#### Islet diabetic phenotype gene sets

#### Color legend:

- T2D expression (C)
- T2D expression (B)
- Glycemic gene-based
- Co-expression
- T2D eQTL
- T2D expression (A)
- Hyperglycemia expression
- T2D methylation (B)
- T2D methylation (A)
- Monogenic
- OMIM
- T2D GWAS/rare variant
- Glycemic GWAS/rare variant

#### Islet biology gene sets

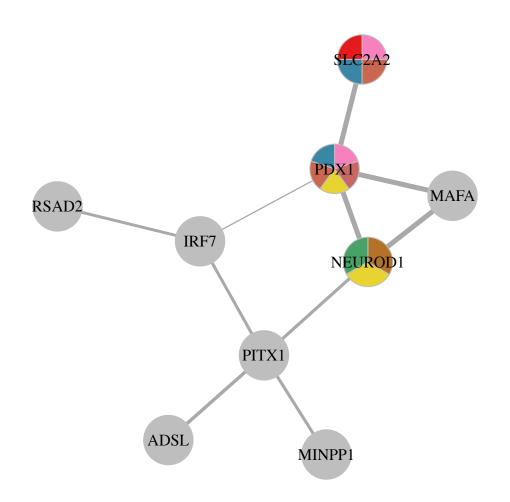
#### Color legend:

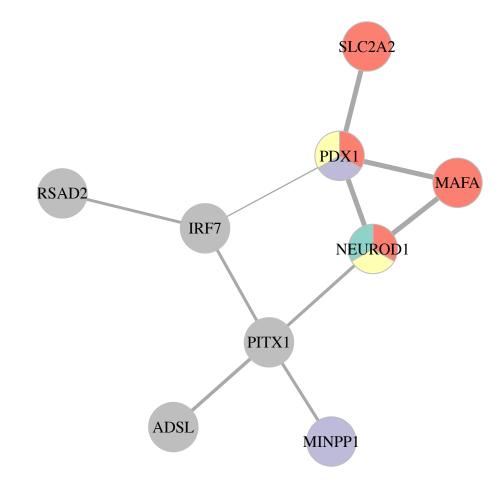
- Islet specific
- Open chromatin
- □ Open chromatin clusters
- Islet biology

Visualization of the 24 complexes with potential T2D dysregulation, where the evidence sources supporting the different genes are annotated.

The first page (of the 25 pages) in this file shows the color legend for the diabetic phenotype and islet related gene sets. Nodes with red boarder indicate targets of FDA approved drugs.

# Complex-1





Emperical P-value: < 1E-5 Number of genes in complex: 9

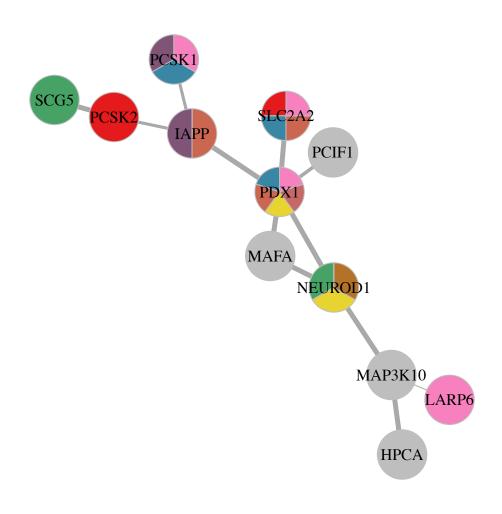
Top coordinated expressed tissues: Colon, Skin, Bone Marrow

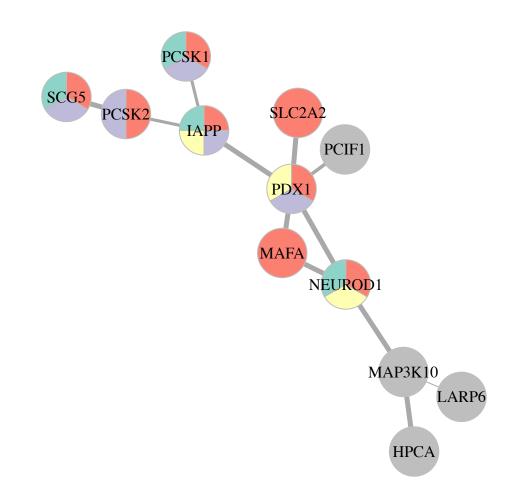
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: < 1E-5 Number of genes in complex: 9

Top coordinated expressed tissues: Colon, Skin, Bone Marrow

# Complex-2





Emperical P-value: < 1E-5 Number of genes in complex: 12

Top coordinated expressed tissues: islet, Pituitary, Pancreas

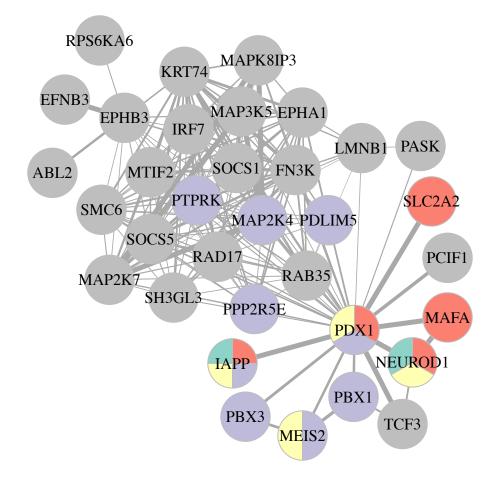
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: < 1E-5 Number of genes in complex: 12

