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Science Foundation Ireland sfi For what's next

SFI Centre for Research Training in GENOMICS DATA SCIENCE

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Computational approaches for the therapeutic target discovery to ameliorate muscle wasting during aging and disease

Msc Karen Guerrero Vazquez

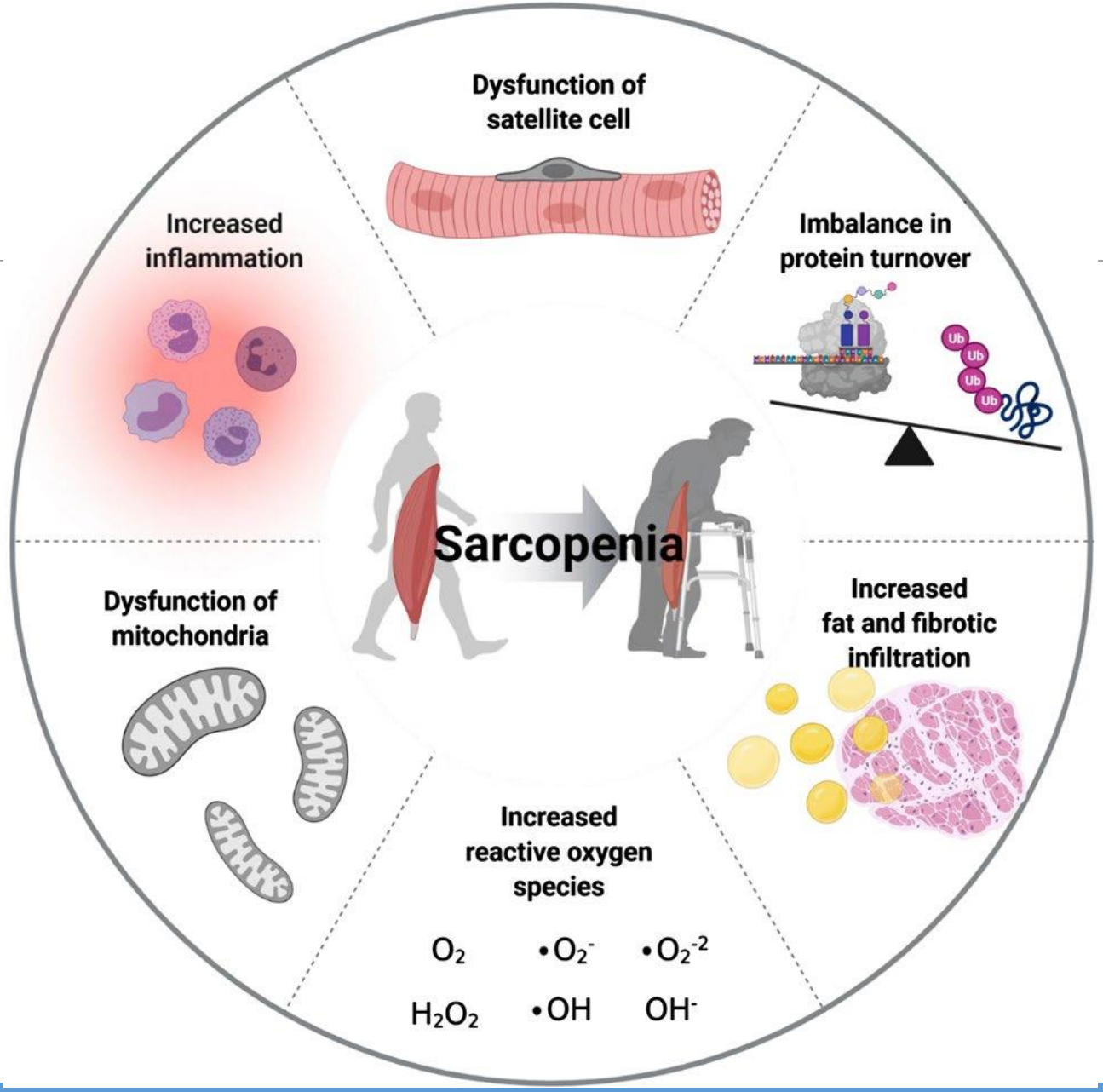
Dr. Katarzyna Whysall

Dr. Pilib O Broin

~3 – 8 %

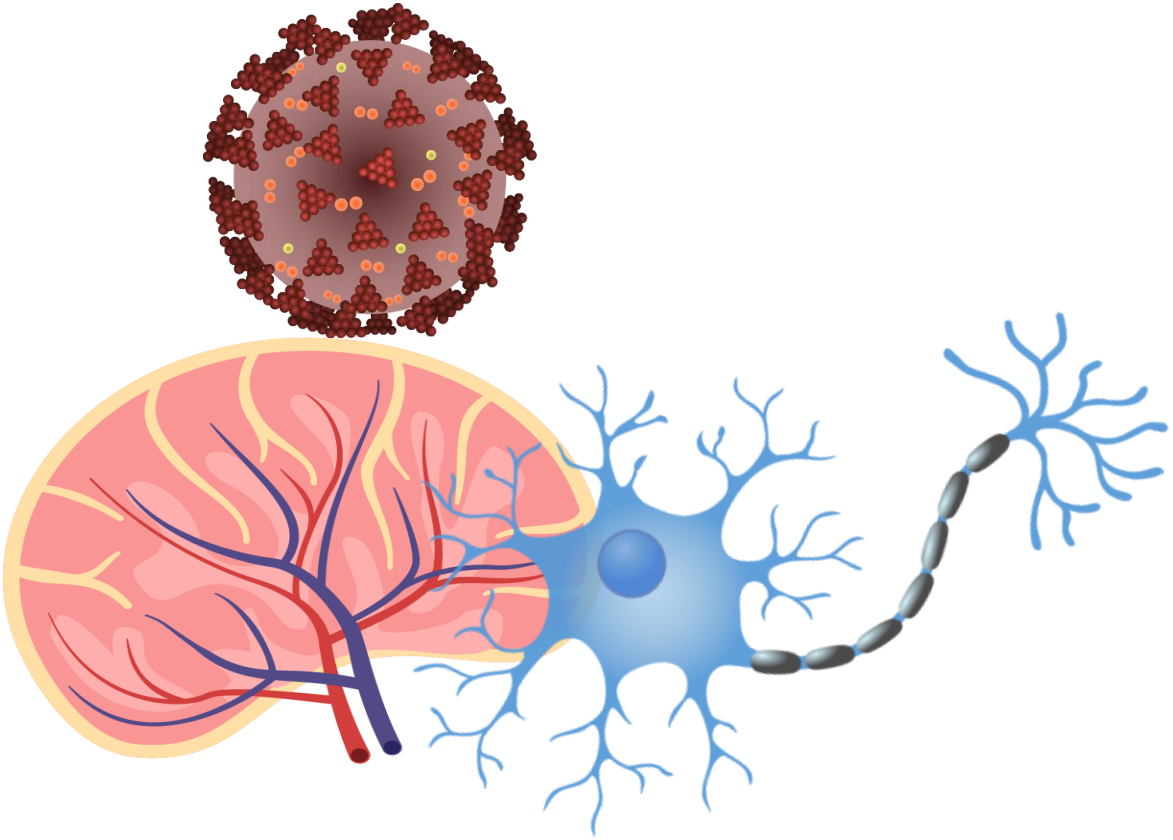
Loss of muscle mass per decade

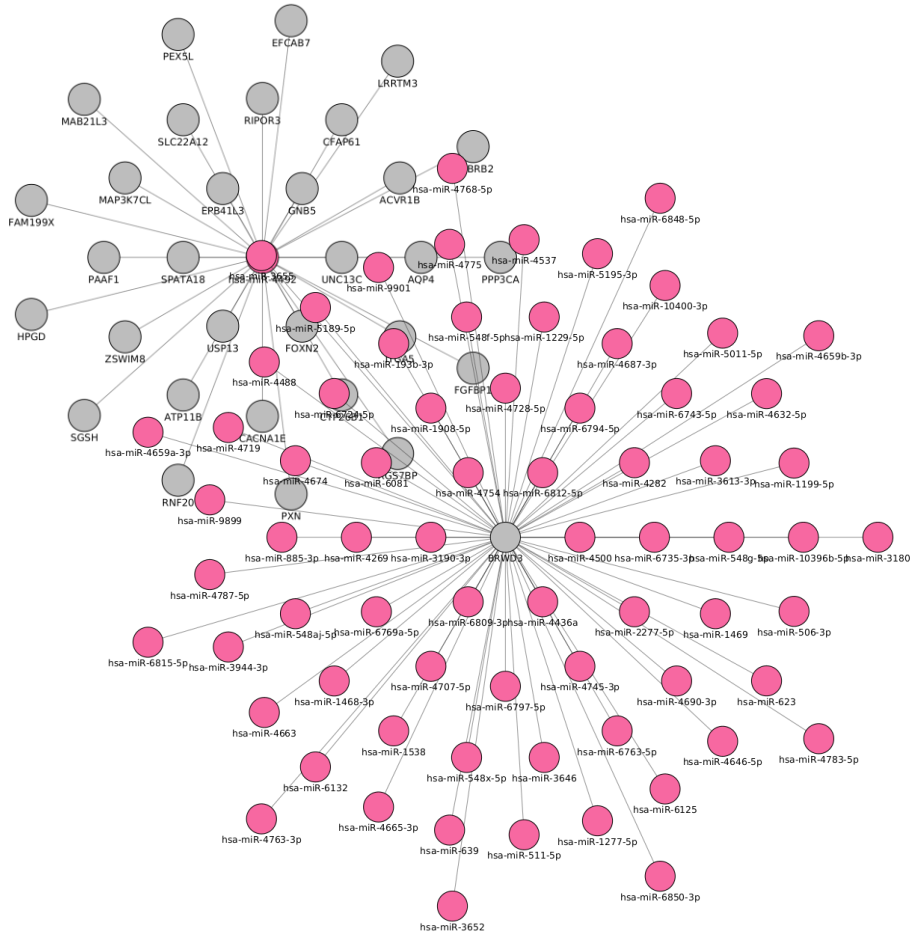
Brocklehurst, 1976


Dysfunction of satellite cell
Increased inflammation
Imbalance in protein turnover
Ub
Ub
Ub
Ub
Sarcopenia
