22q11.2 Deletion Syndrome

A molecular overview

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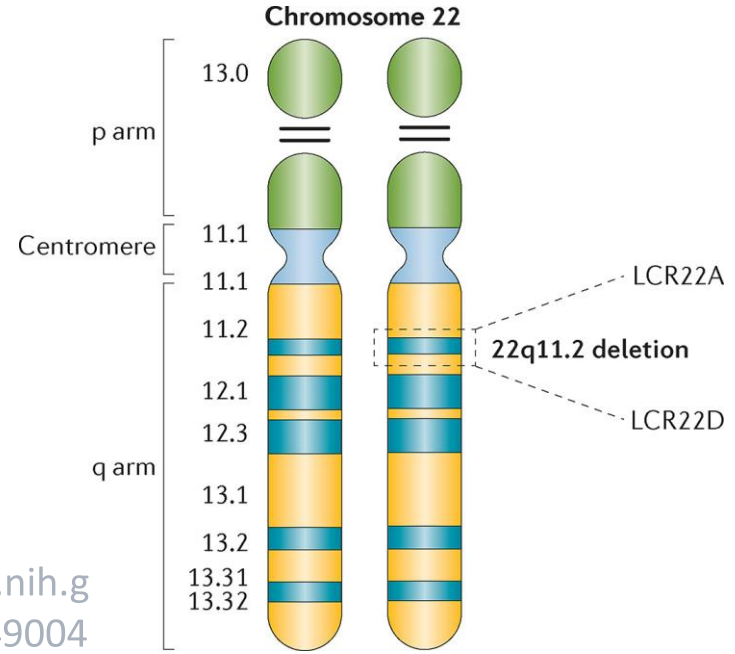
Summary of 22q11.DS

- Occurs in 1 per 3,000-6,000 live births
- Microdeletions of LCR on 22q11.2
- Heterogenous presentation
- 90 known genes for TDR, 46 protein-coding



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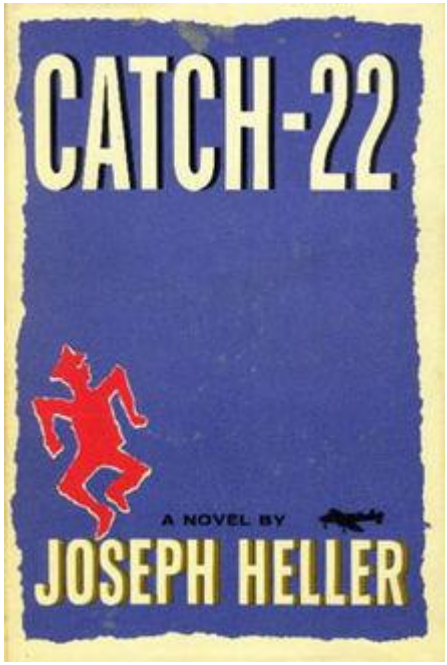
Summary of 22q11.2DS

- Cardiac Abnormalities (75%)
- Abnomal facies
- T-cell deficit (75%)
- Cleft palate(75%)
- Hypocalcemia (50%)
- 22q11.2 deletion



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Catch22.jpg

Summary of 22q11.2DS

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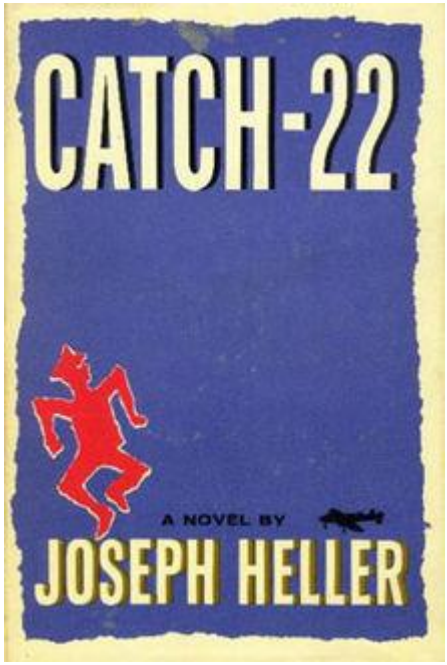
- 22q11.2 deletion
- CNS defects



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Aim

- Creating an interactive pathway involving the most relevant genes and molecules in 22q11.2DS

