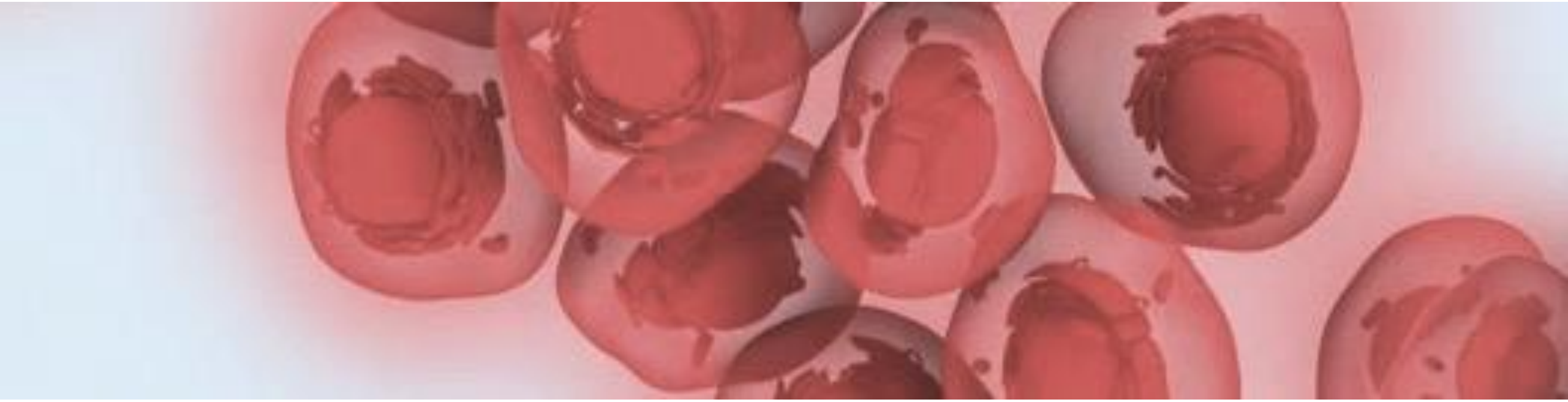

Transcriptomics, Proteomics and Metabolic Changes in the Post-Natal Mouse Heart analyzed with QIAGEN IPA and OmicSoft

Discovery Team, QIAGEN Digital Insights

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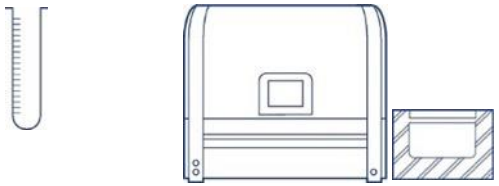
Agenda

- QIAGEN Sample to Insight
- Highlight important results
- Processing 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: Understand what is happening in post-natal mouse heart

- **What transcriptional program underpins the development of heart postnatally?**
  - 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?

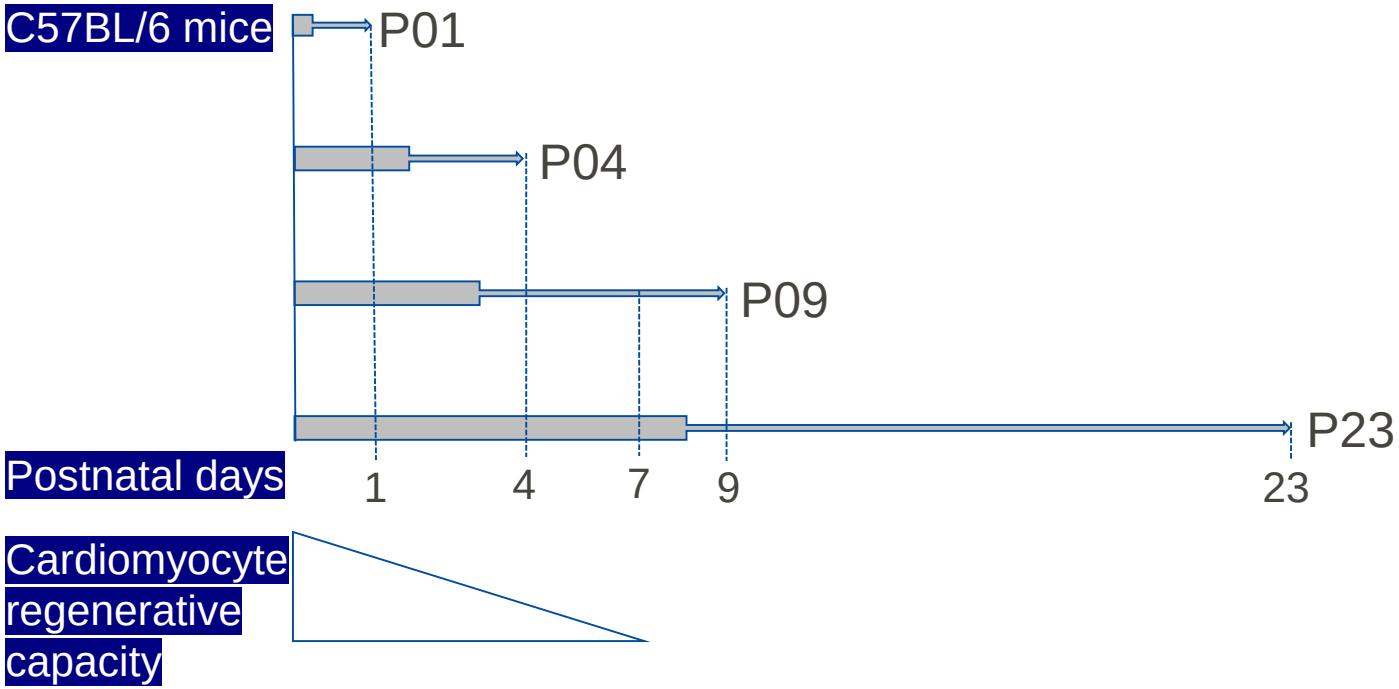
QIAGEN Sample to Insight



Sample 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

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.



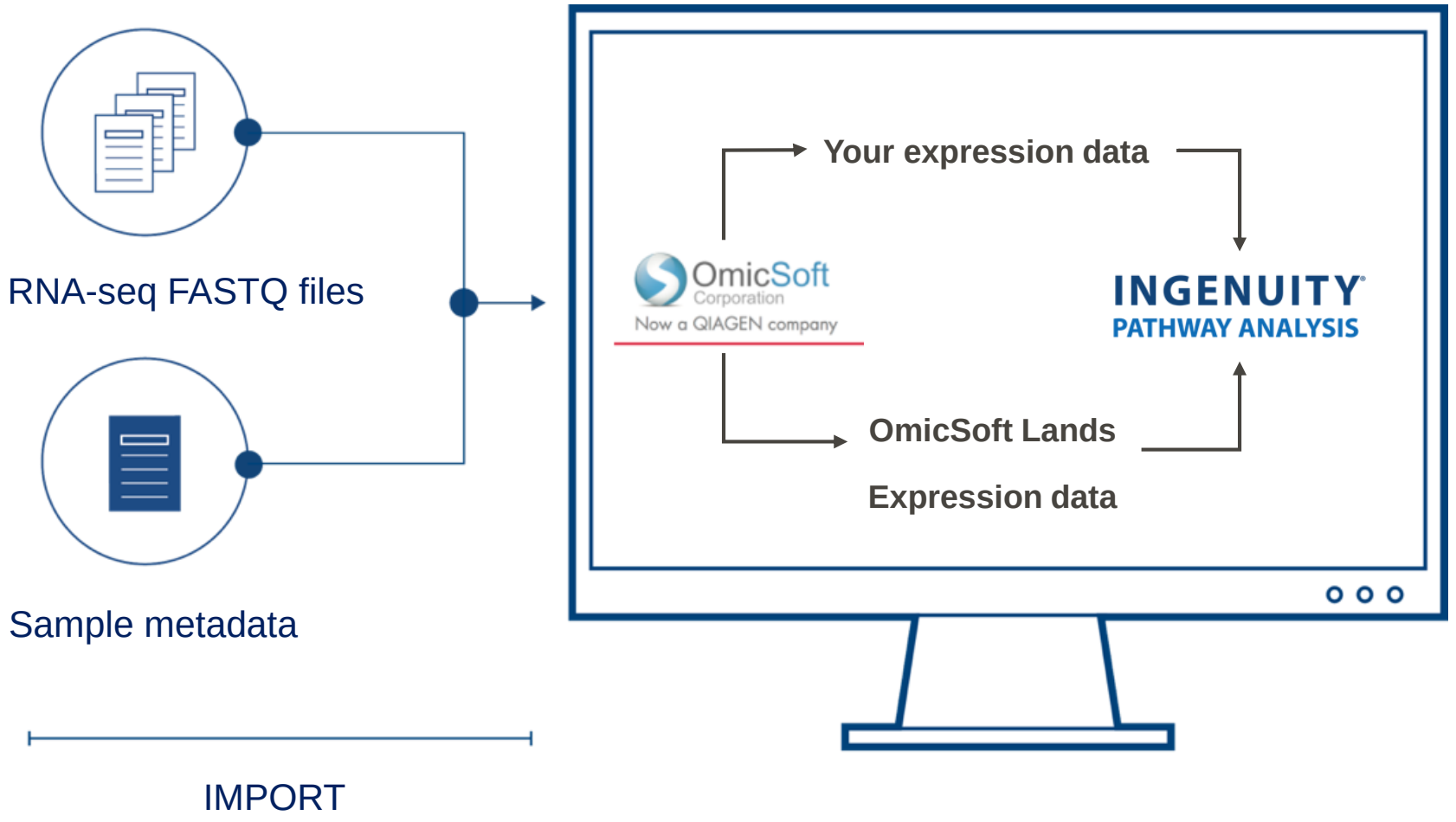
Platform	Omics
RNA-seq	Transcriptomics
LC-MS/MS	Proteomics
LC-MS GCxGC-MS	Metabolomics

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

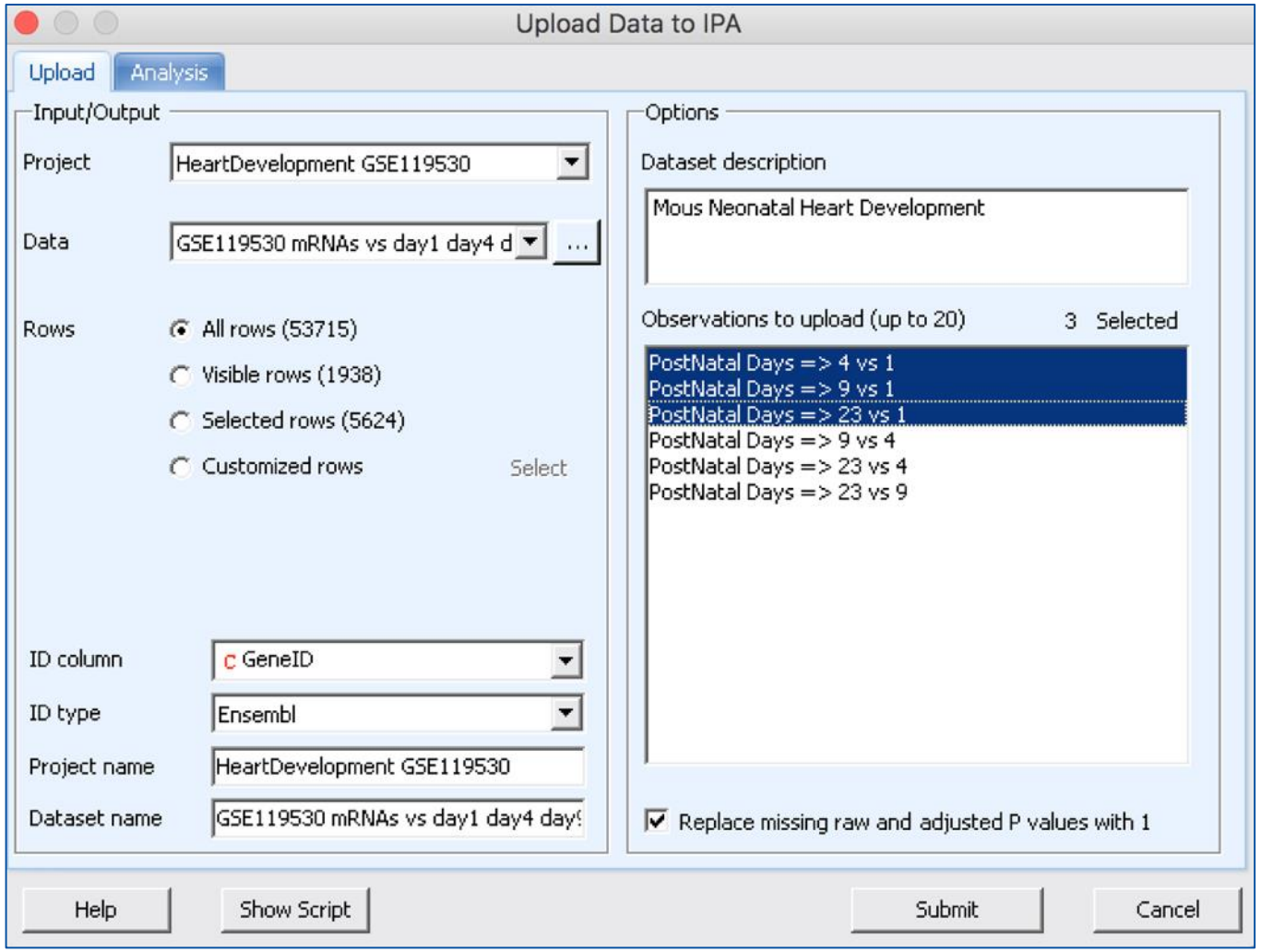
Transcriptomics, Proteomics, Metabolic Changes in Postnatal Mouse Heart

- 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)

OmicSoft → Ingenuity Pathway Analysis (IPA)

