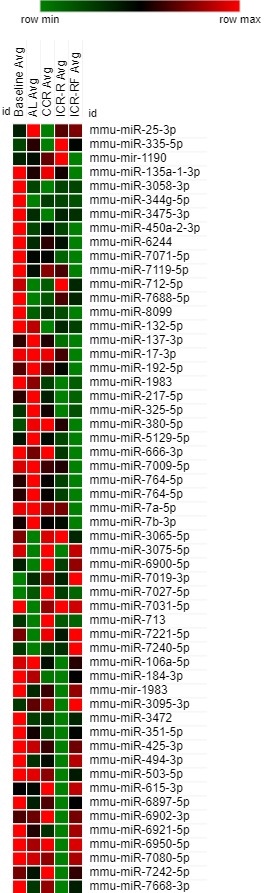
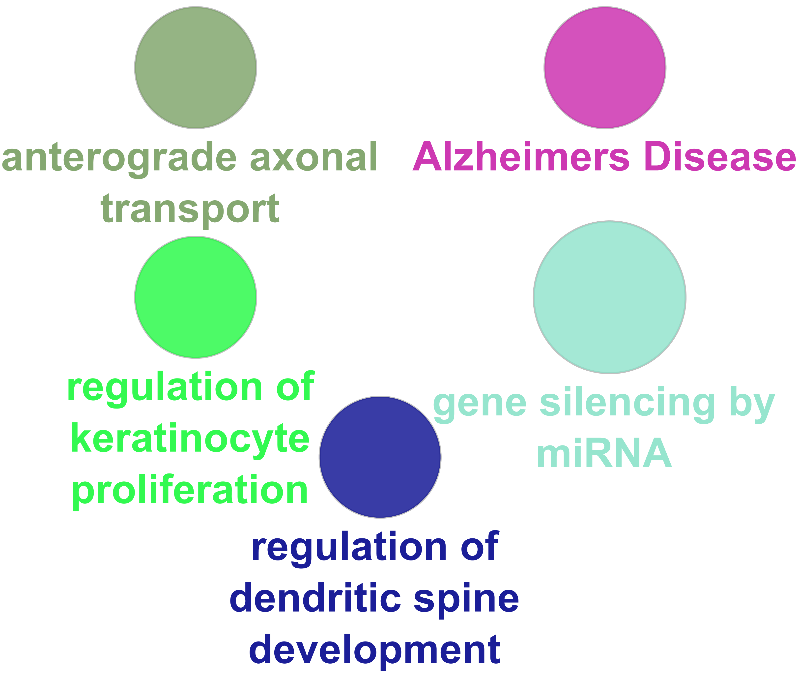
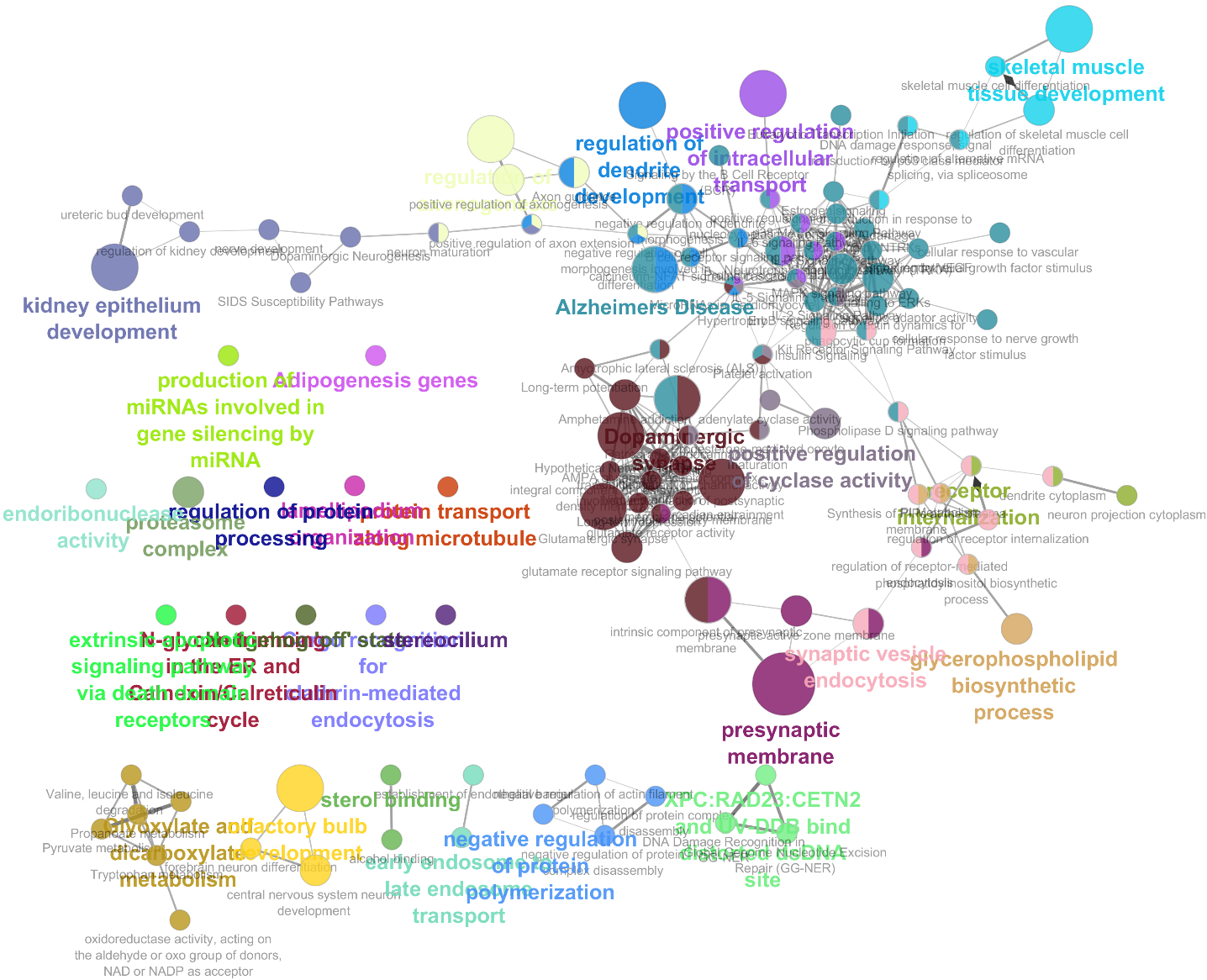
**Supplementary Data**



