	ENSMUST000000292...	○	↑1.975	5.14E-03		ENSMUST000000292...	○	↓-9.772	2.97E-17
2	Ccna2-205	Ccna2-205			protein-coding	ENSMUST000001963...	×	↑1.513	7.45E-02		ENSMUST000001963...	×	↓-3.029	2.88E-02
3	Ccna2-203	Ccna2-203			protein-coding	ENSMUST000001473...	×	↑1.564	1.55E-01		ENSMUST000001473...	×	↓-5.622	1.62E-06
4	Ccna2-202				retained intron		-					-		
5	Ccna2-204				processed transcr...	ENSMUST000001565...	×	↑1.424	1.00E00			-		

CCNA2 is silenced after birth in the mammalian heart and its constitutive expression enhances cardiomyocyte proliferation resulting in cardiac hyperplasia.

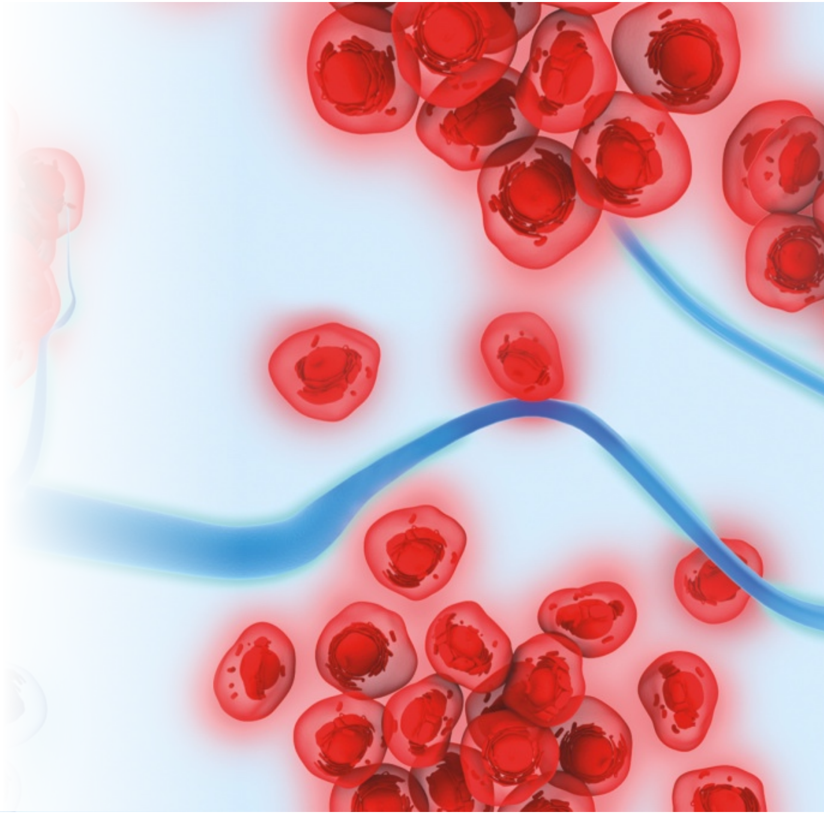


..	Transcript	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1		Add/Remove column(s)		t	transcripts day23 vs day1			
						ID	...	Expr ...	Expr ...		ID	...	Expr...	Expr ...
1	E2f2-201	E2f2 isoform 1		PRINCIPAL:1	protein-coding	ENSMUST000000617...	○	↑1.698	4.92E-03		ENSMUST0...	○	↓-1.972	4.16E-03
2	E2f2-202				processed transcript		-					-		

E2F2 has been shown to promote adult cardiomyocyte proliferation.

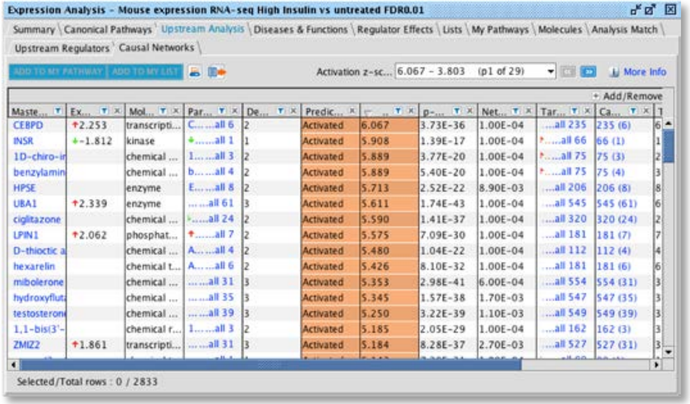
Compare your analysis to pre-computed datasets

Analysis Match – OmicSoft Lands



Introducing Analysis Match

How can you discover which analyses look like yours, to uncover insights from mechanistic similarities and differences?



Expression Analysis - Mouse expression RNA-seq High Insulin vs untreated FDR0.01

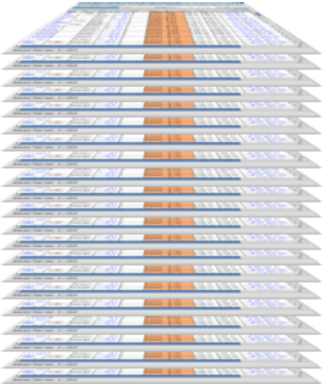
Activation z-sc... 6.067 - 3.803 (p1 of 29)

Maste...	Ex...	Mol...	Par...	De...	Predic...	...	p-...	Net...	Tar...	Ca...	T
CEBPD	↑2.253	transcripti...	C... ...all 6	2	Activated	6.067	3.73E-36	1.00E-04	....all 235	235 (6)	6
INSR	↓-1.812	kinase	↓......all 1	1	Activated	5.908	1.39E-17	1.00E-04	↑.....all 66	66 (1)	1
1D-chiro-i		chemical ...	1... ...all 3	2	Activated	5.889	3.77E-20	1.00E-04	↑.....all 75	75 (3)	2
benzylamin		chemical ...	b... ...all 4	2	Activated	5.889	5.40E-20	1.00E-04	↑.....all 75	75 (4)	3
HPSE		enzyme	E... ...all 8	2	Activated	5.713	2.52E-22	8.90E-03	....all 206	206 (8)	8
UBA1	↑2.339	enzyme	... ...all 61	3	Activated	5.611	1.74E-43	1.00E-04	....all 545	545 (61)	6
ciglitazone		chemical ...	......all 24	2	Activated	5.590	1.41E-37	1.00E-04	....all 320	320 (24)	2
LPIN1	↑2.062	phosphat...	↑......all 7	2	Activated	5.575	7.09E-30	1.00E-04	....all 181	181 (7)	7
D-thioctic a		chemical ...	A... ...all 4	2	Activated	5.480	1.04E-22	1.00E-04	....all 112	112 (4)	4
hexarelin		chemical t...	A... ...all 6	2	Activated	5.426	8.10E-32	1.00E-04	....all 181	181 (6)	6
mibolerone		chemical ...	... ...all 31	3	Activated	5.353	2.98E-41	6.00E-04	....all 554	554 (31)	3
hydroxyfluta		chemical ...	... ...all 35	3	Activated	5.345	1.57E-38	1.70E-03	....all 547	547 (35)	3
testosteron		chemical ...	... ...all 39	3	Activated	5.250	3.22E-39	1.10E-03	....all 549	549 (39)	3
1,1-bis(3'-		chemical r...	1... ...all 3	2	Activated	5.185	2.05E-29	1.00E-04	....all 162	162 (3)	3
ZMIZ2	↑1.861	transcripti...	... ...all 31	3	Activated	5.184	8.28E-37	2.70E-03	....all 527	527 (31)	3

Selected/Total rows : 0 / 2833

Match against

>52,000 analyses



Which analyses have similar Upstream Regulators, Canonical Pathways, Diseases and Functions, etc.?

Analysis Match combines knowledge with data

Array Express
GEO
SRA
TCGA
LINCS
Etc.

Reprocessed using the same pipeline

OmicSoft
Array Studio

>52,000
comparison datasets

Built from
>300,000 samples

Journal articles
Clinical Trials
COSMIC
OMIM
MGD
Etc.

