**Table 1 The fundamental network topology concepts of key modules in Tibetan pig and Rongchang pig tissues**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Pig breed** | **Tissue** | **Key module** | **Density** | **Mean cluster coefficient** | **Centralization** | **Heterogeneity** |
| Tibetan pig | Muscle | M1 | 0.03 | 0.26 | 0.10 | 1.12 |
| Liver | M5 | 0.05 | 0.21 | 0.13 | 1.10 |
| Heart | M2 | 0.03 | 0.14 | 0.09 | 0.91 |
| Spleen | M9 | 0.12 | 0.28 | 0.17 | 0.80 |
| Kideny | M20 | 0.05 | 0.17 | 0.11 | 0.84 |
| Lung | M22 | 0.03 | 0.13 | 0.08 | 0.82 |
| Rongchang | Muscle | M14 | 0.05 | 0.18 | 0.12 | 1.01 |
| Liver | M8 | 0.05 | 0.20 | 0.13 | 1.08 |
| Heart | M21 | 0.05 | 0.18 | 0.11 | 0.97 |
| Spleen | M3 | 0.08 | 0.22 | 0.14 | 0.81 |
| Kideny | M13 | 0.07 | 0.20 | 0.14 | 0.83 |
| Lung | M1 | 0.05 | 0.17 | 0.10 | 0.76 |

**Table 2 Pathways that are only significantly enriched in Tibetan pig tissue modules**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Tissue** | **Category** | **GO/KEGG ID** | **Term** | **p-value** | **Benjamini** |
| Muscle | Cellular Components | GO:0031595 | Nuclear proteasome complex | 1.02E-04 | 3.97E-03 |
| GO:0008540 | Proteasome regulatory particle, base subcomplex | 4.61E-04 | 1.02E-02 |
| KEGG\_Pathway | ssc03050 | Proteasome | 7.28E-06 | 3.15E-04 |
| ssc01200 | Carbon metabolism | 2.70E-04 | 6.64E-03 |
| ssc04152 | AMPK signaling pathway | 6.39E-04 | 1.38E-02 |
| ssc04261 | Adrenergic signaling in cardiomyocytes | 1.28E-03 | 2.18E-02 |
| ssc04931 | Insulin resistance | 2.35E-03 | 3.64E-02 |
| ssc05169 | Epstein-Barr virus infection | 2.60E-03 | 3.69E-02 |
| ssc04722 | Neurotrophin signaling pathway | 3.16E-03 | 3.83E-02 |
| ssc04921 | Oxytocin signaling pathway | 3.15E-03 | 4.11E-02 |
| Heart | KEGG\_Pathway | ssc05412 | Arrhythmogenic right ventricular cardiomyopathy (ARVC) | 1.36E-04 | 1.85E-02 |
| Spleen | Biological Progresses | GO:0006412 | Translation | 1.18E-17 | 6.86E-15 |
| GO:0001731 | Formation of translation preinitiation complex | 4.56E-05 | 1.32E-02 |
| GO:0006446 | Regulation of translational initiation | 9.43E-05 | 1.81E-02 |
| Cellular Components | GO:0022627 | Cytosolic small ribosomal subunit | 3.57E-19 | 6.49E-17 |
| GO:0022625 | Cytosolic large ribosomal subunit | 1.48E-09 | 8.99E-08 |
| GO:0016282 | Cukaryotic 43S preinitiation complex | 4.96E-06 | 1.29E-04 |
| GO:0033290 | Eukaryotic 48S preinitiation complex | 7.72E-06 | 1.76E-04 |
| GO:0005852 | Eukaryotic translation initiation factor 3 complex | 1.08E-04 | 2.17E-03 |
| GO:0005683 | U7 snRNP | 1.56E-03 | 2.35E-02 |
| GO:0042105 | Alpha-beta T cell receptor complex | 1.56E-03 | 2.35E-02 |
| Molecular Function | GO:0003735 | Structural constituent of ribosome | 9.11E-21 | 1.59E-18 |
| GO:0003743 | Translation initiation factor activity | 1.65E-04 | 9.59E-03 |
| KEGG\_Pathway | ssc03010 | Ribosome | 2.54E-21 | 4.10E-19 |
| Lung | KEGG\_Pathway | ssc04510 | Focal adhesion | 2.45E-07 | 3.69E-05 |
| ssc04512 | ECM-receptor interaction | 3.95E-06 | 2.98E-04 |
| ssc04151 | PI3K-Akt signaling pathway | 4.93E-04 | 9.26E-03 |
| ssc04350 | TGF-beta signaling pathway | 1.20E-03 | 1.80E-02 |

