

Appendix G. Functional modules detected from the 221 genes containing rare variants

Network: Blood Vessel

CLUSTER CLUSTER_GENES

NAME

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| M1 | MDC1,DROSHA,PCNT,RSF1,DCLRE1C,BIRC6,ADNP2,FBXO11,RANBP2,NSMAF,MKI67,PIGN,ANKLE2,TPP2,MSH6,HBS1L,AKAP9,MGA,AKAP8,SNAP47,VARS2,RECQL4,TEDC2,VPS13B,MAML1,SYNE2 |
| M2 | TNC,DAAM2,VWF,AHNAK2,TNS1,SVEP1,DPP4,HSPG2,SNED1,AKAP13,MACF1,PIK3C2B,FOXO1,PRUNE2,PLXNA2,COL6A3,PPL,TRIOBP,LAMA5 |
| M3 | BEST2,SLC22A2,NRXN1,SLC1A6,PDIA2,LILRA4,LRP2,ADGRV1,TH,DCHS2,MUC4,CPZ,RYR2 |
| M4 | IGF2R,TM9SF4,PACS2,ADGRG1,SOX13,SREBF1,DNPEP,RPS9,GTF2IRD1,AACS |
| M5 | MADCAM1,PCDHA5,MYO15A,FAM90A1,TTN,MUC5B,MUC16,ACE,BRF1,MYOM2,MEGF8,LILRA6,SPEG,LLGL1,SCAF1,ATP13A5,ATP2C2,ALS2 |

| Cluster | Term Name | GO_ID | Q value | No. of gene | TERM_GENES |
|---------|---|------------|-------------|-------------|------------------------|
| M1 | centrosome localization | GO:0051642 | 1.23477E-05 | 3 | SYNE2,AKAP9,RANBP2 |
| M1 | microtubule organizing center localization | GO:0061842 | 1.23477E-05 | 3 | SYNE2,AKAP9,RANBP2 |
| M1 | maintenance of location in cell | GO:0051651 | 0.008455515 | 2 | SYNE2,AKAP9 |
| M1 | organelle localization | GO:0051640 | 0.008455515 | 3 | SYNE2,AKAP9,RANBP2 |
| M1 | DNA conformation change | GO:0071103 | 0.01808375 | 2 | RECQL4,RSF1 |
| M1 | nucleic acid phosphodiester bond hydrolysis | GO:0090305 | 0.023233266 | 2 | DCLRE1C,DROSHA |
| M1 | maintenance of location | GO:0051235 | 0.024346313 | 2 | SYNE2,AKAP9 |
| M1 | endomembrane system organization | GO:0010256 | 0.034651213 | 2 | ANKLE2,AKAP9 |
| M1 | cellular response to organic cyclic compound | GO:0071407 | 0.055278117 | 2 | AKAP9,DROSHA |
| M1 | cellular response to nitrogen compound | GO:1901699 | 0.055407252 | 2 | DROSHA,AKAP9 |
| M1 | intracellular protein transport | GO:0006886 | 0.063686213 | 2 | PCNT,RANBP2 |
| M1 | microtubule cytoskeleton organization | GO:0000226 | 0.063686213 | 2 | PCNT,AKAP9 |
| M2 | cell-substrate adhesion | GO:0031589 | 0.000420687 | 4 | VWF,MACF1,TRIOBP,LAMA5 |
| M2 | cell morphogenesis involved in differentiation | GO:0000904 | 0.003721779 | 3 | MACF1,TRIOBP,LAMA5 |
| M2 | positive regulation of cell morphogenesis involved in differentiation | GO:0010770 | 0.005899369 | 2 | MACF1,TRIOBP |
| M2 | cell morphogenesis | GO:0000902 | 0.008455515 | 3 | MACF1,TRIOBP,LAMA5 |
| M2 | substrate adhesion-dependent cell spreading | GO:0034446 | 0.008455515 | 2 | TRIOBP,LAMA5 |
| M2 | regulation of cell morphogenesis involved in differentiation | GO:0010769 | 0.008455515 | 2 | MACF1,TRIOBP |
| M2 | cellular component morphogenesis | GO:0032989 | 0.008890533 | 3 | MACF1,TRIOBP,LAMA5 |
| M2 | regulation of cell-substrate adhesion | GO:0010810 | 0.013704603 | 2 | MACF1,TRIOBP |
| M2 | positive regulation of cell development | GO:0010720 | 0.015658423 | 2 | MACF1,TRIOBP |
| M2 | response to oxygen levels | GO:0070482 | 0.016243899 | 2 | DPP4,FOXO1 |
| M2 | response to wounding | GO:0009611 | 0.016243899 | 2 | VWF,TNC |