Top coordinated expressed tissues: islet, Pituitary, Pancreas

#### RPS6KA6 MAPK8IP3 KRT74 EFNB3 MAP3K5 EPHA1 EPHB3 IRF7 LMNB1-PASK SOCS1 FN3K MTIF2 ABL2 PTPRK SMC6 MAP2K4 PDLIM5 SOCS5 RAD17 PCIF1 RAB35 MAP2K7 SH3GL3 PPP2R5E **MAFA** PDX1 NEUROD1 PBX1 PBX3 TCF3 MEIS2

#### Complex-3



Emperical P-value: 2e-05

Number of genes in complex: 34

Top coordinated expressed tissues: Bladder, Ovary, Breast

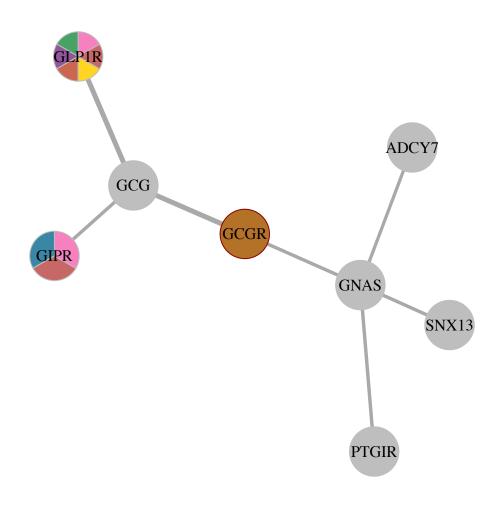
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 2e-05

Number of genes in complex: 34

Top coordinated expressed tissues: Bladder, Ovary, Breast

## Complex-4



GLP1R ADCY7 GCG GCGR **GIPR GNAS** SNX13 **PTGIR** 

Emperical P-value: 3e-05 Number of genes in complex: 8

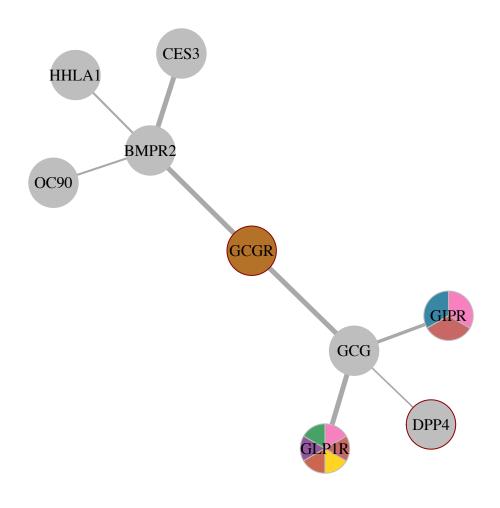
Top coordinated expressed tissues: islet, Pancreas, Small Intestine

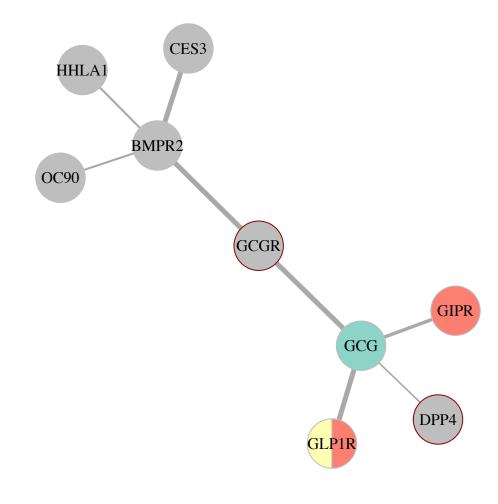
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 3e-05 Number of genes in complex: 8

Top coordinated expressed tissues: islet, Pancreas, Small Intestine

# Complex-5





Emperical P-value: 3e-05 Number of genes in complex: 9

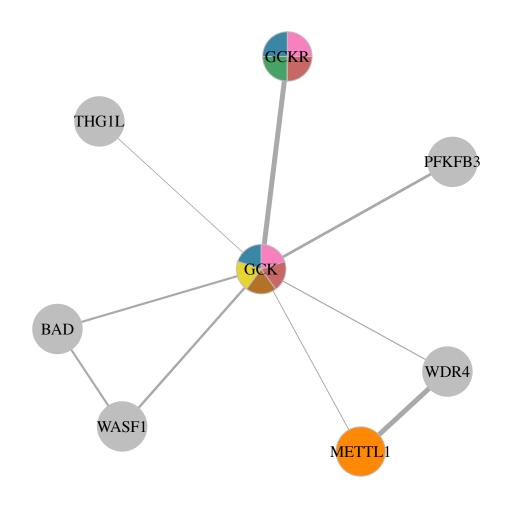
Top coordinated expressed tissues: islet, beta, Bone Marrow