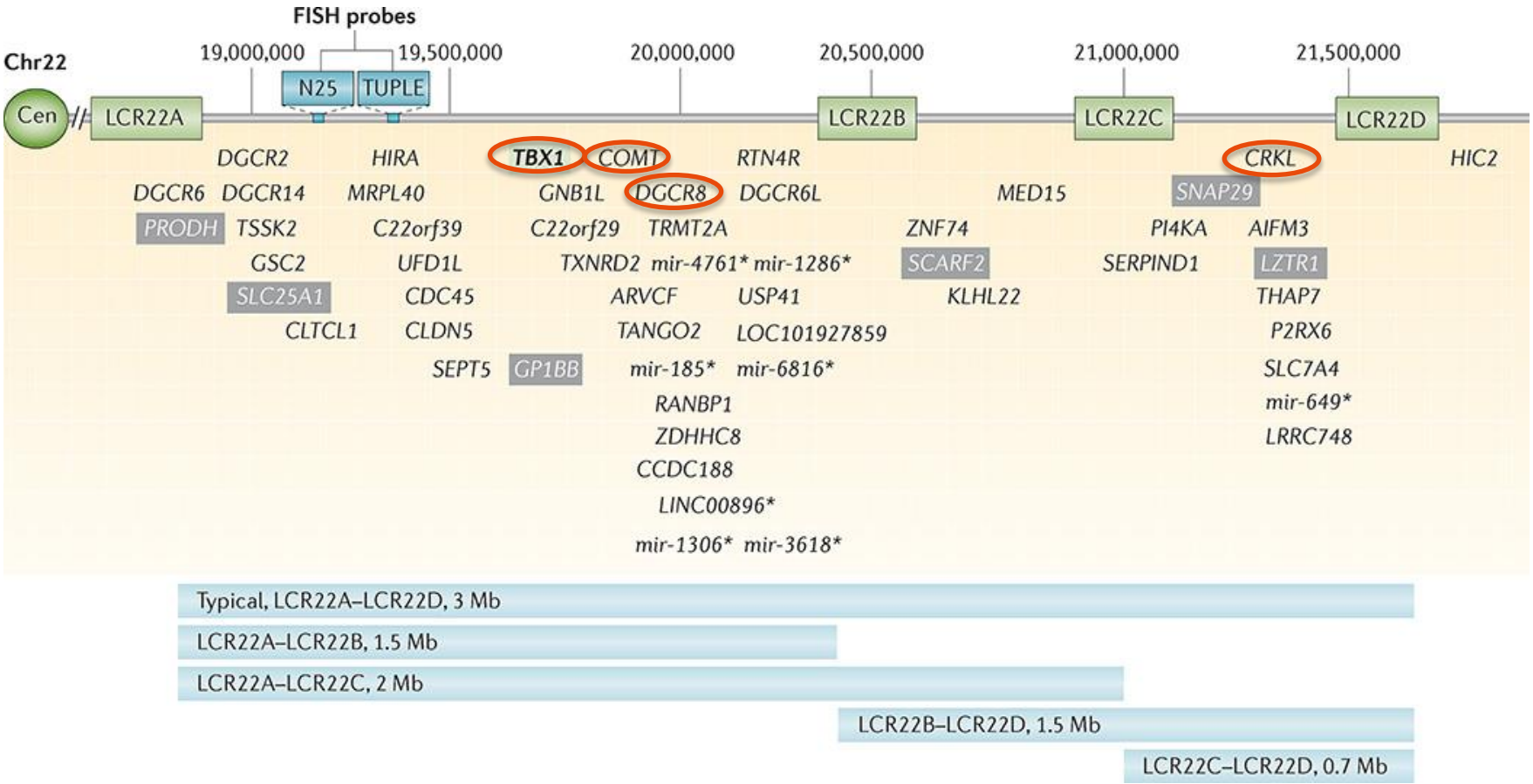
Materials and Methods

- Relevant studies and literature were obtained through **Google Scholar** and **PubMed**
- **OMIM** provided further detail on function of genes and molecules of interest
- **GeneMania**, **KEGG** and **Wikipathways** were used to investigate interactions and downstream pathways of interest

Pathway creation

- **PathVisio** was used to integrate findings into an interactive pathway.
- MIM notation for interactions
- **Ensembl**, **ChEBI** and **miRBase** were used for annotations
- **BridgeDb** was used as a mapping database

Overview of deleted region(s)