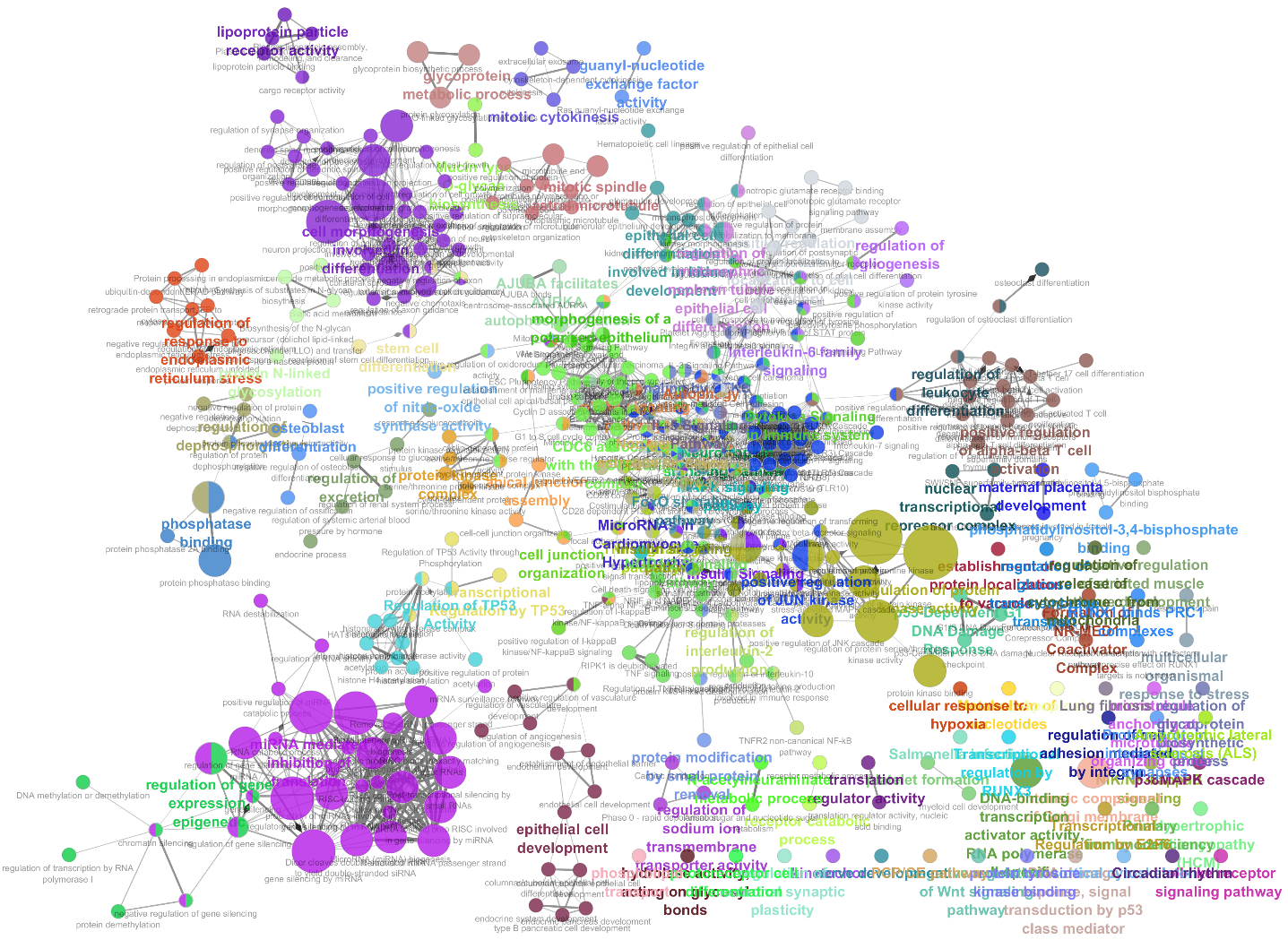
Supplementary Figure 1. K means hierarchical cluster of DE miRNAs with average expression (log2) of each group. K means clustering performed with five main divisions. High, middle and low expressions marked with red, black and green respectively.



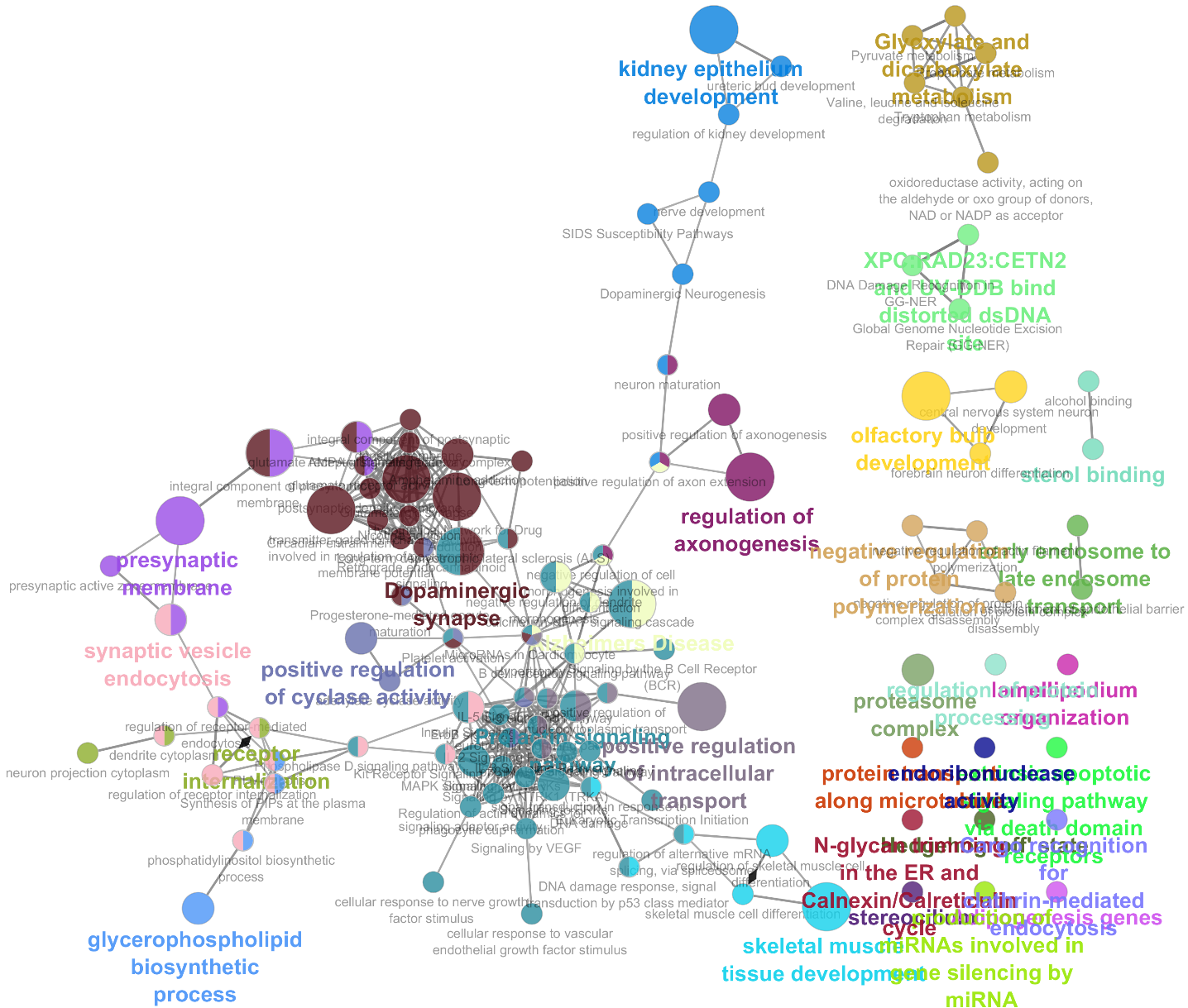
**Supplementary Figure 2.** Visualized ClueGO functional enrichment analysis of common predicted targets of CCR and ICR-R group compared to AL.



**Supplementary Figure 3.** Visualized ClueGO functional enrichment analysis of common predicted targets of AL, ICR-R and ICR-RF group compared to CCR.



**Supplementary Figure 4.** Visualized ClueGO functional enrichment analysis of common predictive targets of CCR and ICR-R group compared to baseline.



**Supplementary Figure 5.** Visualized ClueGO functional enrichment analysis of predicted targets for mmu-miR-713.

**Supplementary Table 1.** Numbers of validated and predicted targets of miRNAs changed with the application of different types of calorie restrictions (A) or by ageing (B) in brain tissue. “Com.” is the common genes in upregulated and downregulated predicted targets. Numbers of GO and KEGG pathway effected by predictive targets of DE miRNAs (C) were given in both different types of calorie restrictions and ageing.