**Table 3 Hub gene information of key modules in Tibetan pigs and Rongchang pigs**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pig breed** | **Tissue** | **Num of hubs** | **Num of overlapping hubs\***  | **Num of hub(TSI>0.9)** | **Num of TFs in hub** |
| Tibetan pig | Muscle | 23 | 22 | 11 | 1 |
| Liver | 41 | 20 | 30 | 0 |
| Heart | 20 | 2 | 8 | 1 |
| Spleen | 40 | 6 | 20 | 1 |
| Kideny | 81 | 45 | 26 | 1 |
| Lung | 32 | 0 | 8 | 6 |
| Rongchang | Muscle | 61 | 22 | 25 | 7 |
| Liver | 39 | 20 | 30 | 0 |
| Heart | 26 | 2 | 3 | 0 |
| Spleen | 123 | 6 | 0 | 13 |
| Kideny | 68 | 45 | 26 | 0 |
| Lung | 14 | 0 | 1 | 0 |

*Note*:\*“Num of overlapping hubs” is the number of overlapping hub genes detected by Tibetan pigs and Rongchang pigs in the same tissue module.

**Table 4 Detailed information of gene regulatory networks in six tissues of Tibetan pigs**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Tissue** | **Num of TFs** | **Num of TF target genes** | **Num of hub regulated by TFs** | **Num of miRNAs** | **Num of miRNAs target genes** | **Num of hub regulated by miRNAs**  |
| Muscle | 9 | 49 | 17 | 8 | 12 | 1 |
| Liver | 3 | 7 | 3 | 3 | 5 | 1 |
| Heart | 1 | 13 | 7 | 3 | 8 | 1 |
| Spleen | 3 | 55 | 33 | 2 | 4 | 1 |
| Kidney | 3 | 4 | 3 | 4 | 13 | 5 |
| Lung | 16 | 118 | 31 | 6 | 12 | 3 |

**Table 5 Motif information in regulatory networks of six tissues in Tibetan pigs**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Motif** | **Name** | **Muscle** | **Liver** | **Heart** | **Spleen** | **Kidney** | **Lung** |
| **Counts** | **Z\*** | **P\*** | **Counts** | **Z** | **P** | **Counts** | **Z** | **P** | **Counts** | **Z** | **P** | **Counts** | **Z-** | **P** | **Counts** | **Z** | **P** |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\23077578bfcfe1b13f124bf163f6f45.png | V-out | 378 | -5.29 | 1.00 | 21 | -0.79 | 0.92 | 67 | -2.18 | 0.99 | 0 | - | 1.00 | 43 | 1.58 | 0.05 | 5160 | -8.94 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\d62d7361ed66135137c762aec127a5c.png | V-in | 24 | 0.46 | 0.38 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 18 | -3.69 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\5040f66cea8d00d09fa96ab97526be6.png | 3-Chain | 21 | -0.05 | 0.57 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 209 | -1.97 | 0.96 | 133 | -2.76 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\6aa83f26542c9790cfc4a04f084290f.png | Mutual in | 408 | -2.12 | 0.98 | 145 | -0.08 | 0.61 | 84 | -2.18 | 0.99 | 0 | - | 1.00 | 0 | - | 1.00 | 380 | -7.70 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\e1981b7bc381930397e5bda343b250f.png | Mutual out | 902 | 1.64 | 0.05 | 26 | 0.41 | 0.39 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 3152 | -0.89 | 0.82 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\380cfcaf9f6b179179c8dee5a888a41.png | Mtual V | 4363 | -12.93 | 1.00 | 2094 | -45.36 | 1.00 | 232 | -3.14 | 0.99 | 8623 | -23.86 | 1.00 | 0 | - | 1.00 | 3098 | -15.01 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\7c0916565bdb5e0c775b0be337be967.png | FFL | 3 | -0.14 | 0.59 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 469 | -1.50 | 0.81 | 135 | 2.51 | <1E-4 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\f7ee12891e6b264038d8a2f9040e3bd.png | 3-Loop | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 29452 | -28.23 | 1.00 | 0 | -0.01 | 1.00 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\6ff2f29dd886980c939e6541f69a083.png | Regulated mutual | 140 | 5.47 | <1E-4 | 3 | 0.79 | 0.32 | 21 | 2.18 | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 810 | 9.34 | <1E-4 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\031f90ae010975ce1893f3609e358d8.png | Regulating mutual | 9 | -0.36 | 0.71 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 88 | 2.67 | <1E-4 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\8fa648e830dc2b42d9da84e587bd2d9.png | Mutual and 3-Chian | 4 | 0.16 | 0.40 | 0 | - | 1.00 | 0 | - | 1.00 | 0 | - | 1.00 | 4 | -1.58 | 0.98 | 28 | 1.88 | 0.03 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\338e3f475304638a2b52c5ff13536fd.png | Semi clique | 309 | -1.68 | 0.95 | 9 | -0.41 | 0.76 | 0 | - | 1.00 | 0 | - | 1.00 | 65 | 1.97 | 0.04 | 382 | -2.11 | 0.98 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\5e1203fc4b08d0c7930d065a3a6eff0.png | Clique | 2333 | 16.14 | <1E-4 | 10769 | 45.80 | <1E-4 | 589 | 3.14 | 0.01 | 11276 | 23.86 | <1E-4 | 48717 | 28.52 | <1E-4 | 1308 | 15.15 | <1E-4 |