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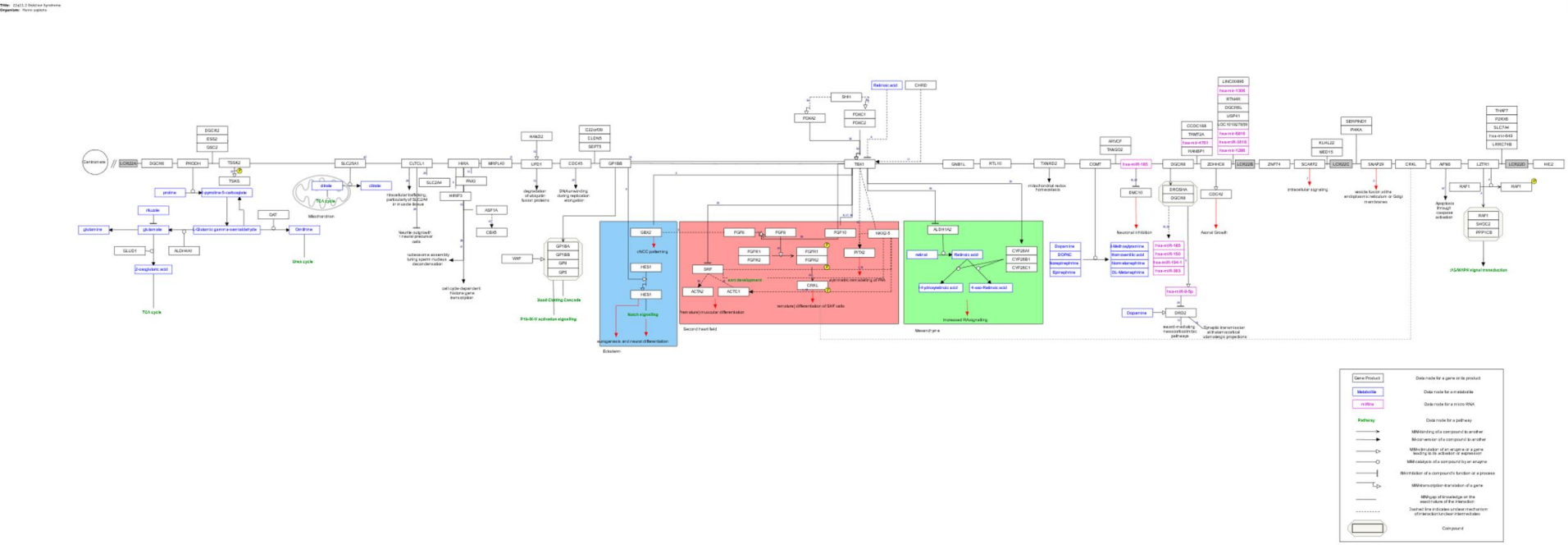
