

Figure S1. Interactive pathway plot for SOD1–ALS network molecules predicted by ShinyGO analysis. Two pathways were considered connected if they shared $\geq 20\%$ genes. Intense green nodes represent highly enriched gene datasets while bigger nodes represent large gene datasets. The thicker lines indicate higher overlapping of genes.

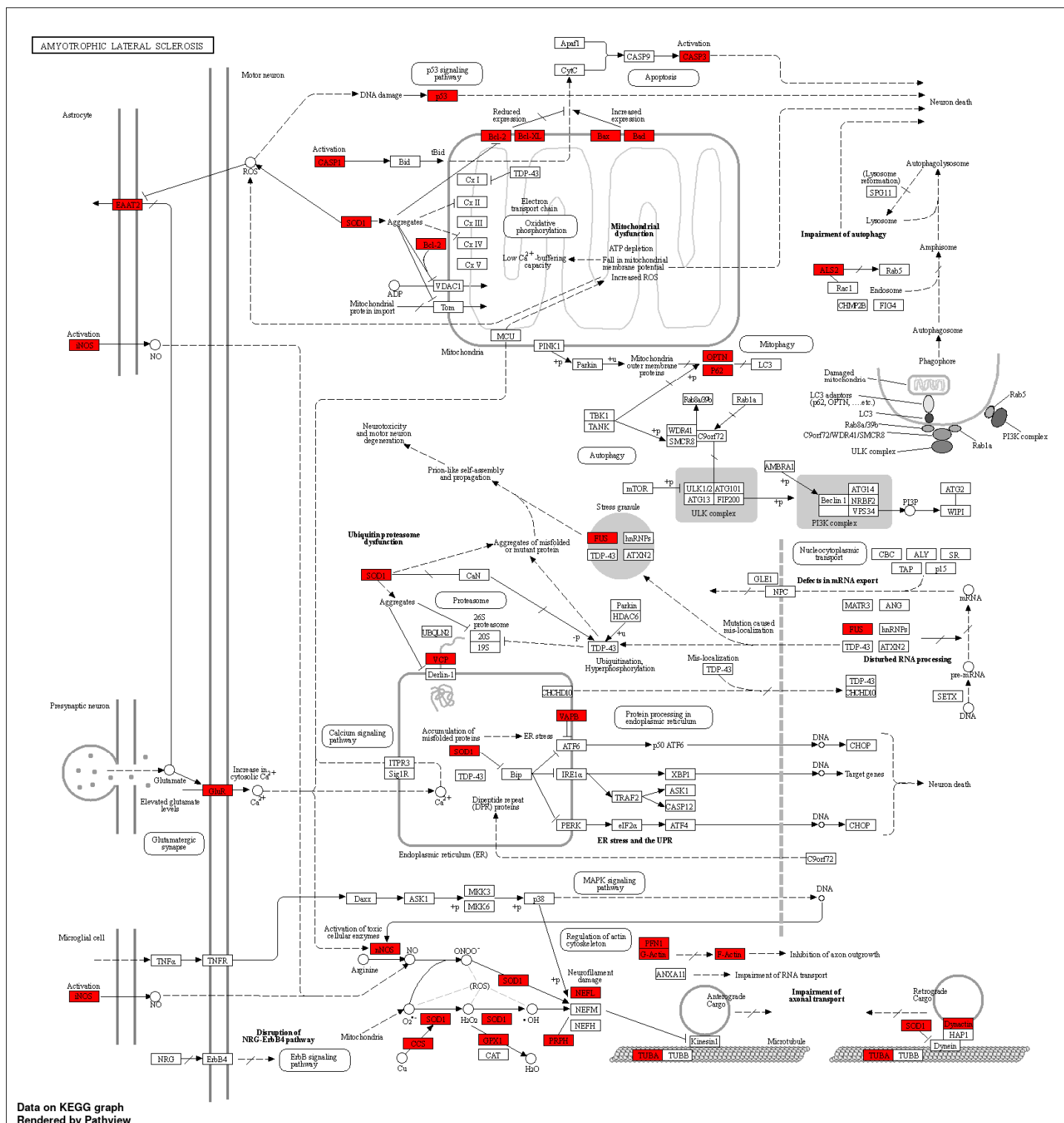


Figure S2. Amyotrophic lateral sclerosis pathway. The SOD1–ALS pathway molecules predicted by IPA are highlighted in red. The molecule boxes were painted red with ShinyGO. Figure source KEGG graph, rendered by Pathview.