**A**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Week 81/82** | **Compared to** | **CCR** | | | **ICR-R** | | | **ICR-RF** | | |  |
| **Up** | **Down** | **Common** | **Up** | **Down** | **Common** | **Up** | **Down** | **Common** |  |
| **AL** | 25 | 31 | - | 36 | 189 | 14 | 104 | - | - | Validated |
| 324 | 757 | 45 | 211 | 994 | 32 | 1210 | 625 | 97 | Predicted |
| **CCR** | - | - | - | 62 | 15 | - | 31 | - | - | Validated |
| - | - | - | 930 | 84 | 4 | 289 | - | - | Predicted |
| **ICR-R** | - | - | - | - | - | - | 17 | - | - | Validated |
| - | - | - | - | - | - | 133 | 130 | 6 | Predicted |

**B**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compared to** | **AL** | | | **CCR** | | | **ICR-R** | | | **ICR-RF** | | |  |
| **Up** | **Dwn** | **Com** | **Up** | **Dwn** | **Com** | **Up** | **Dwn** | **Com** | **Up** | **Dwn** | **Com** |  |
| **Baseline**  **(Week 10)** | 2 | - | - | 53 | - | - | 148 | - | - | 31 | - | - | Validated |
| 426 | - | - | 864 | 698 | 67 | 1521 | - | - | 740 | 149 | 16 | Predicted |

**C**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Compared to** | **AL** | **CCR** | **ICR-R** | **ICR-RF** |  |
| **Week 81/82** | **AL** | - | 271 | 420 | 568 | GO |
| - | 5 | 6 | 16 | KEGG |
| **CCR** | - | - | 227 | 15 | GO |
| - | - | 2 | 2 | KEGG |
| **ICR-R** | - | - | - | 10 | GO |
| - | - | - | - | KEGG |
| **Week 10** | **Baseline** | 20 | 296 | 552 | 218 | GO |
| - | - | 19 | - | KEGG |

**Supplementary Table 2.** Gene Ontology of predicted targets of DE miRNAs among CR groups. GO terms were given with their GO ids, sources, levels, percentage of associated genes and number of predicted genes that found in GO term. However, DE miRNAs in CCR group compared to AL group was given at table 2.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **ICR-R vs AL** | | | | | | |
| **GOID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0007399 | Nervous system development | GO\_BP | 7.61E-17 | [4, 5] | 9.37 | 251.00 |
| GO:0022008 | Neurogenesis | GO\_BP | 1.17E-10 | [4, 5, 6] | 9.25 | 184.00 |
| GO:0048699 | Generation of neurons | GO\_BP | 1.28E-10 | [5, 6, 7] | 9.42 | 174.00 |
| GO:0050767 | Regulation of neurogenesis | GO\_BP | 1.94E-10 | [5, 6, 7, 8] | 10.90 | 117.00 |
| GO:0097458 | Neuron part | GO\_CC | 2.20E-10 | [2, 3] | 8.94 | 199.00 |
| GO:0030182 | Neuron differentiation | GO\_BP | 1.77E-08 | [4, 6, 7, 8] | 9.25 | 154.00 |
| GO:0007417 | Central nervous system development | GO\_BP | 2.43E-08 | [4, 5, 6] | 10.18 | 117.00 |
| GO:0048667 | Cell morphogenesis involved in neuron differentiation | GO\_BP | 2.83E-08 | [5, 6, 7, 8, 9, 10] | 11.88 | 81.00 |
| GO:0098793 | Presynapse | GO\_CC | 8.44E-08 | [2, 3, 4] | 11.84 | 78.00 |
| GO:0050808 | Synapse organization | GO\_BP | 1.52E-07 | [3] | 12.62 | 66.00 |
|  | | | | | | |
| **ICR-RF vs AL** | | | | | | |
| **GOID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0007399 | Nervous system development | GO\_BP | 6.54E-24 | [4, 5] | 13.59 | 364.00 |
| GO:0097458 | Neuron part | GO\_CC | 1.29E-20 | [2, 3] | 13.83 | 308.00 |
| GO:0048699 | Generation of neurons | GO\_BP | 5.43E-20 | [5, 6, 7] | 14.46 | 267.00 |
| GO:0022008 | Neurogenesis | GO\_BP | 7.66E-20 | [4, 5, 6] | 14.13 | 281.00 |
| GO:0048666 | Neuron development | GO\_BP | 2.74E-17 | [4, 5, 7, 8, 9] | 15.19 | 207.00 |
| GO:0043005 | Neuron projection | GO\_CC | 4.22E-17 | [3, 4, 5] | 14.21 | 245.00 |
| GO:0030182 | Neuron differentiation | GO\_BP | 3.58E-16 | [4, 6, 7, 8] | 14.18 | 236.00 |
| GO:0097060 | Synaptic membrane | GO\_CC | 4.47E-14 | [2, 3, 4, 5, 6, 7] | 18.87 | 107.00 |
| GO:0051960 | Regulation of nervous system development | GO\_BP | 6.85E-14 | [4, 5, 6] | 14.98 | 179.00 |
| GO:0031175 | Neuron projection development | GO\_BP | 1.69E-13 | [5, 6, 8, 9, 10] | 14.83 | 179.00 |
|  | | | | | | |
| **ICR-R vs CCR** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0007399 | Nervous system development | GO\_BP | 8.17E-06 | [4, 5] | 6.91 | 185.00 |
| GO:0036477 | Somatodendritic compartment | GO\_CC | 1.25E-05 | [3, 4] | 8.25 | 100.00 |
| GO:0007417 | Central nervous system development | GO\_BP | 1.09E-04 | [4, 5, 6] | 8.09 | 93.00 |
| GO:0097458 | Neuron part | GO\_CC | 2.35E-04 | [2, 3] | 6.92 | 154.00 |
| GO:0097060 | Synaptic membrane | GO\_CC | 3.38E-04 | [2, 3, 4, 5, 6, 7] | 9.70 | 55.00 |
| GO:0045664 | Regulation of neuron differentiation | GO\_BP | 5.85E-04 | [5, 6, 7, 8, 9] | 8.46 | 74.00 |
| GO:0030425 | Dendrite | GO\_CC | 6.65E-04 | [4, 5, 6, 7] | 8.60 | 71.00 |
| GO:0050767 | Regulation of neurogenesis | GO\_BP | 6.83E-04 | [5, 6, 7, 8] | 8.01 | 86.00 |
| GO:0043025 | Neuronal cell body | GO\_CC | 7.37E-04 | [3, 4, 5] | 8.53 | 71.00 |
| GO:0050770 | Regulation of axonogenesis | GO\_BP | 7.63E-04 | [6, 7, 8, 9, 10, 11, 12, 13] | 12.95 | 29.00 |
|  | | | | | | |
| **ICR-RF vs CCR** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0042734 | presynaptic membrane | GO\_CC | 7.78E-03 | [3, 4, 5, 6, 7, 8] | 5.15 | 12.00 |
| GO:0021954 | Central nervous system neuron development | GO\_BP | 1.55E-02 | [5, 6, 7, 8, 9, 10] | 7.02 | 8.00 |
| GO:0098889 | Intrinsic component of presynaptic membrane | GO\_CC | 1.67E-02 | [3, 4, 5, 6, 7, 8, 9] | 6.12 | 9.00 |
| GO:0021537 | Telencephalon development | GO\_BP | 2.44E-02 | [3, 4, 6, 7, 8, 9] | 4.05 | 14.00 |
| GO:0050954 | Sensory perception of mechanical stimulus | GO\_BP | 2.69E-02 | [5] | 5.21 | 10.00 |
| GO:0099240 | Intrinsic component of synaptic membrane | GO\_CC | 3.05E-02 | [2, 3, 4, 5, 6, 7, 8] | 4.41 | 12.00 |
| GO:0043195 | Terminal bouton | GO\_CC | 3.07E-02 | [3, 4, 5, 6, 7, 8, 9, 10] | 7.29 | 7.00 |
| GO:0048787 | Presynaptic active zone membrane | GO\_CC | 3.96E-02 | [3, 4, 5, 6, 7, 8, 9] | 10.64 | 5.00 |
| GO:0021953 | Central nervous system neuron differentiation | GO\_BP | 3.96E-02 | [5, 6, 7, 8, 9] | 4.56 | 11.00 |
|  | | | | | | |
| **ICR-RF vs ICR-R** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0032591 | Dendritic spine membrane | GO\_CC | 3.28E-02 | [3, 4, 5, 6, 7, 8, 9, 10] | 18.75 | 3.00 |