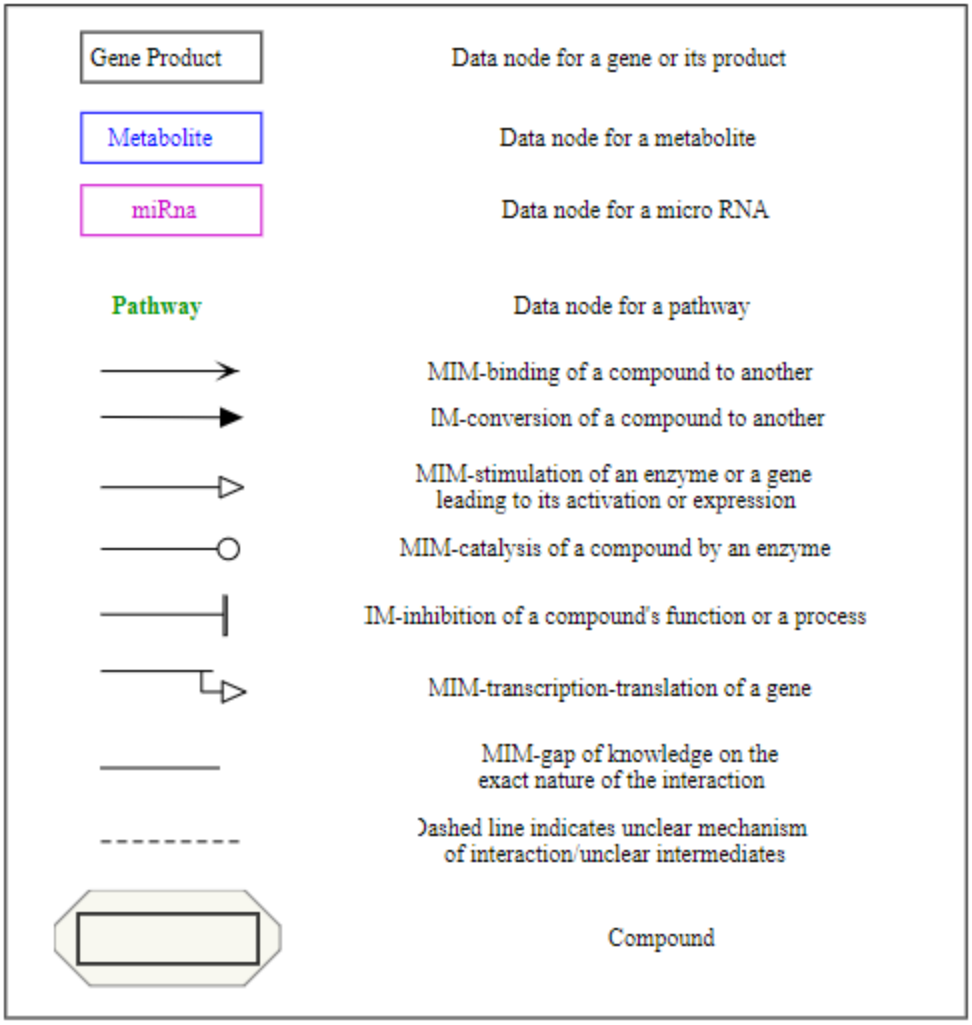