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 3e-05 Number of genes in complex: 9

Top coordinated expressed tissues: islet, beta, Bone Marrow

## Complex-6



**GCKR** THG1L PFKFB3 **GCK BAD** WDR4 WASF1 METTL1

Emperical P-value: 3e-05 Number of genes in complex: 8

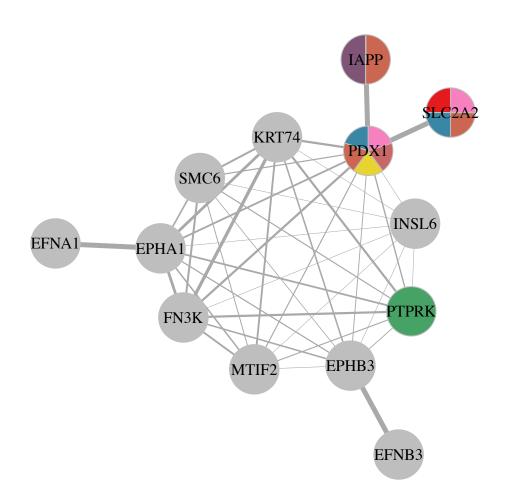
Top coordinated expressed tissues: Nerve, Cervix Uteri, Small Intestine

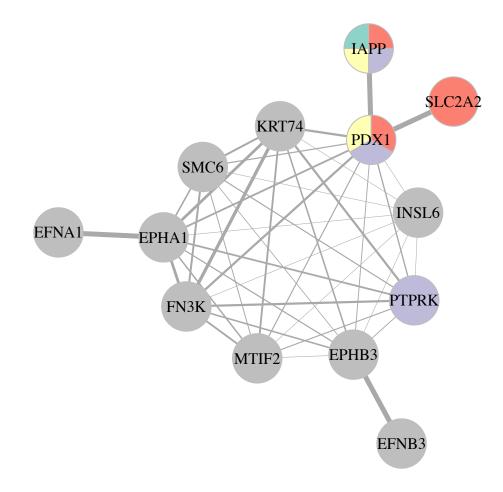
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 3e-05 Number of genes in complex: 8

Top coordinated expressed tissues: Nerve, Cervix Uteri, Small Intestine

# Complex-7





Emperical P-value: 4e-05

Number of genes in complex: 13

Top coordinated expressed tissues: Colon, Bladder, nonbeta

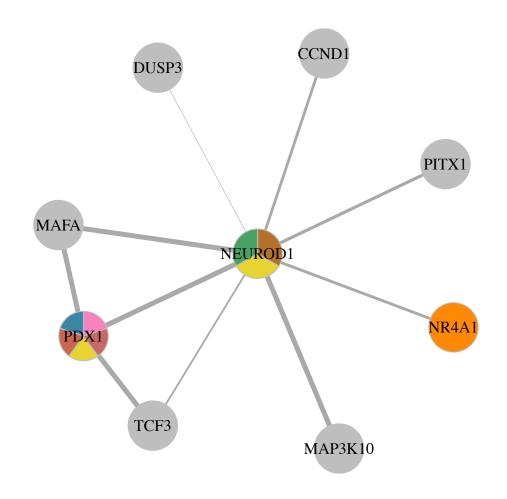
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 4e-05

Number of genes in complex: 13

Top coordinated expressed tissues: Colon, Bladder, nonbeta

# Complex-8



CCND1 DUSP3 PITX1 **MAFA** NEUROD1 NR4A1 PDX1 TCF3 MAP3K10

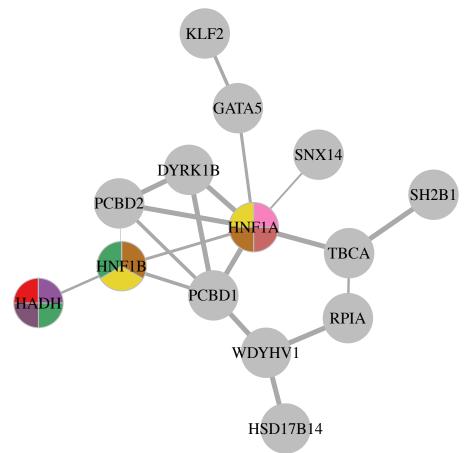
Emperical P-value: 4e-05 Number of genes in complex: 9

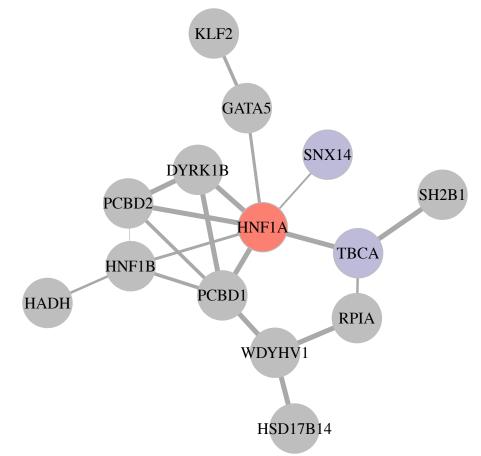
Top coordinated expressed tissues: Skin, Colon, Adrenal Gland

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 4e-05 Number of genes in complex: 9