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|----|---|------------|-------------|---|---------------|
| M2 | regulation of cell morphogenesis | GO:0022604 | 0.019452494 | 2 | MACF1,TRIOBP |
| M2 | positive regulation of cell adhesion | GO:0045785 | 0.020534965 | 2 | DPP4,TRIOBP |
| M2 | regulation of cell development | GO:0060284 | 0.024346313 | 2 | MACF1,TRIOBP |
| M2 | cell activation | GO:0001775 | 0.04057585 | 2 | VWF,DPP4 |
| M3 | tissue homeostasis | GO:0001894 | 0.005899369 | 2 | MUC4,ADGRV1 |
| M3 | multicellular organismal homeostasis | GO:0048871 | 0.008455515 | 2 | MUC4,ADGRV1 |
| M3 | response to mechanical stimulus | GO:0009612 | 0.008455515 | 2 | NRXN1,RYR2 |
| M3 | anatomical structure homeostasis | GO:0060249 | 0.014967971 | 2 | MUC4,ADGRV1 |
| M3 | nervous system process | GO:0050877 | 0.020534965 | 2 | NRXN1,ADGRV1 |
| M3 | response to drug | GO:0042493 | 0.029657437 | 2 | RYR2,TH |
| M4 | regulation of intracellular protein transport | GO:0033157 | 0.008455515 | 2 | SREBF1,TM9SF4 |
| M4 | regulation of intracellular transport | GO:0032386 | 0.014396598 | 2 | SREBF1,TM9SF4 |
| M4 | autophagy | GO:0006914 | 0.016243899 | 2 | SREBF1,PACS2 |
| M4 | process utilizing autophagic mechanism | GO:0061919 | 0.016243899 | 2 | SREBF1,PACS2 |
| M4 | regulation of cellular protein localization | GO:1903827 | 0.019595899 | 2 | SREBF1,TM9SF4 |
| M4 | intracellular protein transport | GO:0006886 | 0.0210012 | 2 | SREBF1,TM9SF4 |
| M5 | heart development | GO:0007507 | 0.013704603 | 2 | TTN,MEGF8 |
| M5 | tissue morphogenesis | GO:0048729 | 0.014396598 | 2 | TTN,MEGF8 |
| M5 | circulatory system process | GO:0003013 | 0.014967971 | 2 | TTN,ACE |
| M5 | blood circulation | GO:0008015 | 0.014967971 | 2 | TTN,ACE |
| M5 | animal organ morphogenesis | GO:0009887 | 0.01808375 | 2 | TTN,MEGF8 |
| M5 | actin cytoskeleton organization | GO:0030036 | 0.029586157 | 2 | TTN,LLGL1 |

Network: Vascular Endothelium

| CLUSTER NAME | CLUSTER_GENES | | | | |
|--------------|--|--|--|--|--|
| M1 | SYNE2,FRY,DPP4,PIK3C2B,COL6A3,VWF,CSPG4,SNED1,PLXNA2,ANK3,CELSR1,HMCN1,PRUNE2,SYNE1 | | | | |
| M2 | RYR2,CACNA1H | | | | |
| M3 | MACF1,FOXO1,AKAP9 | | | | |
| M4 | HYDIN,PCDHA3,BEST2,SLC1A6,OR5V1,CUBN,CNTN2,ADGRV1,ZNF749,LAMC3,ADAM20,LRP2,MYH7B,PCDHA2,NEB,CFTR | | | | |
| M5 | PCDHA5,SLC22A2,MYH2,OR11A1,MYH1,SVEP1,SPEG,PDIA2,LILRA4,TH,CPZ,DCHS2,TTN | | | | |
| M6 | NSMAF,TPP2,DROSHA,ADNP2,ANKLE2,RANBP2,PCNT,MSH6,VPS13B,DCLRE1C,PIGN,MKI67 | | | | |

| Cluster | Term Name | GO_ID | Q value | No. of gene | TERM_GENES |
|---------|--|------------|-------------|-------------|------------------|
| M1 | maintenance of location in cell | GO:0051651 | 3.03621E-05 | 3 | ANK3,SYNE1,SYNE2 |
| M1 | maintenance of protein location in cell | GO:0032507 | 3.03621E-05 | 3 | ANK3,SYNE1,SYNE2 |
| M1 | maintenance of protein location | GO:0045185 | 3.03621E-05 | 3 | ANK3,SYNE1,SYNE2 |
| M1 | cytoskeletal anchoring at nuclear membrane | GO:0090286 | 3.03621E-05 | 2 | SYNE2,SYNE1 |
| M1 | maintenance of location | GO:0051235 | 0.000330468 | 3 | ANK3,SYNE1,SYNE2 |
| M1 | endomembrane system organization | GO:0010256 | 0.009418188 | 2 | ANK3,SYNE1 |
| M1 | cell activation | GO:0001775 | 0.018759555 | 2 | VWF,DPP4 |

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|----|---|------------|-------------|---|----------------|
| M2 | regulation of membrane potential | GO:0042391 | 0.000287447 | 2 | CACNA1H,RYR2 |
| M2 | calcium ion transmembrane transport | GO:0070588 | 0.000287447 | 2 | CACNA1H,RYR2 |
| M2 | response to metal ion | GO:0010038 | 0.000287447 | 2 | CACNA1H,RYR2 |
| M2 | response to inorganic substance | GO:0010035 | 0.000330468 | 2 | CACNA1H,RYR2 |
| M2 | calcium ion transport | GO:0006816 | 0.000330468 | 2 | CACNA1H,RYR2 |
| M2 | divalent metal ion transport | GO:0070838 | 0.000331329 | 2 | CACNA1H,RYR2 |
| M2 | divalent inorganic cation transport | GO:0072511 | 0.000331329 | 2 | CACNA1H,RYR2 |
| M3 | regulation of microtubule-based process | GO:0032886 | 0.000396902 | 2 | MACF1,AKAP9 |
| M4 | multicellular organismal homeostasis | GO:0048871 | 0.0028522 | 2 | CFTR,ADGRV1 |
| M5 | muscle contraction | GO:0006936 | 0.005188135 | 2 | TTN,MYH2 |
| M5 | muscle system process | GO:0003012 | 0.005988174 | 2 | TTN,MYH2 |
| M6 | nucleic acid phosphodiester bond hydrolysis | GO:0090305 | 0.005188135 | 2 | DCLRE1C,DROSHA |
| M6 | intracellular protein transport | GO:0006886 | 0.016702709 | 2 | PCNT,RANBP2 |