Dysfunction of mitochondria
Increased fat and fibrotic infiltration
Increased reactive oxygen species
O_2
$\bullet O_2^-$
$\bullet O_2^{-2}$
H_2O_2
$\bullet OH$
OH^-

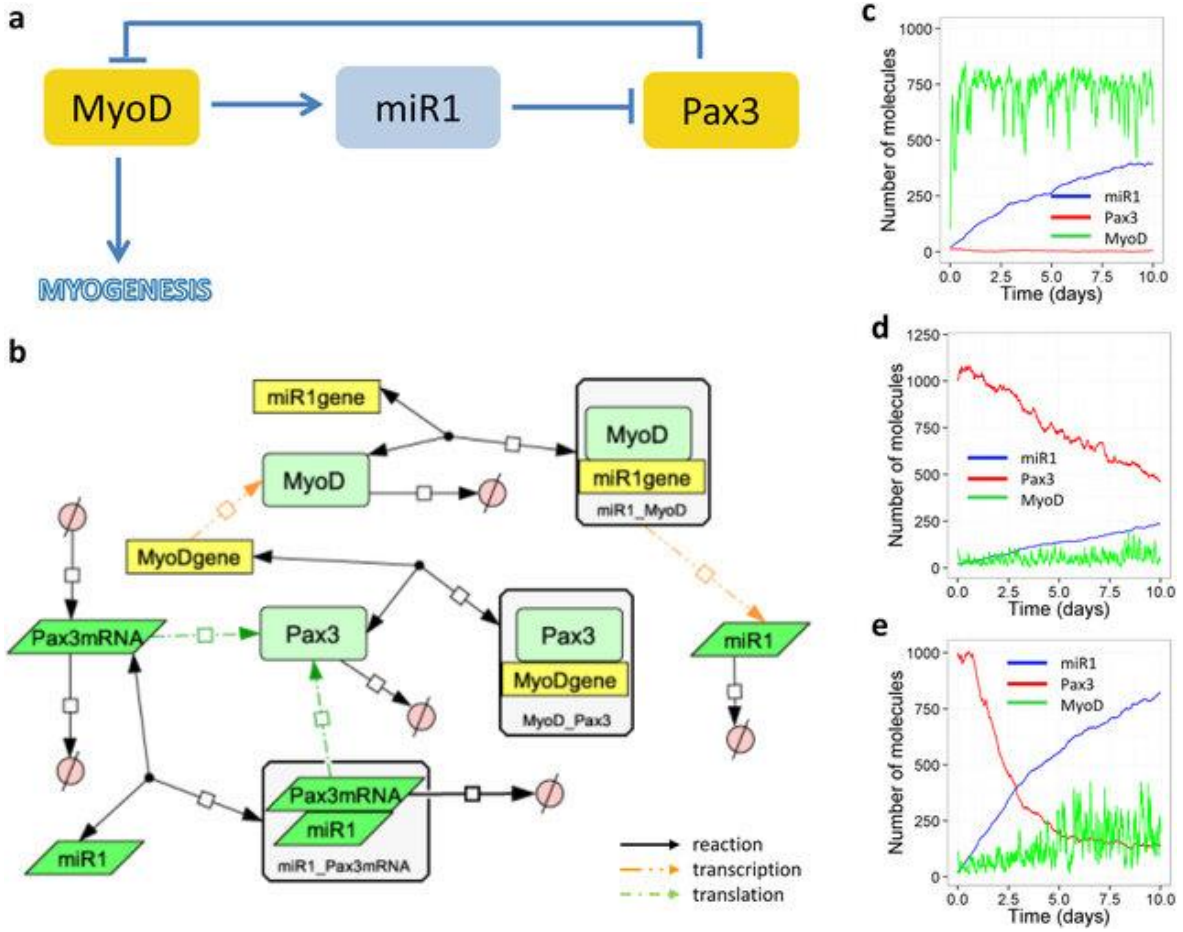
MicroRNA (miRNAs)

MicroRNA (miRNAs)





Objective



- Create independent models and a common model of miR:target interactions in muscle loss during aging and critical illness based on differentially expressed (DE) miRs and genes
- Identification or shortlisted microRNAs as candidates for therapeutics targets against sarcopenia.

Carole J. Proctor & Katarzyna Goljanek-Whysall, 2017, Using computer simulation models to investigate the most promising microRNAs to improve muscle regeneration during ageing