Top coordinated expressed tissues: Skin, Colon, Adrenal Gland





Complex-9

Emperical P-value: 5e-05

Number of genes in complex: 14

Top coordinated expressed tissues: Fallopian Tube, Uterus, Bladder

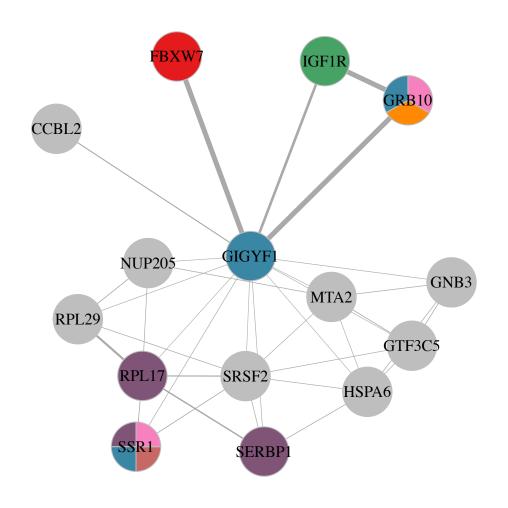
Node color based on: Islet diabetic phenotype gene sets

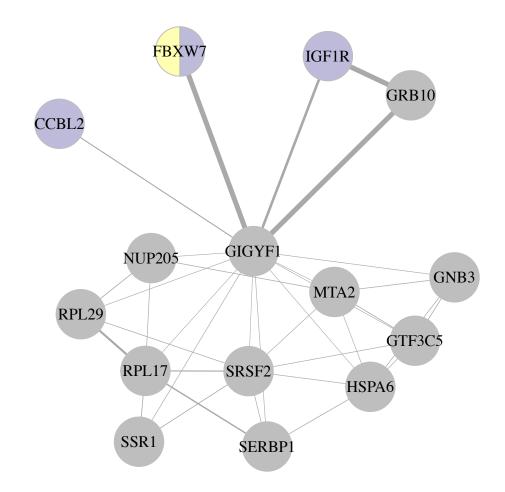
Emperical P-value: 5e-05

Number of genes in complex: 14

Top coordinated expressed tissues: Fallopian Tube, Uterus, Bladder

# Complex-10





Emperical P-value: 6e-05 Number of genes in complex: 15

Top coordinated expressed tissues: Small Intestine, Liver, Brain

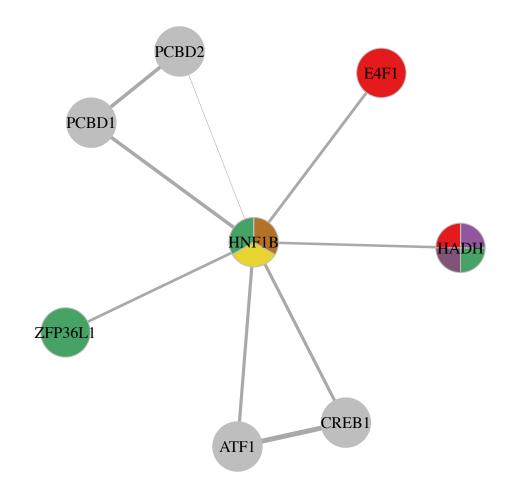
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 6e-05

Number of genes in complex: 15

Top coordinated expressed tissues: Small Intestine, Liver, Brain

# Complex-11



PCBD2 E4F1 PCBD1 HNF1B **HADH** ZFP36L1 CREB1 ATF1

Emperical P-value: 6e-05 Number of genes in complex: 8

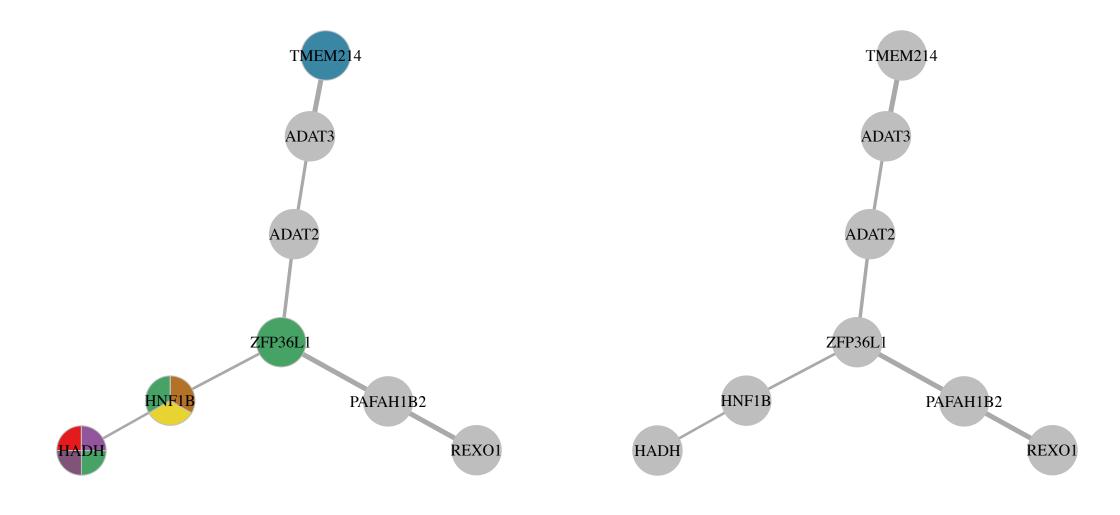
Top coordinated expressed tissues: Bladder, Fallopian Tube, Prostate