>6.7 million
curated
Findings

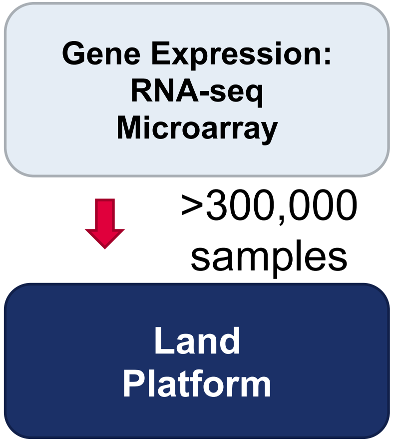
Curation & QA

INGENUITY
PATHWAY ANALYSIS

- Biological analyses of each dataset
- Compare your analysis to all OmicSoft analyses

>52,000 comparison datasets from OmicSoft Lands in IPA

OmicSoft Lands, expression data in IPA



Gene Expression:
RNA-seq
Microarray

>300,000 samples

Land Platform

What >52,000 Land Comparisons represent

DiseaseLand

HumanDisease (7886)
- 486 diseases
- 245 tissues
- 64 expression platforms
- 1162 RNA-seq datasets

MouseDisease (7425)
- 297 diseases
- 207 tissues
- 53 expression platforms
- 1650 RNA-seq datasets

RatDisease (743)
- 34 diseases
- 54 tissues

LINCS (28,234)
- 23 cell lines
- 374 chemical treatments or gene overexpression
- 226 different targets (or groups of target genes)

OncoLand

OncoGeo (2228)
- 135 cancers
- 72 tissues
- 41 expression platforms
- 353 RNA-seq datasets

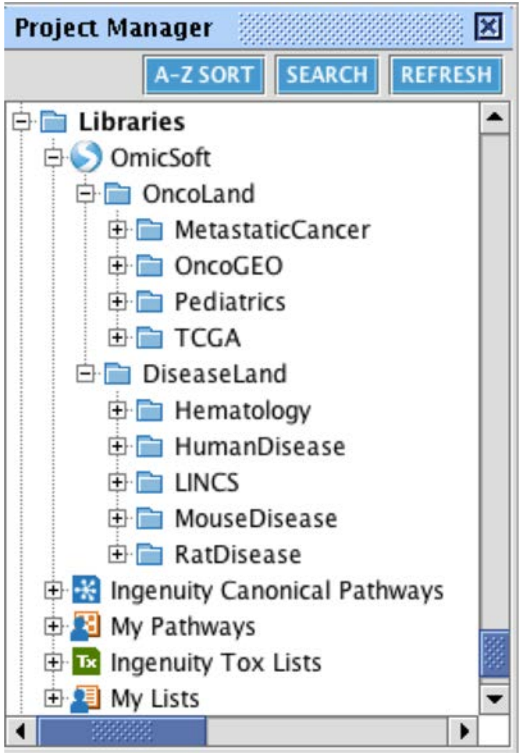
TCGA (4789)
- 33 cancers
- 27 tissues
- 385 different mutational status / clinical signs

Pediatrics (444)
- 47 cancers
- 23 tissues

Metastatic Cancer (81)
- 27 cancers
- 18 tissues

Hematology (1013)
- 36 cancers
- 10 tissues

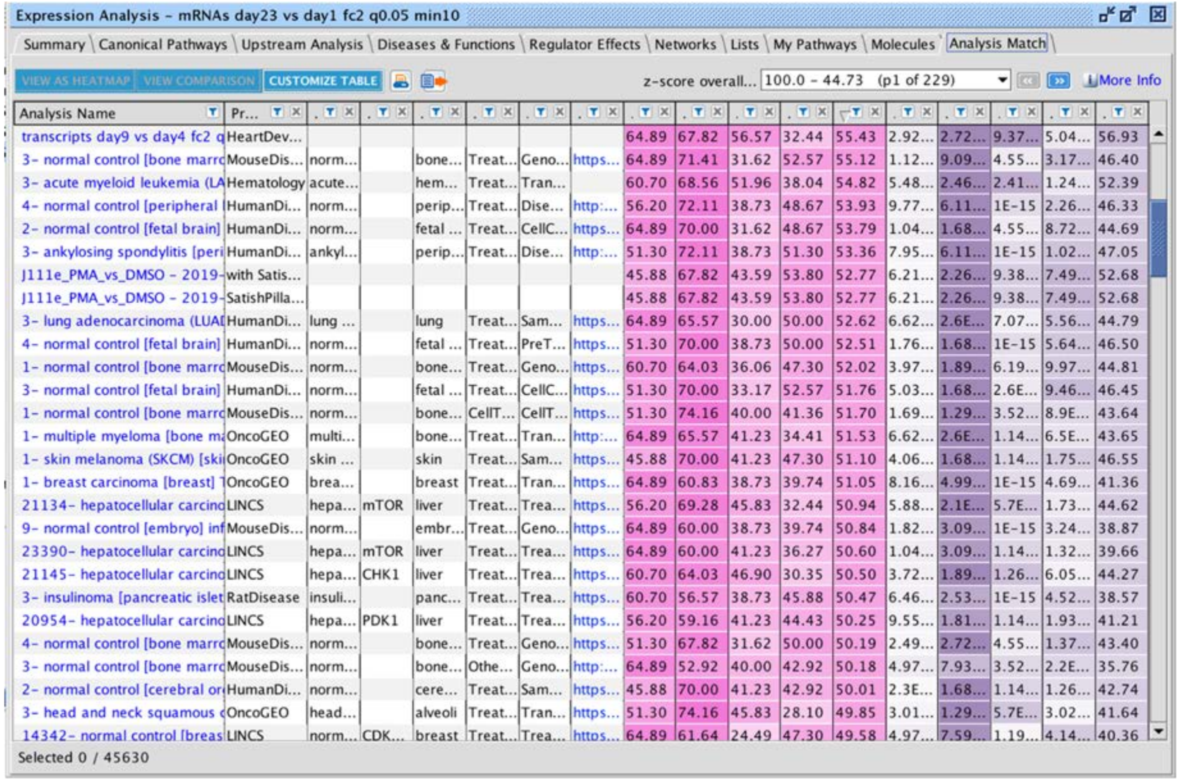
OmicSoft datasets stored and analyzed in IPA



- Libraries
  - OmicSoft
    - OncoLand
      - MetastaticCancer
      - OncoGEO
      - Pediatrics
      - TCGA
    - DiseaseLand
      - Hematology
      - HumanDisease
      - LINCS
      - MouseDisease
      - RatDisease
  - Ingenuity Canonical Pathways
  - My Pathways
  - Ingenuity Tox Lists
  - My Lists

Analysis Match: Postnatal mouse heart day 23 vs. precomputed datasets

Looking for a similar pattern at CP (Canonical Pathways), UR (Upstream Analysis), DEA (Downstream Effect Analysis) and CN (Causal Network) levels



Expression Analysis - mRNAs day23 vs day1 fc2 q0.05 min10

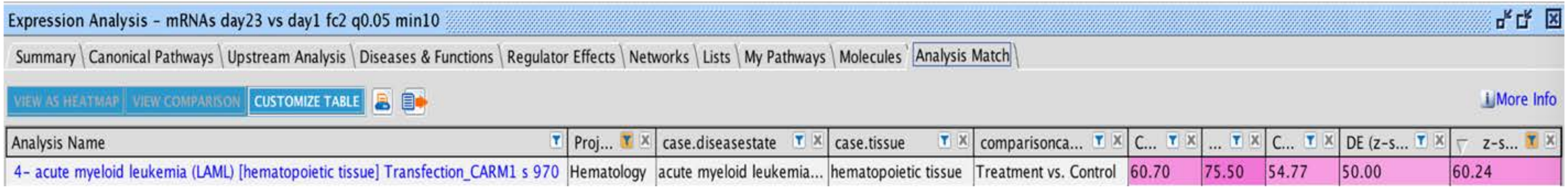
z-score overall... 100.0 - 44.73 (p1 of 229)