**Supplementary Table 3.** Gene Ontology of predicted targets of DE miRNAs with ageing. GO terms were given with their GO ids, sources, levels, percentage of associated genes and number of predicted genes that found in GO term.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **AL vs Baseline** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0048666 | Neuron development | GO\_BP | 9.54E-06 | [4, 5, 7, 8, 9] | 4.18 | 57.00 |
| GO:0050770 | Regulation of axonogenesis | GO\_BP | 1.06E-04 | [6, 7, 8, 9, 10, 11, 12, 13] | 8.04 | 18.00 |
| GO:0031175 | Neuron projection development | GO\_BP | 1.07E-04 | [5, 6, 8, 9, 10] | 4.14 | 50.00 |
| GO:0061564 | Axon development | GO\_BP | 1.50E-04 | [6, 7, 9, 10, 11] | 5.35 | 30.00 |
| GO:0007409 | Axonogenesis | GO\_BP | 6.47E-04 | [6, 7, 8, 9, 10, 11, 12] | 5.30 | 27.00 |
| GO:0048667 | Cell morphogenesis involved in neuron differentiation | GO\_BP | 1.39E-03 | [5, 6, 7, 8, 9, 10] | 4.69 | 32.00 |
| GO:0045664 | Regulation of neuron differentiation | GO\_BP | 2.08E-03 | [5, 6, 7, 8, 9] | 4.23 | 37.00 |
| GO:0010975 | Regulation of neuron projection development | GO\_BP | 3.20E-03 | [6, 7, 8, 9, 10, 11] | 4.53 | 31.00 |
| GO:0050772 | Positive regulation of axonogenesis | GO\_BP | 2.01E-02 | [5, 6, 7, 8, 9, 10, 11, 12, 13, 14] | 8.70 | 10.00 |
|  | | | | | | |
| **CCR vs Baseline** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0007399 | Nervous system development | GO\_BP | 4.22E-09 | [4, 5] | 10.19 | 273.00 |
| GO:0097458 | Neuron part | GO\_CC | 1.33E-08 | [2, 3] | 10.51 | 234.00 |
| GO:0036477 | Somatodendritic compartment | GO\_CC | 3.47E-06 | [3, 4] | 11.39 | 138.00 |
| GO:0043005 | Neuron projection | GO\_CC | 5.39E-06 | [3, 4, 5] | 10.50 | 181.00 |
| GO:0022008 | Neurogenesis | GO\_BP | 5.46E-06 | [4, 5, 6] | 10.21 | 203.00 |
| GO:0030424 | Axon | GO\_CC | 6.36E-06 | [4, 5, 6] | 12.30 | 106.00 |
| GO:0048699 | Generation of neurons | GO\_BP | 2.96E-05 | [5, 6, 7] | 10.18 | 188.00 |
| GO:0007417 | Central nervous system development | GO\_BP | 5.30E-05 | [4, 5, 6] | 11.14 | 128.00 |
| GO:0014069 | Postsynaptic density | GO\_CC | 1.03E-04 | [3, 4, 5] | 14.00 | 64.00 |
| GO:0050767 | Regulation of neurogenesis | GO\_BP | 2.22E-04 | [5, 6, 7, 8] | 11.09 | 119.00 |
|  | | | | | | |
| **ICR-R vs Baseline** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0022008 | Neurogenesis | GO\_BP | 4.65E-20 | [4, 5, 6] | 12.82 | 255.00 |
| GO:0007399 | Nervous system development | GO\_BP | 5.47E-20 | [4, 5] | 11.84 | 317.00 |
| GO:0048699 | Generation of neurons | GO\_BP | 4.85E-19 | [5, 6, 7] | 12.94 | 239.00 |
| GO:0030182 | Neuron differentiation | GO\_BP | 2.48E-16 | [4, 6, 7, 8] | 12.86 | 214.00 |
| GO:0048666 | Neuron development | GO\_BP | 4.96E-15 | [4, 5, 7, 8, 9] | 13.35 | 182.00 |
| GO:0050767 | Regulation of neurogenesis | GO\_BP | 2.40E-14 | [5, 6, 7, 8] | 14.17 | 152.00 |
| GO:0097458 | Neuron part | GO\_CC | 6.26E-14 | [2, 3] | 11.54 | 257.00 |
| GO:0031175 | Neuron projection development | GO\_BP | 1.26E-13 | [5, 6, 8, 9, 10] | 13.50 | 163.00 |
| GO:0048667 | Cell morphogenesis involved in neuron differentiation | GO\_BP | 2.52E-13 | [5, 6, 7, 8, 9, 10] | 15.98 | 109.00 |
| GO:0051960 | Regulation of nervous system development | GO\_BP | 1.19E-12 | [4, 5, 6] | 13.31 | 159.00 |
|  | | | | | | |
| **ICR-RF vs Baseline** | | | | | | |
| **GO ID** | **GO Term** | **GO Source** | **Bonferroni P Val.** | **GO Levels** | **% Assoc. Genes** | **Nr. Genes** |
| GO:0097458 | Neuron part | GO\_CC | 4.52E-13 | [2, 3] | 7.50 | 167.00 |
| GO:0043005 | Neuron projection | GO\_CC | 1.38E-08 | [3, 4, 5] | 7.37 | 127.00 |
| GO:0030424 | Axon | GO\_CC | 1.07E-05 | [4, 5, 6] | 8.24 | 71.00 |
| GO:0007399 | Nervous system development | GO\_BP | 2.98E-05 | [4, 5] | 6.09 | 163.00 |
| GO:0022008 | Neurogenesis | GO\_BP | 4.25E-04 | [4, 5, 6] | 6.28 | 125.00 |
| GO:0048699 | Generation of neurons | GO\_BP | 6.33E-04 | [5, 6, 7] | 6.33 | 117.00 |
| GO:0098793 | Presynapse | GO\_CC | 7.86E-04 | [2, 3, 4] | 8.19 | 54.00 |
| GO:0001505 | Regulation of neurotransmitter levels | GO\_BP | 4.18E-03 | [3] | 9.13 | 38.00 |
| GO:0043009 | Chordate embryonic development | GO\_BP | 4.52E-03 | [5, 6] | 7.33 | 63.00 |
| GO:0098888 | Extrinsic component of presynaptic membrane | GO\_CC | 4.78E-03 | [3, 4, 5, 6, 7, 8, 9] | 50.00 | 6.00 |