Superoxide Radicals Degradation
Overlay: Expected activation state

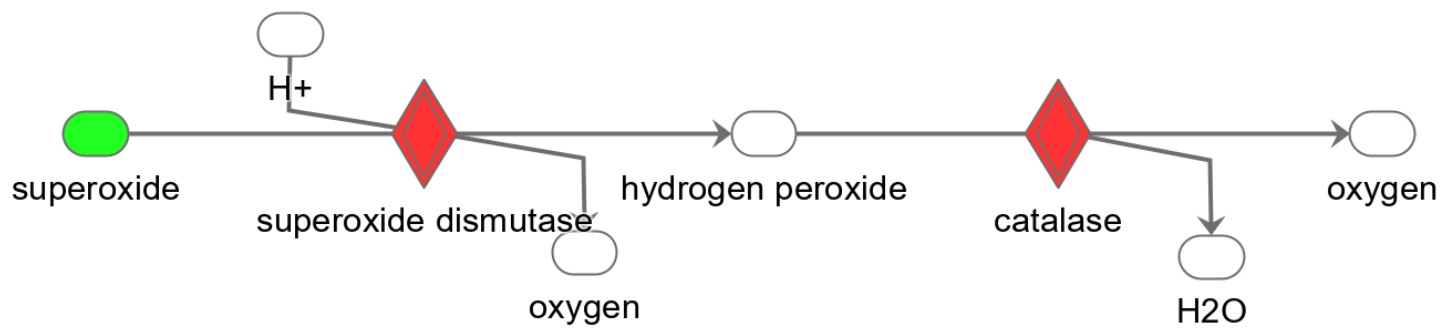


Figure S4. Superoxide radicals' degradation by SOD1. Figure adapted from IPA, QIAGEN.

Apelin is an adipocytokine secreted by adipocytes.
Its main functions are to regulate insulin sensitivity
and to suppress adipogenesis and lipolysis.