Analysis Name	Pr...	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
transcripts day9 vs day4 fc2 q	HeartDev...							64.89	67.82	56.57	32.44	55.43	2.92...	2.72...	9.37...	5.04...	56.93
3- normal control [bone marro	MouseDis...	norm...		bone...	Treat...	Geno...	https...	64.89	71.41	31.62	52.57	55.12	1.12...	9.09...	4.55...	3.17...	46.40
3- acute myeloid leukemia (LA	Hematology	acute...		hem...	Treat...	Tran...		60.70	68.56	51.96	38.04	54.82	5.48...	2.46...	2.41...	1.24...	52.39
4- normal control [peripheral	HumanDi...	norm...		perip...	Treat...	Dise...	http:...	56.20	72.11	38.73	48.67	53.93	9.77...	6.11...	1E-15	2.26...	46.33
2- normal control [fetal brain]	HumanDi...	norm...		fetal ...	Treat...	CellC...	https...	64.89	70.00	31.62	48.67	53.79	1.04...	1.68...	4.55...	8.72...	44.69
3- ankylosing spondylitis [peri	HumanDi...	ankyl...		perip...	Treat...	Dise...	http:...	51.30	72.11	38.73	51.30	53.36	7.95...	6.11...	1E-15	1.02...	47.05
J111e_PMA_vs_DMSO - 2019-	with Satis...							45.88	67.82	43.59	53.80	52.77	6.21...	2.26...	9.38...	7.49...	52.68
J111e_PMA_vs_DMSO - 2019-	SatishPilla...							45.88	67.82	43.59	53.80	52.77	6.21...	2.26...	9.38...	7.49...	52.68
3- lung adenocarcinoma (LUAD	HumanDi...	lung ...		lung	Treat...	Sam...	https...	64.89	65.57	30.00	50.00	52.62	6.62...	2.6E...	7.07...	5.56...	44.79
4- normal control [fetal brain]	HumanDi...	norm...		fetal ...	Treat...	PreT...	https...	51.30	70.00	38.73	50.00	52.51	1.76...	1.68...	1E-15	5.64...	46.50
1- normal control [bone marro	MouseDis...	norm...		bone...	Treat...	Geno...	https...	60.70	64.03	36.06	47.30	52.02	3.97...	1.89...	6.19...	9.97...	44.81
3- normal control [fetal brain]	HumanDi...	norm...		fetal ...	Treat...	CellC...	https...	51.30	70.00	33.17	52.57	51.76	5.03...	1.68...	2.6E...	9.46...	46.45
1- normal control [bone marro	MouseDis...	norm...		bone...	CellT...	CellT...	https...	51.30	74.16	40.00	41.36	51.70	1.69...	1.29...	3.52...	8.9E...	43.64
1- multiple myeloma [bone ma	OncoGEO	multi...		bone...	Treat...	Tran...	http:...	64.89	65.57	41.23	34.41	51.53	6.62...	2.6E...	1.14...	6.5E...	43.65
1- skin melanoma (SKCM) [ski	OncoGEO	skin ...		skin	Treat...	Sam...	https...	45.88	70.00	41.23	47.30	51.10	4.06...	1.68...	1.14...	1.75...	46.55
1- breast carcinoma [breast] T	OncoGEO	brea...		breast	Treat...	Tran...	https...	64.89	60.83	38.73	39.74	51.05	8.16...	4.99...	1E-15	4.69...	41.36
21134- hepatocellular carcino	LINCS	hepa...	mTOR	liver	Treat...	Trea...	https...	56.20	69.28	45.83	32.44	50.94	5.88...	2.1E...	5.7E...	1.73...	44.62
9- normal control [embryo] inf	MouseDis...	norm...		embr...	Treat...	Geno...	https...	64.89	60.00	38.73	39.74	50.84	1.82...	3.09...	1E-15	3.24...	38.87
23390- hepatocellular carcino	LINCS	hepa...	mTOR	liver	Treat...	Trea...	https...	64.89	60.00	41.23	36.27	50.60	1.04...	3.09...	1.14...	1.32...	39.66
21145- hepatocellular carcino	LINCS	hepa...	CHK1	liver	Treat...	Trea...	https...	60.70	64.03	46.90	30.35	50.50	3.72...	1.89...	1.26...	6.05...	44.27
3- insulinoma [pancreatic islet	RatDisease	insuli...		panc...	Treat...	Trea...	https...	60.70	56.57	38.73	45.88	50.47	6.46...	2.53...	1E-15	4.52...	38.57
20954- hepatocellular carcino	LINCS	hepa...	PDK1	liver	Treat...	Trea...	https...	56.20	59.16	41.23	44.43	50.25	9.55...	1.81...	1.14...	1.93...	41.21
4- normal control [bone marro	MouseDis...	norm...		bone...	Treat...	Geno...	https...	51.30	67.82	31.62	50.00	50.19	2.49...	2.72...	4.55...	1.37...	43.40
3- normal control [bone marro	MouseDis...	norm...		bone...	Othe...	Geno...	http:...	64.89	52.92	40.00	42.92	50.18	4.97...	7.93...	3.52...	2.2E...	35.76
2- normal control [cerebral or	HumanDi...	norm...		cere...	Treat...	Sam...	https...	45.88	70.00	41.23	42.92	50.01	2.3E...	1.68...	1.14...	1.26...	42.74
3- head and neck squamous c	OncoGEO	head...		alveoli	Treat...	Tran...	https...	51.30	74.16	45.83	28.10	49.85	3.01...	1.29...	5.7E...	3.02...	41.64
14342- normal control [breas	LINCS	norm...	CDK...	breast	Treat...	Trea...	https...	64.89	61.64	24.49	47.30	49.58	4.97...	7.59...	1.19...	4.14...	40.36

Selected 0 / 45630

Analysis Match: Postnatal mouse heart day 23 vs. precomputed datasets

Filtering with unique criteria on overall Z-score indicating highest similar pattern possible between day 23 vs day 1 and others precomputed analyses.



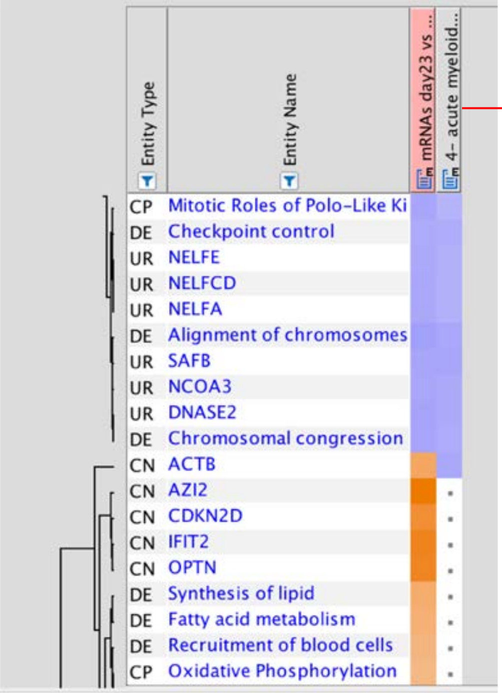
Expression Analysis - mRNAs day23 vs day1 fc2 q0.05 min10

Analysis Name	Proj...	case.diseasestate	case.tissue	comparisonca...	C...	...	C...	DE (z-s...	z-s...
4- acute myeloid leukemia (LAML) [hematopoietic tissue] Transfection_CARM1 s 970	Hematology	acute myeloid leukemia...	hematopoietic tissue	Treatment vs. Control	60.70	75.50	54.77	50.00	60.24

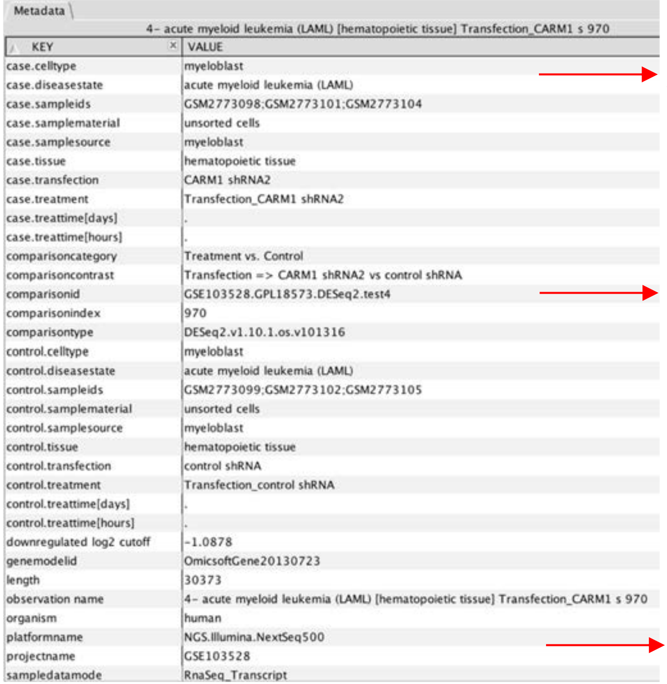
Z-score % > 60

Analysis Match: Postnatal mouse heart day 23 vs. precomputed datasets

Highest similarity at Canonical Pathways, Upstream Regulators, Causal Networks and Diseases & Functions is found with a cancer dataset.