Tools to analyze miRNAs

Tools to analyze miRNAs

Tools to analyze miRNAs

miRDB

miRBase

miTED

Tools to analyze miRNA

miRWalk 2.0

miRDB

miRBase

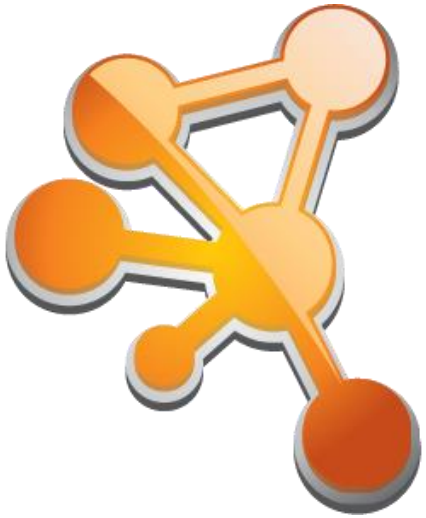
miTED

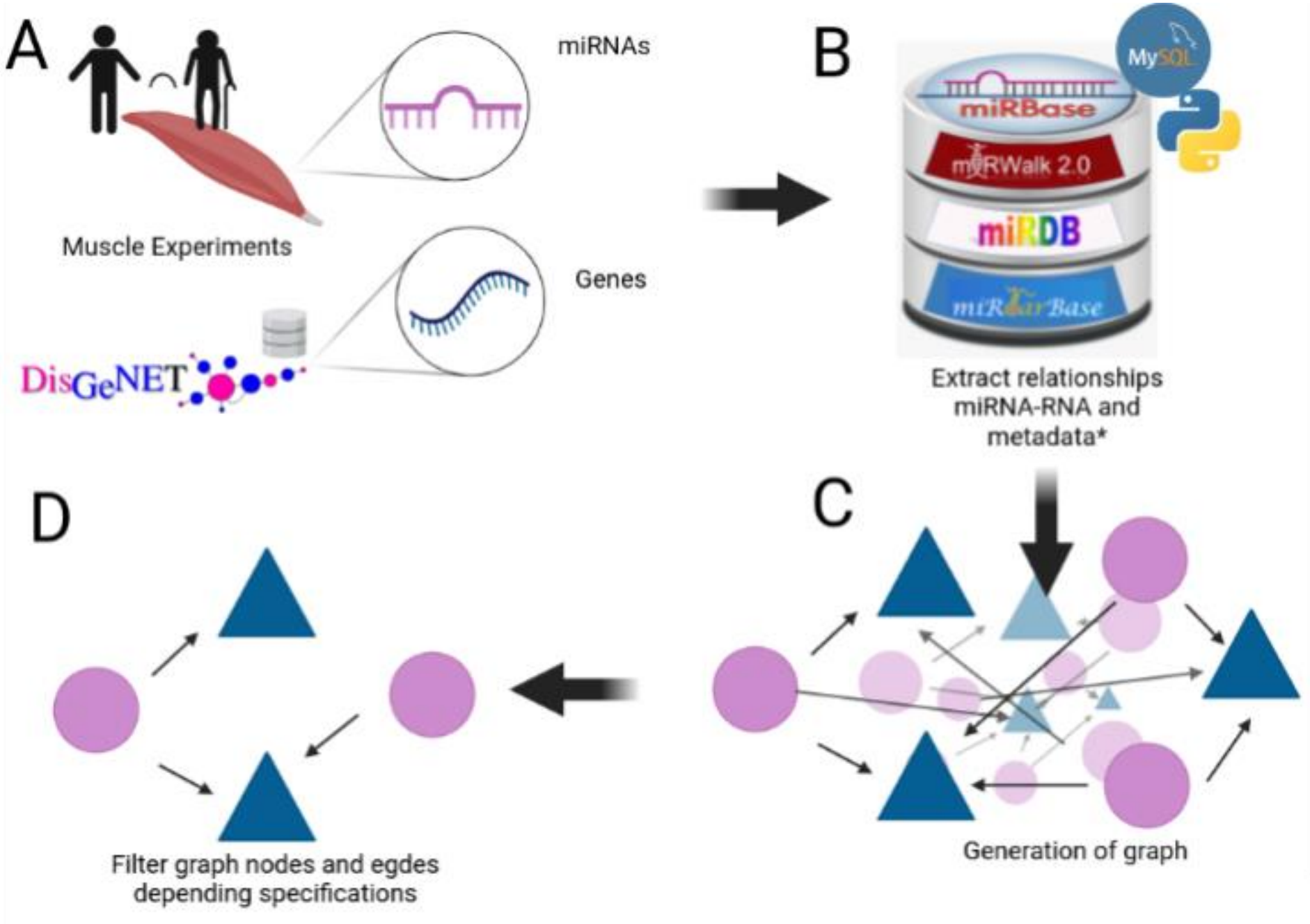
Tools to analyze miRNAs

Tools to analyze miRNAs

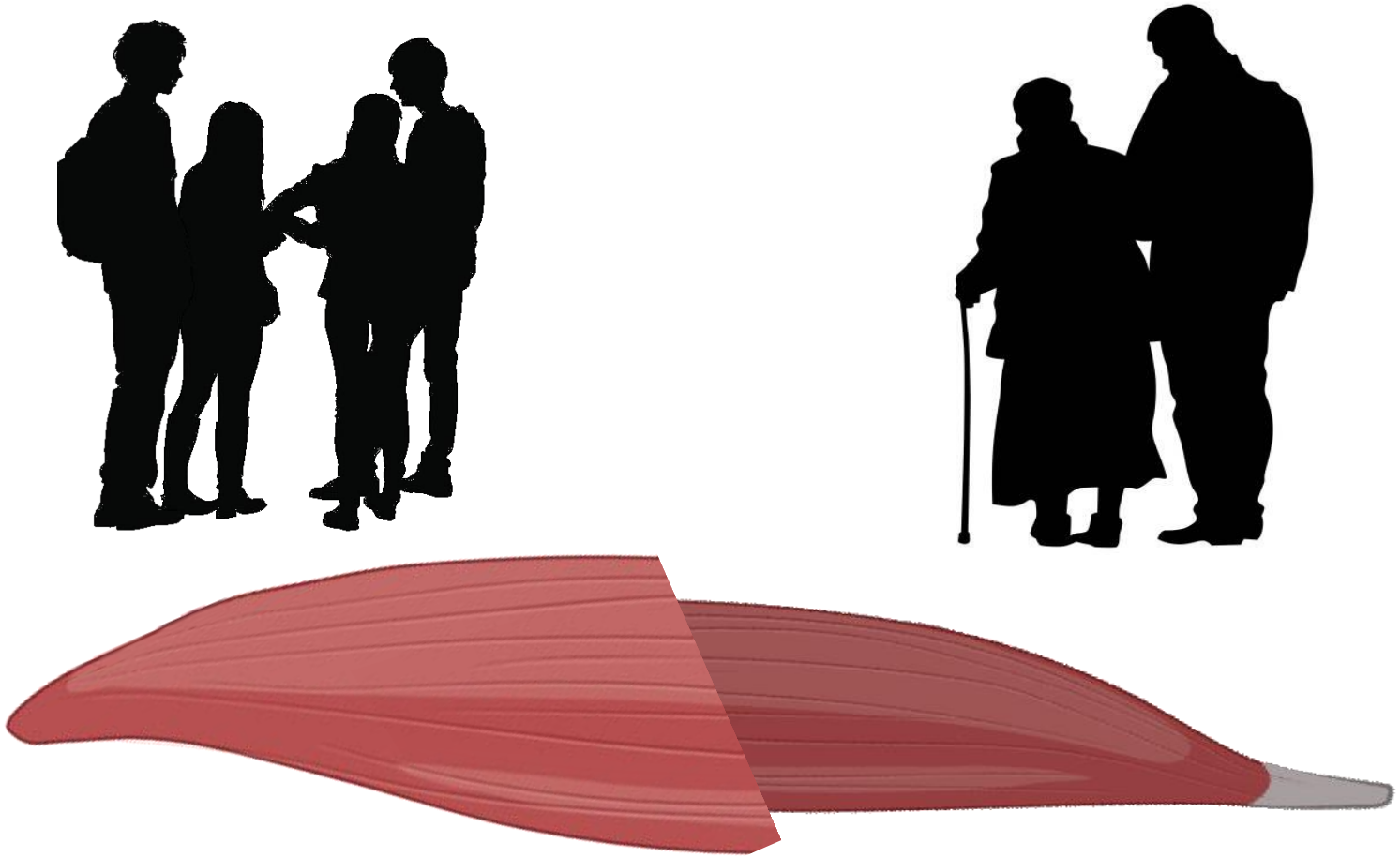
Tools to analyze miRNAs

Tools to analyze miRNAs




A
miRNAs
Muscle Experiments
Genes
DisGeNET
B
MySQL
miRBase
miRWalk 2.0
miRDB
miRTarBase
Extract relationships
miRNA-RNA and
metadata*
C
Generation of graph
D
Filter graph nodes and egdes
depending specifications