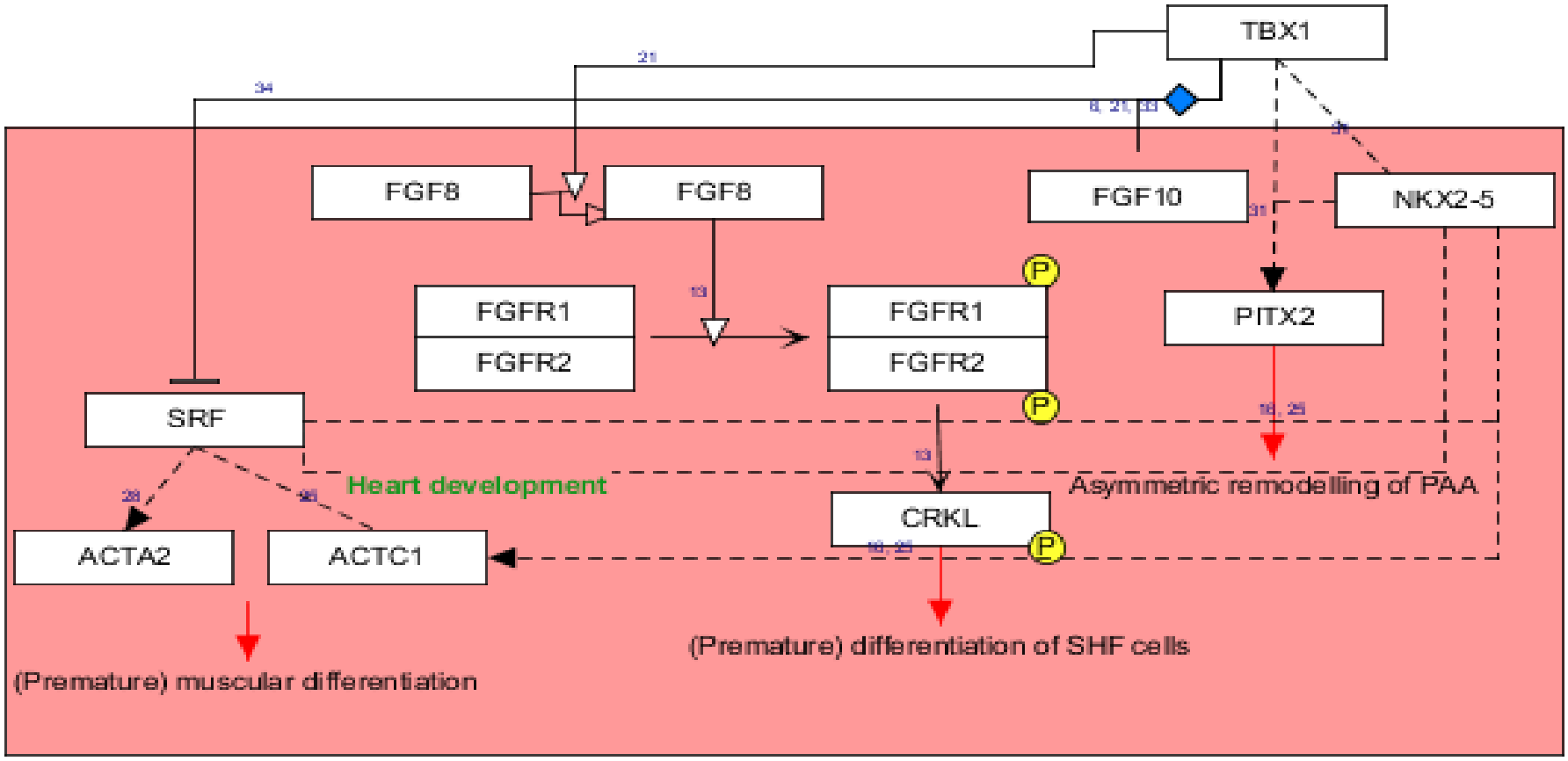
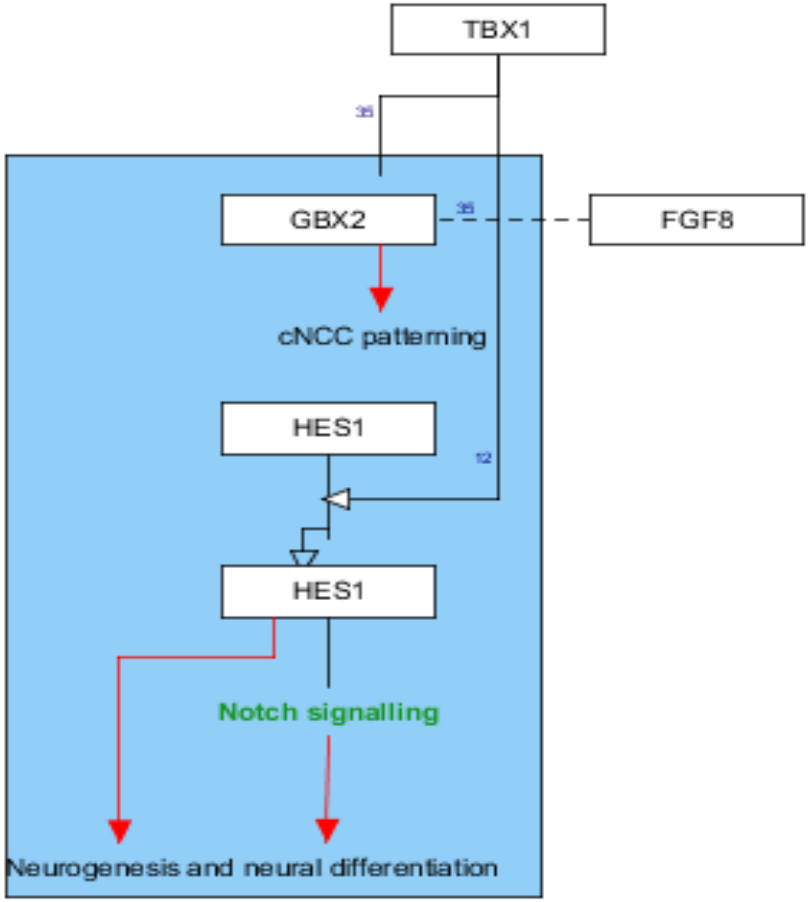
The result