Entity Type	Entity Name
CP	Mitotic Roles of Polo-Like Ki
DE	Checkpoint control
UR	NELFE
UR	NELFCD
UR	NELFA
DE	Alignment of chromosomes
UR	SAFB
UR	NCOA3
UR	DNASE2
DE	Chromosomal congression
CN	ACTB
CN	AZI2
CN	CDKN2D
CN	IFIT2
CN	OPTN
DE	Synthesis of lipid
DE	Fatty acid metabolism
DE	Recruitment of blood cells
CP	Oxidative Phosphorylation



4- acute myeloid leukemia (LAML) [hematopoietic tissue] Transfection_CARM1 s 970

KEY	VALUE
case.celltype	myeloblast
case.diseasestate	acute myeloid leukemia (LAML)
case.sampleids	GSM2773098;GSM2773101;GSM2773104
case.samplematerial	unsorted cells
case.samplesource	myeloblast
case.tissue	hematopoietic tissue
case.transfection	CARM1 shRNA2
case.treatment	Transfection_CARM1 shRNA2
case.treattime[days]	.
case.treattime[hours]	.
comparisoncategory	Treatment vs. Control
comparisoncontrast	Transfection => CARM1 shRNA2 vs control shRNA
comparisonid	GSE103528.GPL18573.DESeq2.test4
comparisonindex	970
comparisontype	DESeq2.v1.10.1.os.v101316
control.celltype	myeloblast
control.diseasestate	acute myeloid leukemia (LAML)
control.sampleids	GSM2773099;GSM2773102;GSM2773105
control.samplematerial	unsorted cells
control.samplesource	myeloblast
control.tissue	hematopoietic tissue
control.transfection	control shRNA
control.treatment	Transfection_control shRNA
control.treattime[days]	.
control.treattime[hours]	.
downregulated log2 cutoff	-1.0878
genemodelid	OmicsoftGene20130723
length	30373
observation name	4- acute myeloid leukemia (LAML) [hematopoietic tissue] Transfection_CARM1 s 970
organism	human
platformname	NGS.Illumina.NextSeq500
projectname	GSE103528
sampledatamode	RnaSeq_Transcript

Acute Myeloid Leukemia

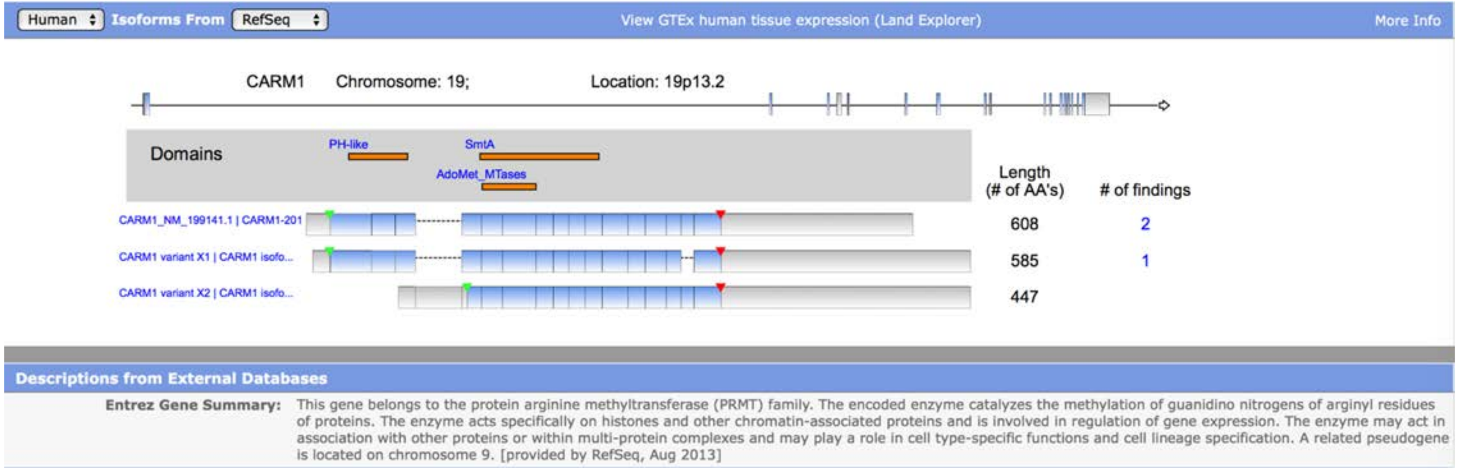
CARM1 shRNA vs control shRNA

GSE103528

What we know about CARM1…

CARM1 is an important regulator in embryonic development and cellular differentiation.

- CARM1 is “Co-activator-associated arginine methyltransferase 1”
- CARM1 adds asymmetric dimethylation to arginine residues in histones, with specificity for H3R17 and H3R26 and other protein substrates (RUNX1, and members of the SWI/SNF,…).
- CARM1 regulates critical cellular processes such as RNA splicing and autophagy.
- In solid tumors, overexpression of CARM1 correlates with cancer cell proliferation, metastasis, and poor survival outcomes.



CARM1 Chromosome: 19; Location: 19p13.2

	Length (# of AA's)	# of findings
CARM1_NM_199141.1 | CARM1-201	608	2
CARM1 variant X1 | CARM1 isofo...	585	1
CARM1 variant X2 | CARM1 isofo...	447	

Descriptions from External Databases

Entrez Gene Summary: This gene belongs to the protein arginine methyltransferase (PRMT) family. The encoded enzyme catalyzes the methylation of guanidino nitrogens of arginyl residues of proteins. The enzyme acts specifically on histones and other chromatin-associated proteins and is involved in regulation of gene expression. The enzyme may act in association with other proteins or within multi-protein complexes and may play a role in cell type-specific functions and cell lineage specification. A related pseudogene is located on chromosome 9. [provided by RefSeq, Aug 2013]

Unique analysis sharing similar pattern with mRNA day 23 is GS103528

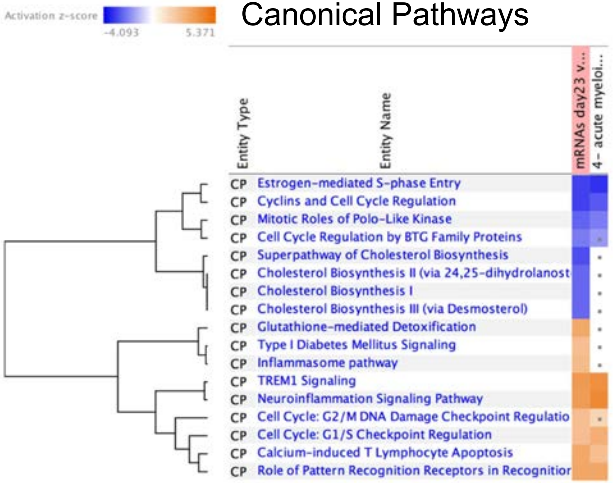
GSE103528: CARM1 is essential for myeloid leukemogenesis but dispensable for normal hematopoiesis. Greenblatt SM et al. Cancer Cell, 2018.

- 3 leukemia cell lines treated with short hairpin inhibition of CARM1 or short hairpin scramble control.
- Knockdown of CARM1 impairs cell cycle progression, induces apoptosis and downregulated E2F target genes in leukemia cell lines

Hypothesis: CARM1 may be involved as well in the post-natal mouse heart biology

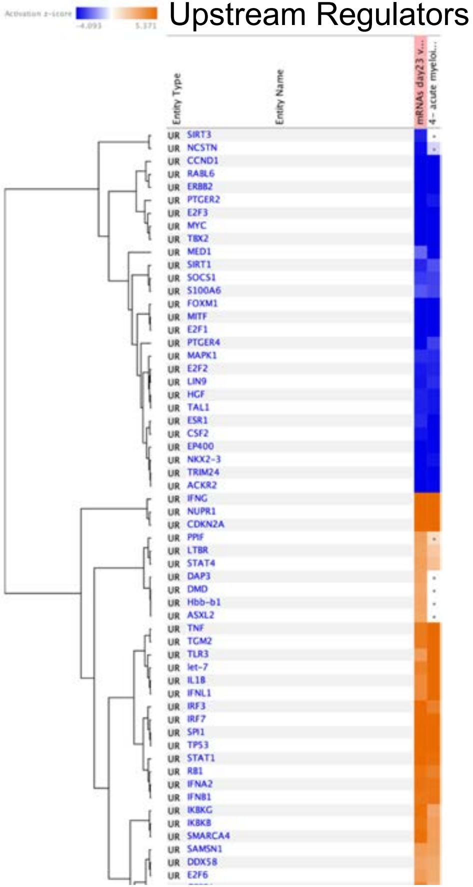
Knockdown of CARM1 induces a similar program to day 23 post-natal heart