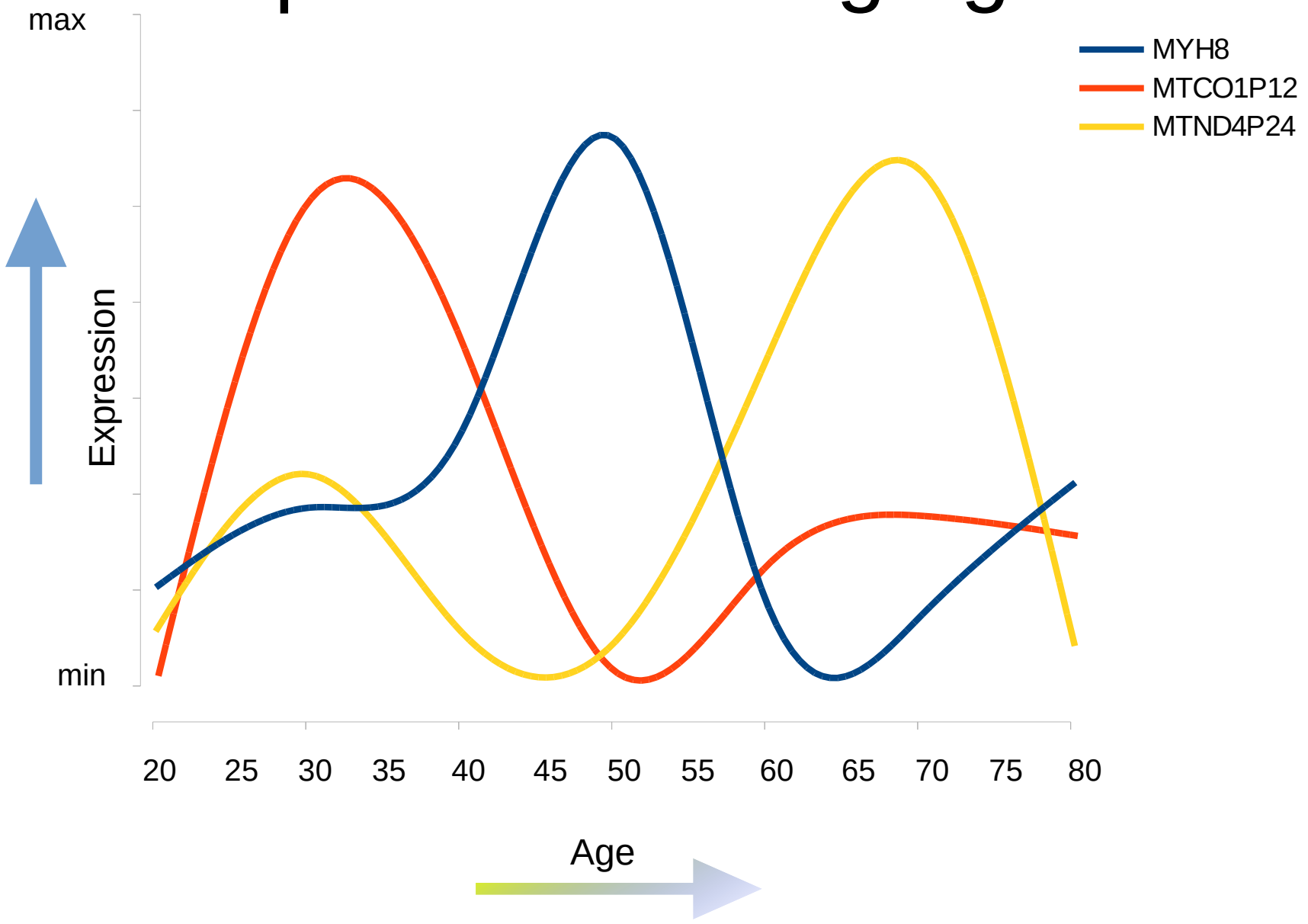
How to start



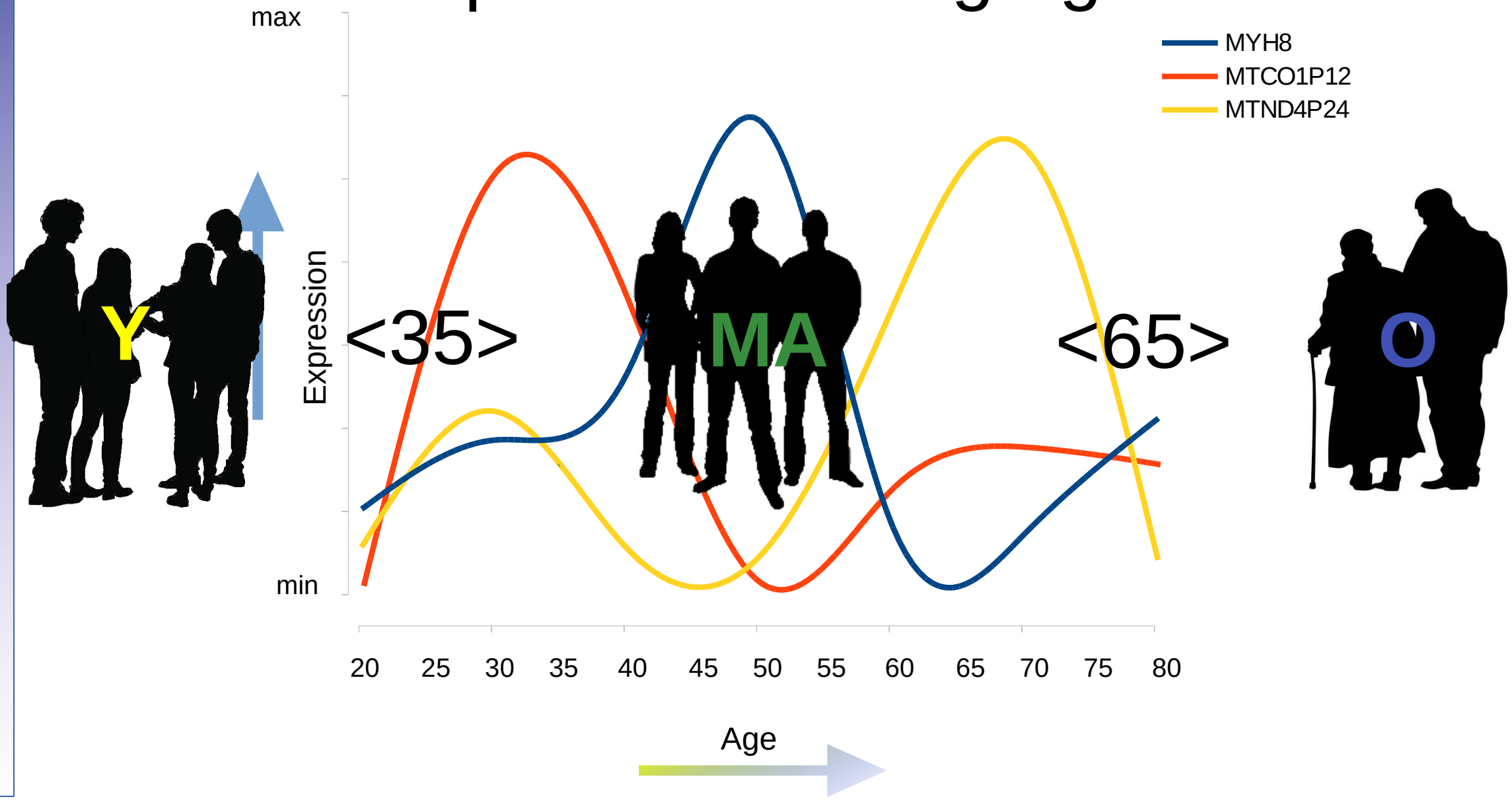
My Experiments

Target	Type	N. Experiments	Healthy	Non healthy
mRNA	RNAseq	3	3	0
	Microarray	4	2	2
miRNA	Microarray	2	2	0
	miRSeq	1	0	1