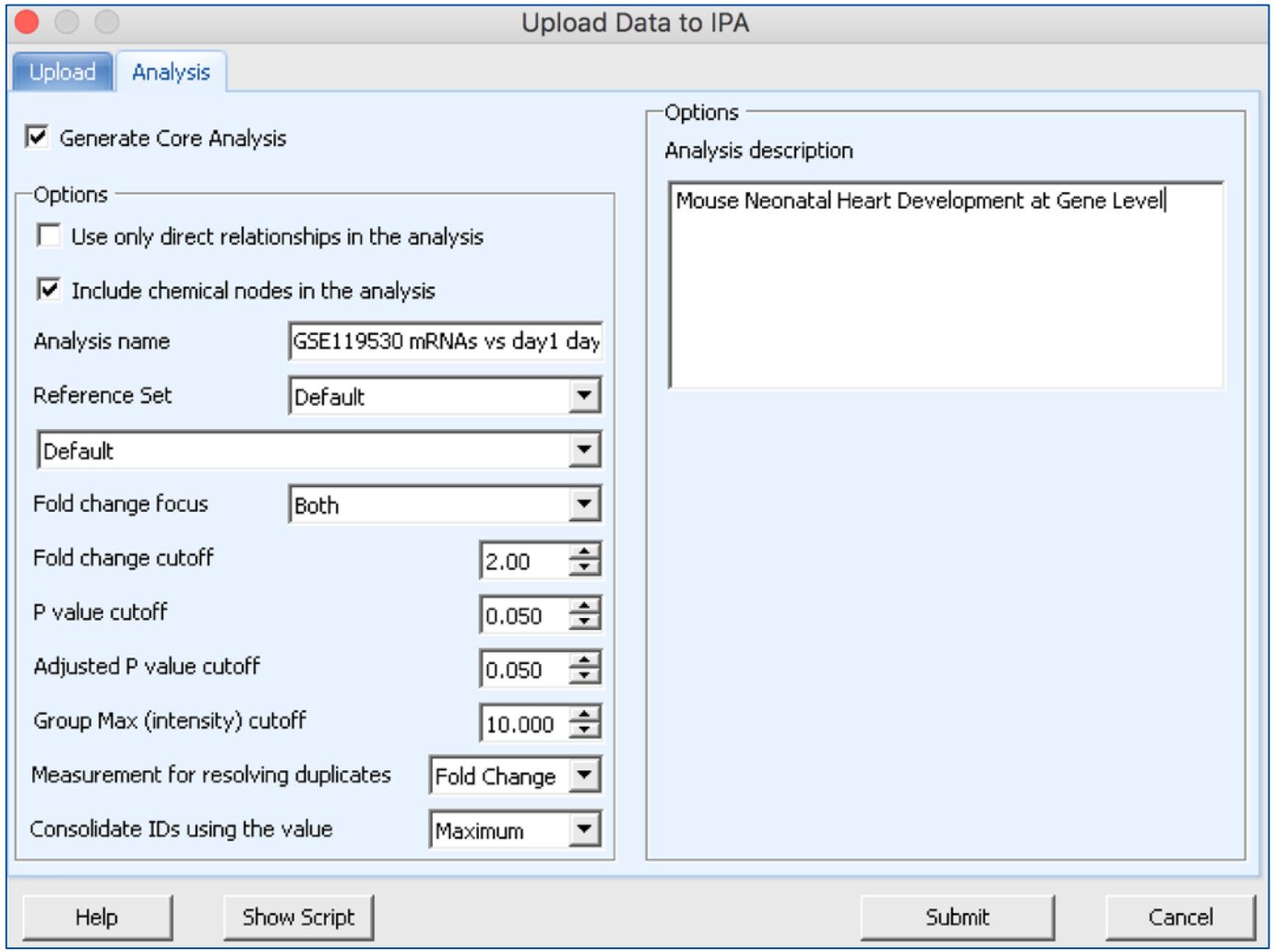


Upload dataset to IPA



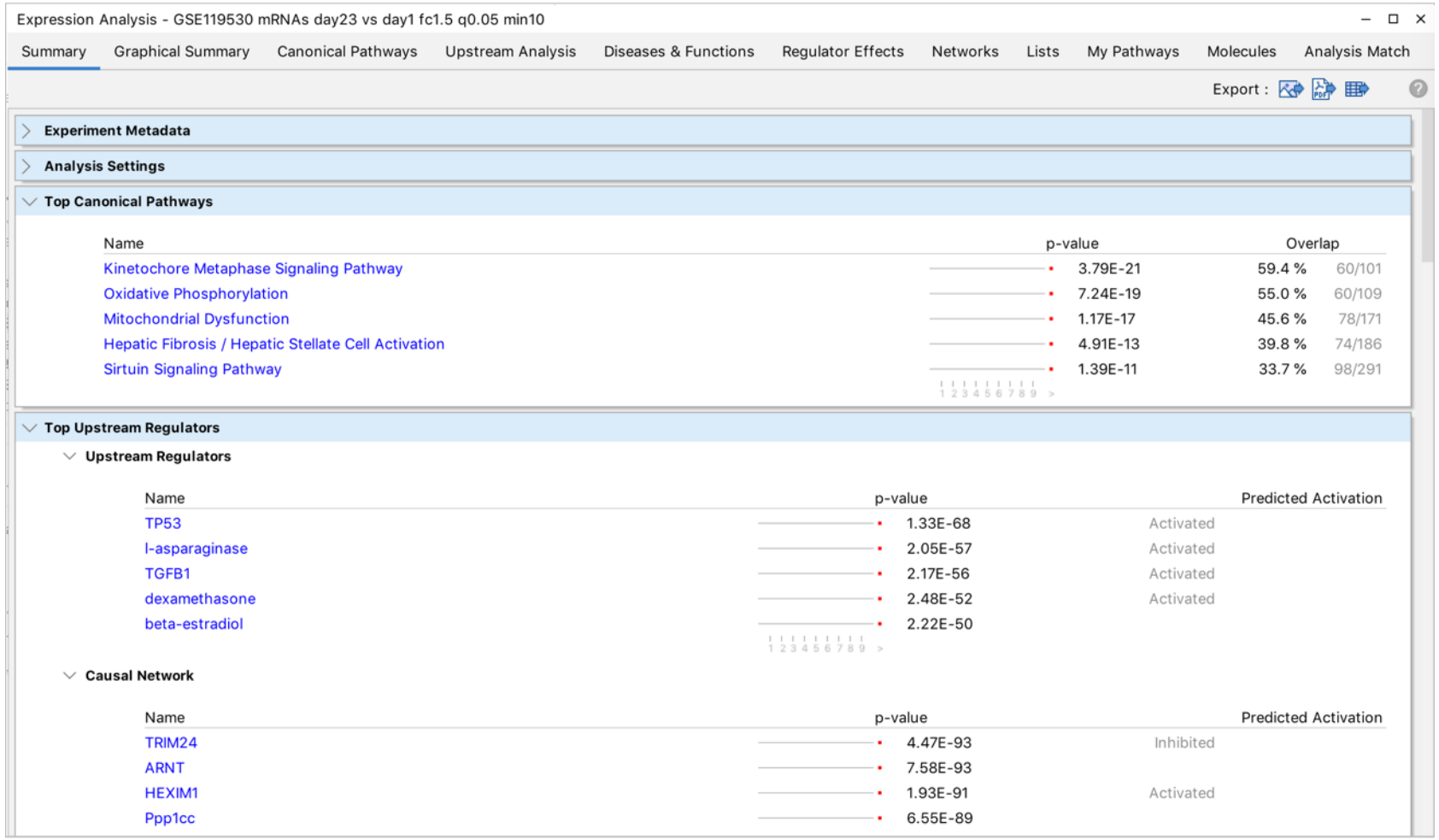
OS-IPA integration:
Analyzed dataset in AS is sent to IPA via Plugin

Auto-submit IPA core analysis from Array Studio dataset



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

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



Summary at the gene level

- |fold change|>1.5
- q<0.05
- min counts >10 in day 23 or day 1

Core Analysis: day 4 vs day 1 (example)

Experiment Metadata

Raw Data (9957) | Dataset Summary (9903) | Metadata

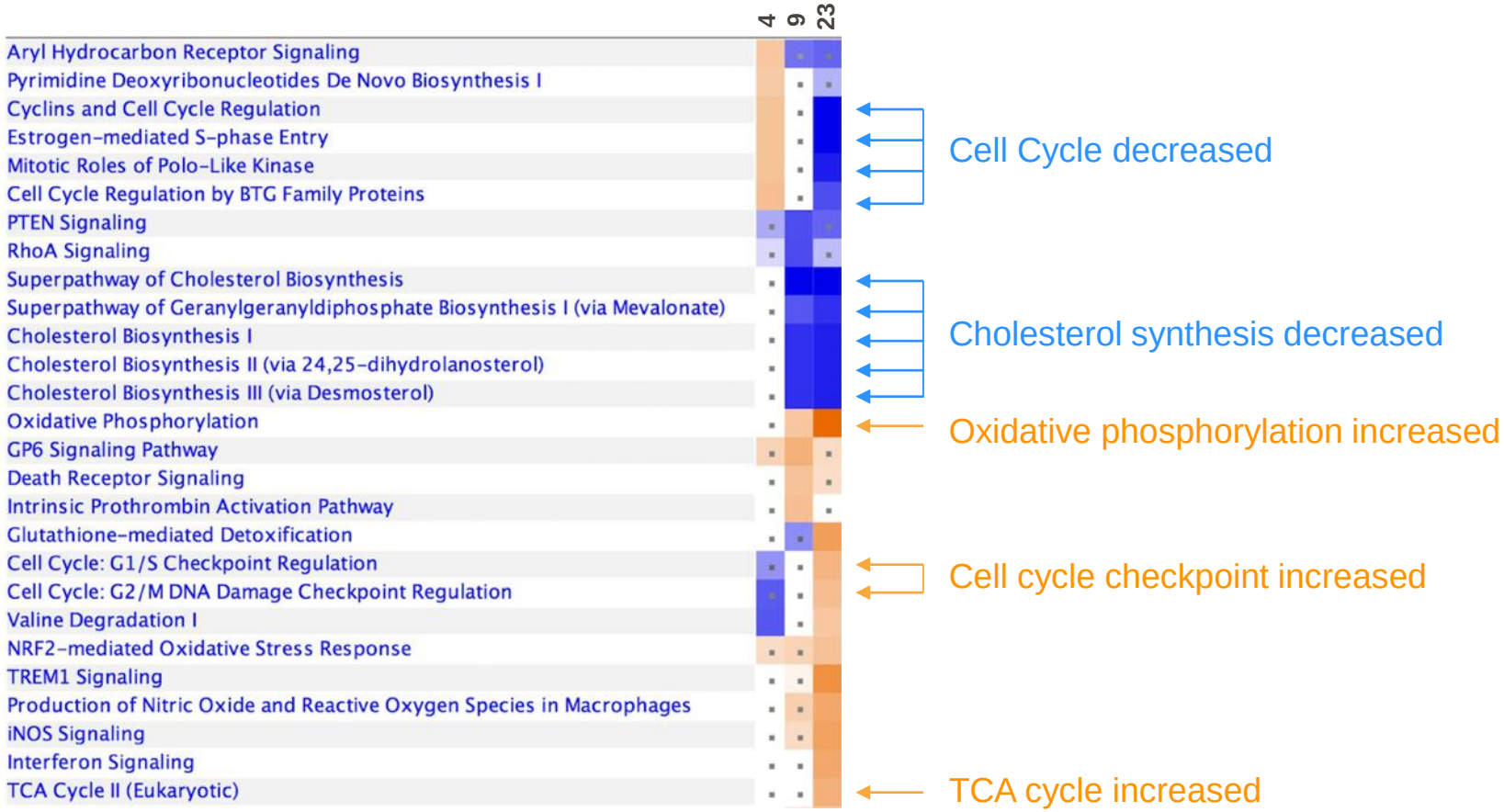
There are 13 metadata fields with values in this dataset.
Fill-in metadata using pre-defined fields, or add a field of your own.
Note that only rows with **values** will be saved in the dataset.

Show Rows With Empty Values

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 Ensembl92
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

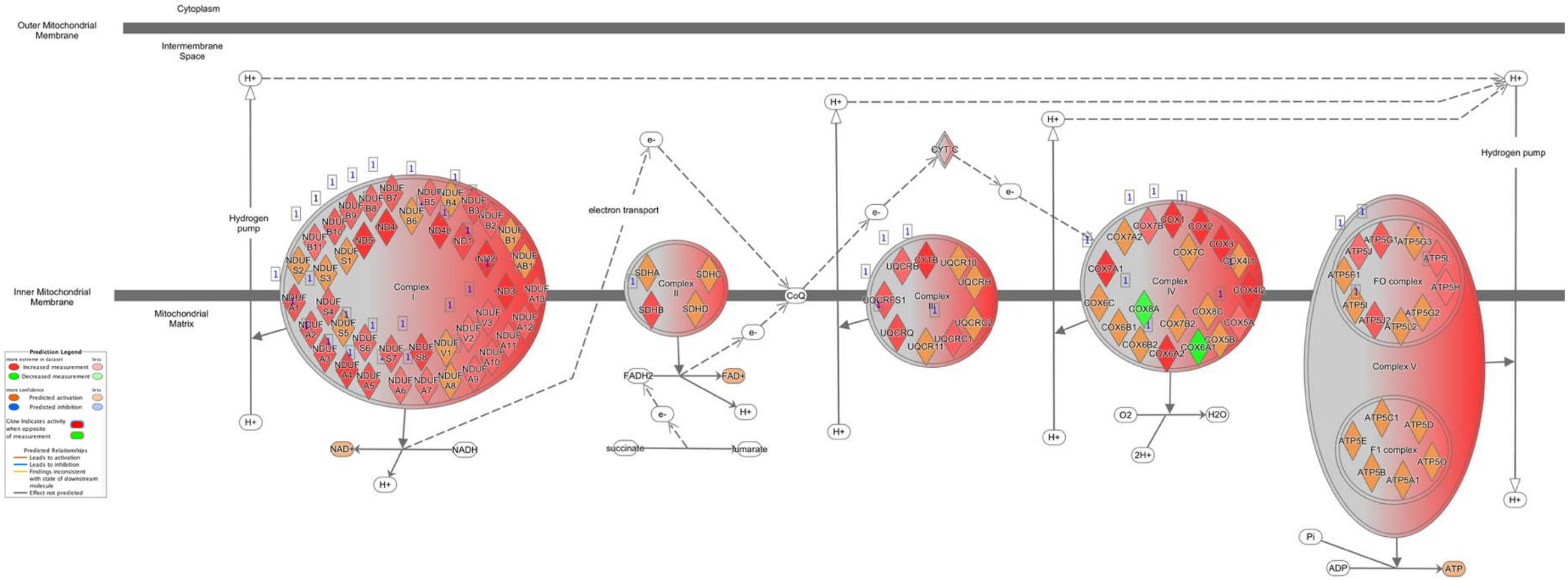
Canonical Pathways comparison indicate switch in energy metabolism and changes in cell cycle



Post-natal cardiomyocytes arrest cell cycle progression and increase ox. phos. starting at day 9 after birth

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

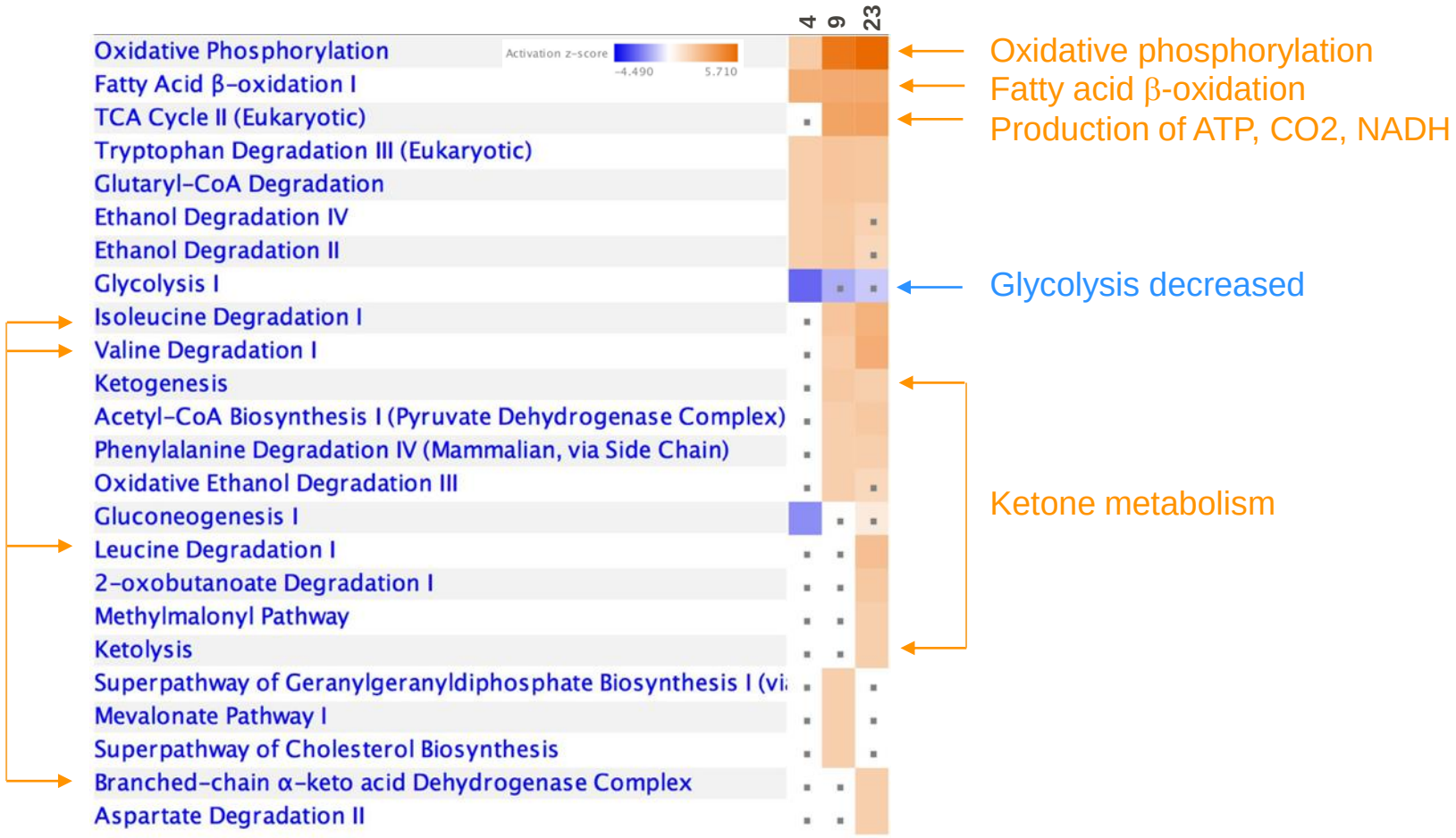
Comparison of transcriptomics analysis indicates that oxidative phosphorylation pathway is activated from day 9 on