*Note*:\* “Z” and “P” in the table are the Z score and p-value calculated by mfinder1.2 software for each motif.

**Table 6 The top 25% of** $S\_{node}$ **genes in the Tibetan pig lung gene regulatory network**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Ranking** | **Gene** | **Full name** | **Type(Hub/TF)\*** | **Snode** |
| 1 | *KLF4* | Kruppel like factor 4 | Hub & TF | 0.4485 |
| 2 | *BCL6B* | BCL6B transcription repressor | Hub & TF | 0.3506 |
| 3 | *EGR1* | Early growth response 1 | Hub & TF | 0.3184 |
| 4 | *TBX3* | T-box 3 | TF | 0.1885 |
| 5 | *EPAS1* | Endothelial PAS domain protein 1 | Hub & TF | 0.1789 |
| 6 | *SMAD6* | SMAD family member 6 | Hub & TF | 0.1516 |
| 7 | *MAFF* | MAF bZIP transcription factor F | TF | 0.1189 |
| 8 | *CCN1* | Cellular communication network factor 1 | Hub | 0.0814 |
| 9 | *GJA5* | Gap junction protein, alpha 5 | Hub | 0.0784 |
| 10 | *JUNB* | JunB proto-oncogene, AP-1 transcription factor subunit  | TF | 0.0744 |
| 11 | *CALCRL* | Calcitonin receptor like receptor | Hub | 0.0712 |
| 12 | *FOS* | Fos proto-oncogene, AP-1 transcription factor subunit | TF | 0.0707 |
| 13 | *JCAD* | Junctional cadherin 5 associated | Hub | 0.0705 |
| 14 | *MRC2* | Mannose receptor C type 2 | Hub | 0.0683 |
| 15 | *PECAM1* | Platelet and endothelial cell adhesion molecule 1 | Hub | 0.0646 |
| 16 | *TJP1* | Tight junction protein 1 | Hub | 0.0645 |
| 17 | *CD93* | CD93 molecule  | Hub | 0.0636 |
| 18 | *LHFPL6* | LHFPL tetraspan subfamily member 6 | TG | 0.0611 |
| 19 | *COL16A1* | Collagen, type XVI, alpha 1 | Hub | 0.0588 |
| 20 | *PTPRB* | Protein tyrosine phosphatase receptor type B | Hub | 0.0570 |
| 21 | *SMAD7* | SMAD family member 7  | Hub | 0.0556 |
| 22 | *MCAM* | Melanoma cell adhesion molecule | Hub | 0.0540 |
| 23 | *HYAL2* | Hyaluronidase 2 | Hub | 0.0525 |
| 24 | *SLIT2* | Slit guidance ligand 2 | Hub | 0.0515 |
| 25 | *HSPA12B* | Heat shock protein family A (Hsp70) member 12B | Hub | 0.0495 |
| 26 | *PPP1R15A* | Protein phosphatase 1, regulatory subunit 15A | Hub | 0.0464 |
| 27 | *EHD2* | EH domain containing 2 | Hub | 0.0461 |
| 28 | *PHLDA2* | Pleckstrin homology like domain family A member 2 | Hub | 0.0451 |
| 29 | *KANK3* | KN motif and ankyrin repeat domains 3 | Hub | 0.0442 |
| 30 | *MMP23B* | Matrix metallopeptidase 23B | Hub | 0.0394 |
| 31 | *LOXL1* | Lysyl oxidase like 1 | Hub | 0.0333 |
| 32 | *TBX2* | T-box 2 | TF | 0.0251 |
| 33 | *FAM171A1* | Family with sequence similarity 171 member A1 | Hub | 0.0250 |
| 34 | *KDR* | Kinase insert domain receptor | Hub | 0.0212 |
| 35 | *MYO1C* | Myosin IC  | Hub | 0.0211 |
| 36 | *ATOH8* | Atonal bHLH transcription factor 8 | TF | 0.0193 |
| 37 | *AGRN* | Agrin | Hub | 0.0178 |
| 38 | *NPC2* | NPC intracellular cholesterol transporter 2 | TG | 0.0169 |
| 39 | *PLAC9* | Placenta associated 9 | TG | 0.0163 |
| 40 | *SLC9A3R2* | SLC9A3 regulator 2 | TG | 0.0157 |