Expression during age

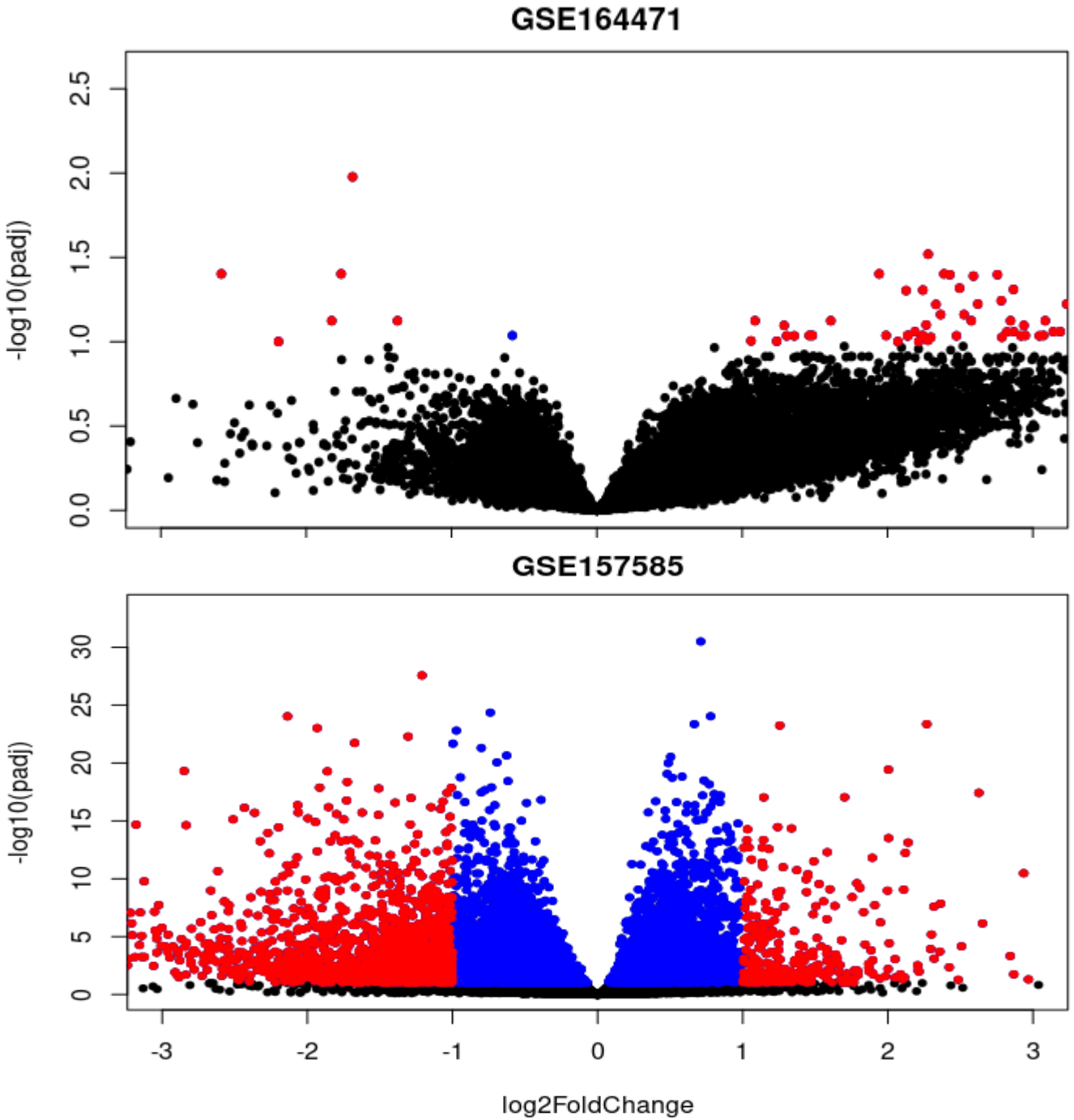


Expression during age



Experiments

GEO number	Samples	Min Age	Max Age	Reference
GSE152558	5	41	85	Tharakan, R., Ubaida-Mohien, C., Piao, Y., Gorospe, M., & Ferrucci, L. (2021).
GSE164471	53	34	80	Tumasian III, R. A., Harish, A., Kundu, G., Yang, J. H., Ubaida-Mohien, C., Gonzalez-Freire, M., ... & Ferrucci, L. (2021).
GSE157585	136	19	>65	Kulkarni, A. S., Peck, B. D., Walton, R. G., Kern, P. A., Mar, J. C., Windham, S. T., ... & Peterson, C. A. (2020).
GSE87105	16	30	78	Mercken, E. M., Capri, M., Carboneau, B. A., Conte, M., Heidler, J., Santoro, A., ... & de Cabo, R. (2017)..
GSE23527	36	29	76	Drummond, M. J., McCarthy, J. J., Sinha, M., Spratt, H. M., Volpi, E., Esser, K. A., & Rasmussen, B. B. (2011)



1)GSE152558

2)GSE164471

3)GSE157585

4)GSE87105

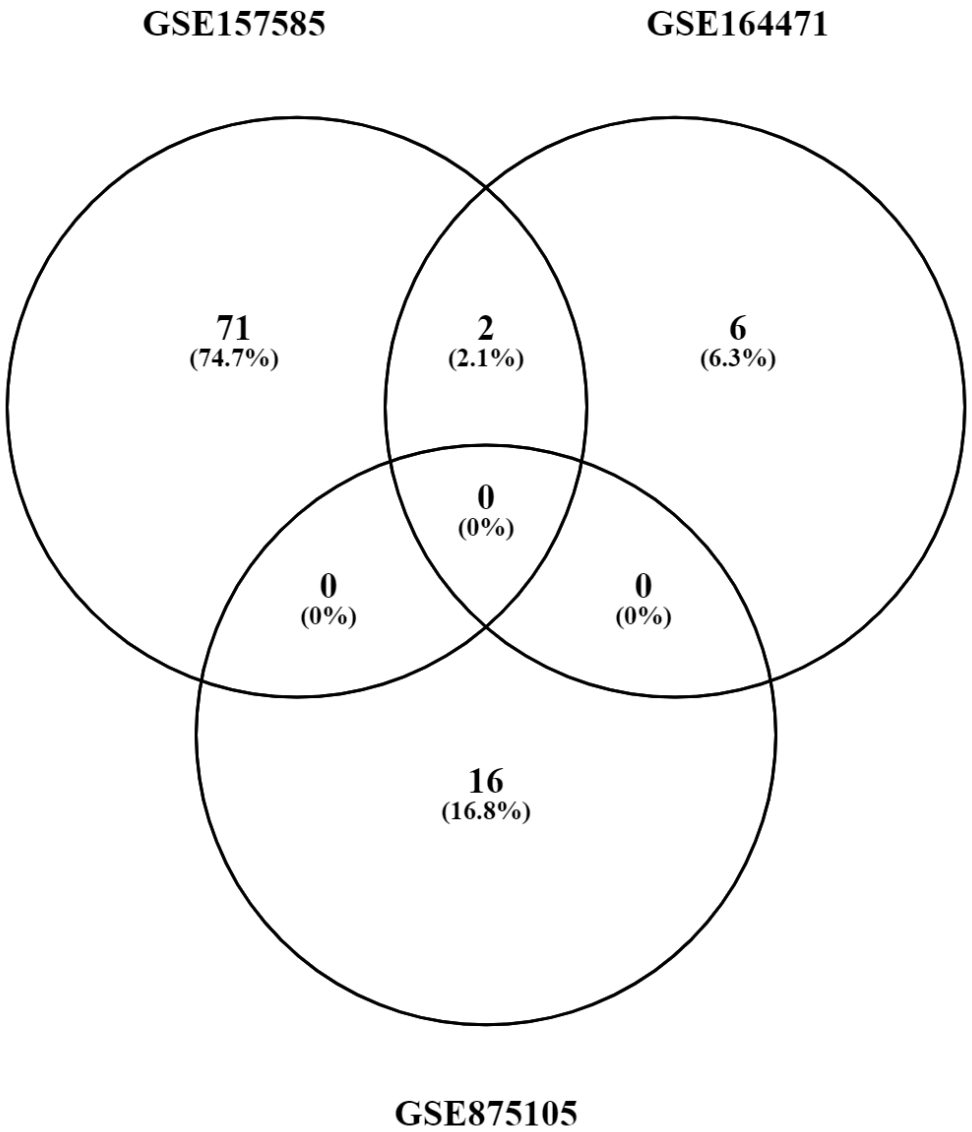
5)GSE23527

Differentially Expressed Genes

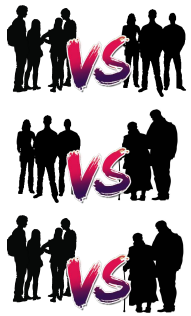
Experiment	Evaluation	Regulation	Genes
GSE152558	MO	UP	8
GSE152558	MO	Down	9
GSE157585	YO	UP	9
GSE157585	YO	Down	73
GSE164471	YO	UP	5
GSE164471	YM	UP	2
GSE164471	MO	UP	6
GSE164471	YO	Down	8
GSE164471	YM	Down	2
GSE164471	MO	Down	11
GSE23527	YO	Up	1
GSE23527	YO	Down	5
GSE875105	OY	Down	88
GSE875105	MO	Up	6
GSE875105	OY	Up	18

Old vs Young (up or down)