Canonical Pathways



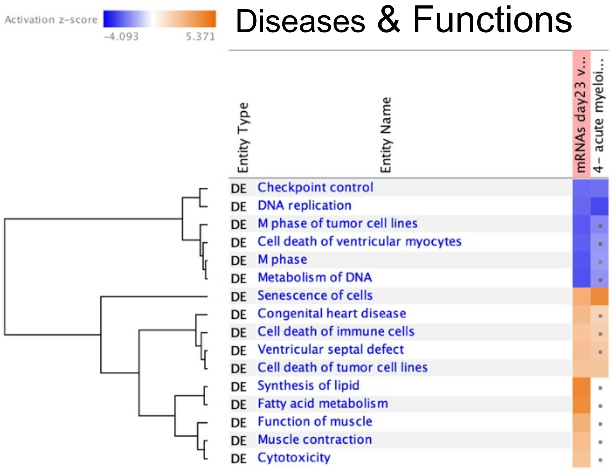
Entity Type	Entity Name
CP	Estrogen-mediated S-phase Entry
CP	Cyclins and Cell Cycle Regulation
CP	Mitotic Roles of Polo-Like Kinase
CP	Cell Cycle Regulation by BTG Family Proteins
CP	Superpathway of Cholesterol Biosynthesis
CP	Cholesterol Biosynthesis II (via 24,25-dihydrolanost
CP	Cholesterol Biosynthesis I
CP	Cholesterol Biosynthesis III (via Desmosterol)
CP	Glutathione-mediated Detoxification
CP	Type I Diabetes Mellitus Signaling
CP	Inflammasome pathway
CP	TREM1 Signaling
CP	Neuroinflammation Signaling Pathway
CP	Cell Cycle: G2/M DNA Damage Checkpoint Regulatio
CP	Cell Cycle: G1/S Checkpoint Regulation
CP	Calcium-induced T Lymphocyte Apoptosis
CP	Role of Pattern Recognition Receptors in Recognitior

Upstream Regulators



Entity Type	Entity Name
UR	SIRT3
UR	NCSTN
UR	CCND1
UR	RABL6
UR	ERBB2
UR	PTGER2
UR	E2F3
UR	MYC
UR	TBX2
UR	MED1
UR	SIRT1
UR	SOCS1
UR	S100A6
UR	FOXM1
UR	MITF
UR	E2F1
UR	PTGER4
UR	MAPK1
UR	E2F2
UR	LIN9
UR	HGF
UR	TAL1
UR	ESR1
UR	CSF2
UR	EP400
UR	NKX2-3
UR	TRIM24
UR	ACKR2
UR	IFNG
UR	NUPR1
UR	CDKN2A
UR	PPIF
UR	LTBR
UR	STAT4
UR	DAP3
UR	DMD
UR	Hbb-b1
UR	ASXL2
UR	TNF
UR	TGM2
UR	TLR3
UR	let-7
UR	IL1B
UR	IFNL1
UR	IRF3
UR	IRF7
UR	SPI1
UR	TP53
UR	STAT1
UR	RB1
UR	IFNA2
UR	IFNB1
UR	IKBKG
UR	IKBKB
UR	SMARCA4
UR	SAMSN1
UR	DDX58
UR	E2F6

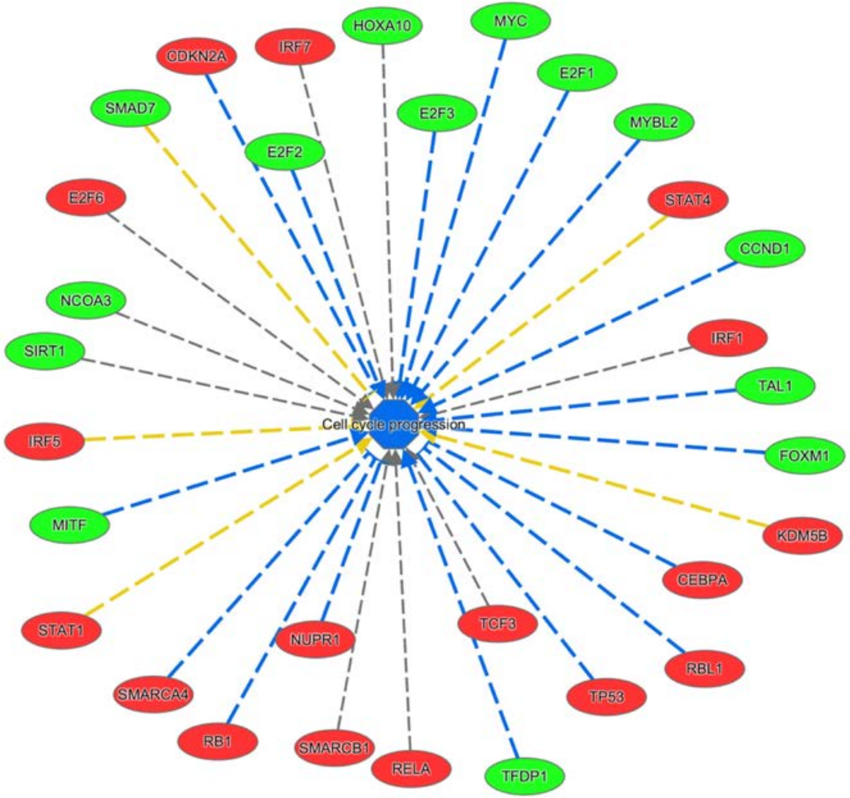
Diseases & Functions



Entity Type	Entity Name
DE	Checkpoint control
DE	DNA replication
DE	M phase of tumor cell lines
DE	Cell death of ventricular myocytes
DE	M phase
DE	Metabolism of DNA
DE	Senescence of cells
DE	Congenital heart disease
DE	Cell death of immune cells
DE	Ventricular septal defect
DE	Cell death of tumor cell lines
DE	Synthesis of lipid
DE	Fatty acid metabolism
DE	Function of muscle
DE	Muscle contraction
DE	Cytotoxicity

Upstream Regulator Analysis indicates inhibition of cell cycle progression

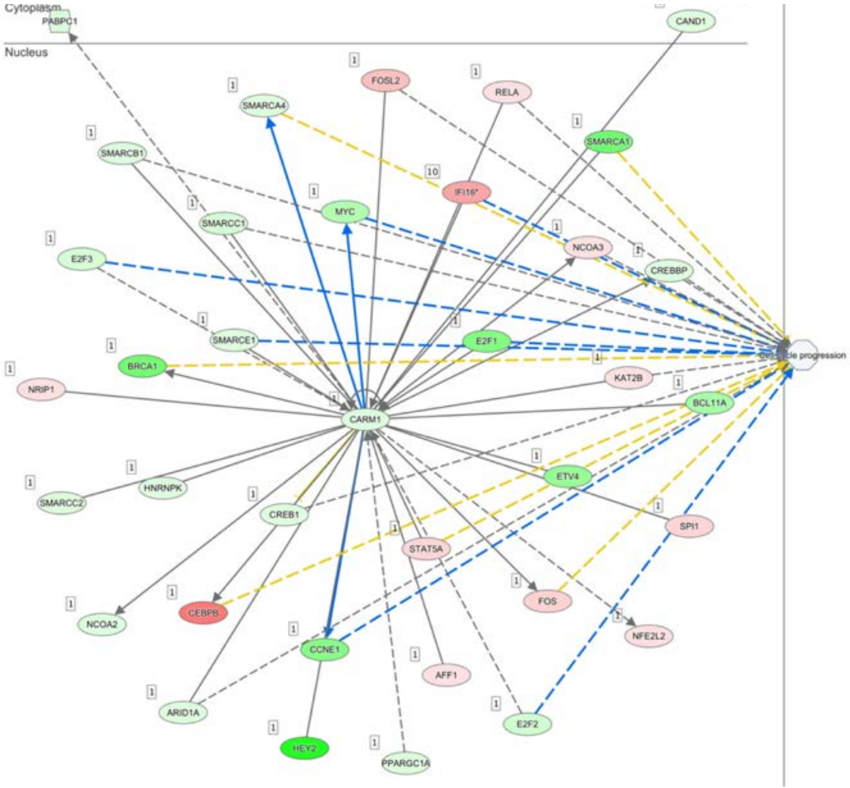
All upstream regulators (only transcription factors) predicted to be inhibited and activated at day 23 vs day 1