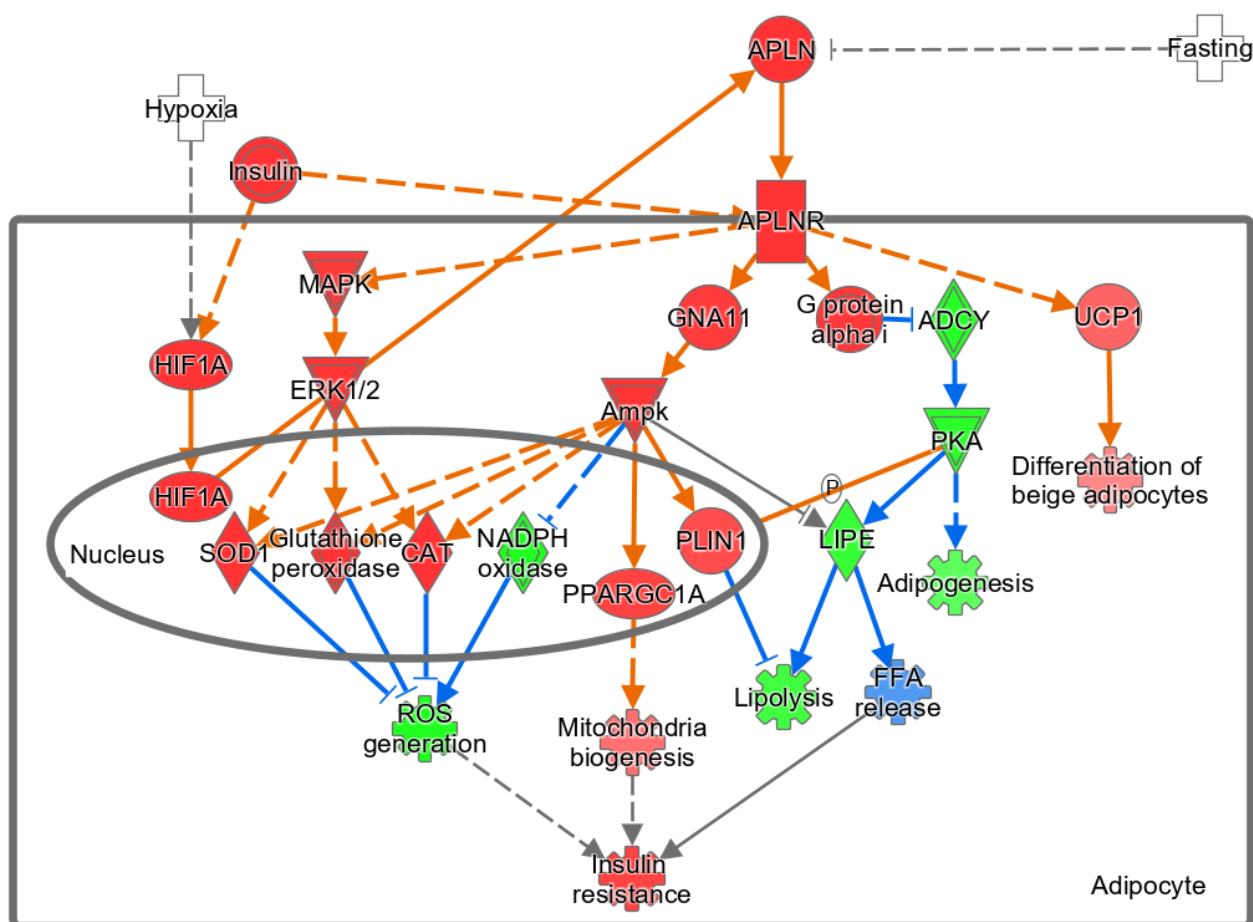
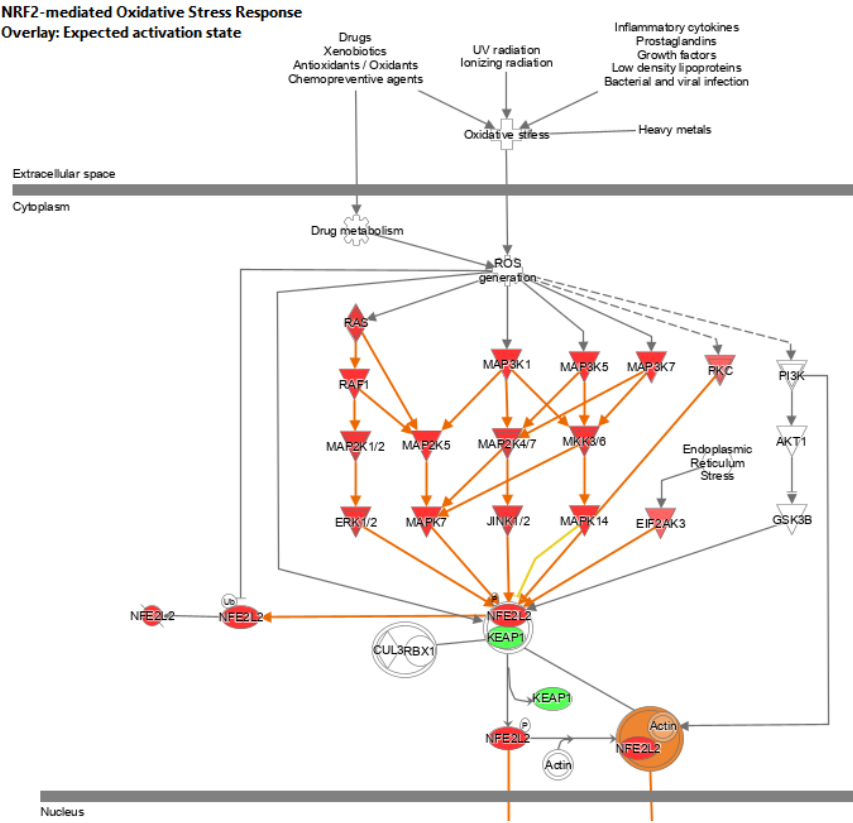


Figure S5. The role of SOD1 in the apelin adipocyte signaling pathway. Figure adapted from IPA, QIAGEN.