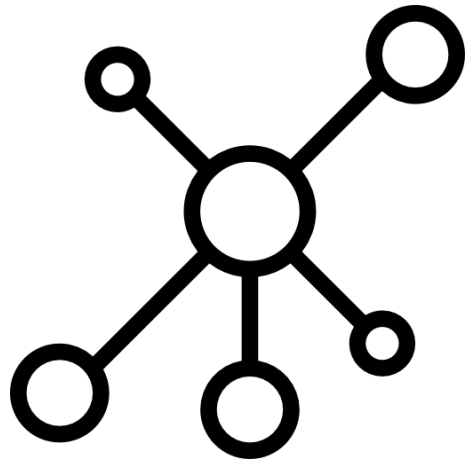
- MYH8
- HCN1



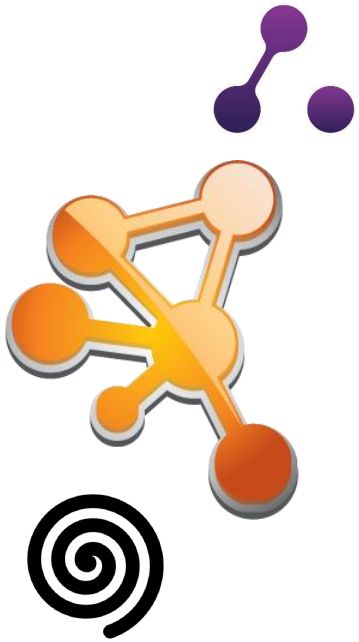

2.0


VS
VS
VS


2.0

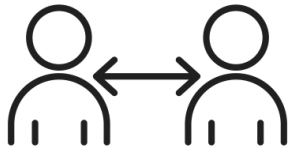


20 genes



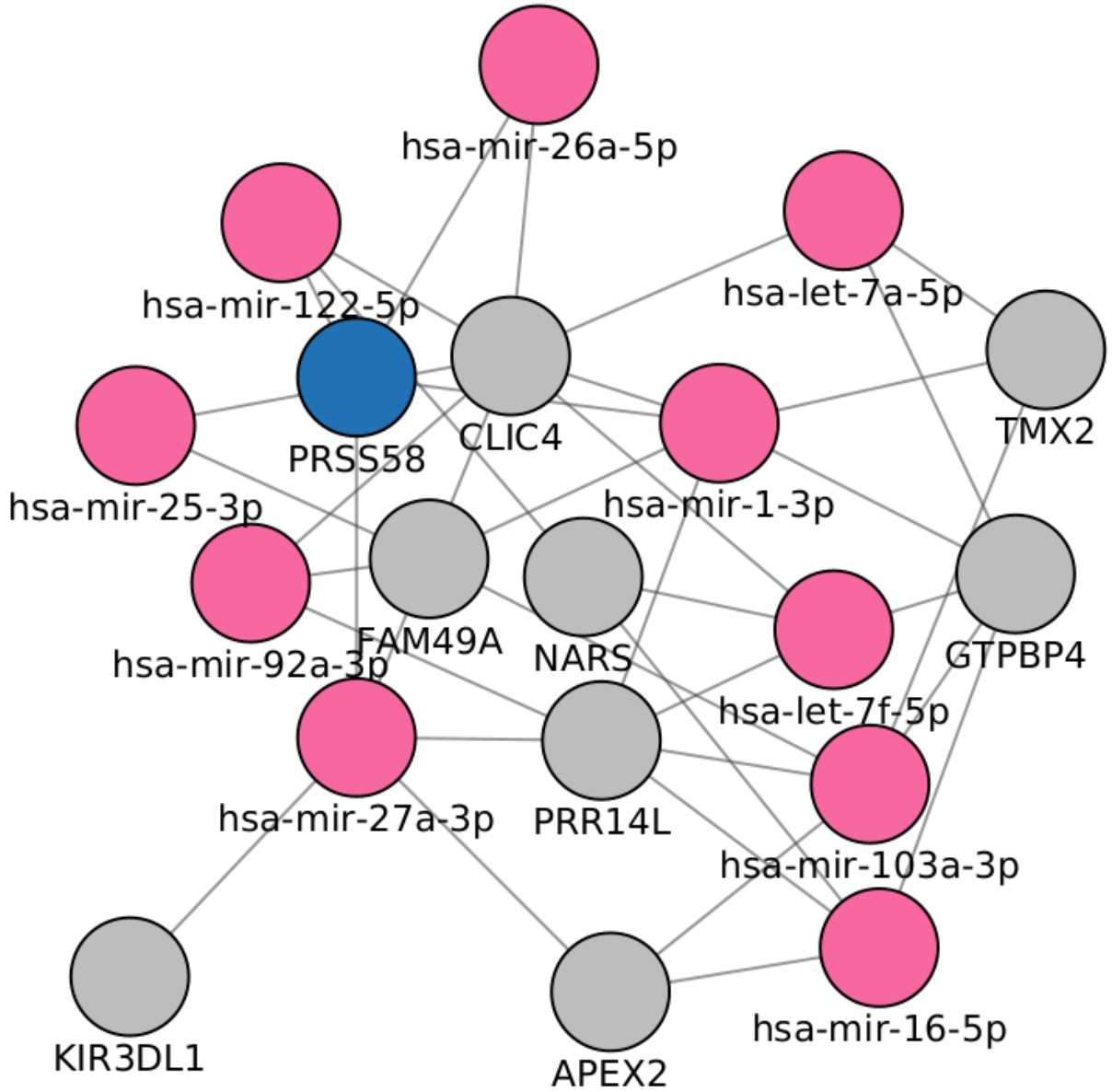
446 genes
1.2k edges

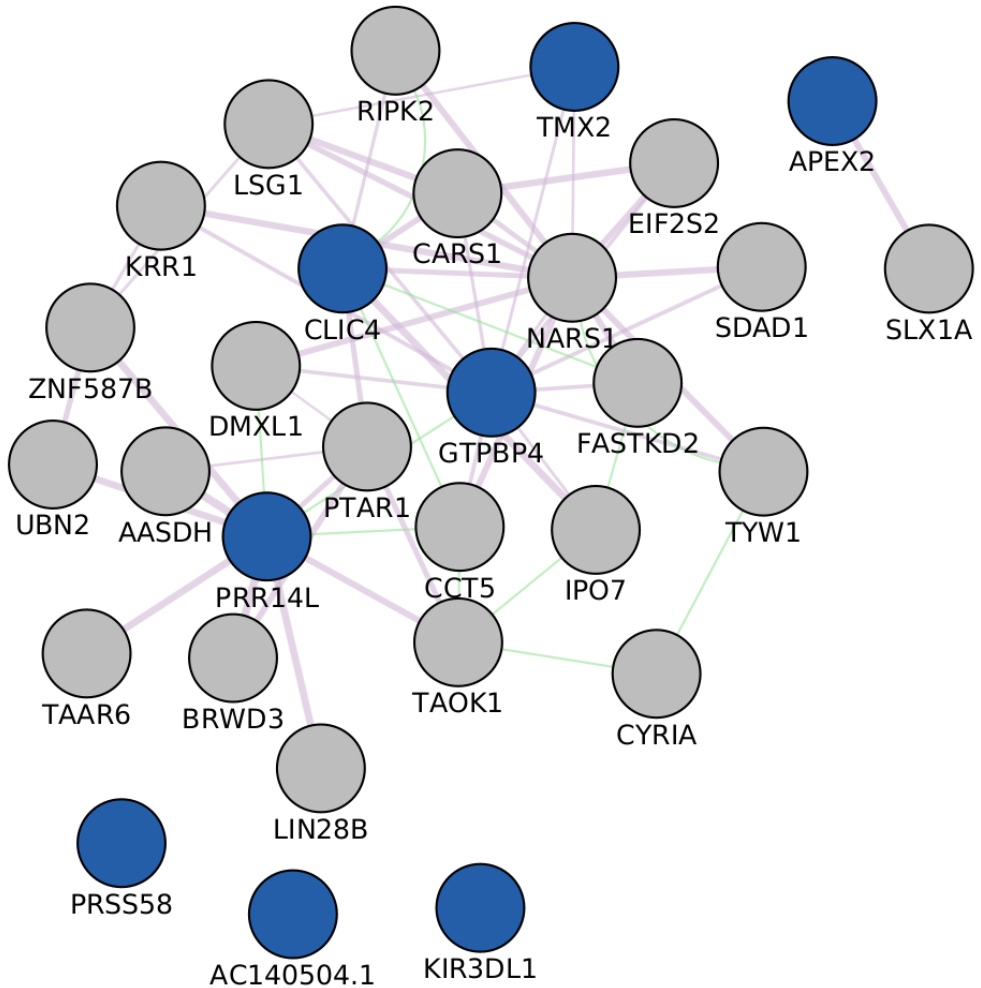
446 genes
2k miRNAs
3.5 edges

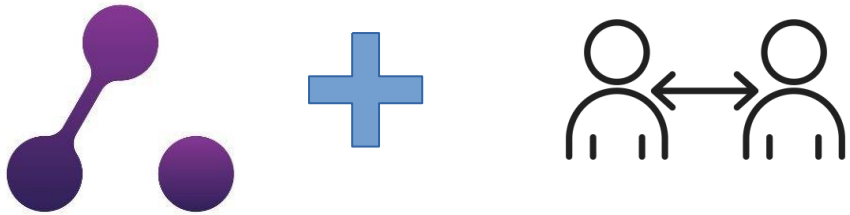


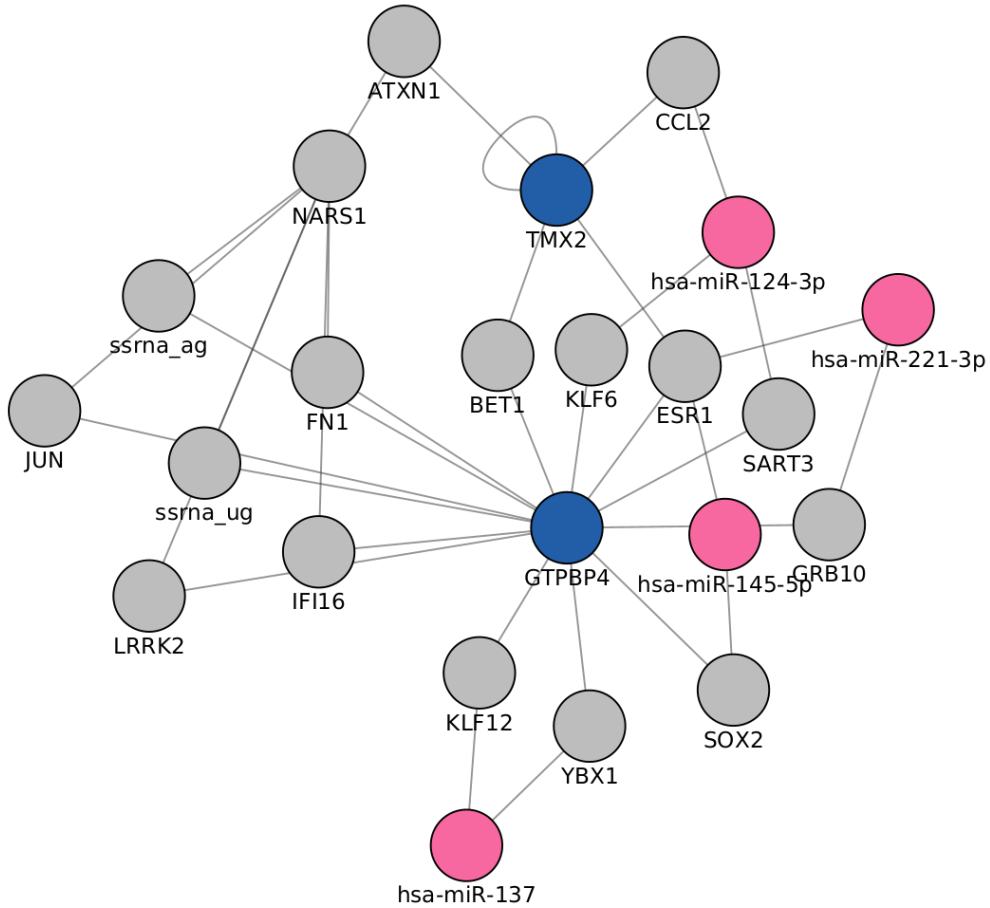
5 miRNAs
146 genes
163 edges

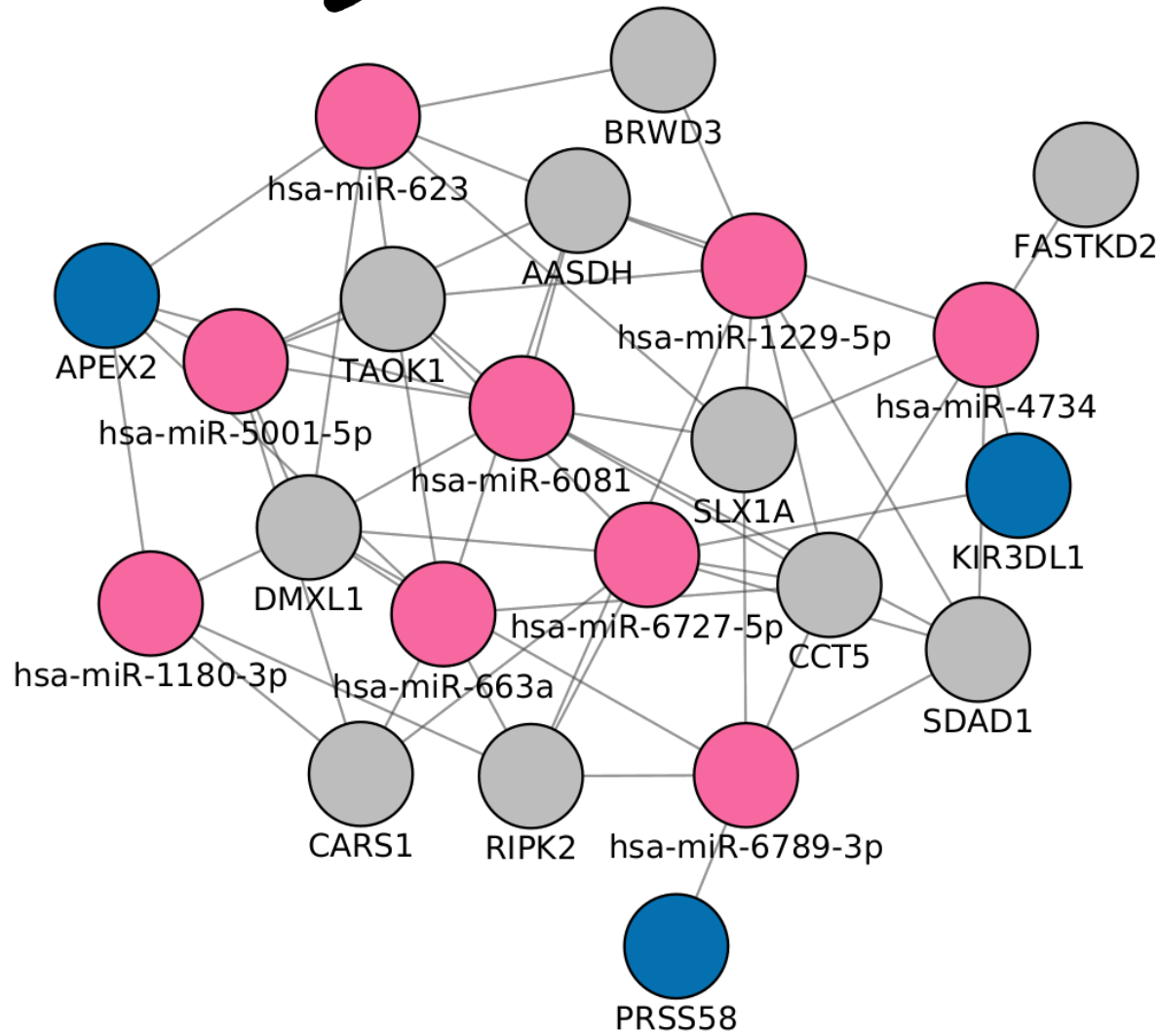

2.0

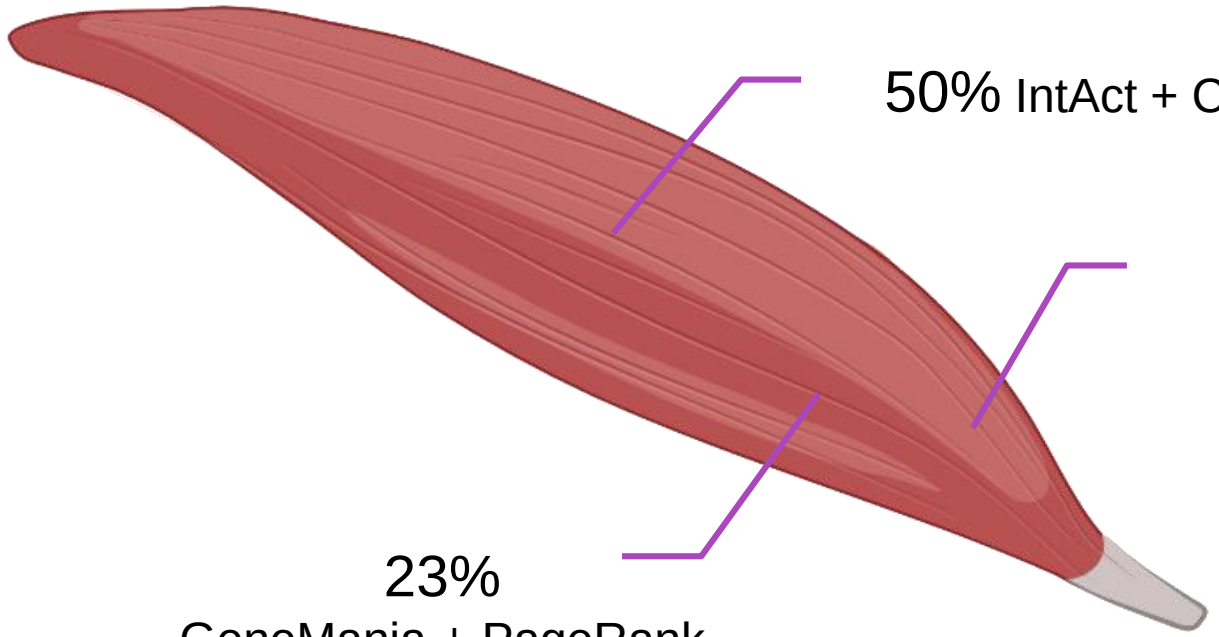

hsa-mir-26a-5p
hsa-mir-122-5p
hsa-let-7a-5p
PRSS58
CLIC4
TMX2
hsa-mir-25-3p
hsa-mir-1-3p
FAM49A
NARS
GTPBP4
hsa-mir-92a-3p
hsa-let-7f-5p