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

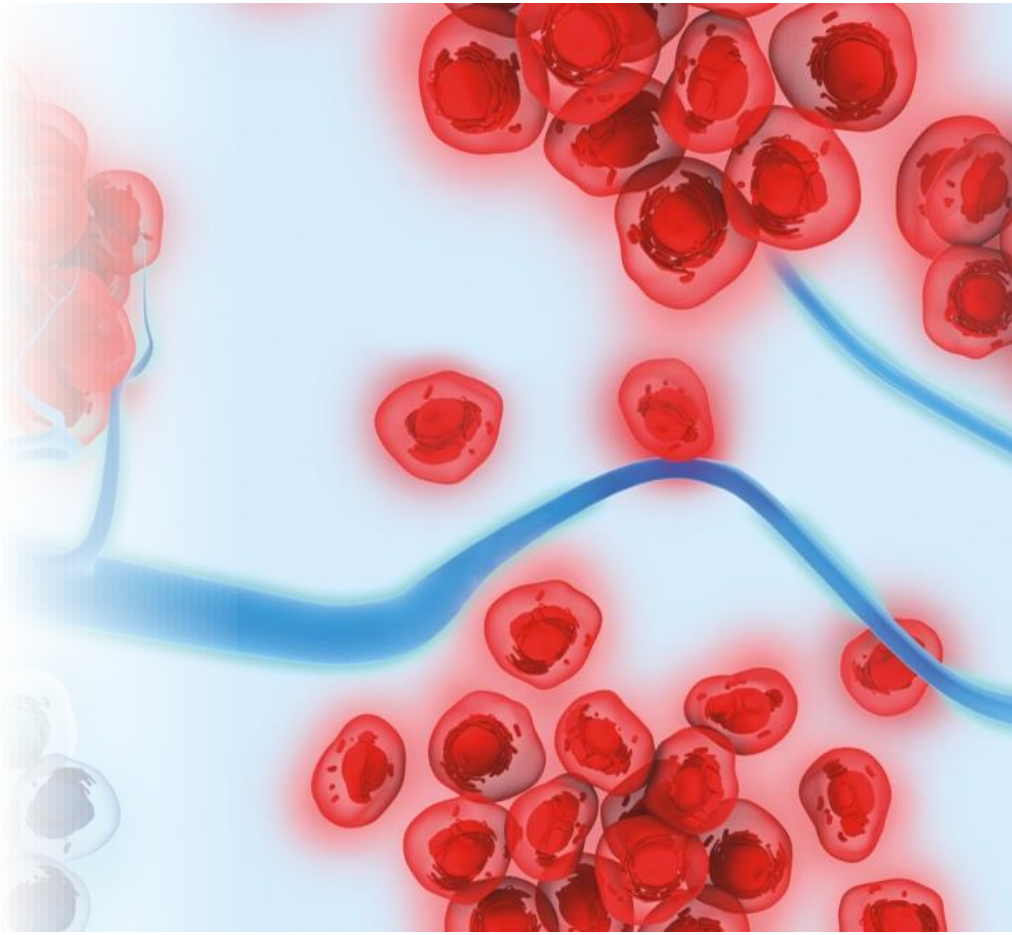
Proteomics indicate major switch in energy metabolism and energy substrates after birth.



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

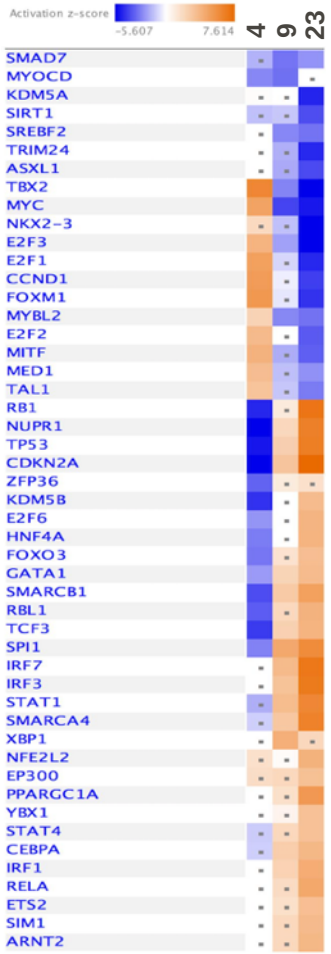
Explore the underlying transcriptional programs

Upstream Analysis

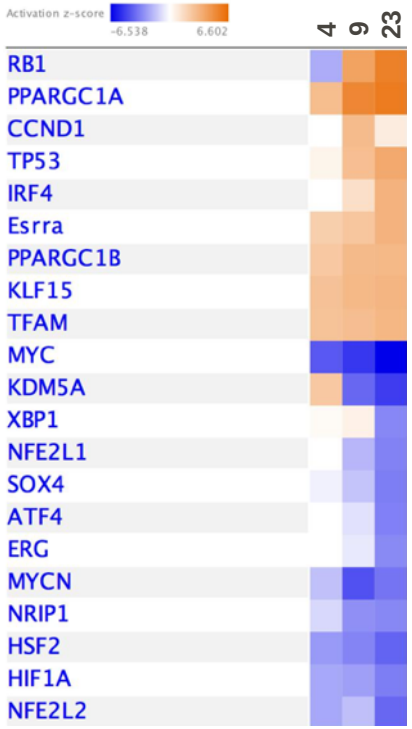


Multi-omics analysis indicate similar transcriptional drivers

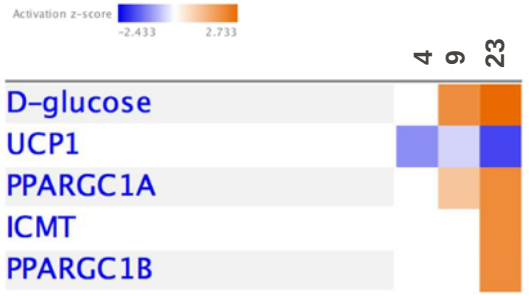
Transcriptomic



Proteomic



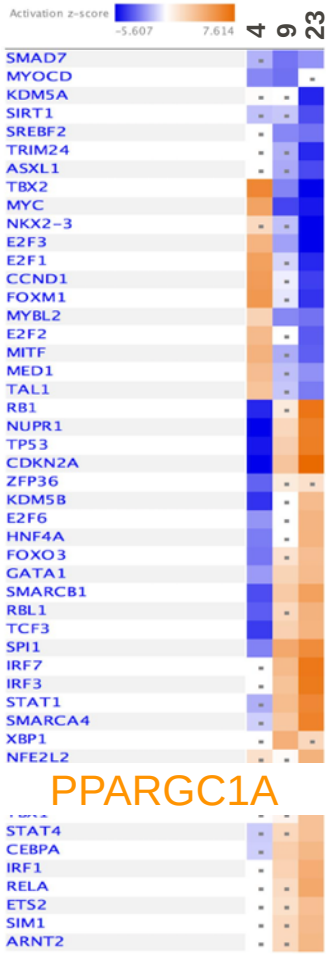
Metabolomic



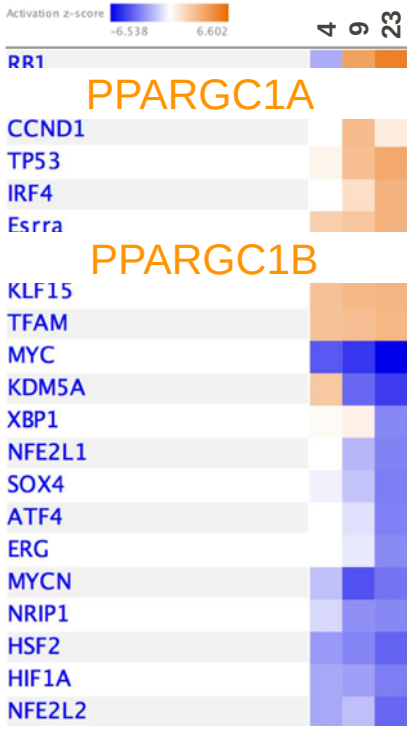
Upstream Regulators Analysis of transcriptomics, proteomics and metabolomics show induction of fatty oxidation regulation by PPARG coactivators.

Multi-omics analysis indicate similar transcriptional drivers

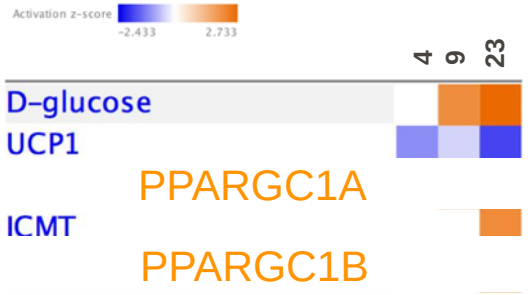
Transcriptomic



Proteomic

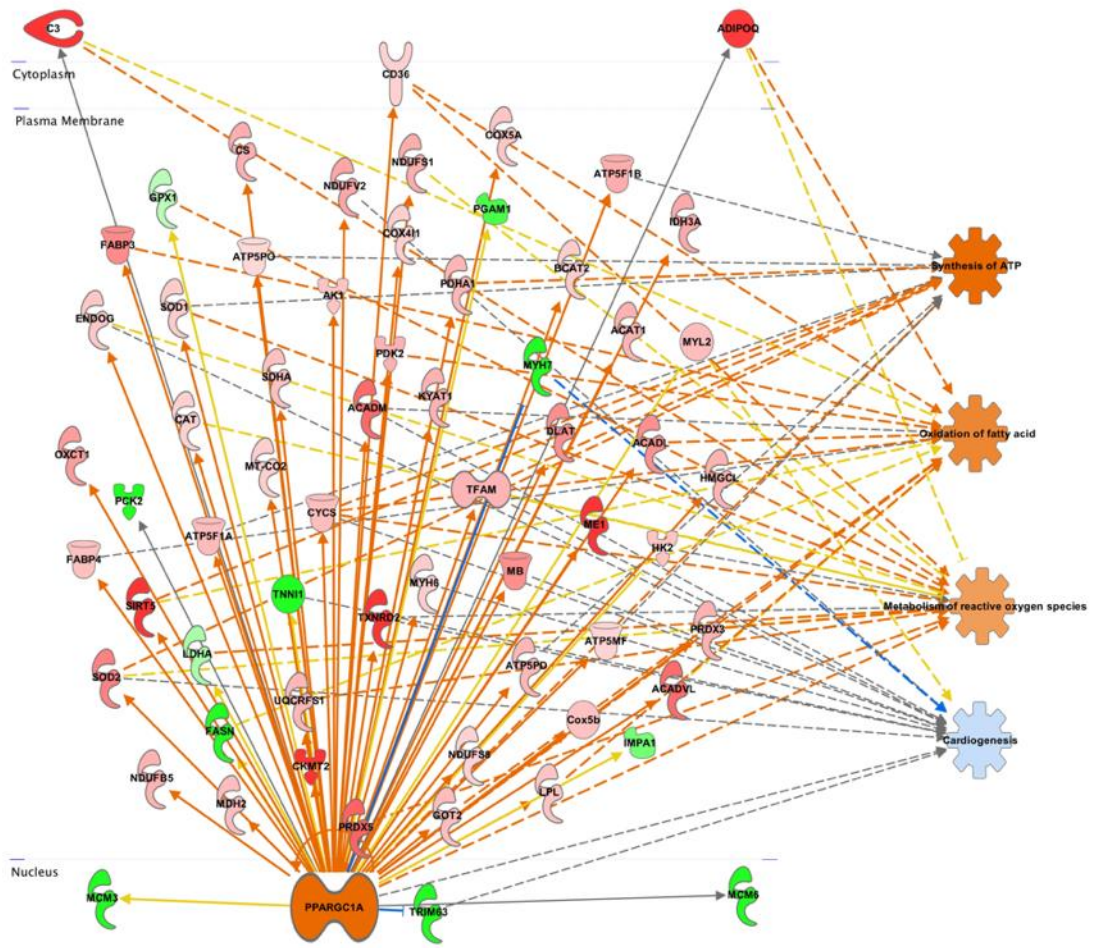


Metabolomic



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

PPARGC1A is predicted to induce ATP synthesis



PPARGC1A

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

Synthesis of ATP (p-value 8.01E-15)

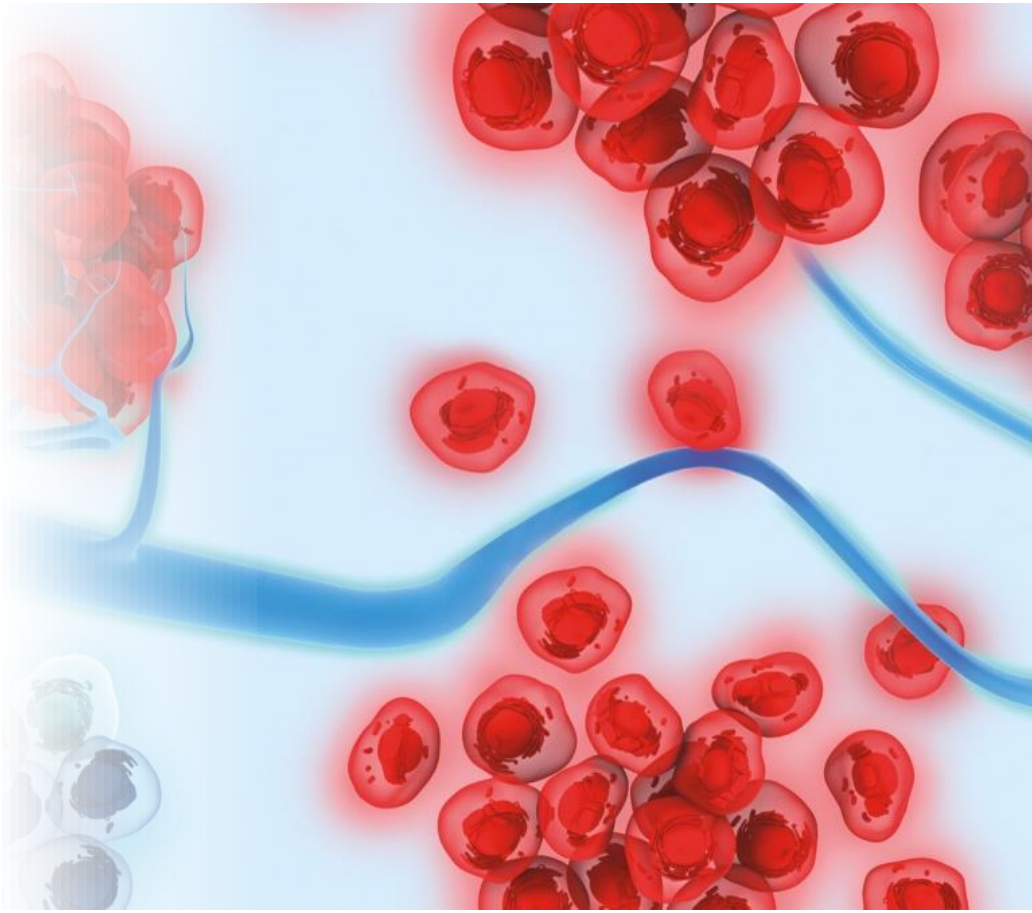
Oxidation of Fatty acid (p-value 4.61E-16)

Metabolism of ROS (p-value 7.65E-12)