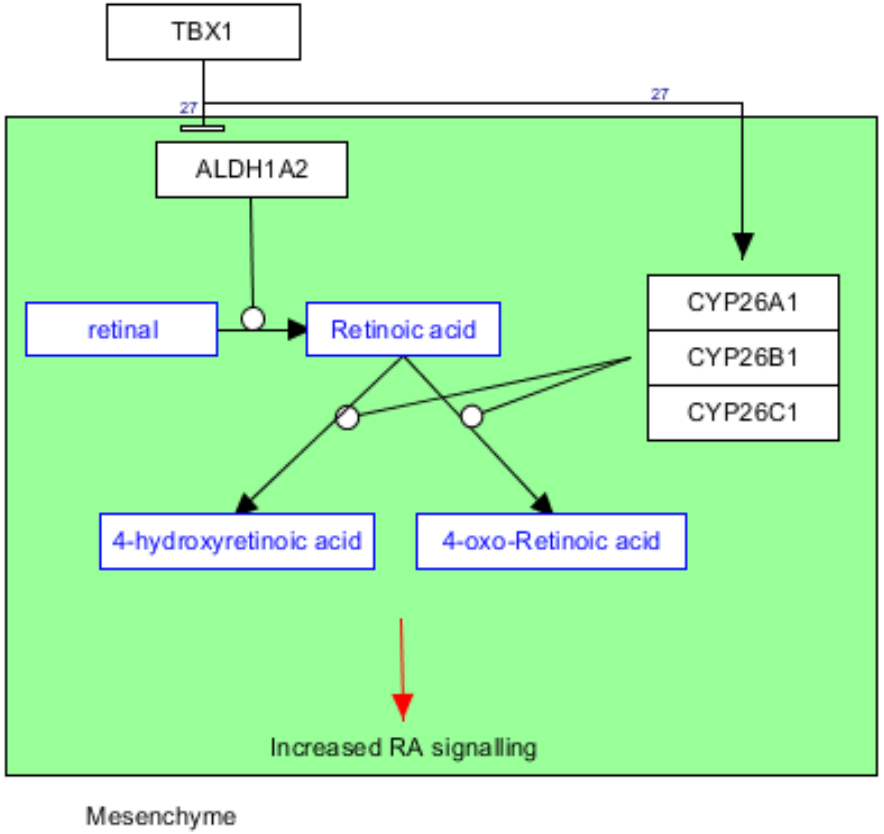


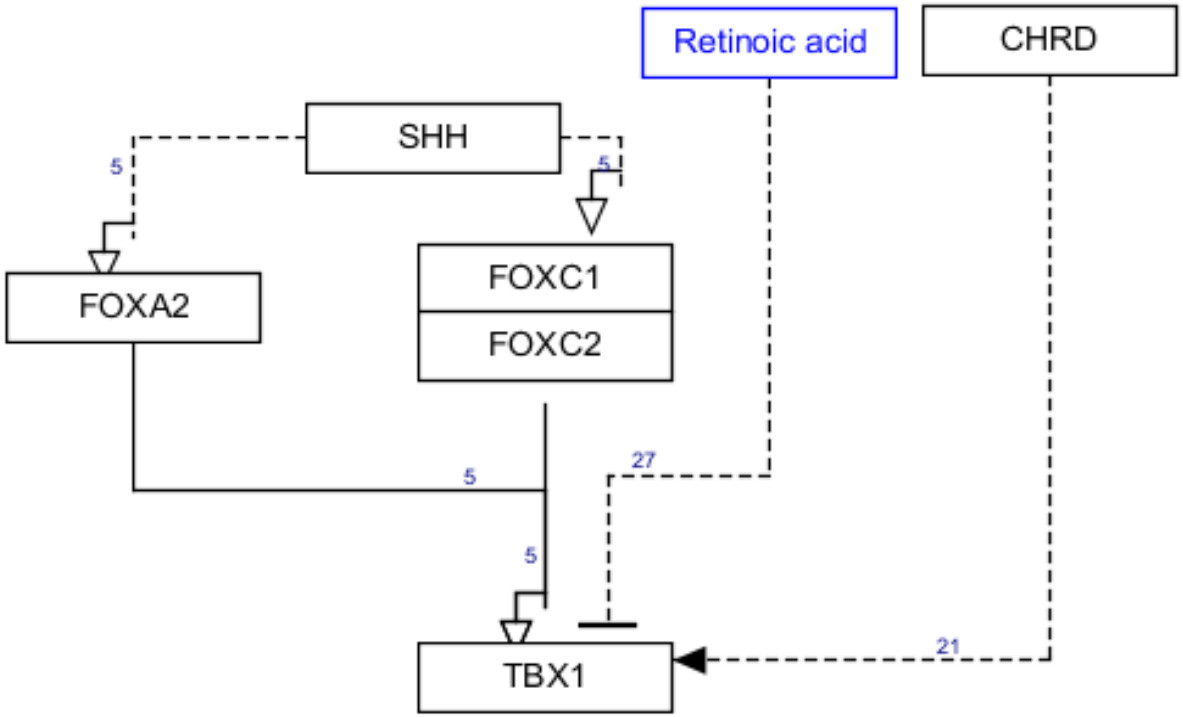
The Legend

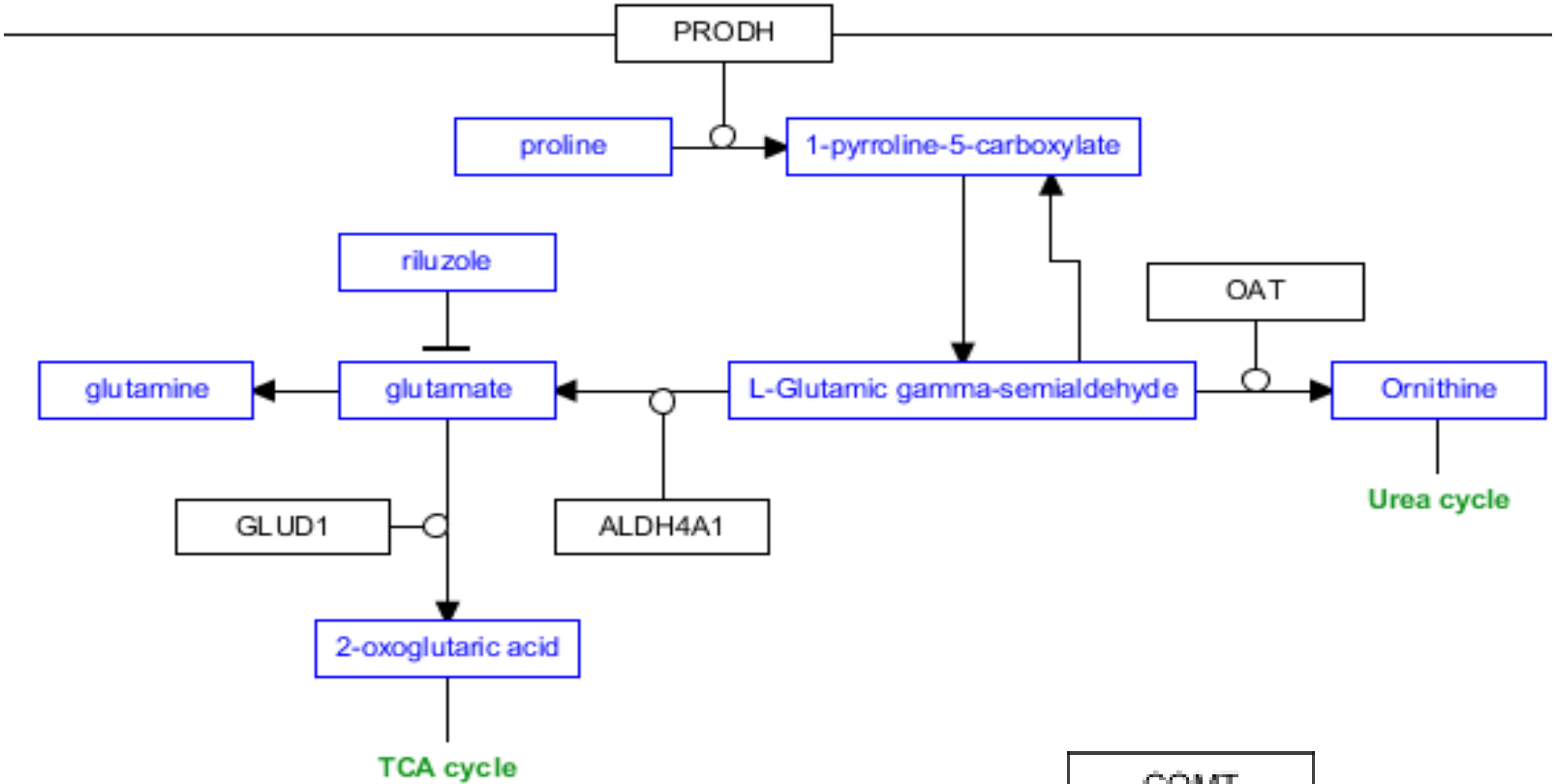

Gene Product
Data node for a gene or its product
Metabolite
Data node for a metabolite
miRna
Data node for a micro RNA
Pathway
Data node for a pathway
MIM-binding of a compound to another
IM-conversion of a compound to another
MIM-stimulation of an enzyme or a gene leading to its activation or expression
MIM-catalysis of a compound by an enzyme