**Supplementary Table 4.** KEGG pathway analysis of predicted targets of DE miRNAs among CR groups. KEGG pathways were given with their Term IDs, number of predicted genes that found in KEGG pathway, percentage of associated genes and genes. However, DE miRNAs in CCR group compared to AL group was given at Table 3.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ICR-R vs AL** | | | | | |
| **Term ID** | **KEGG Pathway** | **Count** | **%** | **Bonferroni P Val.** | **Genes** |
| mmu05205 | Proteoglycans in cancer | 30 | 2.56 | 9.04E-04 | TFAP4, ERBB4, WNT3A, PDCD4, TIMP3, KRAS, WNT3, PIK3CA, PIK3R3, CAMK2A, PIK3R1, TWIST1, PRKCA, PIK3CB, ROCK2, MET, ESR1, IGF1, FZD5, PPP1CB, FZD7, ITPR2, KDR, FZD6, PTPN11, CTSL, CCND1, VEGFA, HBEGF, WNT7A |
| mmu04550 | Signaling pathways regulating pluripotency of stem cells | 22 | 1.88 | 7.85E-03 | BMI1, PIK3CB, WNT3A, IGF1, REST, FZD5, MEIS1, ZIC3, FZD7, ACVR1C, FZD6, WNT3, KRAS, RIF1, PIK3CA, AXIN2, PIK3R3, ZFHX3, WNT7A, PIK3R1, KAT6A, BMPR1A |
| mmu04360 | Axon guidance | 21 | 1.79 | 9.20E-03 | ABLIM1, PLXNA2, ROCK2, MET, PPP3R1, NTNG1, SLIT1, EPHA2, EPHA4, EPHA7, KRAS, PAK2, ROBO1, SEMA7A, SEMA3E, SEMA4C, SEMA3D, PPP3CA, SEMA3A, SEMA4D, RASA1 |
| mmu04960 | Aldosterone-regulated sodium reabsorption | 11 | 0.94 | 1.49E-02 | PRKCA, ATP1B1, KRAS, ATP1B3, PIK3CB, NR3C2, IGF1, PIK3CA, PIK3R3, INSR, PIK3R1 |
| mmu04310 | Wnt signaling pathway | 21 | 1.79 | 3.28E-02 | CER1, PRKCA, AF366264, NKD1, ROCK2, WNT3A, BTRC, PPP3R1, FZD5, FZD7, FZD6, CCND1, WNT3, CCND2, PPP3CA, AXIN2, PLCB1, FOSL1, CAMK2A, WNT7A, FBXW11 |
| mmu04015 | Rap1 signaling pathway | 27 | 2.3 | 4.70E-02 | PRKCA, FGF5, FGF7, TLN2, PIK3CB, CSF1, MET, IGF1, FGF13, KIT, RALGDS, EPHA2, DOCK4, KDR, KRAS, GNAQ, CNR1, P2RY1, VEGFA, PIK3CA, RAP1B, PLCB1, RAPGEF2, PIK3R3, CRK, INSR, PIK3R1 |
|  | | | | | |
| **ICR-RF vs AL** | | | | | |
| **Term ID** | **KEGG Pathway** | **Count** | **%** | **Bonferroni P Val.** | **Genes** |
| mmu04012 | ErbB signaling pathway | 24 | 1.38 | 5.98E-05 | PRKCA, NRG3, ERBB4, BRAF, PIK3CD, ELK1, RAF1, PRKCG, RPS6KB1, SRC, PAK6, CBLB, CDKN1B, EREG, NCK1, GSK3B, CAMK2B, SHC1, PIK3R5, PIK3R3, CRK, ABL2, PIK3R1, AKT2 |
| mmu04015 | Rap1 signaling pathway | 41 | 2.36 | 9.14E-05 | FGF7, ADCY2, TLN2, EFNA3, FGF16, FGF11, LPAR4, CTNND1, KIT, SRC, PFN2, TEK, RAPGEF6, PIK3R5, THBS1, RAPGEF2, PLCB1, PIK3R3, INSR, PIK3R1, AKT2, PRKCA, MAGI2, BRAF, GRIN1, PIK3CD, SIPA1L2, RAF1, IGF1, PRKCG, KITL, PRKD1, VEGFC, MAPK14, EFNA5, RAP1B, PARD6G, CRK, PRKD3, CALM1, LCP2 |
| mmu04150 | mTOR signaling pathway | 19 | 1.09 | 1.24E-04 | PRKCA, BRAF, PIK3CD, IGF1, PRKCG, RPS6KB1, RICTOR, RRAGD, DDIT4, EIF4B, PDPK1, TSC1, ULK2, PRKAA1, PIK3R5, MLST8, PIK3R3, PIK3R1, AKT2 |
| mmu04151 | PI3K-Akt signaling pathway | 56 | 3.22 | 2.63E-04 | FGF7, PPP2R5A, EFNA3, PPP2R5C, FGF16, FGF11, LPAR4, RPS6KB1, CHAD, PDPK1, CREB3L2, MLST8, INSR, AKT2, SYK, PPP2R1B, PRKCA, SGK1, PIK3CD, PKN2, DDIT4, VEGFC, G6PC, CCND3, GNB1, CHRM1, EFNA5, PHLPP2, MCL1, COL3A1, GNG11, COL2A1, KIT, PPP2CA, TEK, PIK3R5, PRKAA1, PIK3R3, THBS1, PPP2R2D, PIK3R1, COL4A4, TNXB, RAF1, IGF1, ITGA4, KITL, EIF4B, ITGA9, HSP90B1, CDKN1B, TSC1, ITGA5, GSK3B, IKBKG, YWHAQ |
| mmu04910 | Insulin signaling pathway | 30 | 1.73 | 4.55E-04 | HK2, MKNK1, RHOQ, PDE3B, ELK1, RPS6KB1, PRKAR2B, PDPK1, HK3, PRKAA1, SHC1, PIK3R5, PIK3R3, INSR, PIK3R1, AKT2, IRS4, BRAF, PIK3CD, PRKAB1, RAF1, SOCS4, PPARGC1A, PPP1CB, CBLB, G6PC, TSC1, GSK3B, CRK, CALM1 |
| mmu04810 | Regulation of actin cytoskeleton | 39 | 2.24 | 5.98E-04 | GNA13, FGD1, ENAH, FGF7, FGF16, SSH2, WASF2, FGF11, ABI2, ARHGAP35, ARPC5, PXN, IQGAP1, SRC, MYL9, PAK6, PFN2, ARPC2, PIK3R5, MSN, PIK3R3, PIK3R1, APC, BRAF, ARHGEF7, LIMK1, ARHGEF6, PIK3CD, RAF1, ITGA4, ARHGEF12, VAV2, PPP1CB, ITGA9, ITGA5, CHRM1, CYFIP2, CRK, PIP4K2C |
| mmu05100 | Bacterial invasion of epithelial cells | 21 | 1.21 | 6.22E-04 | CAV1, CLTA, SEPT3, WASF2, PIK3CD, ARPC5, CLTC, CD2AP, SRC, ELMO2, PXN, CBLB, ARPC2, ITGA5, SHC1, PIK3R5, PIK3R3, CRK, DNM1, SEPT8, PIK3R1 |
| mmu04510 | Focal adhesion | 37 | 2.13 | 2.02E-03 | CAV1, TLN2, COL3A1, ELK1, ARHGAP35, COL2A1, PXN, SRC, MYL9, CHAD, PAK6, PDPK1, PIK3R5, SHC1, THBS1, PIK3R3, PIK3R1, AKT2, PRKCA, COL4A4, TNXB, BRAF, PIK3CD, RAF1, IGF1, PRKCG, ITGA4, VAV2, CAPN2, PPP1CB, ITGA9, VEGFC, CCND3, ITGA5, GSK3B, RAP1B, CRK |
| mmu04152 | AMPK signaling pathway | 26 | 1.5 | 6.85E-03 | PPP2R1B, IRS4, RAB2A, PFKFB4, PPP2R5A, PPP2R5C, PIK3CD, PRKAB1, IGF1, RPS6KB1, PPARGC1A, LEP, PDPK1, G6PC, TSC1, PPP2CA, RAB11B, CREB3L2, EEF2K, PIK3R5, PRKAA1, PIK3R3, INSR, PPP2R2D, PIK3R1, AKT2 |
| mmu04713 | Circadian entrainment | 22 | 1.27 | 7.15E-03 | PRKCA, ADCY2, GRIN1, CACNA1I, PRKCG, GNG11, GRIA4, KCNJ3, FOS, GRIA2, GRIA1, GNB1, RYR3, PER2, GUCY1A2, CACNA1G, CACNA1H, CAMK2B, PLCB1, RASD1, CACNA1D, CALM1 |
|  | | | | | |
| **ICR-R vs CCR** | | | | | |
| **Term ID** | **KEGG Pathway** | **Count** | **%** | **Bonferroni P Val.** | **Genes** |
| mmu04630 | Jak-STAT signaling pathway | 20 | 1.98 | 1.34E-02 | PIK3CG, IL2RA, IL23R, IL5, OSMR, IL6ST, GRB2, IL7, STAT5A, LIFR, IL7R, IL22, IFNAR2, CCND1, IL23A, PRLR, CCND2, PRL, PIK3R1, GHR |
| mmu04071 | Sphingolipid signaling pathway | 18 | 1.78 | 1.86E-02 | PPP2R1B, PIK3CG, ADORA3, GNAI3, SPHK2, ROCK1, GNAI2, SGPP1, CERS5, CERS4, GAB2, CERS1, BCL2, MAPK14, ABCC1, PLCB1, PIK3R1, OPRD1 |
|  | | | | | |
| **ICR-RF vs CCR** | | | | | |
| **Term ID** | **KEGG Pathway** | **Count** | **%** | **Bonferroni P Val.** | **Genes** |
| mmu04728 | Dopaminergic synapse | 11 | 3.81 | 2.38E-03 | PRKCA, SCN1A, GNAI3, GRIA2, MAPK14, GSK3B, PPP3CB, GRIA3, GRIA4, PPP3CA, ITPR2 |
| mmu04724 | Glutamatergic synapse | 10 | 3.46 | 4.54E-03 | PRKCA, GRM4, GNAI3, GRIA2, ADCY7, PPP3CB, GRIA3, GRIA4, PPP3CA, ITPR2 |