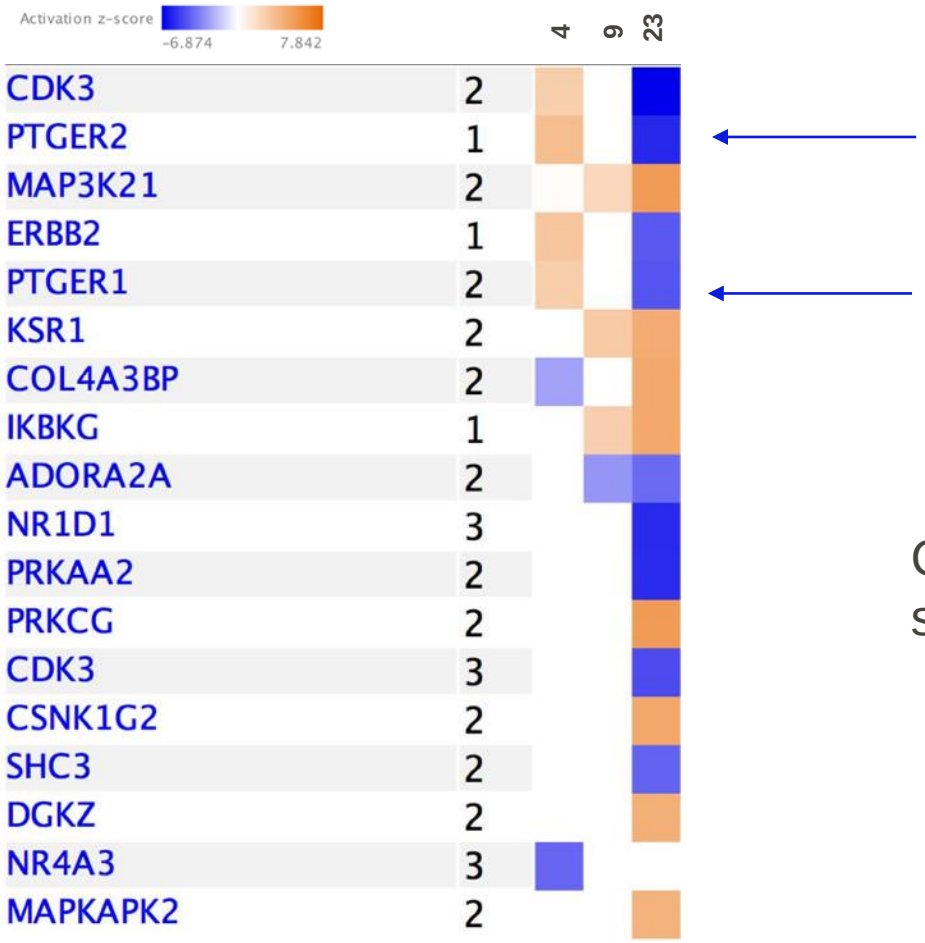
Cardiogenesis (P-value 4.03E-10)

Generate hypotheses to validate in the lab

Causal Network



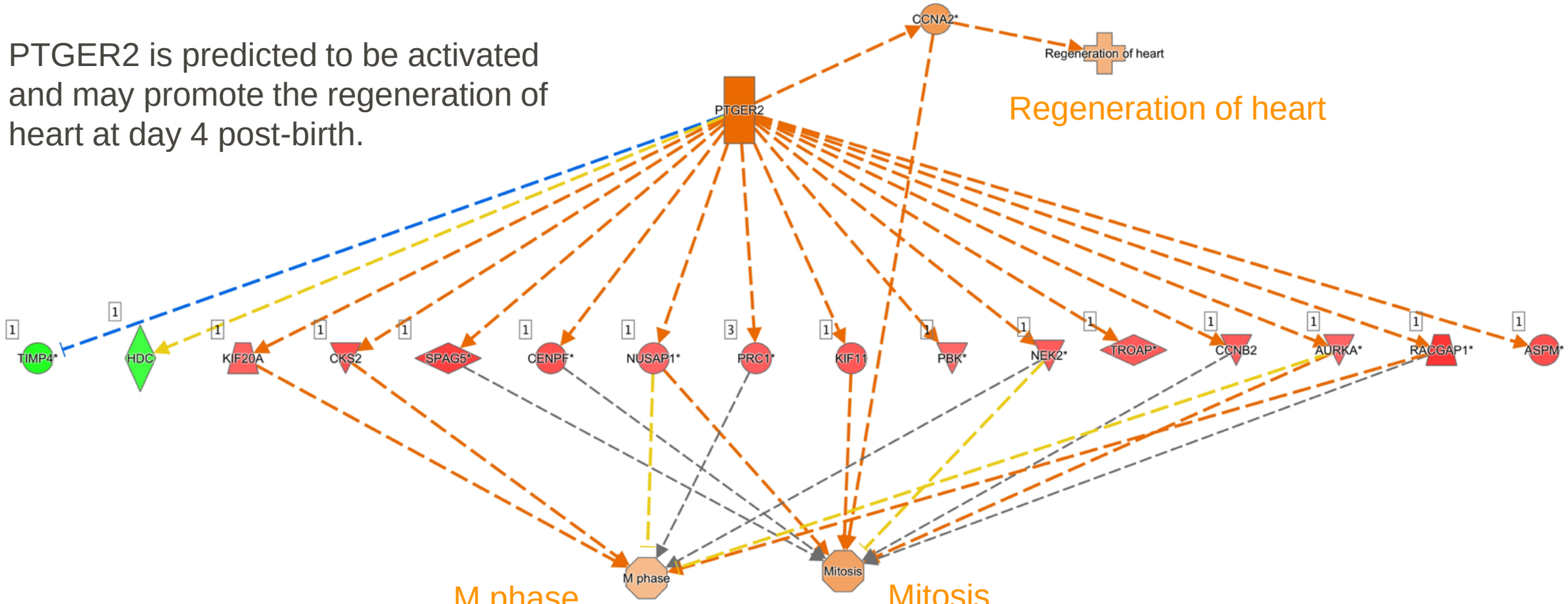
Causal Network Analysis of transcriptomics in post-natal mouse heart



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

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.

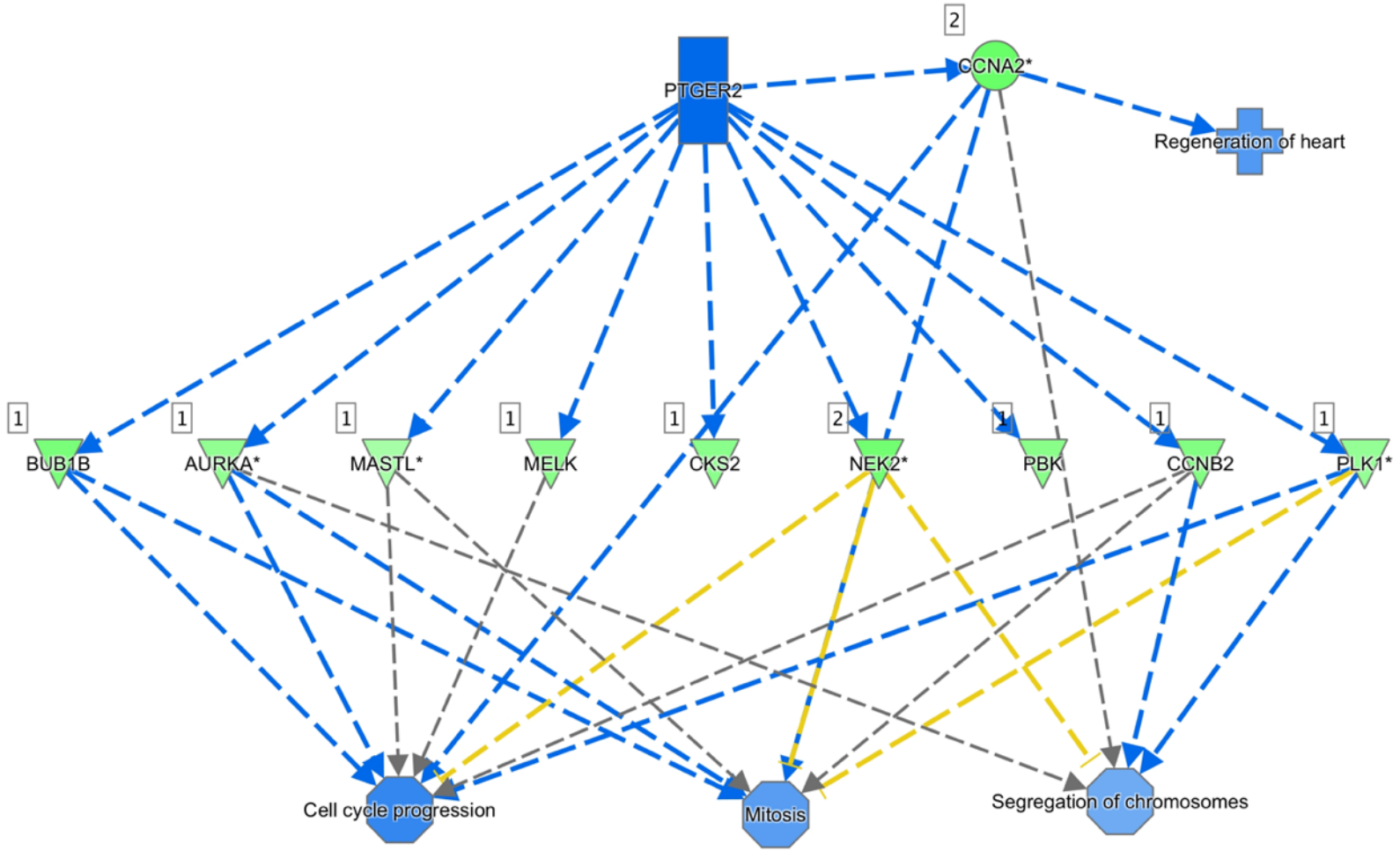


Regeneration of heart

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



Regeneration of heart

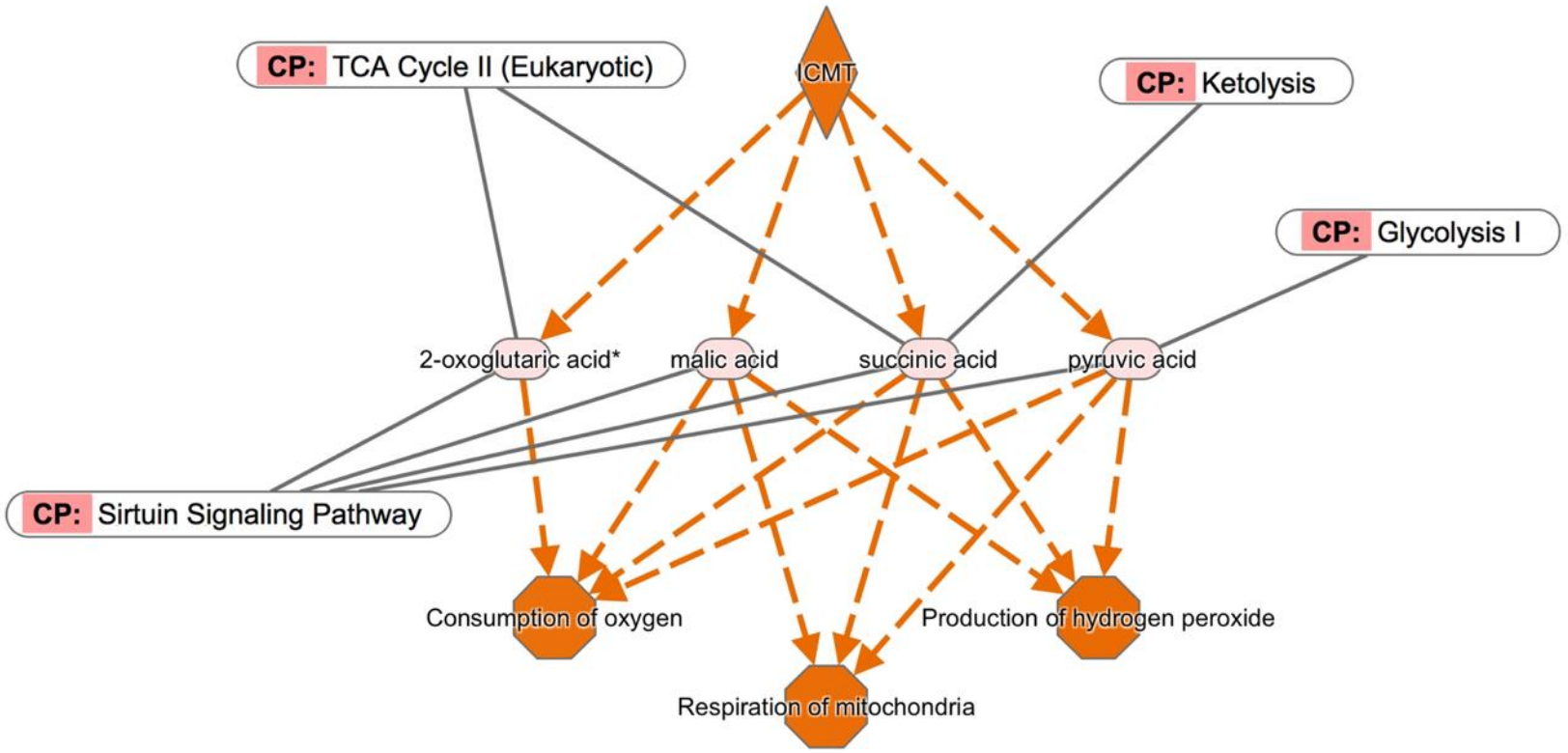
PTGER2 is predicted to be inhibited and may inhibit the regeneration of heart at day 23 post-birth.

Cell cycle progression
p-value 2.33E-08

Mitosis
p-value 2.33E-08

Segregation of chromosomes
p-value 2.33E-08

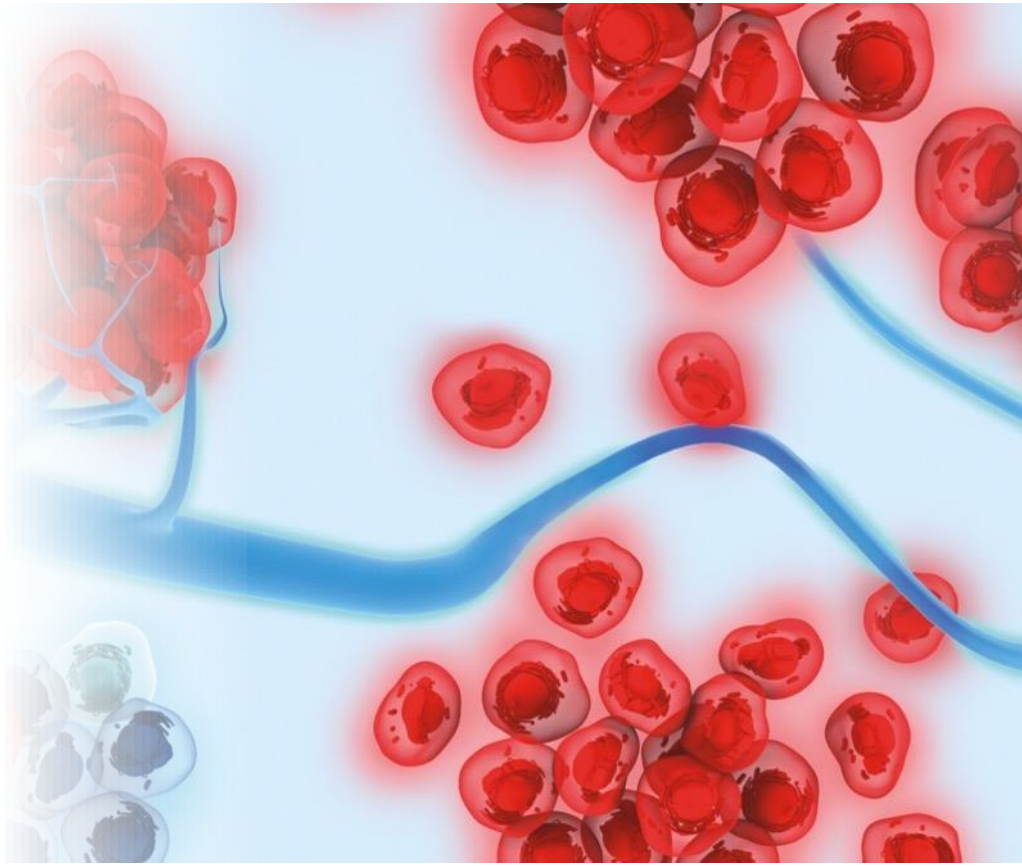
Regulator Effects predicts ICMT as a player in post-natal mouse heart



Comparison of metabolomics analysis predicts that ICMT (Isoprenylcysteine carboxyl methyltransferase) increases O2 consumption and oxidative phosphorylation at day 23 in post-natal mouse heart.