*Note:*\* There are 4 types of genes, including “Hub&TF”, “Hub”, “TF” and “TG”. Among them, type “Hub & TF” represents that the gene is both TF and hub genes. Type “Hub” represents that the gene is a hub gene, and type “TF” represents that the gene is TF. Type “TG” means that the gene is neither hub nor TF, but only a target gene of TF.

**Table 7 The motifs formed between the “*KLF4-EGR1-BCL6B*” triad and its regulatory genes in the lung**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Motif type** | **Name** | **Num of Transitive triplets** | **Motif** | **Smotif** | **Ranking** |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\031f90ae010975ce1893f3609e358d8.png | Regulating mutual | 2 | *KLF4-EGR1-BCL6B* | 1.1695 | 1 |
| *KLF4-EGR1-EPAS1* | 1.0766 | 2 |
| *KLF4-EGR1-CCN1* | 1.0129 | 13 |
| *KLF4-EGR1-SMAD6* | 1.0073 | 16 |
| *KLF4-EGR1-MMP23B* | 0.9544 | 43 |
| *KLF4-EGR1-ATOH8* | 0.9293 | 65 |
| *KLF4-EGR1-SMAD7* | 0.9031 | 97 |
| *KLF4-EGR1-KDR* | 0.9025 | 98 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\6ff2f29dd886980c939e6541f69a083.png | Regulated mutual | 2 | *KLF4-SMAD6-BCL6B* | 1.0108 | 15 |
| C:\Users\Gemini\AppData\Local\Temp\WeChat Files\7c0916565bdb5e0c775b0be337be967.png | FFL | 1 | *KLF4-BCL6B-EPAS1* | 1.0717 | 3 |
| *KLF4-BCL6B-CCN1* | 1.0212 | 9 |
| *EGR1-BCL6B-EPAS1* | 1.0006 | 19 |
| *KLF4-BCL6B-ATOH8* | 0.9463 | 50 |
| *KLF4-EPAS1-SMAD6* | 0.9423 | 55 |
| *KLF4-BCL6B-KDR* | 0.9199 | 77 |
| *EGR1-BCL6B-CCN1* | 0.9125 | 87 |
| *KLF4-EPAS1-MMP23B* | 0.8839 | 117 |
| *EGR1-EPAS1-SMAD6* | 0.8806 | 121 |