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 6e-05 Number of genes in complex: 8

Top coordinated expressed tissues: Bladder, Fallopian Tube, Prostate





Emperical P-value: 6e-05 Number of genes in complex: 8

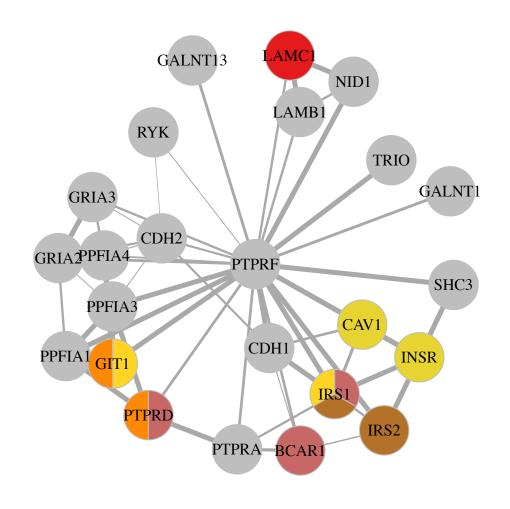
Top coordinated expressed tissues: Bladder, Fallopian Tube, Cervix Uteri

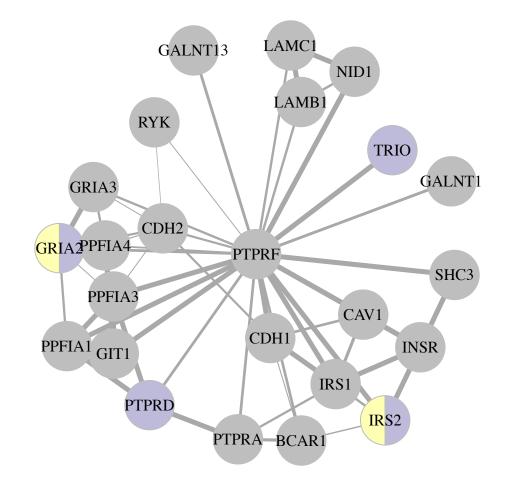
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 6e-05 Number of genes in complex: 8

Top coordinated expressed tissues: Bladder, Fallopian Tube, Cervix Uteri

# Complex-13





Emperical P-value: 7e-05

Number of genes in complex: 24

Top coordinated expressed tissues: beta, islet, Testis

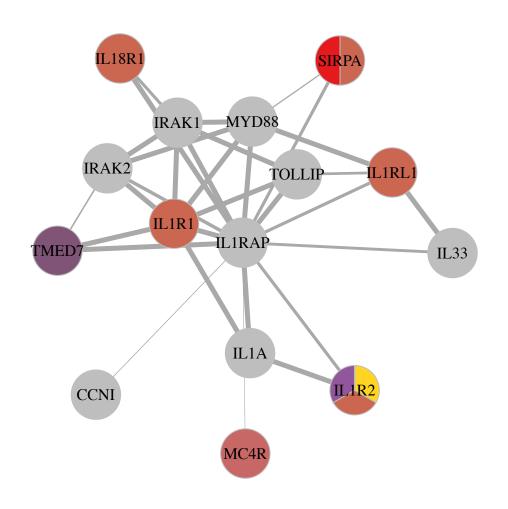
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 7e-05

Number of genes in complex: 24

Top coordinated expressed tissues: beta, islet, Testis

# Complex-14



IL18R1 **SIRPA** IRAK1 MYD88 IRAK2 TOLLIP IL1RL1 IL1R1 IL1RAP TMED7 IL33 IL1A IL1R2 **CCNI** MC4R

Emperical P-value: 9e-05

Number of genes in complex: 15

Top coordinated expressed tissues: Fallopian Tube, Nerve, Blood Vessel

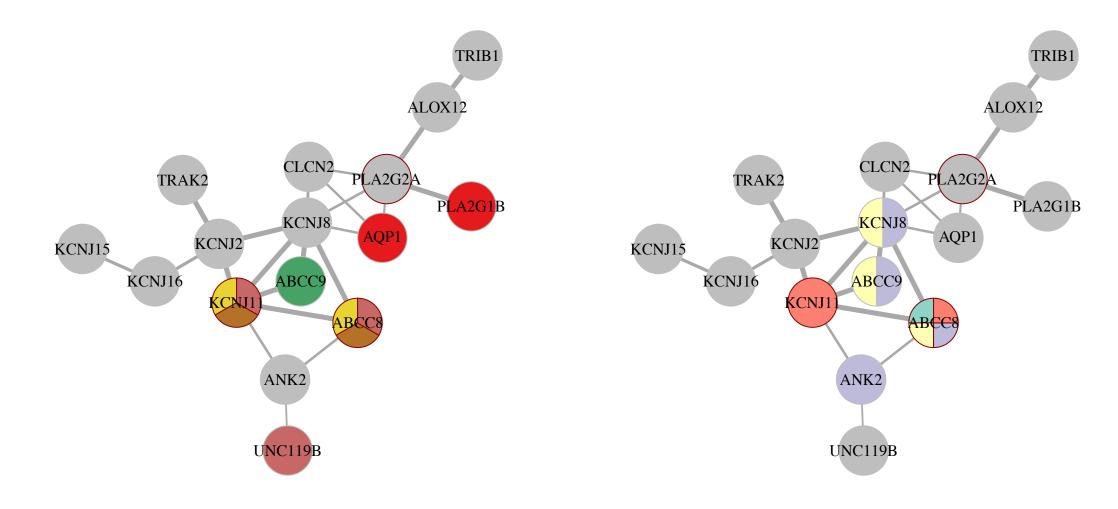
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 9e-05