Identify tissue-enriched splicing variant and its expression pattern

IsoProfiler



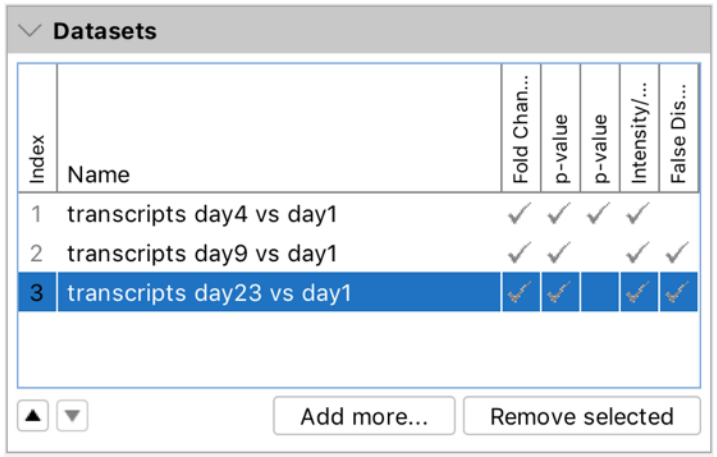
Isoforms differentially expressed observed in post-natal mouse heart

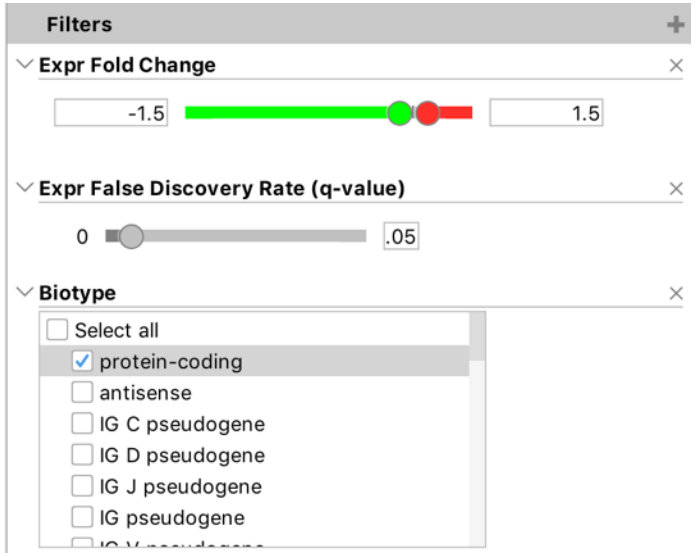
Add To My Pathway | Add To My List | IsoProfiler Findings | Create Dataset | Customize Table

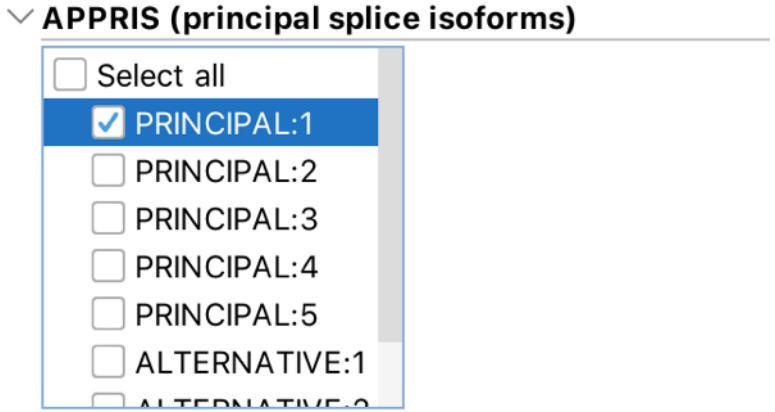
Sy...	Molecul...	Gene-level Disease or Func...	Gene-level Fi...	Expressi...	Max Ex...
ABCC9	ion channel	Abnormal ST segment, Antivir... ...all 67	320	2 -- 3 more	↑1.340
				3 --	↑1.711
ABCD1	transporter	Abnormal conduction by nerves,...all 74	383	1 - -	
				2 - -	
				3 -	↑1.471
ABCD2	transporter	Abnormal conduction by nerves ...all 55	103	1 - --	
				2 --	↑1.448
				3 --	↑2.602
ABCD3	transporter	Abnormal composition of bile,.....all 24	51	1 ---- - -	
				2 ---- - -	
				3 -----	↓-1.990
ABCE1	transporter	Antiviral response,Apoptosis o.....all 10	30	1 - -	↑1.457
				2 - - - -	
				3 - -	↑1.691

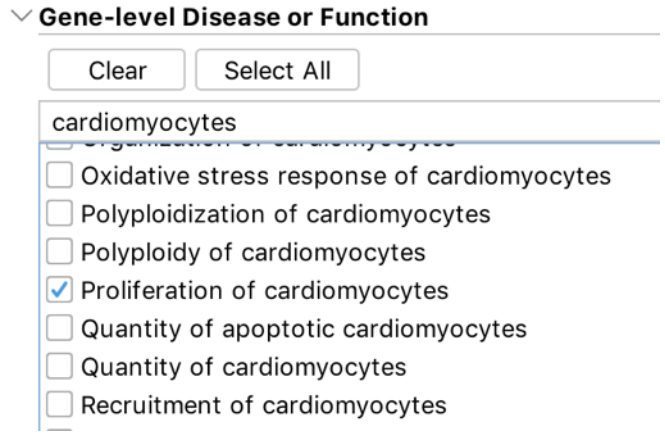
At q<0.05, 2256, 2965 and 6639 differentially expressed isoforms are found at day 4, day 9 and day 23 post-birth, respectively.

IsoProfiler to filter transcripts from post-natal mouse 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		↑1.636 ↓-2.084
BIRC5	other	Accumulation of breast ca.....all 297		↑1.873 ↓-1.702 ↓-12.801
CCNA2	other	Activation of R... Acute my... ...all 74		↑1.975 ↓-9.772
E2F2	transcription reg...	Abnormal function of immu... ...all 96		↑1.698 ↓-1.972

Four isoforms are differentially expressed between day 4 and day 23

..	Transcript	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1					transcripts day23 vs day1				
						ID	...	E...	Exp...	ID	ID	...	Ex...	Exp...	
1	Aldh1a2-201	Aldh1a2-201		PRINCIPAL:1	protein-coding	ENSMUST000...	×	↑1.636	8.54E-04	E...	ENS...		↓-2.084	2.46E-06	

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

	Trans...	Protein	Sc...	APPRIS	Biotype	transcripts day4 vs day1				transcripts day9 vs day1				transcripts day23 vs day1			
						ID	...	E...	Exp...	ID	...	Ex...	Exp...	ID	...	Ex...	Exp...
1	Birc5-201	Birc5 isoform 1		PRINCIPAL:1	protein-coding	ENSMU...		↑1.873	2.33E-05	ENSMUS...		↓-1.702	9.22E-04	ENSMUS...		↓-12.801	2.89E-26
2	Birc5-202	Birc5 isoform 3			protein-coding	ENSMU...		↑2.071	1.88E-05	ENSMUS...		↓-1.348	2.72E-01	ENSMUS...		↓-4.534	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				tran...		transcripts day23 vs day1				
						ID	...	E...	Exp...	ID	...	ID	...	Ex...	Exp...	E...
1	Ccna2-201	Ccna2-201		PRINCIPAL:1	protein-coding	ENSM...		↑1.975	5.14E-03		–	ENSMU...		↓-9.772	2.97E-17	385.647
2	Ccna2-205	Ccna2-205			protein-coding	ENSM...	×	↑1.513	7.45E-02		–	ENSMU...	×	↓-3.029	2.88E-02	5.311
3	Ccna2-203	Ccna2-203			protein-coding	ENSM...	×	↑1.564	1.55E-01		–	ENSMU...	×	↓-5.622	1.62E-06	175.989
4	Ccna2-202				retained intron		–				–		–			
5	Ccna2-204				processed transcr...	ENSM...	×	↑1.424	1.00E00		–		–			

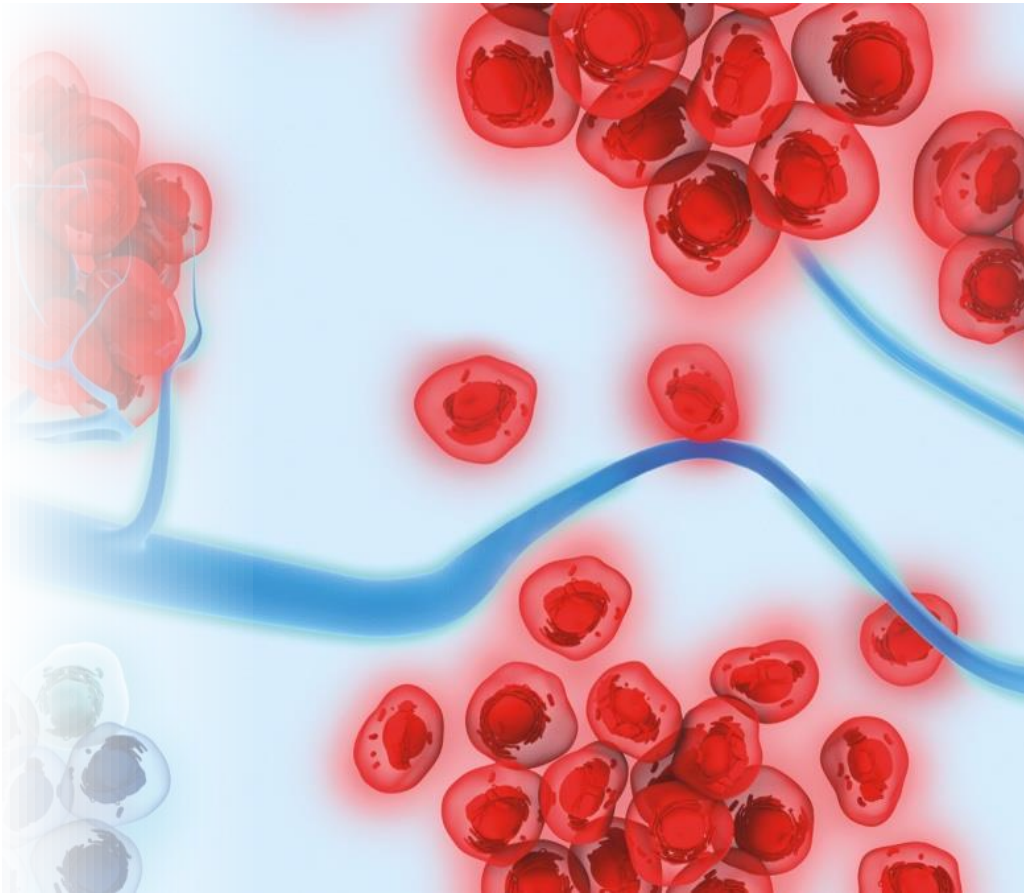
CCNA2 is silenced after birth in the mammalian heart and its constitutive expression enhances cardiomyocyte proliferation resulting in cardiac hyperplasia.

..	Trans...	Protein	Schematic	APPRIS	Biotype	transcripts day4 vs day1				tran...		transcripts day23 vs day1				
						ID	...	E...	Exp...	ID		ID	...	Ex...	Ex...	E...
1	E2f2-201	E2f2 isoform 1		PRINCIPAL:1	protein-coding	ENSMU...		↑1.698	4.92E-03		–	ENSMU...		↓-1.972	4.16E-03	42.649
2	E2f2-202				processed transcri...		–				–		–			

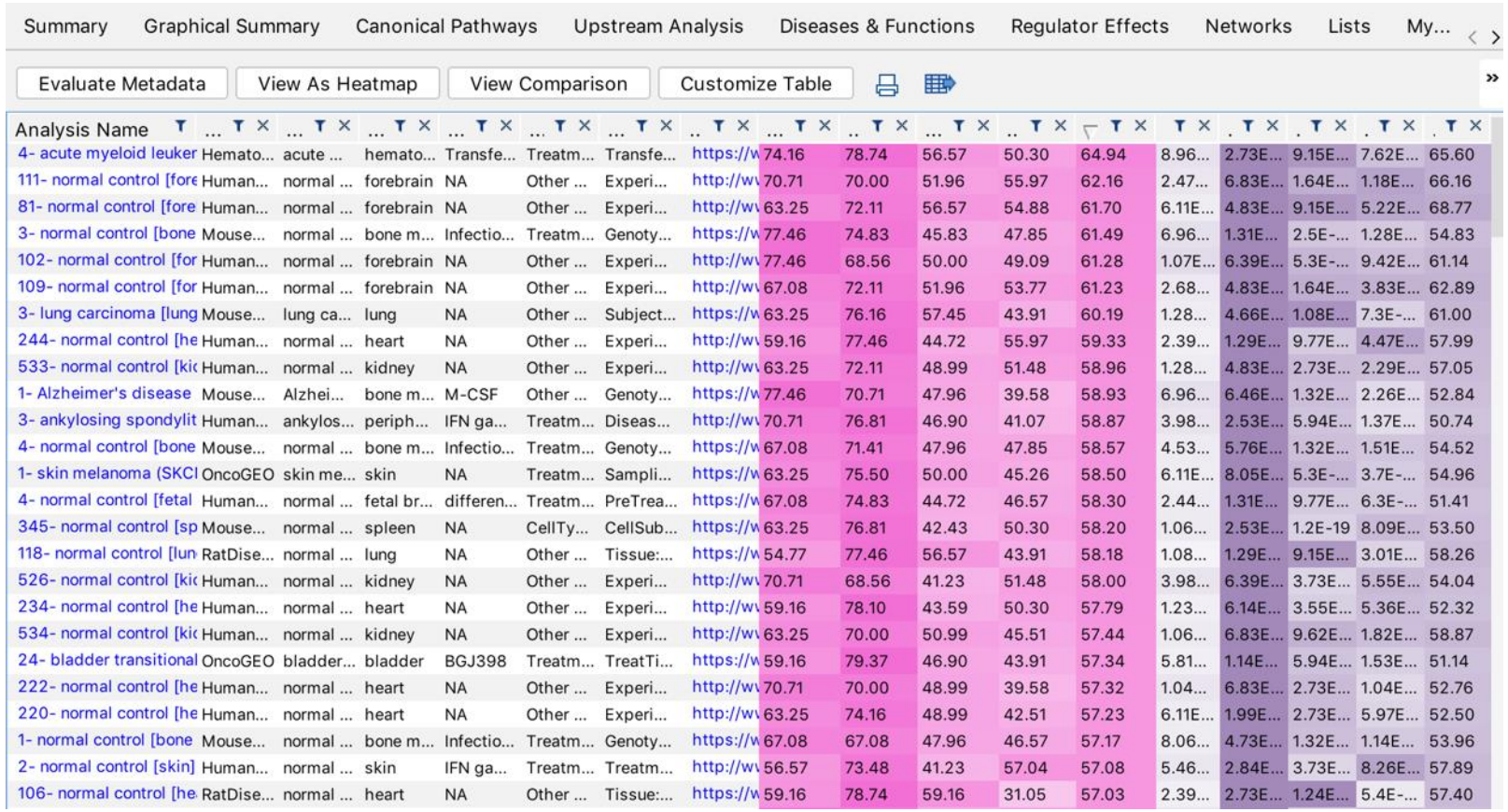
E2F2 has been shown to promote adult cardiomyocyte proliferation.

Compare your analysis to pre-computed datasets

Analysis Match – OmicSoft Lands



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



Summary | Graphical Summary | Canonical Pathways | Upstream Analysis | Diseases & Functions | Regulator Effects | Networks | Lists | My...