hsa-mir-27a-3p
PRR14L
hsa-mir-103a-3p
KIR3DL1
APEX2
hsa-mir-16-5p


RIPK2
TMX2
APEX2
LSG1
EIF2S2
KRR1
CARS1
CLIC4
NARS1
SDAD1
SLX1A
ZNF587B
DMXL1
GTPBP4
FASTKD2
UBN2
AASDH
PTAR1
TYW1
PRR14L
CCT5
IPO7
TAAR6
BRWD3
TAOK1
CYRIA
LIN28B
PRSS58
AC140504.1
KIR3DL1

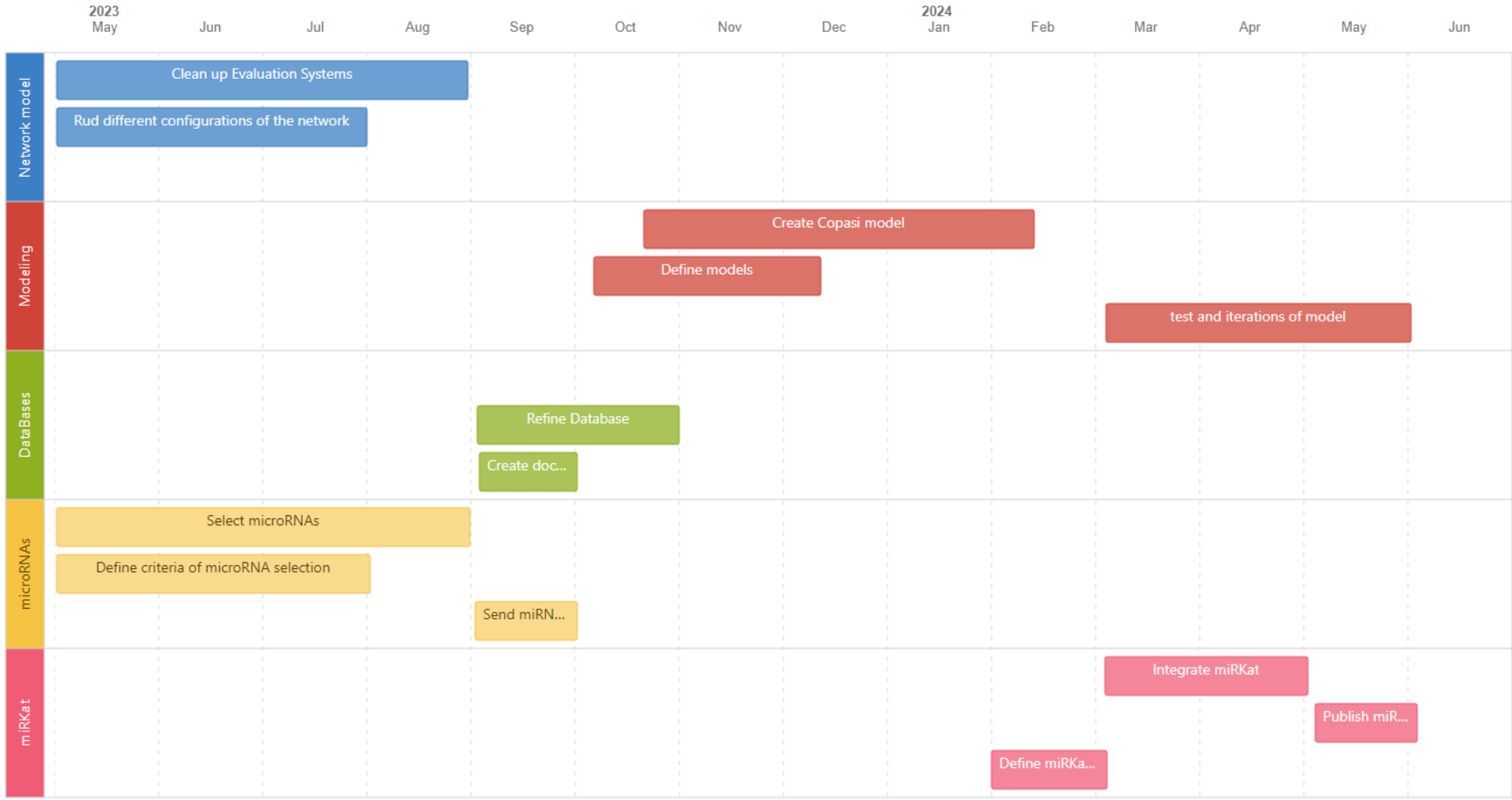



ATXN1
CCL2
NARS1
TMX2
hsa-miR-124-3p
ssrna_ag
hsa-miR-221-3p
BET1
KLF6
ESR1
FN1
JUN
SART3
ssrna_ug
GTPBP4
hsa-miR-145-5p
GRB10
IFI16
LRRK2
KLF12
SOX2
YBX1
hsa-miR-137


BRWD3
hsa-miR-623
FASTKD2
AASDH
APEX2
TAOK1
hsa-miR-1229-5p
hsa-miR-4734
hsa-miR-5001-5p
hsa-miR-6081
SLX1A
KIR3DL1
DMXL1
hsa-miR-6727-5p
CCT5
hsa-miR-1180-3p
hsa-miR-663a
SDAD1
CARS1
RIPK2
hsa-miR-6789-3p
PRSS58



Differentially expressed?


2023
May
Jun
Jul
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Sep
Oct
Nov
Dec
2024
Jan
Feb
Mar
Apr
May
Jun
Network model
Clean up Evaluation Systems
Rud different configurations of the network
Modeling
Create Copasi model
Define models
test and iterations of model
DataBases
Refine Database
Create doc...
microRNAs
Select microRNAs
Define criteria of microRNA selection
Send miRN...
miRKat
Integrate miRKat
Publish miR...
Define miRKa...

Questions?

?

Thank You

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Acknowledgements

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