Cell cycle progression decreased

CARM1 itself is downregulated in post-natal mouse heart at day 23

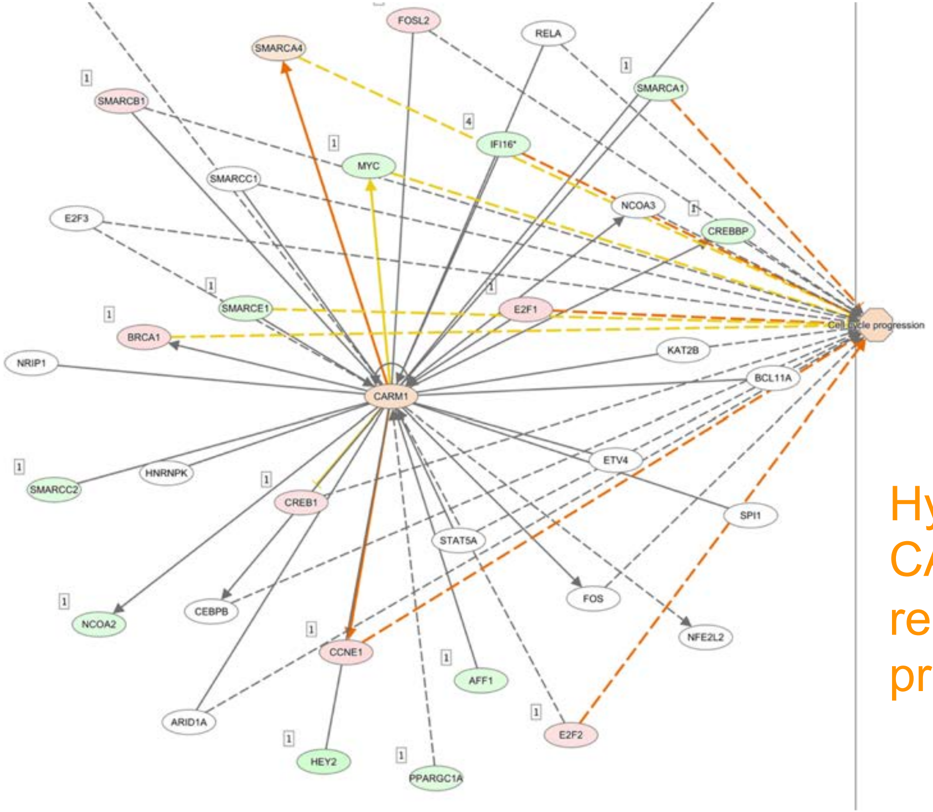
CARM1 (down-regulated) is connected to transcription regulators and induces a decrease of cycle progression at day 23



Cell cycle progression

Activation of CARM1 may allow cell cycle to progress again

CARM1 is upregulated at day 4 and is driving increase of cell cycle progression

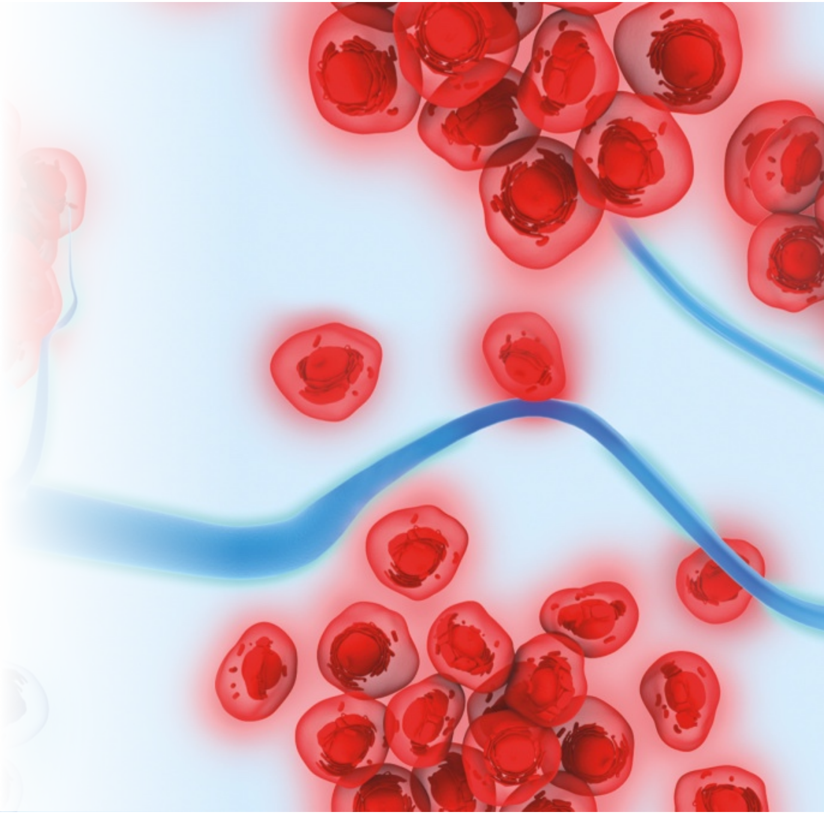


Cell cycle progression

Hypothesis: activating CARM1 at day 23 would re-initiate cell cycle progress

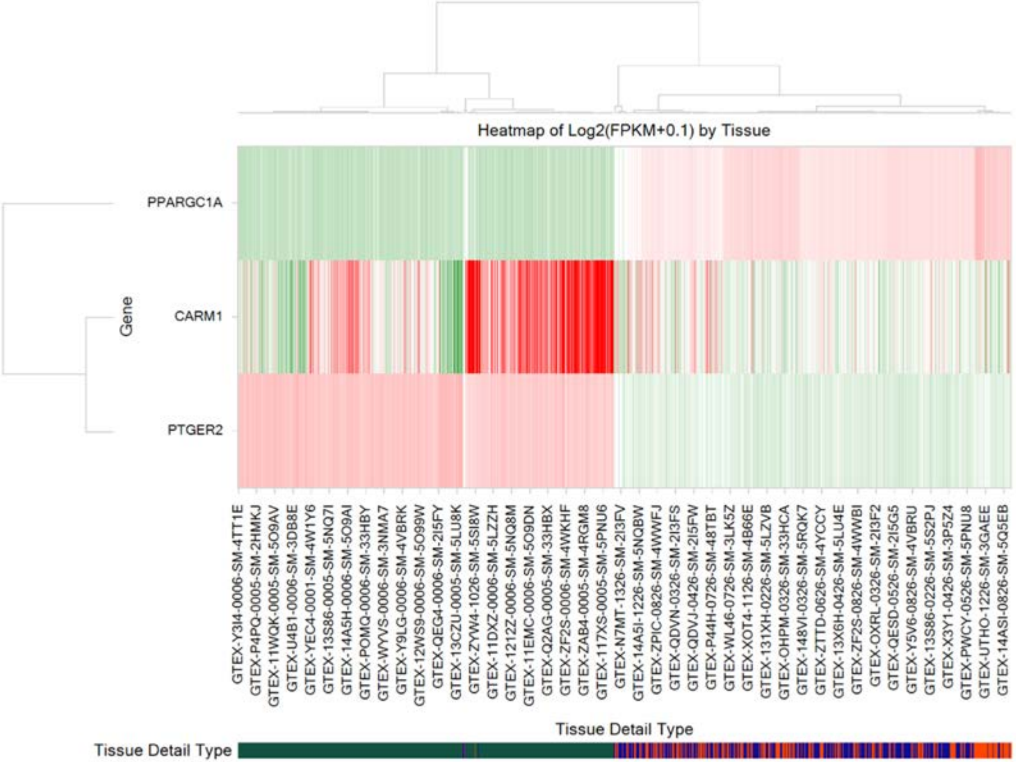
Visualize the connections of important genes in fetal heart and post-natal mouse heart

OmicSoft



Expression of important genes in GTEX and connections to predictions

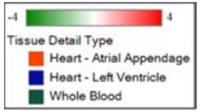
CARM1, PPARGC1A, and PTGER2 expression profile in normal heart tissue or in blood