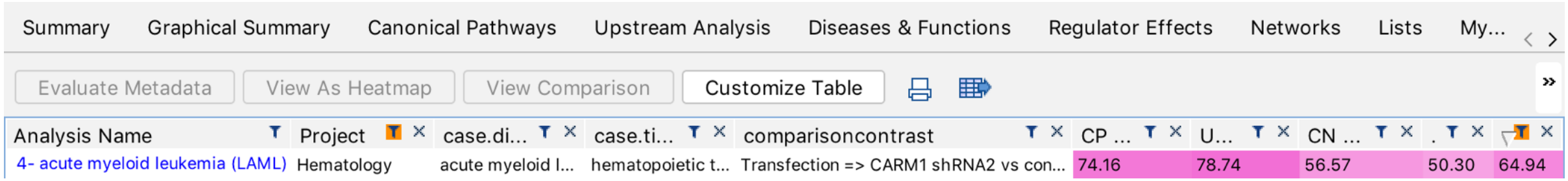
Evaluate Metadata | View As Heatmap | View Comparison | Customize Table

Analysis Name	...	...	...	...	...	...	..	...	..	...	..			.	.	.	.
4- acute myeloid leuker	Hemato...	acute ...	hemato...	Transfe...	Treatm...	Transfe...	https://w	74.16	78.74	56.57	50.30	64.94	8.96...	2.73E...	9.15E...	7.62E...	65.60
111- normal control [fore	Human...	normal ...	forebrain	NA	Other ...	Experi...	http://wv	70.71	70.00	51.96	55.97	62.16	2.47...	6.83E...	1.64E...	1.18E...	66.16
81- normal control [fore	Human...	normal ...	forebrain	NA	Other ...	Experi...	http://wv	63.25	72.11	56.57	54.88	61.70	6.11E...	4.83E...	9.15E...	5.22E...	68.77
3- normal control [bone	Mouse...	normal ...	bone m...	Infectio...	Treatm...	Genoty...	https://w	77.46	74.83	45.83	47.85	61.49	6.96...	1.31E...	2.5E-...	1.28E...	54.83
102- normal control [for	Human...	normal ...	forebrain	NA	Other ...	Experi...	http://wv	77.46	68.56	50.00	49.09	61.28	1.07E...	6.39E...	5.3E-...	9.42E...	61.14
109- normal control [for	Human...	normal ...	forebrain	NA	Other ...	Experi...	http://wv	67.08	72.11	51.96	53.77	61.23	2.68...	4.83E...	1.64E...	3.83E...	62.89
3- lung carcinoma [lung	Mouse...	lung ca...	lung	NA	Other ...	Subject...	https://w	63.25	76.16	57.45	43.91	60.19	1.28...	4.66E...	1.08E...	7.3E-...	61.00
244- normal control [he	Human...	normal ...	heart	NA	Other ...	Experi...	http://wv	59.16	77.46	44.72	55.97	59.33	2.39...	1.29E...	9.77E...	4.47E...	57.99
533- normal control [kic	Human...	normal ...	kidney	NA	Other ...	Experi...	http://wv	63.25	72.11	48.99	51.48	58.96	1.28...	4.83E...	2.73E...	2.29E...	57.05
1- Alzheimer's disease	Mouse...	Alzhei...	bone m...	M-CSF	Other ...	Genoty...	https://w	77.46	70.71	47.96	39.58	58.93	6.96...	6.46E...	1.32E...	2.26E...	52.84
3- ankylosing spondylit	Human...	ankylos...	periph...	IFN ga...	Treatm...	Diseas...	http://wv	70.71	76.81	46.90	41.07	58.87	3.98...	2.53E...	5.94E...	1.37E...	50.74
4- normal control [bone	Mouse...	normal ...	bone m...	Infectio...	Treatm...	Genoty...	https://w	67.08	71.41	47.96	47.85	58.57	4.53...	5.76E...	1.32E...	1.51E...	54.52
1- skin melanoma (SKCI	OncoGEO	skin me...	skin	NA	Treatm...	Sampli...	https://w	63.25	75.50	50.00	45.26	58.50	6.11E...	8.05E...	5.3E-...	3.7E-...	54.96
4- normal control [fetal	Human...	normal ...	fetal br...	differen...	Treatm...	PreTrea...	https://w	67.08	74.83	44.72	46.57	58.30	2.44...	1.31E...	9.77E...	6.3E-...	51.41
345- normal control [sp	Mouse...	normal ...	spleen	NA	CellTy...	CellSub...	https://w	63.25	76.81	42.43	50.30	58.20	1.06...	2.53E...	1.2E-19	8.09E...	53.50
118- normal control [lun	RatDise...	normal ...	lung	NA	Other ...	Tissue:...	https://w	54.77	77.46	56.57	43.91	58.18	1.08...	1.29E...	9.15E...	3.01E...	58.26
526- normal control [kic	Human...	normal ...	kidney	NA	Other ...	Experi...	http://wv	70.71	68.56	41.23	51.48	58.00	3.98...	6.39E...	3.73E...	5.55E...	54.04
234- normal control [he	Human...	normal ...	heart	NA	Other ...	Experi...	http://wv	59.16	78.10	43.59	50.30	57.79	1.23...	6.14E...	3.55E...	5.36E...	52.32
534- normal control [kic	Human...	normal ...	kidney	NA	Other ...	Experi...	http://wv	63.25	70.00	50.99	45.51	57.44	1.06...	6.83E...	9.62E...	1.82E...	58.87
24- bladder transitional	OncoGEO	bladder...	bladder	BGJ398	Treatm...	TreatTi...	https://w	59.16	79.37	46.90	43.91	57.34	5.81...	1.14E...	5.94E...	1.53E...	51.14
222- normal control [he	Human...	normal ...	heart	NA	Other ...	Experi...	http://wv	70.71	70.00	48.99	39.58	57.32	1.04...	6.83E...	2.73E...	1.04E...	52.76
220- normal control [he	Human...	normal ...	heart	NA	Other ...	Experi...	http://wv	63.25	74.16	48.99	42.51	57.23	6.11E...	1.99E...	2.73E...	5.97E...	52.50
1- normal control [bone	Mouse...	normal ...	bone m...	Infectio...	Treatm...	Genoty...	https://w	67.08	67.08	47.96	46.57	57.17	8.06...	4.73E...	1.32E...	1.14E...	53.96
2- normal control [skin]	Human...	normal ...	skin	IFN ga...	Treatm...	Treatm...	http://wv	56.57	73.48	41.23	57.04	57.08	5.46...	2.84E...	3.73E...	8.26E...	57.89
106- normal control [he	RatDise...	normal ...	heart	NA	Other ...	Tissue:...	https://w	59.16	78.74	59.16	31.05	57.03	2.39...	2.73E...	1.24E...	5.4E-...	57.40

Looking for a similar pattern in

- CP (Canonical Pathways)
- UR (Upstream Regulators)
- DE (Downstream Effects)
- CN (Causal Networks)

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

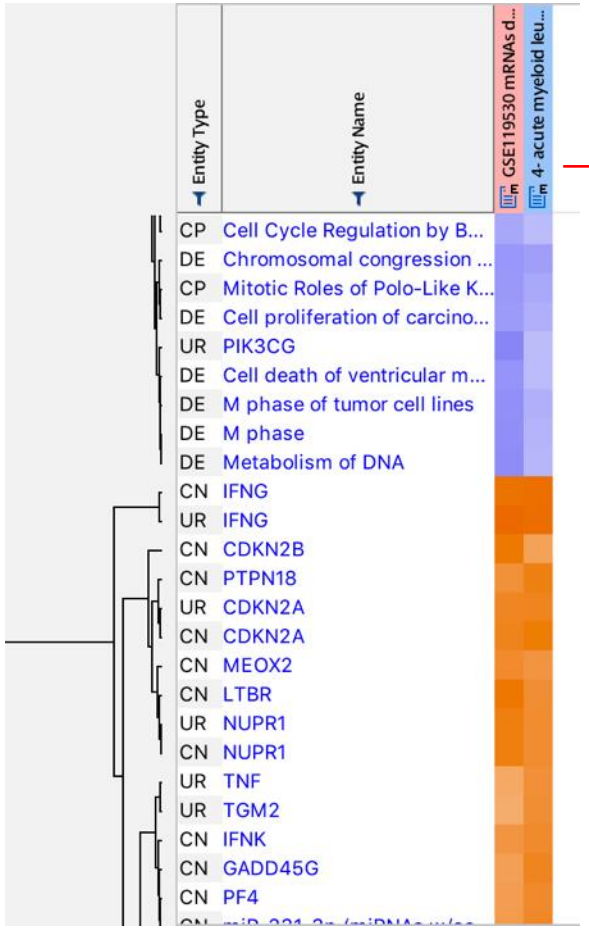


Z-score % > 60

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

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.



Metadata

4- acute myeloid leukemia (LAML) [hematopoietic tissue] Transfection_CARM1 1240

KEY	VALUE
case.celltype	myeloblast
case.diseasestate	acute myeloid leukemia (LAML)
case.sampleids	GSM2773098;GSM2773101;GSM2773104
case.samplematerial	unsorted cells
case.samplesource	myeloblast
case.samplingtime[hours]	.
case.tissue	hematopoietic tissue
case.transfection	CARM1 shRNA2
case.treatment	Transfection_CARM1 shRNA2
case.treattime[days]	.
case.treattime[hours]	.
case.treattime[minutes]	.
comparisoncategory	Treatment vs. Control
comparisoncontrast	Transfection => CARM1 shRNA2 vs control shRNA
comparisonid	GSE103528.GPL18573.DESeq2.test4
comparisonindex	1240
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] Transfe...
organism	human
platformname	NGS.Illumina.NextSeq500
projectname	GSE103528
sampledatamode	RnaSeq_Transcript
upregulated log2 cutoff	1.1452
weblink	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE103528

Acute Myeloid Leukemia

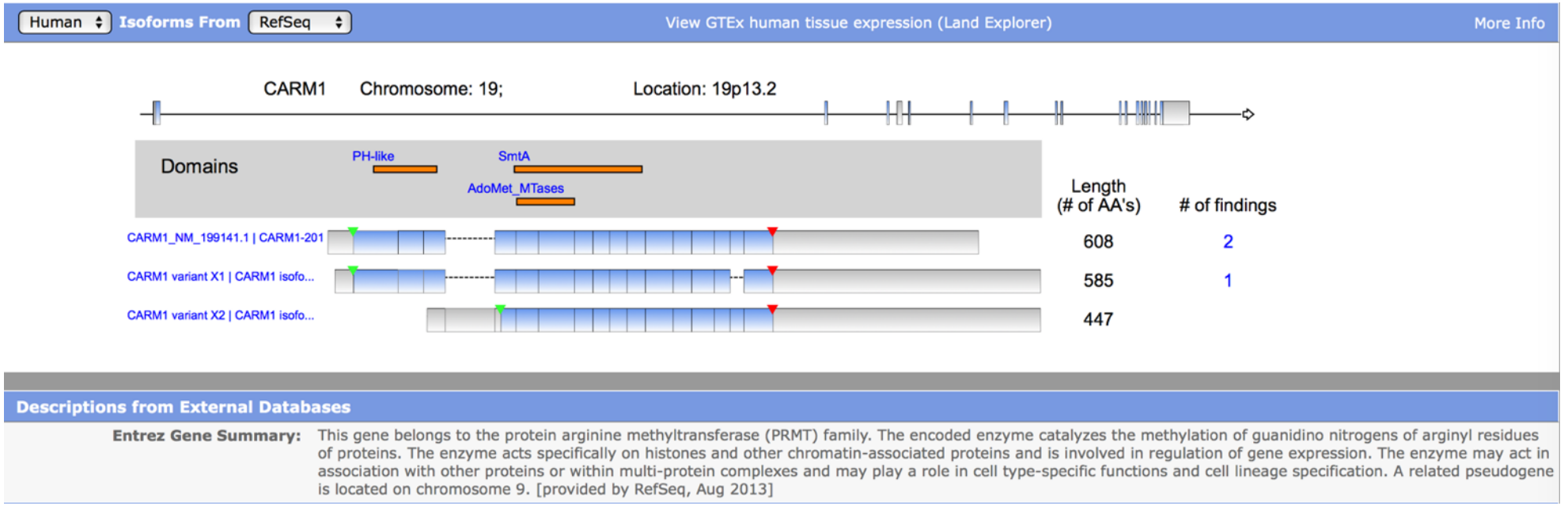
CARM1 shRNA vs control shRNA

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 demethylation 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.



Unique analysis sharing similar pattern with mRNA day 23 is GS103528

GSE103528: CARM1 is essential for myeloid leukemogenesis but dispensable for normal hematopoiesis

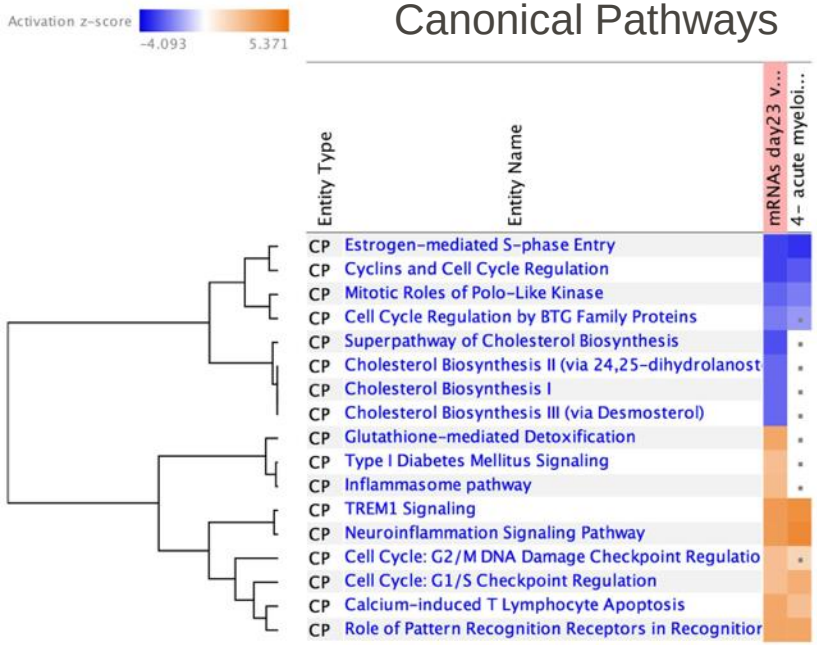
Greenblatt SM et al. Cancer Cell, 2018.

- 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

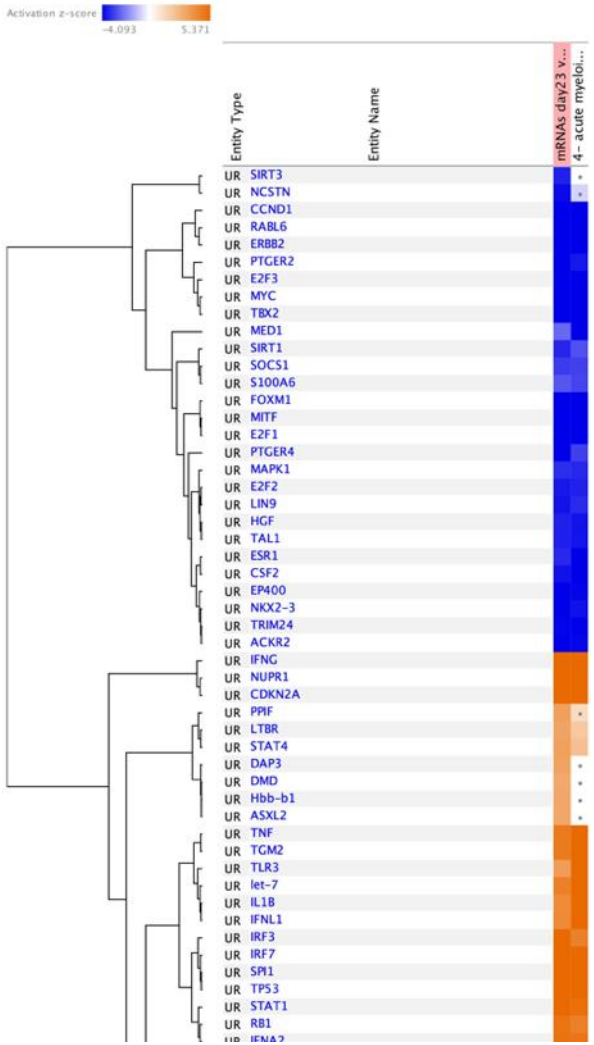
Hypothesis: CARM1 may be involved as well in the post-natal mouse heart biology