IM-inhibition of a compound's function or a process
MIM-transcription-translation of a gene
MIM-gap of knowledge on the exact nature of the interaction
Dashed line indicates unclear mechanism of interaction/unclear intermediates
Compound

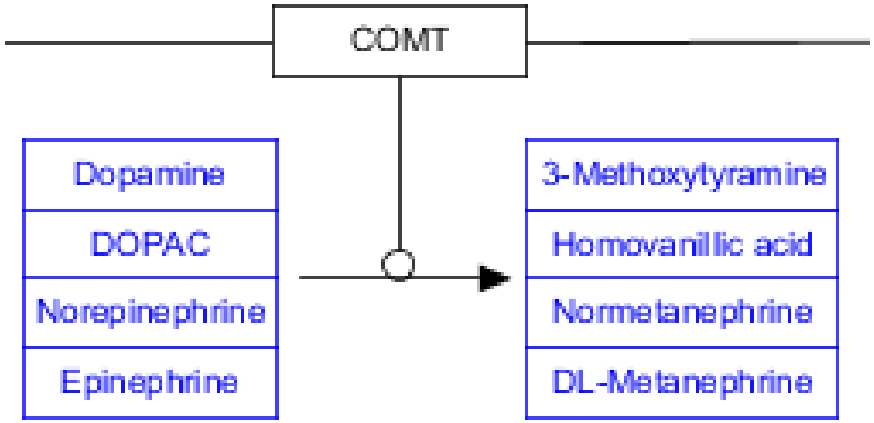

TBX1
FGF8
FGF8
FGF10
NKX2-5
FGFR1
FGFR2
FGFR1
FGFR2
PITX2
SRF
Heart development
Asymmetric remodelling of PAA
CRKL
ACTA2
ACTC1
(Premature) differentiation of SHF cells
(Premature) muscular differentiation
Second heart field