PPARGC1A is enriched in heart
and predicted to be activated at day 23

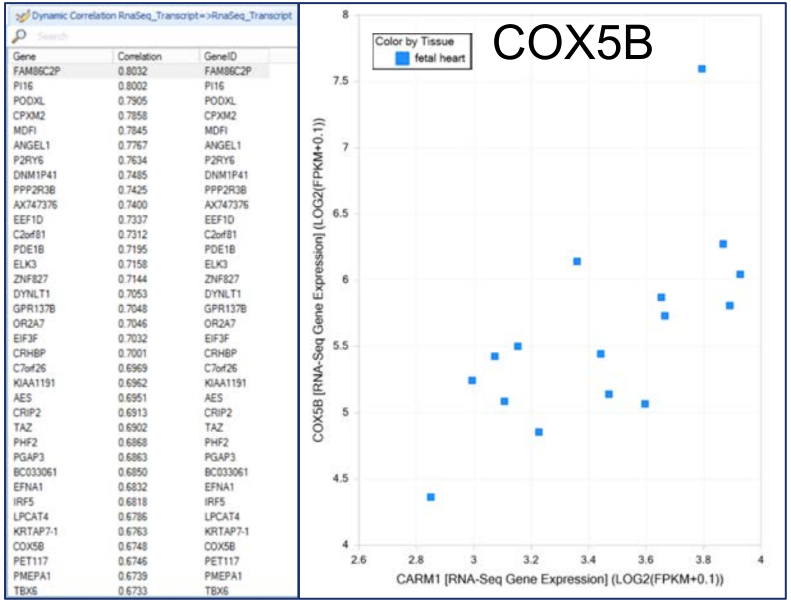
CARM1A is not enriched in heart and
down-regulated at day 23

PTGER2 is not enriched in heart
and predicted to be inhibited at day 23

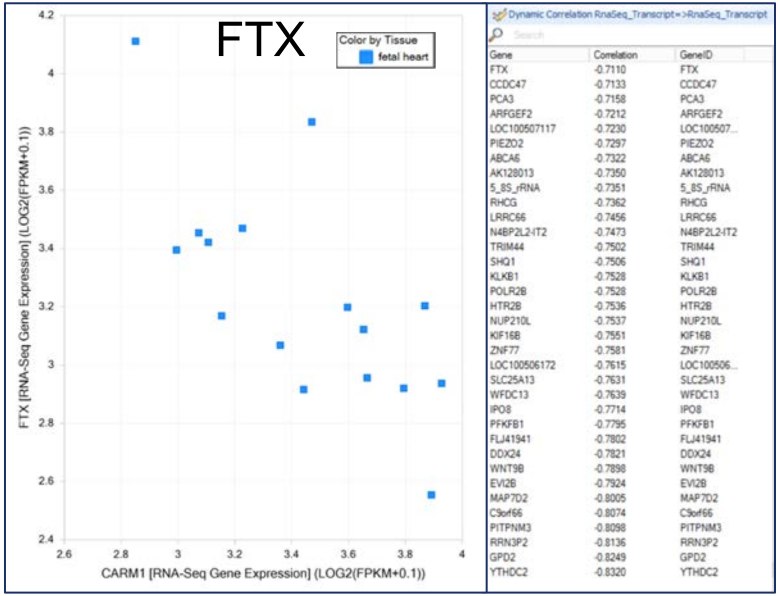


Dynamic correlation with CARM1 in fetal heart

COX5B is positively correlated with CARM1 and FTX is negatively correlated with CARM1.



Gene	Correlation	GeneID
FAM86C2P	0.8032	FAM86C2P
PI16	0.8002	PI16
PODXL	0.7905	PODXL
CPXM2	0.7858	CPXM2
MDFI	0.7845	MDFI
ANGEL1	0.7767	ANGEL1
P2RY6	0.7634	P2RY6
DNM1P41	0.7485	DNM1P41
PPP2R3B	0.7425	PPP2R3B
AX747376	0.7400	AX747376
EEF1D	0.7337	EEF1D
C2orf81	0.7312	C2orf81
PDE1B	0.7195	PDE1B
ELK3	0.7158	ELK3
ZNF827	0.7144	ZNF827
DYNLT1	0.7053	DYNLT1
GPR137B	0.7048	GPR137B
OR2A7	0.7046	OR2A7
EIF3F	0.7032	EIF3F
CRHBP	0.7001	CRHBP
C7orf26	0.6969	C7orf26
KIAA1191	0.6962	KIAA1191
AES	0.6951	AES
CRIP2	0.6913	CRIP2
TAZ	0.6902	TAZ
PHF2	0.6868	PHF2
PGAP3	0.6863	PGAP3
BC033061	0.6850	BC033061
EFNA1	0.6832	EFNA1
IRF5	0.6818	IRF5
LPCAT4	0.6786	LPCAT4
KRTAP7-1	0.6763	KRTAP7-1
COX5B	0.6748	COX5B
PET117	0.6746	PET117
PMEPA1	0.6739	PMEPA1
TBX6	0.6733	TBX6

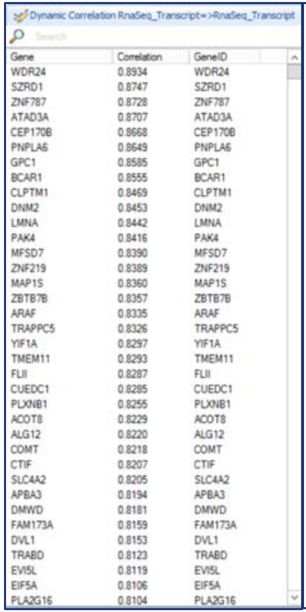


Gene	Correlation	GeneID
FTX	-0.7110	FTX
CCDC47	-0.7133	CCDC47
PCA3	-0.7158	PCA3
ARFGEF2	-0.7212	ARFGEF2
LOC100507117	-0.7230	LOC100507...
PIEZO2	-0.7297	PIEZO2
ABCA6	-0.7322	ABCA6
AK128013	-0.7350	AK128013
5_8S_rRNA	-0.7351	5_8S_rRNA
RHCG	-0.7362	RHCG
LRRC66	-0.7456	LRRC66
N4BP2L2-IT2	-0.7473	N4BP2L2-IT2
TRIM44	-0.7502	TRIM44
SHQ1	-0.7506	SHQ1
KLKB1	-0.7528	KLKB1
POLR2B	-0.7528	POLR2B
HTR2B	-0.7536	HTR2B
NUP210L	-0.7537	NUP210L
KIF16B	-0.7551	KIF16B
ZNF77	-0.7581	ZNF77
LOC100506172	-0.7615	LOC100506...
SLC25A13	-0.7631	SLC25A13
WFDC13	-0.7639	WFDC13
IPO8	-0.7714	IPO8
PFKFB1	-0.7795	PFKFB1
FLJ41941	-0.7802	FLJ41941
DDX24	-0.7821	DDX24
WNT9B	-0.7898	WNT9B
EVI2B	-0.7924	EVI2B
MAP7D2	-0.8005	MAP7D2
C9orf66	-0.8074	C9orf66
PITPNM3	-0.8098	PITPNM3
RRN3P2	-0.8136	RRN3P2
GPD2	-0.8249	GPD2
YTHDC2	-0.8320	YTHDC2

COX5B is correlated with CARM1 in fetal heart and is the terminal enzyme in the mitochondria respiratory chain. FTX is a long non-coding RNA is involves in cardiomyocyte apoptosis and is inversely correlated with CARM1.

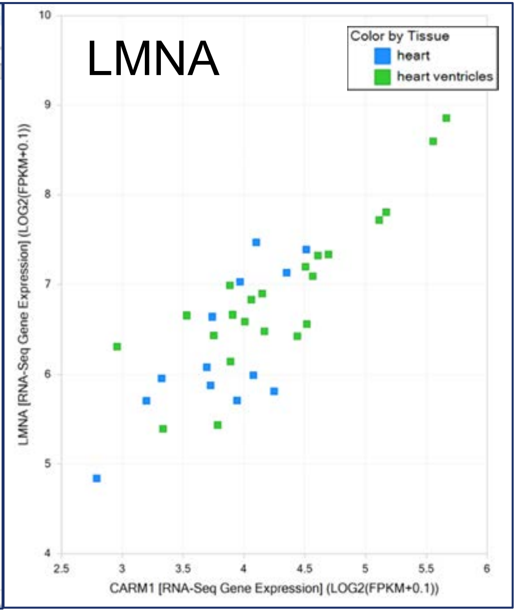
Dynamic correlation with CARM1 in post-natal heart

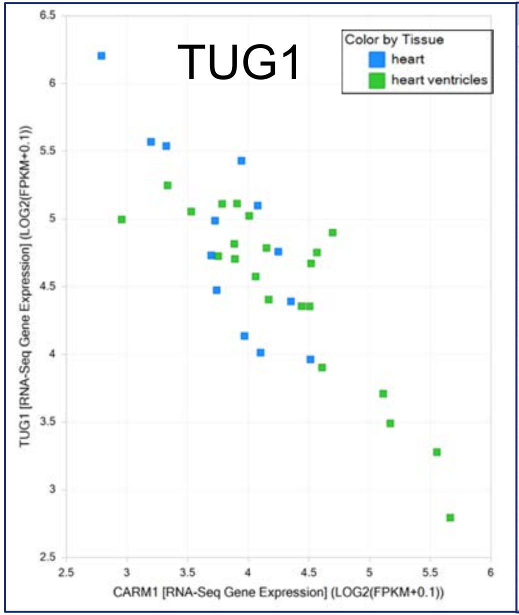
Laminin A is correlated positively with CARM1, TUG1 is negatively correlated with CARM1 in adult heart.