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

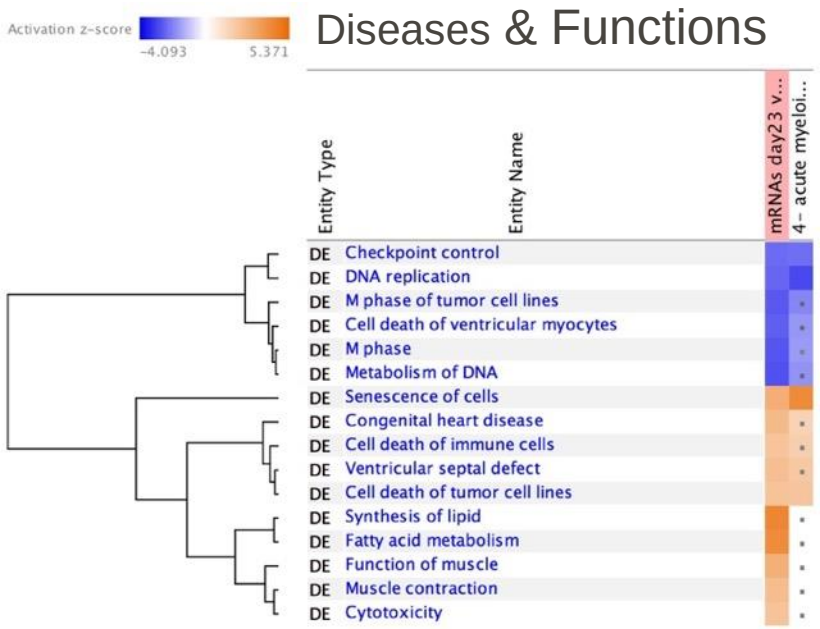
Canonical Pathways



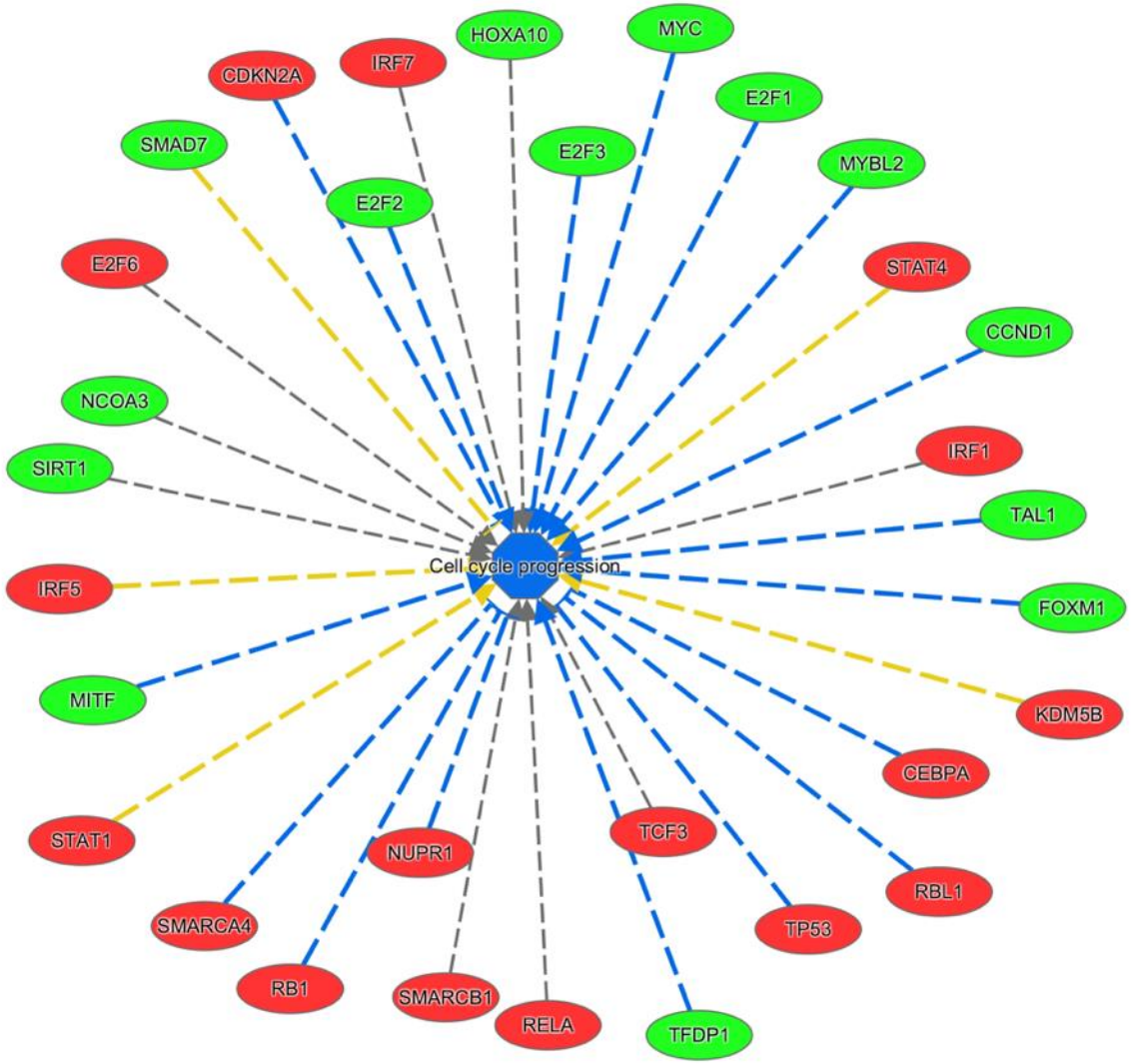
Upstream Regulators



Diseases & Functions



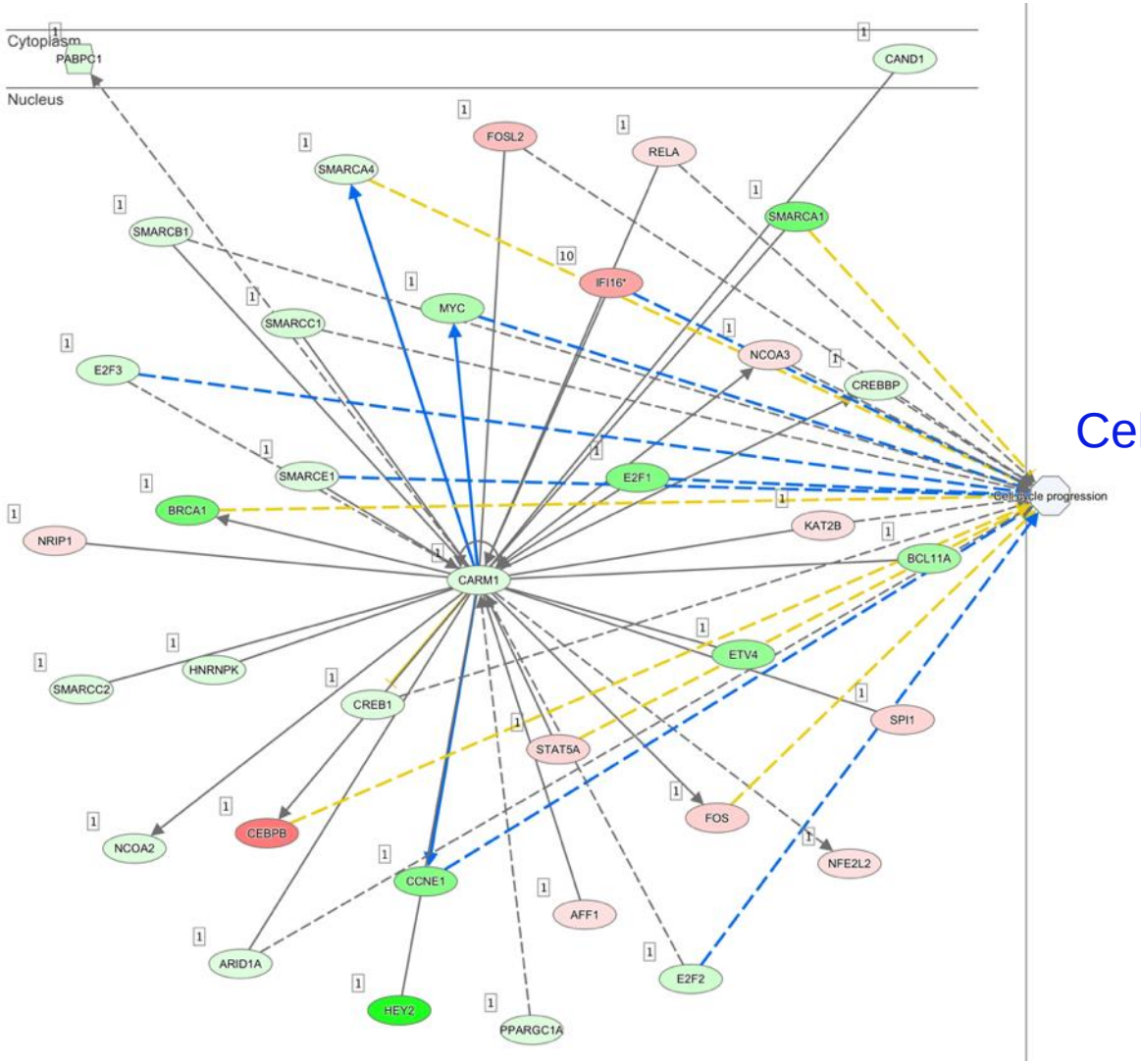
Upstream Regulator Analysis indicates inhibition of cell cycle progression



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

Cell cycle progression decreased

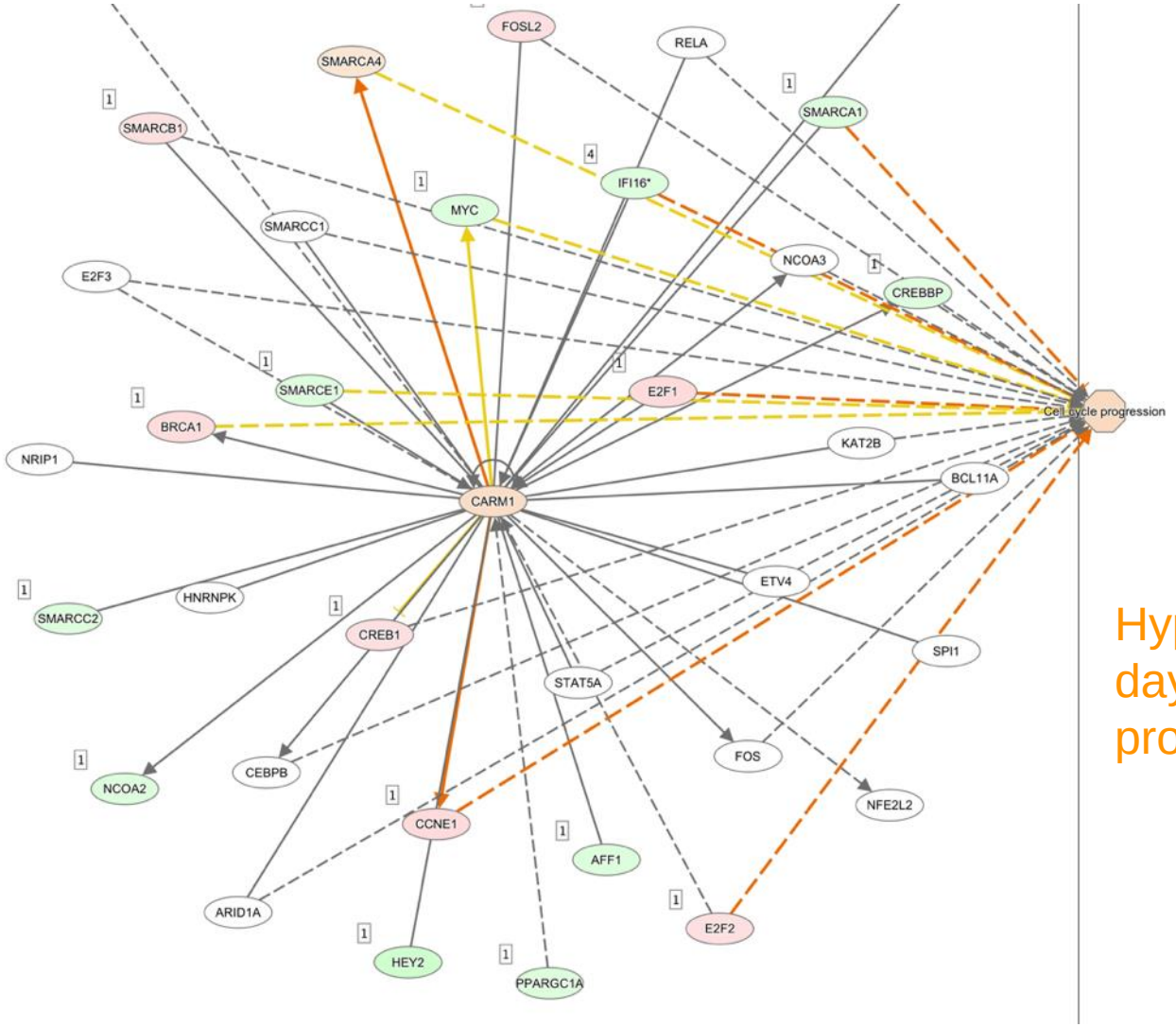
CARM1 itself is downregulated in post-natal mouse heart at day 23



Cell cycle progression

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

Activation of CARM1 may allow cell cycle to progress again



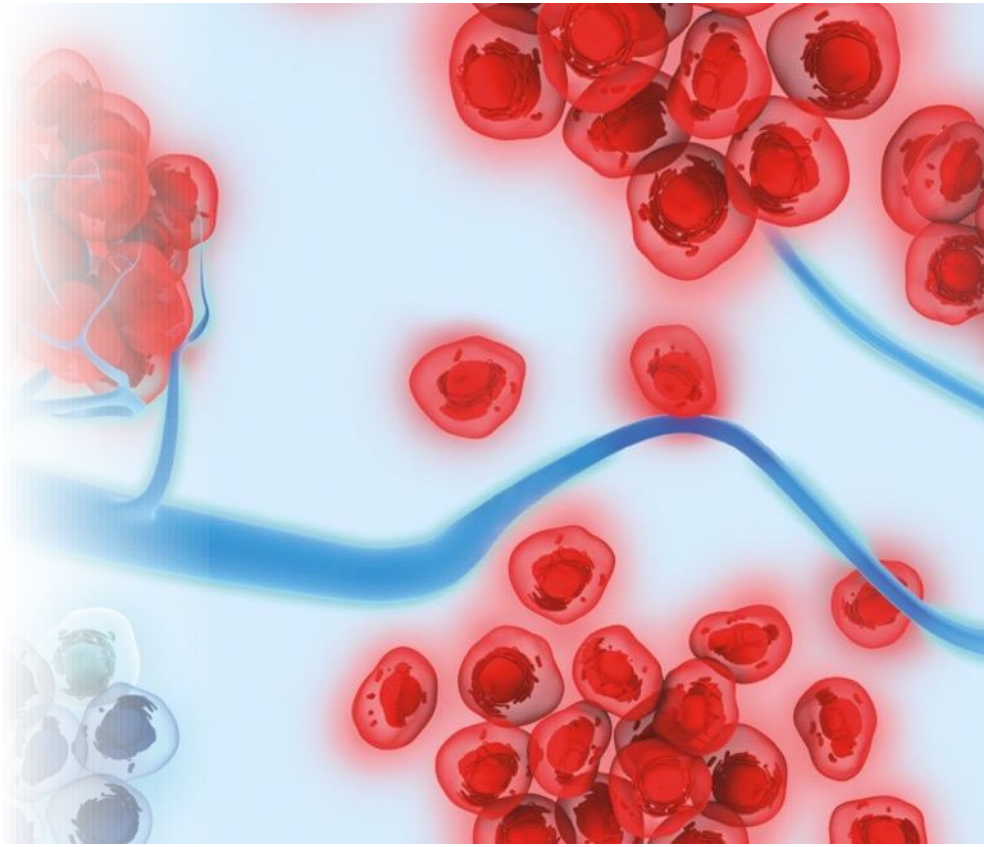
CARM1 is upregulated at day 4 and is driving increase of cell cycle progression