**Supplementary Table 5.** KEGG pathway analysis of predicted targets of DE miRNAs with ageing. KEGG pathways were given with their term ids, number of predicted genes that found in KEGG pathway, percentage of associated genes and genes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ICR-R vs Baseline** | | | | | |
| **Term ID** | **KEGG Pathway** | **Count** | **%** | **Bonferroni P Val.** | **Genes** |
| mmu04010 | MAPK signaling pathway | 47 | 3.09 | 4.21E-07 | FGF7, PDGFB, MRAS, FGF17, MKNK2, CACNB1, PPP3R1, GNG12, SRF, MAP3K5, KRAS, MAP3K2, MAP3K1, SOS1, JUND, FGF1, TRAF6, NFATC3, MAP2K7, AKT3, RASA2, TAOK1, TGFBR2, PTPRR, MAPK11, CACNG2, RPS6KA5, RPS6KA6, DUSP2, RPS6KA4, RPS6KA1, RASGRF2, MAPK12, PDGFRA, MAPK8IP2, RAP1A, MAPK9, RAP1B, MAP3K14, CACNA1C, MAP3K13, CRK, DUSP8, MAP3K12, DUSP7, CACNA1B, DUSP6 |
| mmu04144 | Endocytosis | 41 | 2.7 | 6.98E-04 | CLTA, CLTB, RAB5B, RAB5C, CYTH1, TSG101, ASAP1, VPS37B, ARF6, EEA1, ARF5, AMPH, DAB2, GBF1, WIPF2, VPS4B, RAB11A, NEDD4L, WIPF1, TRAF6, IQSEC1, IQSEC2, STAMBP, GIT1, PARD6B, KIF5A, KIF5C, TGFBR2, SMAD3, LDLRAP1, EPS15, RAB11FIP5, ACAP3, PSD, IST1, RAB22A, PDGFRA, SMURF1, RAB10, VPS26A, RAB11FIP1 |
| mmu04360 | Axon guidance | 26 | 1.71 | 8.73E-04 | PLXNA1, PPP3R1, LRRC4C, EPHB4, PAK7, KRAS, SEMA7A, SEMA3C, UNC5C, NFATC3, ROCK1, ROCK2, EFNB1, NTNG1, DPYSL5, NTN3, EPHA4, EPHA7, SEMA4G, SEMA4F, CFL2, SRGAP3, SEMA4C, SEMA4B, SEMA4D, SRGAP1 |
| mmu04550 | Signaling pathways regulating pluripotency of stem cells | 27 | 1.78 | 9.64E-04 | IL6ST, WNT3A, BMPR2, REST, MEIS1, LIF, WNT1, KRAS, PCGF6, AKT3, PIK3R1, APC, TBX3, OTX1, SMAD5, LIFR, SMAD3, NEUROG1, MAPK11, FZD2, STAT3, MAPK12, WNT9B, WNT11, ZFHX3, WNT7A, BMPR1A |
| mmu04722 | Neurotrophin signaling pathway | 24 | 1.58 | 3.46E-03 | MAPK11, RPS6KA5, RPS6KA6, MAP3K5, PDPK1, KRAS, RPS6KA1, MAPK12, PRDM4, MAP3K1, SOS1, BCL2, GAB1, RAP1A, MAPK9, RAP1B, TRAF6, MAP2K7, CRK, FRS2, PIK3R1, AKT3, CALM1, SHC4 |
| mmu04151 | PI3K-Akt signaling pathway | 48 | 3.16 | 4.14E-03 | PHLPP1, CRTC2, FGF7, PHLPP2, MCL1, PDGFB, FGF17, LPAR4, ITGA10, GNG12, IL7R, PTEN, CCNE1, PDPK1, LAMB3, KRAS, ITGB8, BCL2, SOS1, PPP2CA, PDGFC, PRKAA2, FGF1, THBS2, THBS3, AKT3, PIK3R1, GHR, RBL2, CREB1, PKN2, CDK6, BCL2L11, IL6RA, OSM, ITGA9, CCND1, CDKN1A, CDKN1B, YWHAH, LAMA3, CHRM2, CCND2, ITGA8, VEGFA, PDGFRA, IFNA12, PPP2R2A |
| mmu04068 | FoxO signaling pathway | 25 | 1.64 | 5.53E-03 | USP7, RBL2, TGFBR2, SMAD3, MAPK11, IL7R, PTEN, SIRT1, CCNG2, BCL2L11, STAT3, CCNB1, PDPK1, CCND1, CDKN1A, KRAS, CDKN1B, MAPK12, SLC2A4, CCND2, SOS1, MAPK9, PRKAA2, AKT3, PIK3R1 |
| mmu05218 | Melanoma | 17 | 1.12 | 7.44E-03 | E2F1, E2F2, E2F3, FGF7, PDGFB, FGF17, CDK6, RB1, PTEN, CDKN1A, CCND1, KRAS, PDGFRA, PDGFC, FGF1, AKT3, PIK3R1 |
| mmu04710 | Circadian rhythm | 11 | 0.72 | 9.10E-03 | NPAS2, BTRC, CREB1, RORB, RORA, PRKAA2, BHLHE40, ARNTL, BHLHE41, CLOCK, CUL1 |
| mmu05215 | Prostate cancer | 19 | 1.25 | 9.66E-03 | E2F1, E2F2, E2F3, PDGFB, CREB1, RB1, PTEN, CCNE1, CDKN1A, CCND1, PDPK1, KRAS, CDKN1B, SOS1, BCL2, PDGFRA, PDGFC, AKT3, PIK3R1 |