A)

NRF2-mediated Oxidative Stress Response
Overlay: Expected activation state



B)

NRF2-mediated Oxidative Stress Response

Overlay: Expected activation state

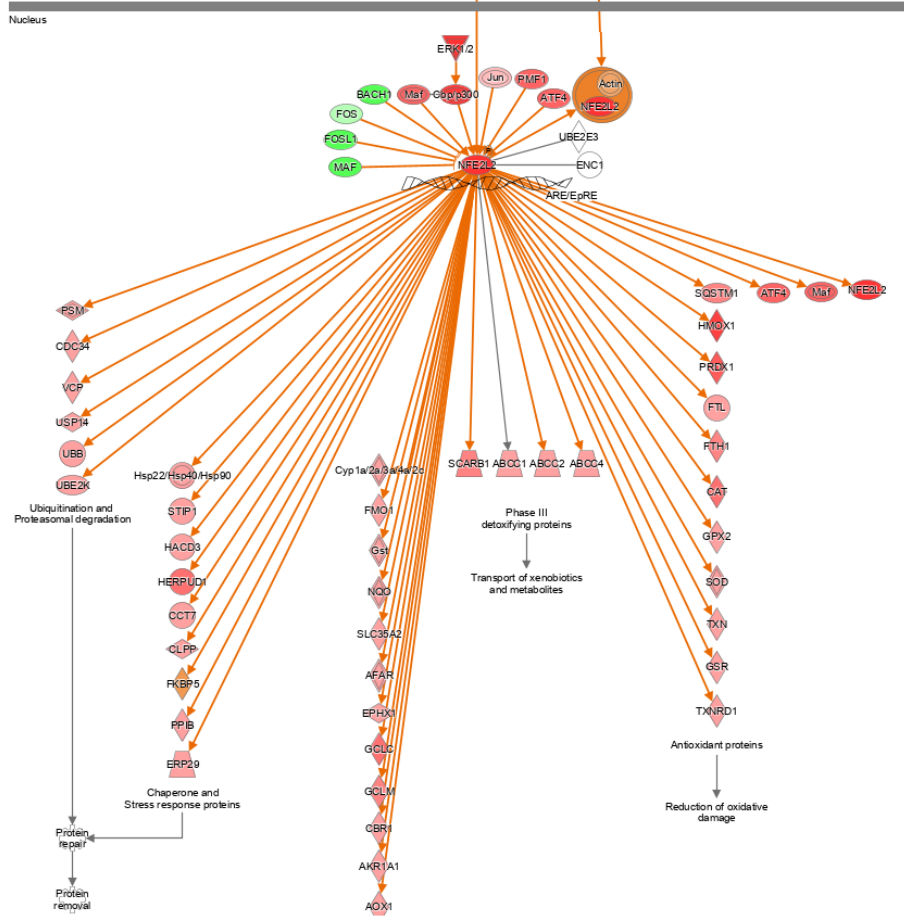


Figure S6. A) NRF2-mediated oxidative stress response signaling pathway in the extracellular space and cytoplasm. Figure adapted from IPA, QIAGEN. **B)** The role of SOD1 in the NRF2-mediated oxidative stress response signaling pathway in the nucleus. Figure credit to IPA, QIAGEN.