Cell cycle progression

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

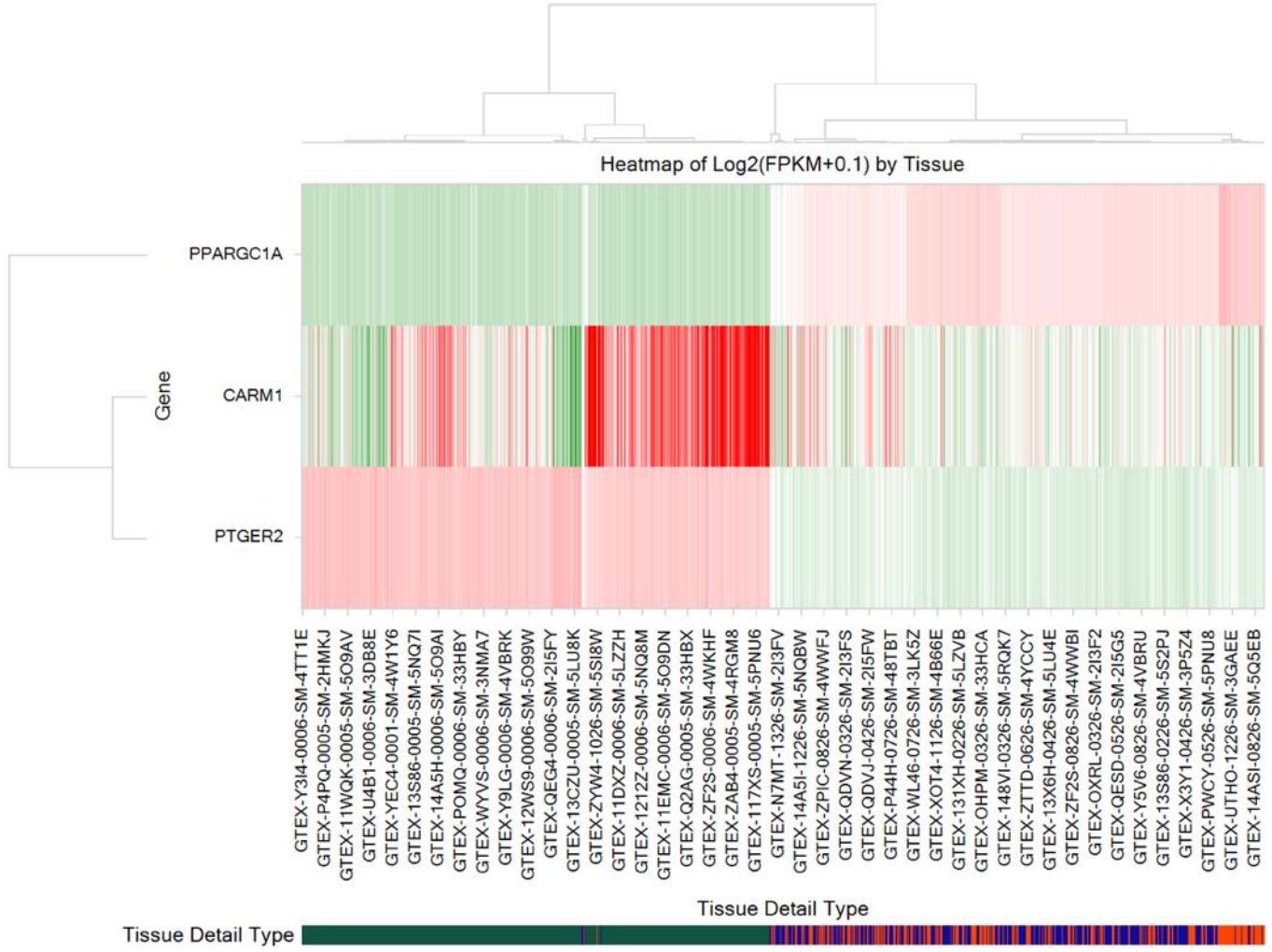
Visualize the connections of important genes in fetal heart and post-natal mouse heart

OmicSoft



Expression of important genes in GTEX and connections to predictions

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



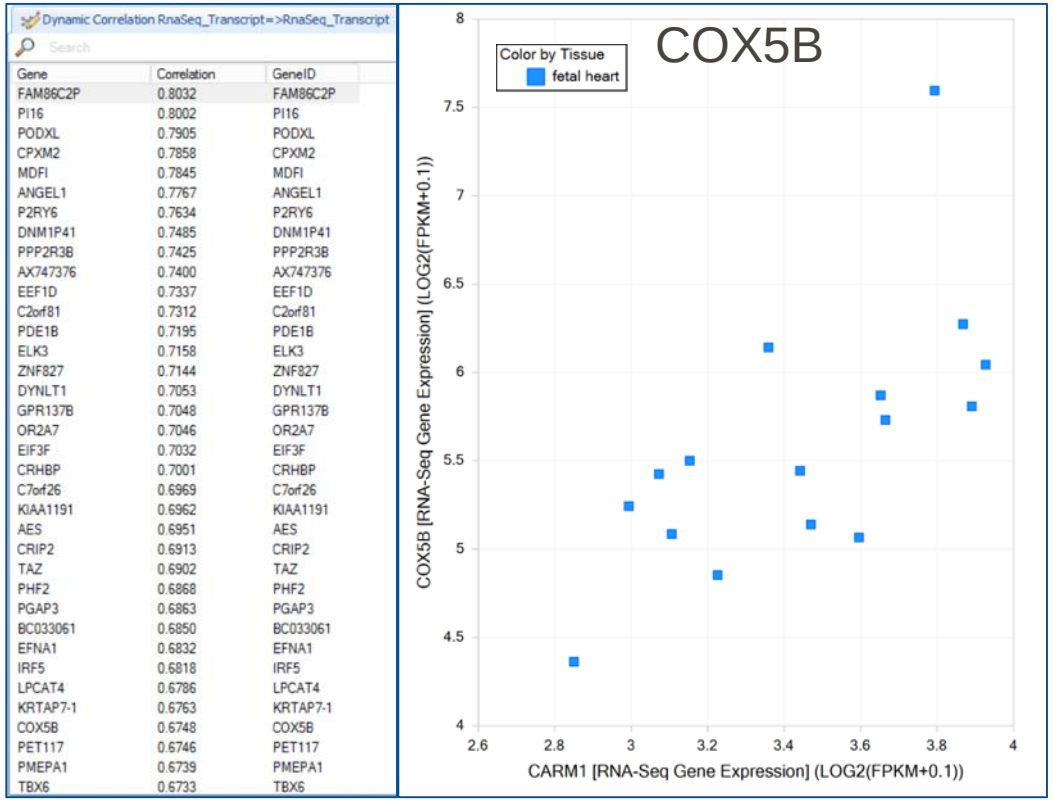
PPARGC1A is enriched in heart and predicted to be activated at day 23

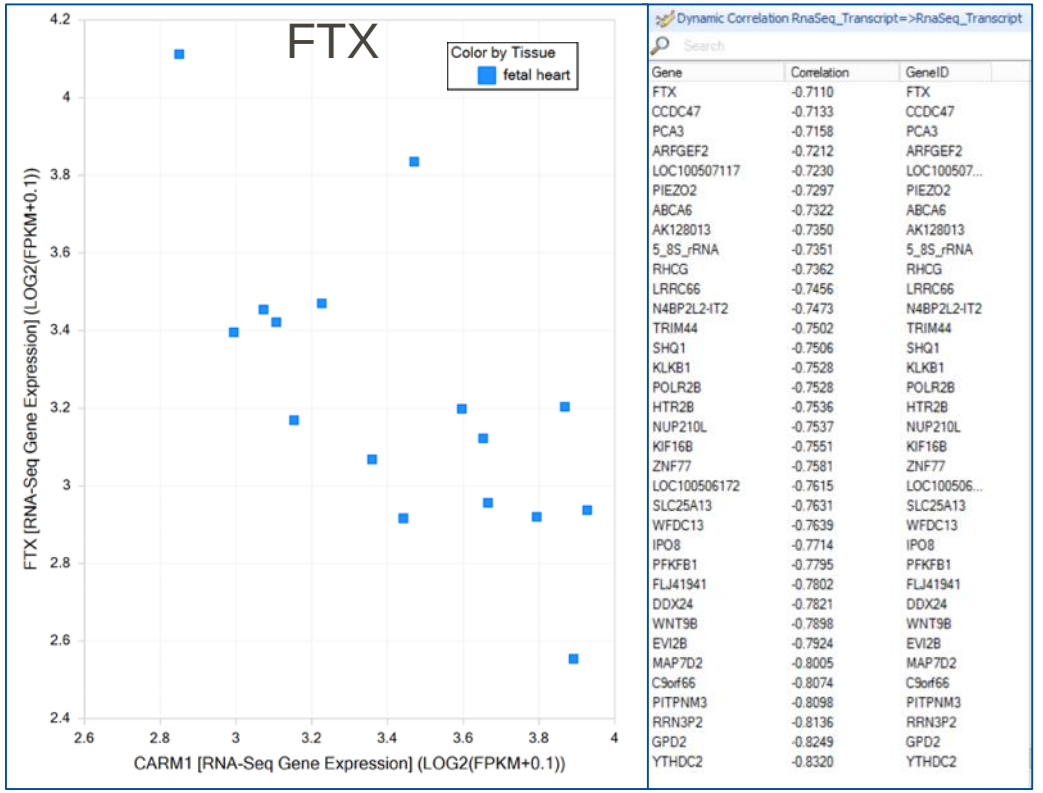
CARM1A is not enriched in heart and down-regulated at day 23

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.





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

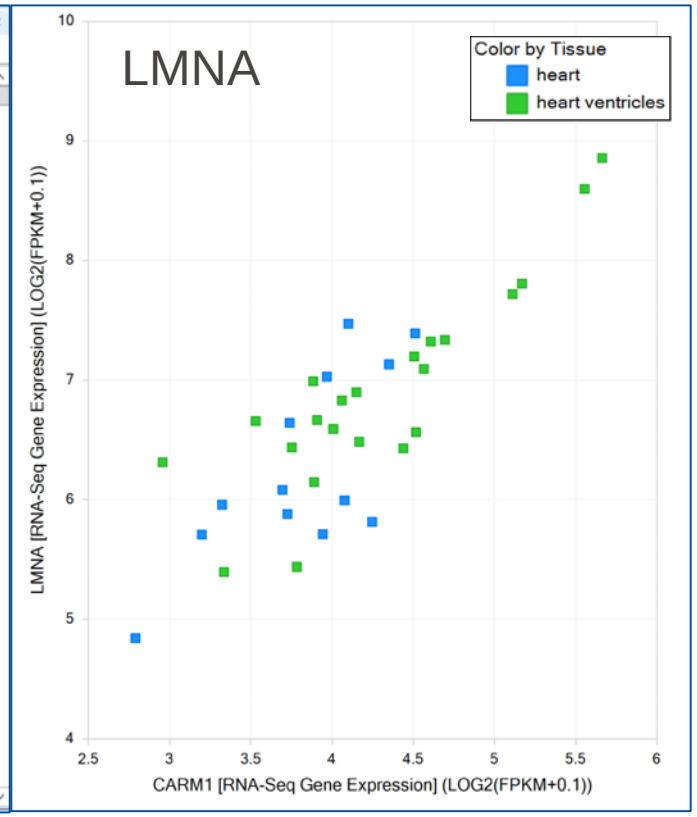
Dynamic correlation with CARM1 in post-natal heart

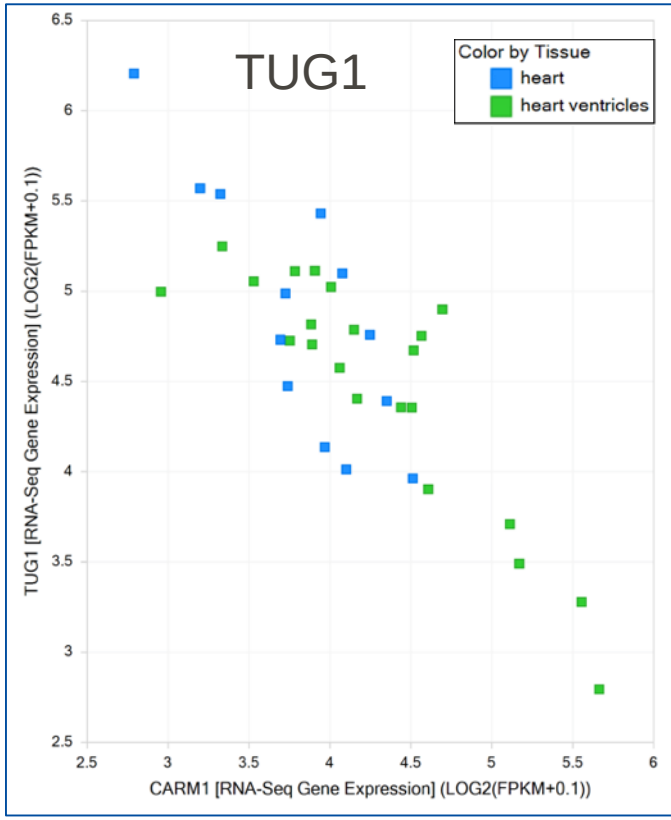
Laminin A is correlated positively with CARM1, TUG1 is negatively correlated with CARM1 in adult heart.

Dynamic Correlation RnaSeq_Transcript=>RnaSeq_Transcript

Search

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

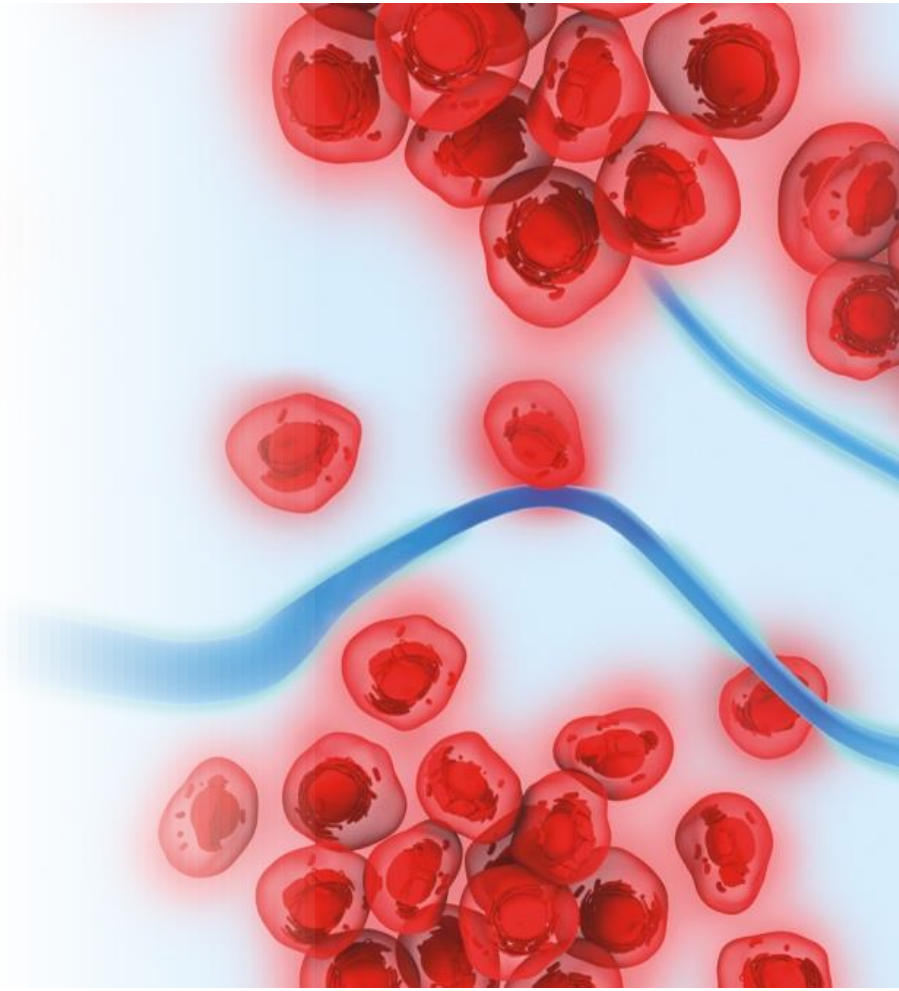
Search

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

- 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

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- German toll: +49 (0)341 33975301

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AdvancedGenomicsSupport@qiagen.com

Websites:

www.qiagenbioinformatics.com

http://tv.qiagenbioinformatics.com

Resources

QIAGEN IPA

- IPA product info: https://digitalinsights.qiagen.com/products-overview/discovery-insights-portfolio/analysis-and-visualization/qiagen-ipa
- IPA Analysis Match: https://tv.qiagenbioinformatics.com/video/37242337/exploring-ipas-analysis-match-an
- Land Explorer: https://digitalinsights.qiagen.com/products-overview/discovery-insights-portfolio/content-exploration-and-databases/qiagen-omicsoft-land-explorer/
- Coronavirus Network Explorer: https://digitalinsights.qiagen.com/coronavirus-network-explorer/

QIAGEN OmicSoft:

- Product Info: https://digitalinsights.qiagen.com/products-overview/discovery-insights-portfolio/qiagen-omicsoft/

QIAGEN CLC Genomics

- Product info: https://digitalinsights.qiagen.com/products-overview/analysis-and-visualization/qiagen-clc-genomics-workbench/

QIAGEN expands integrated coronavirus NGS and software solutions to accelerate COVID-19 research

- QIAseq SARS-CoV-2 Primer Panel converts viral RNA samples into libraries ready for sequencing
- QIAGEN Digital Insights solutions support COVID-19 drug, vaccine and epidemiology research
- For an overview of QIAGEN's coronavirus testing solutions, please visit http://www.qiagen.com/coronavirus.
- To explore QIAGEN's NGS-specific solutions for COVID-19 research, please visit https://go.qiagen.com/CoronavirusNGS
- For details of QIAGEN's SARS-CoV-2 Whole Genome Sequencing Service, please visit https://www.qiagen.com/applications/genomic-services/sars-cov-2-whole-genome-sequencing-services

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