Number of genes in complex: 15

Top coordinated expressed tissues: Fallopian Tube, Nerve, Blood Vessel





Emperical P-value: 9e-05

Number of genes in complex: 16

Top coordinated expressed tissues: Salivary Gland, islet, Bone Marrow

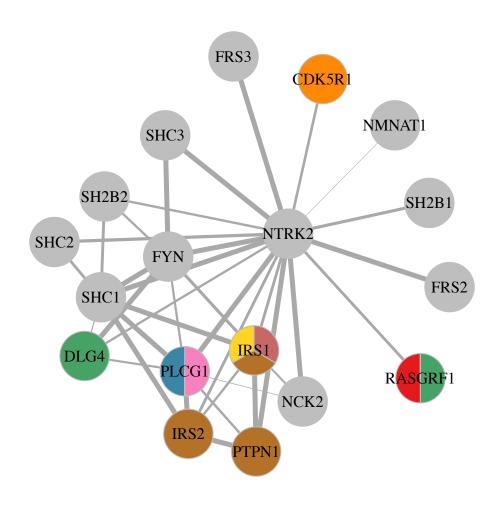
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 9e-05

Number of genes in complex: 16

Top coordinated expressed tissues: Salivary Gland, islet, Bone Marrow

## Complex-16



FRS3 CDK5R1 NMNAT1 SHC3 SH2B2 SH2B1 NTRK2 SHC2 **FYN** FRS2 SHC1 IRS1 DLG4 PLCG1 RASGRF1 NCK2 IRS2 PTPN1

Emperical P-value: 1e-04 Number of genes in complex: 18

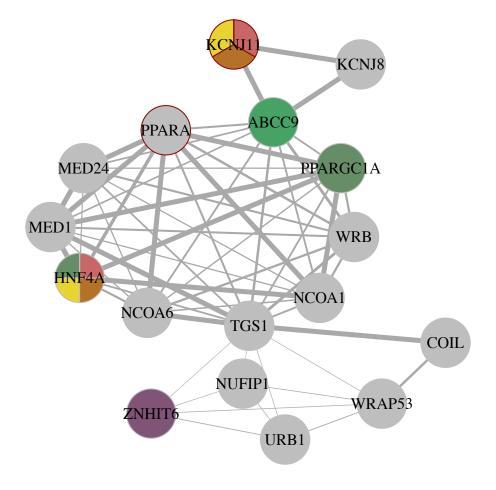
Top coordinated expressed tissues: Stomach, Vagina, Colon

Node color based on: Islet diabetic phenotype gene sets

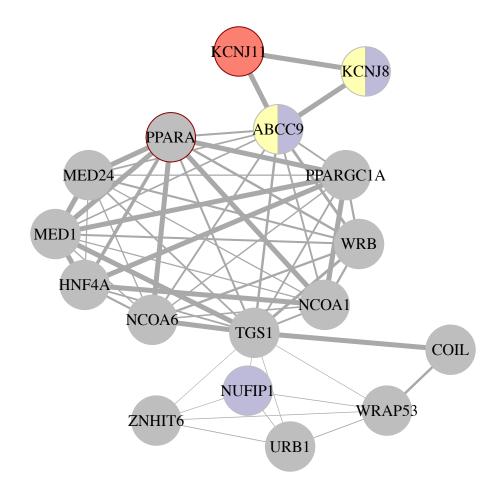
Emperical P-value: 1e-04

Number of genes in complex: 18

Top coordinated expressed tissues: Stomach, Vagina, Colon



## Complex-17



Emperical P-value: 1e-04 Number of genes in complex: 17

Top coordinated expressed tissues: islet, Vagina, Cervix Uteri

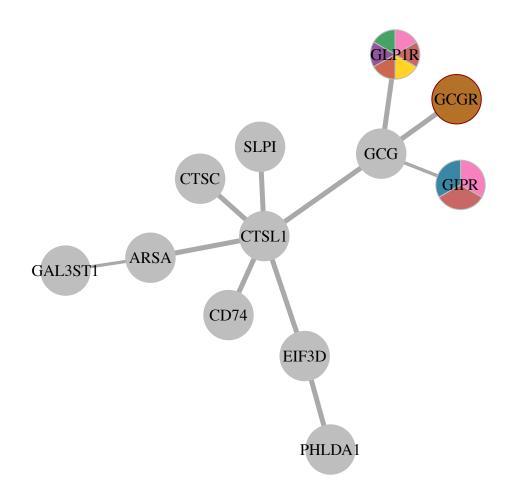
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 1e-04