Table S1. SOD1 variants causing amyotrophic lateral sclerosis.

| | | | | | |
|--------------|-------------|-------------|-------------|------------|-------------|
| A141A | D12Y | G11G | H121L | L68P | T55R |
| A141G | D77V | G11R | H44R | L68R | T89_D91del |
| A146G | D77Y | G11V | H47D | L85F | V119KfsTer5 |
| A146T | D84G | G128R | H47R | L85V | V119L |
| A5F | D84N | G128VfsTer7 | H49Q | L9Q | V119M |
| A5S | D91A | G139E | H49R | L9V | V120F |
| A5T | D91A | G13R | H72Y | N139H | V149A |
| A5V | D91N | G142A | H81R | N140D | V149G |
| A90T | D91V | G142E | I100V | N140K | V15G |
| A90V | D91_K92insN | G142R | I105F | N140N | V15M |
| A96T | D97MfsTer8 | G142X | I113M | N20S | V30A |
| c.170-108T>A | D97N | G148 | I113T | N66S | V30Dfs*8 |
| c.239+62T>C | E101G | G148C | I114F | N87D | V30M |
| c.240-7T>G | E101K | G148D | I114T | N87I | V32A |
| c.358-10A>G | E122G | G148R | I150T | N87K | V48A |
| c.358-10T>G | E133DfsTer2 | G16A | I150V | N87S | V48F |
| c.358-11A>G | E133insTT | G17A | I152S | P67R | V6L |
| c.358-304C>G | E133K | G28_P29del | I152T | P67S | V88A |
| C112Y | E133VfsX31 | G38R | I19del | Q154Q | V88M |
| C147R | E134del | G38V | K129PfsX6 | Q22H | V8E |
| C147X | E134K | G42D | K129WfsX6 | Q23L | V95A |
| C7F | E134V | G42S | K137X | Q23R | V98L |
| C7G | E22G | G62R | K4E | R116C | V98M |
| C7S | E22K | G73C | K92RfsX9 | R116G | |
| C7W | E41G | G73D | L106V | S105del | |
| C7Y | E50K | G73S | L107F | S106L | |
| D102G | F21C | G86R | L118V | S108LfsX15 | |
| D102H | F21L | G86S | L127GfsTer6 | S135N | |
| D102N | F46C | G94A | L127S | S135T | |
| D102Y | F46S | G94C | L127X | S60I | |
| D110Y | F65L | G94D | L145F | S60S | |
| D125G | G109V | G94R | L145S | T117T | |
| D125V | G10A | G94S | L39R | T138A | |
| D126H | G115A | G94V | L39V | T138R | |

Reference: ALSoD – Amyotrophic Lateral Sclerosis online Database. Available at: <https://alsod.ac.uk/output/gene.php/SOD1> (accessed on 10 November 2022).

Table S2. The list of SOD1–ALS pathway molecules identified by IPA, genes used for ShinyGO analysis, and construction of a molecular interaction network on STRING.

| No | SOD1–ALS pathway molecules | Genes used for ShinyGO analysis | Genes used for STRING molecular interaction network construction |
|----|----------------------------|---------------------------------|--|
|----|----------------------------|---------------------------------|--|