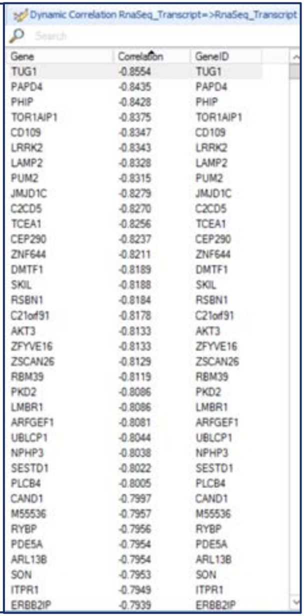


Dynamic Correlation RnaSeq_Transcript=>RnaSeq_Transcript

Gene	Correlation	GeneID
WDR24	0.8934	WDR24
SZRD1	0.8747	SZRD1
ZNF787	0.8728	ZNF787
ATAD3A	0.8707	ATAD3A
CEP170B	0.8668	CEP170B
PNPLA6	0.8649	PNPLA6
GPC1	0.8585	GPC1
BCAR1	0.8555	BCAR1
CLPTM1	0.8469	CLPTM1
DNM2	0.8453	DNM2
LMNA	0.8442	LMNA
PAK4	0.8416	PAK4
MFSD7	0.8390	MFSD7
ZNF219	0.8389	ZNF219
MAP1S	0.8360	MAP1S
ZBTB7B	0.8357	ZBTB7B
ARAF	0.8335	ARAF
TRAPPC5	0.8326	TRAPPC5
YIF1A	0.8297	YIF1A
TMEM11	0.8293	TMEM11
FLII	0.8287	FLII
CUEDC1	0.8285	CUEDC1
PLXNB1	0.8255	PLXNB1
ACOT8	0.8229	ACOT8
ALG12	0.8220	ALG12
COMT	0.8218	COMT
CTIF	0.8207	CTIF
SLC4A2	0.8205	SLC4A2
APBA3	0.8194	APBA3
DMWD	0.8181	DMWD
FAM173A	0.8159	FAM173A
DVL1	0.8153	DVL1
TRABD	0.8123	TRABD
EVI5L	0.8119	EVI5L
EIF5A	0.8106	EIF5A
PLA2G16	0.8104	PLA2G16







Dynamic Correlation RnaSeq_Transcript=>RnaSeq_Transcript

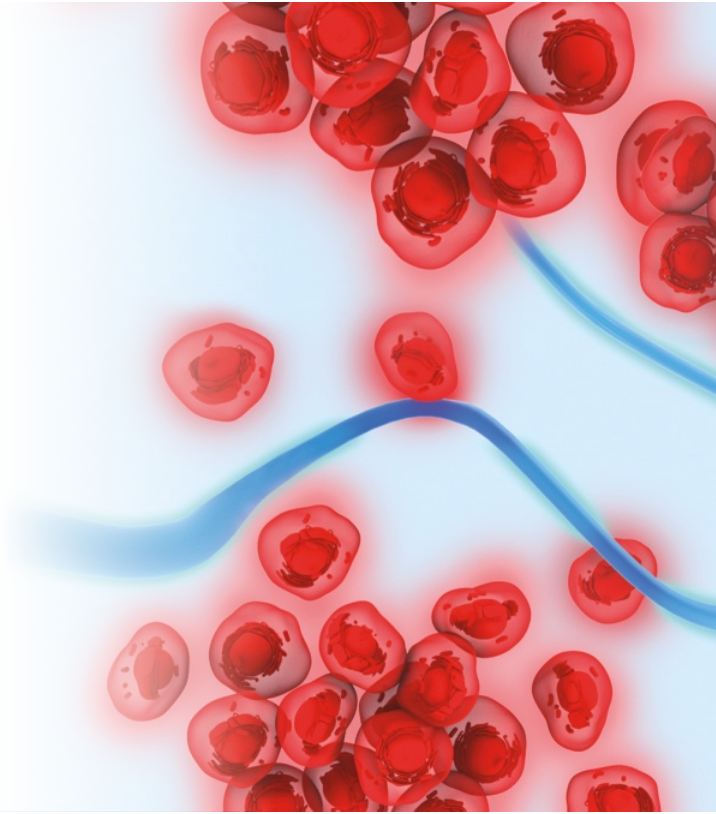
Gene	Correlation	GeneID
TUG1	-0.8554	TUG1
PAPD4	-0.8435	PAPD4
PHIP	-0.8428	PHIP
TOR1AIP1	-0.8375	TOR1AIP1
CD109	-0.8347	CD109
LRRK2	-0.8343	LRRK2
LAMP2	-0.8328	LAMP2
PUM2	-0.8315	PUM2
JMJD1C	-0.8279	JMJD1C
C2CD5	-0.8270	C2CD5
TCEA1	-0.8256	TCEA1
CEP290	-0.8237	CEP290
ZNF644	-0.8211	ZNF644
DMTF1	-0.8189	DMTF1
SKIL	-0.8188	SKIL
RSBN1	-0.8184	RSBN1
C21orf91	-0.8178	C21orf91
AKT3	-0.8133	AKT3
ZFYVE16	-0.8133	ZFYVE16
ZSCAN26	-0.8129	ZSCAN26
RBM39	-0.8119	RBM39
PKD2	-0.8086	PKD2
LMBR1	-0.8086	LMBR1
ARFGEF1	-0.8081	ARFGEF1
UBLCP1	-0.8044	UBLCP1
NPHP3	-0.8038	NPHP3
SESTD1	-0.8022	SESTD1
PLCB4	-0.8005	PLCB4
CAND1	-0.7997	CAND1
M55536	-0.7957	M55536
RYBP	-0.7956	RYBP
PDE5A	-0.7954	PDE5A
ARL13B	-0.7954	ARL13B
SON	-0.7953	SON
ITPR1	-0.7949	ITPR1
ERBB2IP	-0.7939	ERBB2IP

LMNA is correlated with CARM1 in adult heart and is important in structural scaffolding of nuclear lamina. TUG1 is a long-non-coding RNA and is participating in hypoxia mechanism in myocardial injury involving WNT pathway essential in heart development.

Conclusion: Multi-omics analyses in postnatal mouse heart

Some ideas to pursue and hypotheses to test

- A potential transcriptional program with TFs (PPARGC1A, PPARGC1B, etc.) is detected and drives the metabolism switch in post-natal heart
- One master regulator, PTGER2, is predicted to be inhibited at day 23, its activation could revert the arrest of cell cycle in post-natal heart
- Four isoforms connected to heart development are specifically down-regulated in post-natal heart (ALDH1A2-201, BIRC5-201, CCNA2-201, E2F2-201)
- A common signature between post-natal mouse heart and AML was detected, this signature indicates CARM1 as a major player in cell cycle progression in post-natal heart
- CARM1 is correlated with important genes involved in myocardial function or structure (COX5B, FTX, LMNA, TUG1)



Conclusion

Secondary analysis in Array Studio of RNAseq data

- Find differentially-expressed genes/transcripts
- Send the data to IPA

Biological interpretation of the whole transcriptome, proteome, and metabolome

- Identify significantly differentially expressed isoforms and their association to post-natal mouse heart
- Generate novel regulatory networks as hypotheses suggesting drivers of the expression changes observed in postnatal mouse heart.
- Compare this analysis across a repository of processed datasets from OmicSoft Lands (Analysis Match)
- Visualize a specific gene of interest in OmicSoft Lands

Thank you for your attention

Questions?

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