Number of genes in complex: 17

Top coordinated expressed tissues: islet, Vagina, Cervix Uteri





GLP1R **GCGR SLPI** GCG **CTSC GIPR** CTSL1 **ARSA** GAL3ST1 **CD74** EIF3D PHLDA1

Emperical P-value: 0.00011 Number of genes in complex: 12

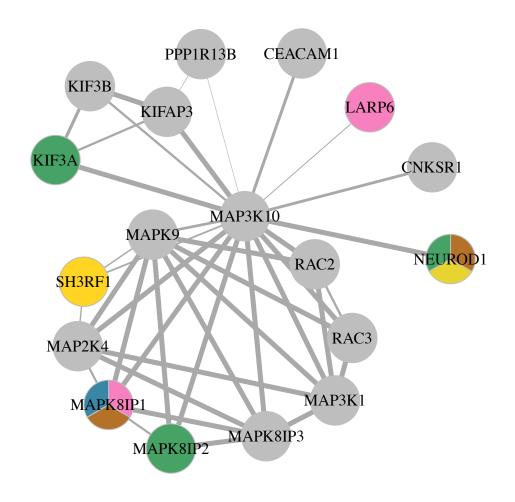
Top coordinated expressed tissues: Blood Vessel, Nerve, Thyroid

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00011 Number of genes in complex: 12

Top coordinated expressed tissues: Blood Vessel, Nerve, Thyroid

# Complex-19



PPP1R13B CEACAM1 KIF3B LARP6 KIFAP3 KIF3A CNKSR1 MAP3K10 MAPK9 NEUROD1 RAC2 SH3RF1 RAC3 MAP2K4 MAP3K1 MAPK8IP1 MAPK8IP3 MAPK8IP2

Emperical P-value: 0.00011 Number of genes in complex: 18

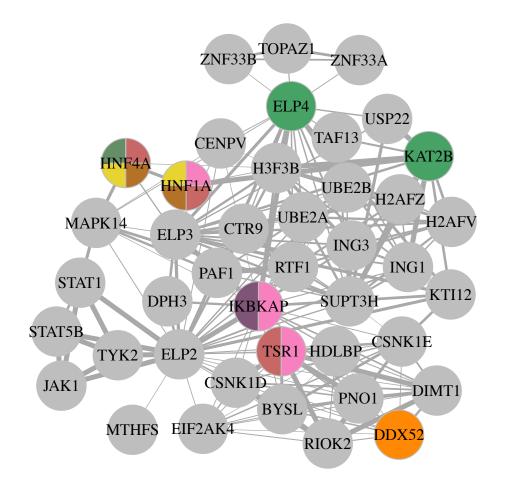
Top coordinated expressed tissues: Adrenal Gland, Prostate, Liver

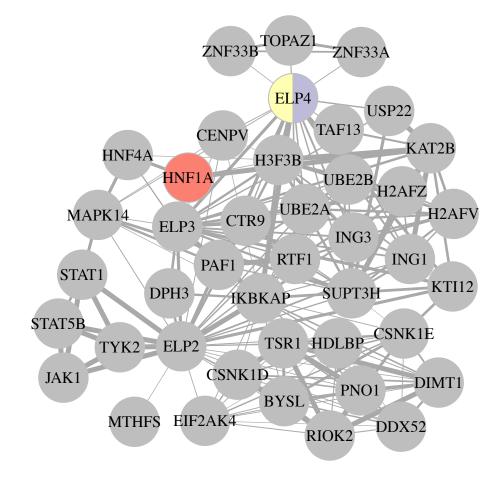
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00011 Number of genes in complex: 18

Top coordinated expressed tissues: Adrenal Gland, Prostate, Liver

## Complex-20





Emperical P-value: 0.00012 Number of genes in complex: 42

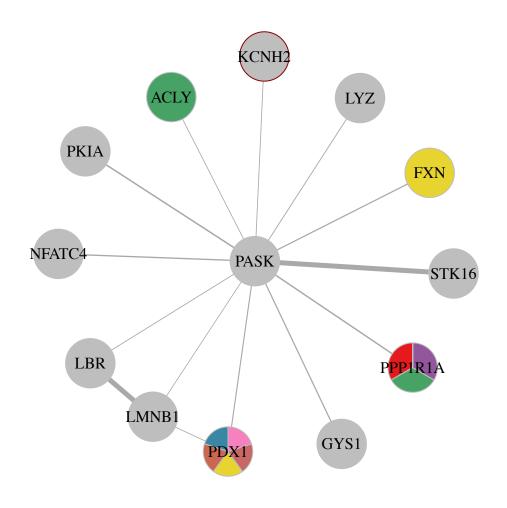
Top coordinated expressed tissues: Brain, Heart, Cervix Uteri

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00012 Number of genes in complex: 42