| | | | |
|----|------------------------------|--------|--------|
| 1 | 8-oxo-7-hydrodeoxyguano-sine | ACTB | ACTB |
| 2 | ACTB | ADRB2 | ADRB2 |
| 3 | ADRB2 | ALS2 | ALS2 |
| 4 | ALS2 | ANXA1 | ANXA1 |
| 5 | ANXA1 | ANXA5 | ANXA5 |
| 6 | ANXA5 | APOE | APOE |
| 7 | APOE | APP | APP |
| 8 | APP | BAD | BAD |
| 9 | BAD | BAX | BAX |
| 10 | BAX | BCL2 | BCL2 |
| 11 | BCL2 | BCL2L1 | BCL2L1 |
| 12 | BCL2L1 | CALM1 | CALM1 |
| 13 | Ca ²⁺ | CASP1 | CASP1 |
| 14 | CALM1 (includes others) | CASP3 | CASP3 |
| 15 | CASP1 | CCS | CCS |
| 16 | CASP3 | CCT2 | CCT2 |
| 17 | CCS | CD36 | CD36 |
| 18 | CCT2 | CHGB | CHGB |
| 19 | CD36 | CLU | CLU |
| 20 | CHGB | COL1A1 | COL1A1 |
| 21 | CLU | DAO | DAO |
| 22 | COL1A1 | DCTN1 | DCTN1 |
| 23 | Cytochrome C | DPYSL3 | DPYSL3 |
| 24 | DAO | ENO3 | ENO3 |
| 25 | DCTN1 | ETS2 | ETS2 |
| 26 | DPYSL3 | EWSR1 | EWSR1 |
| 27 | ENO3 | EZR | EZR |
| 28 | ETS2 | FAS | FAS |
| 29 | EWSR1 | FUS | FUS |
| 30 | EZR | GABRA4 | GABRA4 |
| 31 | FAS | GABRD | GABRD |
| 32 | FUS | GABRG3 | GABRG3 |
| 33 | GABRA4 | GFAP | GFAP |
| 34 | GABRD | GPX3 | GPX3 |
| 35 | GABRG3 | GRIN1 | GRIN1 |
| 36 | GFAP | HPRT1 | HPRT1 |
| 37 | GPX3 | HSPA1A | HSPA1A |
| 38 | GRIN1 | IGF1 | IGF1 |
| 39 | HPRT1 | IL6 | IL6 |
| 40 | Hsp70 | IL10 | IL10 |
| 41 | IGF1 | IL1B | IL1B |
| 42 | IL6 | JPT1 | HN1 |
| 43 | IL10 | LPL | LPL |
| 44 | IL1B | MIF | MIF |
| 45 | Iron | MOG | MOG |
| 46 | JPT1 | NEFH* | NEFH |
| 47 | Lipid | NEFL | NEFL |
| 48 | LPL | NFIL3 | NFIL3 |
| 49 | MIF | NOS1 | NOS1 |
| 50 | mir-1 | NOS2 | NOS2 |
| 51 | miR-1-3p | OPTN | OPTN |
| 52 | miR-17-5p | PARK7 | PARK7 |

| | | | |
|----|-------------------------|--------|--------|
| 53 | MOG | PAWR | PAWR |
| 54 | NEFH | PFN1 | PFN1 |
| 55 | NEFL | PPIA | PPIA |
| 56 | Neurofilament | PRPH | PRPH |
| 57 | NFIL3 | PSAP | PSAP |
| 58 | NOS1 | PTGS2 | PTGS2 |
| 59 | NOS2 | RHOA | RHOA |
| 60 | OPTN | SCN1B | SCN1B |
| 61 | PARK7 | SCN2B | SCN2B |
| 62 | PAWR | SLC1A2 | SLC1A2 |
| 63 | PFN1 | SOD1 | SOD1 |
| 64 | PPIA | SOD2 | SOD2 |
| 65 | PRPH | SPP1 | SPP1 |
| 66 | PSAP | SQSTM1 | SQSTM1 |
| 67 | PTGS2 | SREBF2 | SREBF2 |
| 68 | Reactive oxygen species | TFRC | TFRC |
| 69 | RHOA | TP53 | TP53 |
| 70 | SCN1B | TUBA1A | TUBA1A |
| 71 | SCN2B | VAPB | VAPB |
| 72 | SLC1A2 | VCP | VCP |
| 73 | SOD1 | VEGFA | VEGFA |
| 74 | SOD2 | VPS35 | VPS35 |
| 75 | Sod | XIAP | XIAP |
| 76 | SPP1 | | |
| 77 | SQSTM1 | | |
| 78 | SREBF2 | | |
| 79 | TFRC | | |
| 80 | TP53 | | |
| 81 | Triacylglycerol | | |
| 82 | TUBA1A | | |
| 83 | Ubiquitin | | |
| 84 | VAPB | | |
| 85 | VCP | | |
| 86 | Vegf | | |
| 87 | VPS35 | | |
| 88 | XIAP | | |
| | | | |

*Not mapped in ShinyGO analysis, HSPA1A was mapped for Hsp70, blue color indicates that these molecules do not represent genes.