**Supplementary Table 6.** Functional enrichment analysis of common predicted targets among CR groups. Results were given with their category, term, numbers of predicted genes that found in term, p value, Bonferroni corrected p value and fold enrichment.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Common between CCR and ICR-R compared to AL** | | | | | | |
| **Annotation Cluster 1** | **Enrichment Score: 4.24** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Transcription regulation | 21 | 28.00 | 7.97E-07 | 1.18E-04 | 3.53 |
| UP\_KEYWORDS | Transcription | 21 | 28.00 | 1.33E-06 | 1.97E-04 | 3.42 |
| UP\_KEYWORDS | Nucleus | 34 | 45.33 | 1.40E-06 | 2.07E-04 | 2.27 |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated | 21 | 28.00 | 1.23E-05 | 6.88E-03 | 2.92 |
| GOTERM\_MF\_DIRECT | GO:0000977~RNA polymerase II regulatory region sequence-specific DNA binding | 8 | 10.67 | 2.64E-05 | 5.31E-03 | 9.02 |
| UP\_KEYWORDS | Activator | 11 | 14.67 | 3.41E-05 | 5.03E-03 | 5.33 |
| GOTERM\_MF\_DIRECT | GO:0003700~transcription factor activity, sequence-specific DNA binding | 14 | 18.67 | 3.63E-05 | 7.30E-03 | 3.95 |
| GOTERM\_BP\_DIRECT | GO:0045893~positive regulation of transcription, DNA-templated | 11 | 14.67 | 5.48E-05 | 3.02E-02 | 5.00 |
| GOTERM\_BP\_DIRECT | GO:0006355~regulation of transcription, DNA-templated | 22 | 29.33 | 5.93E-05 | 3.26E-02 | 2.53 |
| GOTERM\_MF\_DIRECT | GO:0000978~RNA polymerase II core promoter proximal region sequence-specific DNA binding | 9 | 12.00 | 8.33E-05 | 1.67E-02 | 6.25 |
| GOTERM\_CC\_DIRECT | GO:0005634~nucleus | 38 | 50.67 | 8.52E-05 | 1.36E-02 | 1.75 |
| GOTERM\_MF\_DIRECT | GO:0001077~transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding | 8 | 10.67 | 9.36E-05 | 1.87E-02 | 7.38 |
| GOTERM\_BP\_DIRECT | GO:0045944~positive regulation of transcription from RNA polymerase II promoter | 13 | 17.33 | 3.02E-04 | 1.56E-01 | 3.42 |
| UP\_KEYWORDS | DNA-binding | 15 | 20.00 | 6.07E-04 | 8.59E-02 | 2.83 |
| GOTERM\_MF\_DIRECT | GO:0003677~DNA binding | 16 | 21.33 | 5.04E-03 | 6.40E-01 | 2.16 |
| GOTERM\_MF\_DIRECT | GO:0043565~sequence-specific DNA binding | 8 | 10.67 | 1.24E-02 | 9.19E-01 | 3.15 |
|  | | | | | | |
| **Annotation Cluster 2** | **Enrichment Score: 2.05** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| GOTERM\_CC\_DIRECT | GO:0043198~dendritic shaft | 4 | 5.33 | 1.34E-03 | 1.94E-01 | 18.16 |
| GOTERM\_CC\_DIRECT | GO:0043197~dendritic spine | 4 | 5.33 | 1.58E-02 | 9.24E-01 | 7.48 |
| GOTERM\_CC\_DIRECT | GO:0045202~synapse | 6 | 8.00 | 3.39E-02 | 9.96E-01 | 3.29 |
|  | | | | | | |
| **Common between AL, ICR-R, ICR-RF compared to CCR** | | | | | | |
| **Annotation Cluster 1** | **Enrichment Score: 4.61** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Transcription | 48 | 20.34 | 8.46E-09 | 2.12E-06 | 2.48 |
| UP\_KEYWORDS | Transcription regulation | 47 | 19.92 | 8.93E-09 | 2.24E-06 | 2.51 |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated | 49 | 20.76 | 3.43E-07 | 4.31E-04 | 2.16 |
| UP\_KEYWORDS | Nucleus | 78 | 33.05 | 2.52E-06 | 6.31E-04 | 1.65 |
| GOTERM\_BP\_DIRECT | GO:0006355~regulation of transcription, DNA-templated | 49 | 20.76 | 6.18E-05 | 7.49E-02 | 1.78 |
| GOTERM\_MF\_DIRECT | GO:0003700~transcription factor activity, sequence-specific DNA binding | 24 | 10.17 | 2.06E-04 | 8.06E-02 | 2.36 |
| GOTERM\_CC\_DIRECT | GO:0005634~nucleus | 95 | 40.25 | 2.37E-04 | 6.51E-02 | 1.37 |
| UP\_KEYWORDS | Activator | 17 | 7.20 | 8.43E-04 | 1.91E-01 | 2.62 |
| GOTERM\_BP\_DIRECT | GO:0045944~positive regulation of transcription from RNA polymerase II promoter | 25 | 10.59 | 8.99E-04 | 6.78E-01 | 2.08 |
| UP\_KEYWORDS | DNA-binding | 31 | 13.14 | 1.23E-03 | 2.65E-01 | 1.86 |
| GOTERM\_MF\_DIRECT | GO:0003677~DNA binding | 33 | 13.98 | 1.15E-02 | 9.91E-01 | 1.55 |
|  | | | | | | |
| **Annotation Cluster 2** | **Enrichment Score: 2.21** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| GOTERM\_MF\_DIRECT | GO:0008046~axon guidance receptor activity | 4 | 1.69 | 7.97E-05 | 3.21E-02 | 43.40 |
| KEGG\_PATHWAY | mmu04360:Axon guidance | 8 | 3.39 | 6.52E-04 | 1.19E-01 | 5.36 |
| UP\_KEYWORDS | Developmental protein | 21 | 8.90 | 2.98E-03 | 5.28E-01 | 2.07 |
| UP\_KEYWORDS | Neurogenesis | 9 | 3.81 | 4.36E-03 | 6.66E-01 | 3.50 |
| UP\_KEYWORDS | Differentiation | 15 | 6.36 | 7.65E-03 | 8.54E-01 | 2.23 |
| GOTERM\_BP\_DIRECT | GO:0007275~multicellular organism development | 22 | 9.32 | 1.23E-02 | 1.00E+00 | 1.77 |
| GOTERM\_BP\_DIRECT | GO:0007399~nervous system development | 11 | 4.66 | 1.60E-02 | 1.00E+00 | 2.42 |
| GOTERM\_BP\_DIRECT | GO:0030154~cell differentiation | 17 | 7.20 | 2.62E-02 | 1.00E+00 | 1.81 |
| GOTERM\_BP\_DIRECT | GO:0007411~axon guidance | 3 | 1.27 | 5.36E-01 | 1.00E+00 | 1.67 |