Top coordinated expressed tissues: Brain, Heart, Cervix Uteri

# Complex-21



**KCNH ACLY** LYZ **PKIA FXN** NFATC4 **PASK** STK16 LBR PPP1R1A LMNB1 GYS1 PDX1

Emperical P-value: 0.00018 Number of genes in complex: 13

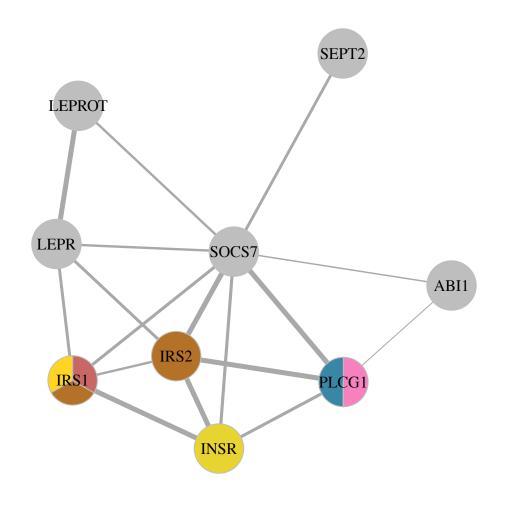
Top coordinated expressed tissues: Pituitary, Spleen, Liver

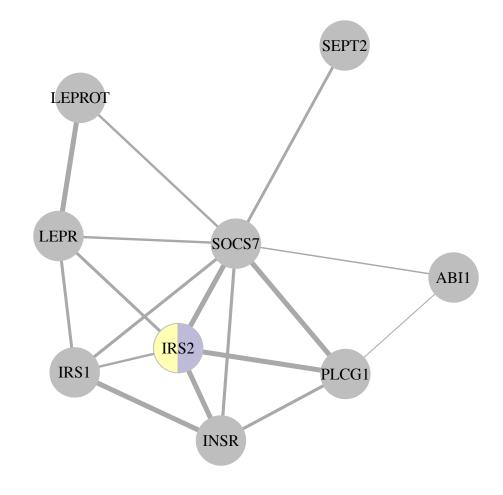
Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00018 Number of genes in complex: 13

Top coordinated expressed tissues: Pituitary, Spleen, Liver

# Complex-22





Emperical P-value: 2e-04 Number of genes in complex: 9

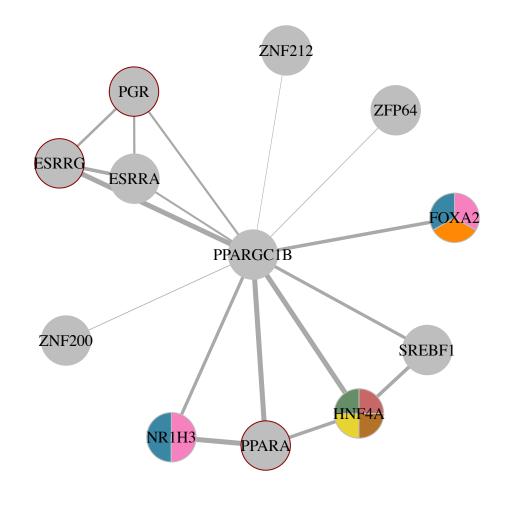
Top coordinated expressed tissues: Ovary, nonbeta, Colon

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 2e-04 Number of genes in complex: 9

Top coordinated expressed tissues: Ovary, nonbeta, Colon

Complex-23



ZNF212 PGR ZFP64 ESRRG **ESRRA** FOXA2 PPARGC1B **ZNF200** SREBF1 HNF4A NR1H3 PPARA

Emperical P-value: 0.00024 Number of genes in complex: 12

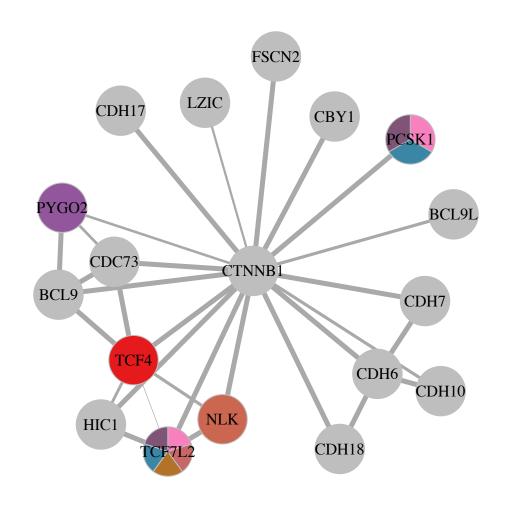
Top coordinated expressed tissues: Skin, beta, Colon

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00024 Number of genes in complex: 12

Top coordinated expressed tissues: Skin, beta, Colon

## Complex-24



FSCN2 **LZIC** CDH17 CBY1 PCSK1 PYGO2 BCL9L CDC73 CTNNB1 BCL9 CDH7 TCF4 CDH6 CDH<sub>10</sub> NLK HIC1 CDH<sub>18</sub> TCF7L2

Emperical P-value: 0.00028 Number of genes in complex: 18

Top coordinated expressed tissues: Cervix Uteri, Vagina, Stomach

Node color based on: Islet diabetic phenotype gene sets

Emperical P-value: 0.00028 Number of genes in complex: 18

Top coordinated expressed tissues: Cervix Uteri, Vagina, Stomach