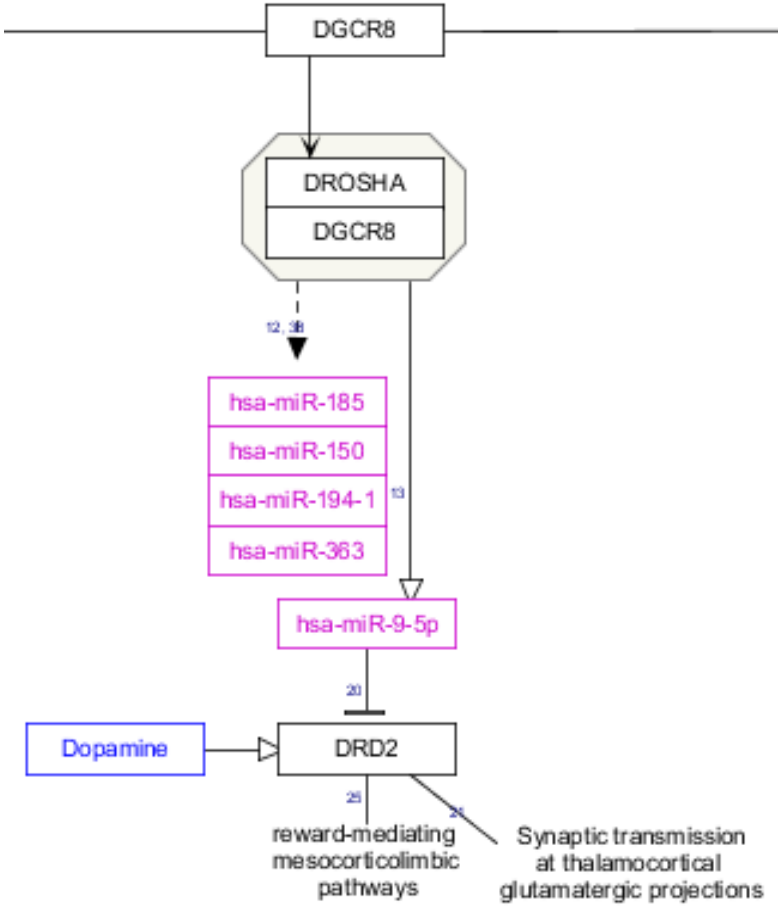

TBX1
35
GBX2
35
FGF8
cNCC patterning
HES1
12
HES1
Notch signalling
Neurogenesis and neural differentiation
Ectoderm

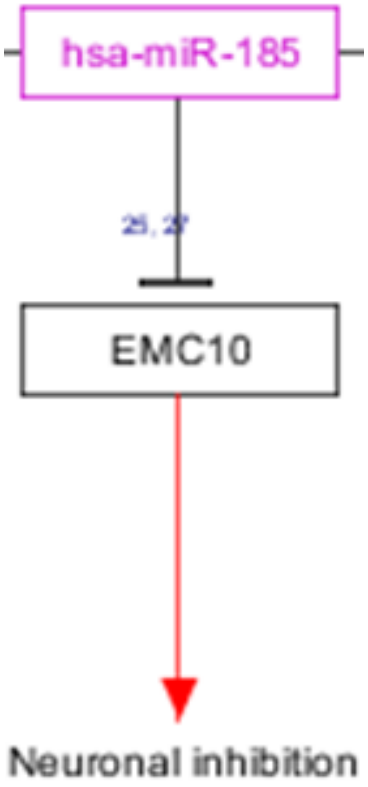

TBX1
27
27
ALDH1A2
retinal
Retinoic acid
CYP26A1
CYP26B1
CYP26C1
4-hydroxyretinoic acid
4-oxo-Retinoic acid
Increased RA signalling
Mesenchyme


Retinoic acid
CHRD
SHH
5
5
FOXA2
FOXC1
FOXC2
5
27
5
21
TBX1


PRODH
proline
1-pyrroline-5-carboxylate
riluzole
OAT
glutamine
glutamate
L-Glutamic gamma-semialdehyde
Ornithine
Urea cycle
GLUD1
ALDH4A1
2-oxoglutaric acid
TCA cycle


COMT
Dopamine
DOPAC
Norepinephrine
Epinephrine
3-Methoxytyramine
Homovanillic acid
Normetanephrine
DL-Metanephrine


DGCR8
DROSHA
DGCR8
hsa-miR-185
hsa-miR-150
hsa-miR-194-1
hsa-miR-363
hsa-miR-9-5p
Dopamine
DRD2
reward-mediating mesocorticolimbic pathways
Synaptic transmission at thalamocortical glutamatergic projections


hsa-miR-185
EMC10
Neuronal inhibition

Summary

- TBX1 is responsible for most of the defects associated with 22q11.2DS
- PRODH, COMT, DGCR8 and miR-185 play important roles in psychiatric pathologies

Discussion

- Limitations:
  - Vastly heterogenous disease
  - Uncertainty of importance of some factors

- Model for microdeletion disorders
- More research needed to explain variance in phenotypes so as to facilitate more individualized approaches

Acknowledgements

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&
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BiGCaT bioinformatics

Thank you for your attention!

- Questions?