**Supplementary Table 7.** Functional enrichment analysis of common predicted targets changed with ageing. Functional enrichment results were given with their category, term, number of predicted genes that found in term, p value, bonferroni corrected p value and fold enrichment.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Common between CCR, ICR-R compared to Baseline** | | | | | | |
| **Annotation Cluster 1** | **Enrichment Score: 6.09** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Transcription regulation | 74 | 17.33 | 2.89E-10 | 7.33E-08 | 2.18 |
| UP\_KEYWORDS | Transcription | 75 | 17.56 | 5.04E-10 | 1.28E-07 | 2.14 |
| UP\_KEYWORDS | Nucleus | 135 | 31.62 | 1.09E-08 | 2.77E-06 | 1.58 |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated | 76 | 17.80 | 2.90E-08 | 5.05E-05 | 1.92 |
| GOTERM\_BP\_DIRECT | GO:0006355~regulation of transcription, DNA-templated | 80 | 18.74 | 3.26E-06 | 5.67E-03 | 1.67 |
| GOTERM\_CC\_DIRECT | GO:0005634~nucleus | 161 | 37.70 | 7.51E-05 | 2.70E-02 | 1.30 |
| GOTERM\_MF\_DIRECT | GO:0003677~DNA binding | 64 | 14.99 | 9.02E-05 | 4.66E-02 | 1.63 |
| UP\_KEYWORDS | DNA-binding | 51 | 11.94 | 2.97E-04 | 7.26E-02 | 1.69 |
| GOTERM\_MF\_DIRECT | GO:0003700~transcription factor activity, sequence-specific DNA binding | 35 | 8.20 | 5.66E-04 | 2.59E-01 | 1.87 |
|  | | | | | | |
| **Annotation Cluster 2** | **Enrichment Score: 5.69** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Zinc-finger | 62 | 14.52 | 4.61E-08 | 1.17E-05 | 2.10 |
| UP\_KEYWORDS | Zinc | 74 | 17.33 | 1.83E-07 | 4.65E-05 | 1.87 |
| UP\_KEYWORDS | Metal-binding | 100 | 23.42 | 3.51E-06 | 8.91E-04 | 1.56 |
| GOTERM\_MF\_DIRECT | GO:0008270~zinc ion binding | 46 | 10.77 | 9.22E-06 | 4.86E-03 | 2.02 |
| GOTERM\_MF\_DIRECT | GO:0046872~metal ion binding | 101 | 23.65 | 1.25E-04 | 6.42E-02 | 1.42 |
|  | | | | | | |
| **Annotation Cluster 3** | **Enrichment Score: 2.24** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Cell cycle | 28 | 6.56 | 6.11E-05 | 1.54E-02 | 2.38 |
| GOTERM\_BP\_DIRECT | GO:0007049~cell cycle | 25 | 5.85 | 2.61E-03 | 9.89E-01 | 1.94 |
| UP\_KEYWORDS | Cell division | 16 | 3.75 | 4.84E-03 | 7.09E-01 | 2.28 |
| GOTERM\_BP\_DIRECT | GO:0051301~cell division | 16 | 3.75 | 1.25E-02 | 1.00E+00 | 2.04 |
| UP\_KEYWORDS | Mitosis | 10 | 2.34 | 5.62E-02 | 1.00E+00 | 2.05 |
| GOTERM\_BP\_DIRECT | GO:0007067~mitotic nuclear division | 11 | 2.58 | 6.65E-02 | 1.00E+00 | 1.89 |
|  | | | | | | |
| **Annotation Cluster 4** | **Enrichment Score: 2.09** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Developmental protein | 34 | 7.96 | 8.63E-04 | 1.97E-01 | 1.85 |
| GOTERM\_BP\_DIRECT | GO:0007275~multicellular organism development | 36 | 8.43 | 3.26E-03 | 9.97E-01 | 1.67 |
| UP\_KEYWORDS | Differentiation | 22 | 5.15 | 1.08E-02 | 9.37E-01 | 1.81 |
| GOTERM\_BP\_DIRECT | GO:0030154~cell differentiation | 22 | 5.15 | 1.43E-01 | 1.00E+00 | 1.35 |
|  | | | | | | |
| **Annotation Cluster 5** | **Enrichment Score: 2.05** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| INTERPRO | IPR011011:Zinc finger, FYVE/PHD-type | 11 | 2.58 | 4.10E-04 | 2.69E-01 | 4.04 |
| INTERPRO | IPR019786:Zinc finger, PHD-type, conserved site | 7 | 1.64 | 1.72E-03 | 7.33E-01 | 5.47 |
| UP\_SEQ\_FEATURE | zinc finger region:PHD-type | 6 | 1.41 | 2.21E-03 | 9.41E-01 | 6.47 |
| INTERPRO | IPR001965:Zinc finger, PHD-type | 8 | 1.87 | 2.30E-03 | 8.29E-01 | 4.39 |
| INTERPRO | IPR019787:Zinc finger, PHD-finger | 7 | 1.64 | 4.38E-03 | 9.65E-01 | 4.54 |
| SMART | SM00249:PHD | 8 | 1.87 | 6.54E-03 | 7.33E-01 | 3.61 |
| UP\_KEYWORDS | Chromatin regulator | 10 | 2.34 | 6.90E-02 | 1.00E+00 | 1.97 |
| GOTERM\_BP\_DIRECT | GO:0016569~covalent chromatin modification | 9 | 2.11 | 1.95E-01 | 1.00E+00 | 1.61 |
| GOTERM\_MF\_DIRECT | GO:0035064~methylated histone binding | 3 | 0.70 | 2.62E-01 | 1.00E+00 | 3.01 |

**Supplementary Table 8**. Functional enrichment analysis of predicted targets of mmu-miR-713. Functional enrichment results were given with their category, term, number of predicted genes that found in term, p value, bonferroni corrected p value and fold enrichment.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **mmu-miR-713** | | | | | | |
| **Annotation Cluster 1** | **Enrichment Score: 4.43** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Transcription | 47 | 20.17 | 1.61E-08 | 4.02E-06 | 2.46 |
| UP\_KEYWORDS | Transcription regulation | 46 | 19.74 | 1.72E-08 | 4.31E-06 | 2.49 |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated | 48 | 20.60 | 5.63E-07 | 7.04E-04 | 2.14 |
| UP\_KEYWORDS | Nucleus | 77 | 33.05 | 2.94E-06 | 7.35E-04 | 1.65 |
| GOTERM\_CC\_DIRECT | GO:0005654~nucleoplasm | 42 | 18.03 | 5.72E-05 | 1.59E-02 | 1.91 |
| GOTERM\_BP\_DIRECT | GO:0006355~regulation of transcription, DNA-templated | 48 | 20.60 | 8.81E-05 | 1.04E-01 | 1.77 |
| GOTERM\_MF\_DIRECT | GO:0003700~transcription factor activity, sequence-specific DNA binding | 24 | 10.30 | 1.64E-04 | 6.46E-02 | 2.39 |
| GOTERM\_CC\_DIRECT | GO:0005634~nucleus | 93 | 39.91 | 3.81E-04 | 1.01E-01 | 1.36 |
| GOTERM\_BP\_DIRECT | GO:0045944~positive regulation of transcription from RNA polymerase II promoter | 25 | 10.73 | 7.38E-04 | 6.03E-01 | 2.11 |
| UP\_KEYWORDS | Activator | 16 | 6.87 | 2.02E-03 | 3.97E-01 | 2.50 |
| UP\_KEYWORDS | DNA-binding | 30 | 12.88 | 2.02E-03 | 3.97E-01 | 1.82 |
| GOTERM\_MF\_DIRECT | GO:0003677~DNA binding | 32 | 13.73 | 1.59E-02 | 9.99E-01 | 1.53 |
|  | | | | | | |
| **Annotation Cluster 2** | **Enrichment Score: 1.97** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| UP\_KEYWORDS | Golgi apparatus | 17 | 7.30 | 4.84E-03 | 7.02E-01 | 2.20 |
| GOTERM\_CC\_DIRECT | GO:0005794~Golgi apparatus | 23 | 9.87 | 1.58E-02 | 9.88E-01 | 1.70 |
| GOTERM\_CC\_DIRECT | GO:0000139~Golgi membrane | 11 | 4.72 | 1.65E-02 | 9.90E-01 | 2.41 |
|  | | | | | | |
| **Annotation Cluster 3** | **Enrichment Score: 1.85** | | | | | |
| **Category** | **Term** | **Count** | **%** | **P Value** | **Bonferroni** | **Fold Enrichment** |
| GOTERM\_MF\_DIRECT | GO:0008046~axon guidance receptor activity | 4 | 1.72 | 7.62E-05 | 3.05E-02 | 44.06 |
| KEGG\_PATHWAY | mmu04360:Axon guidance | 7 | 3.00 | 3.30E-03 | 4.73E-01 | 4.74 |
| UP\_KEYWORDS | Developmental protein | 20 | 8.58 | 5.70E-03 | 7.60E-01 | 1.99 |
| UP\_KEYWORDS | Neurogenesis | 8 | 3.43 | 1.39E-02 | 9.70E-01 | 3.15 |
| GOTERM\_BP\_DIRECT | GO:0007275~multicellular organism development | 21 | 9.01 | 2.02E-02 | 1.00E+00 | 1.72 |
| UP\_KEYWORDS | Differentiation | 13 | 5.58 | 3.42E-02 | 1.00E+00 | 1.96 |
| GOTERM\_BP\_DIRECT | GO:0007399~nervous system development | 10 | 4.29 | 3.59E-02 | 1.00E+00 | 2.23 |
| GOTERM\_BP\_DIRECT | GO:0030154~cell differentiation | 15 | 6.44 | 8.03E-02 | 1.00E+00 | 1.62 |
| GOTERM\_BP\_DIRECT | GO:0007411~axon guidance | 3 | 1.29 | 5.29E-01 | 1.00E+00 | 1.69 |