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## **Supporting Information:**



Fig. S1. Physiochemical characterization of GO. (a) AFM analysis of GO after sonification.(b) Raman spectrum of GO. (c) Size distribution of GO after sonication.



Fig. S2. Transcriptome-wide sequencing of circRNAs. (a) Length distribution for circRNAs.(b) Chromosome distribution of circRNAs. (c) Genome region distribution of circRNAs.



Fig. S3. RNAi efficiency confirmation of five circRNAs (*circ\_0000115, circ\_0000201, circ\_0000247, circ\_0000308* and *circ\_0000665*). Bars represent means  $\pm$  SD. \*\*p < 0.01 vs wild-type N2.



**Fig. S4.** IFC-2 expression in GO exposed nematodes. (a) Effect of GO exposure on *ifc-2* expression. (b) Effect of *circ\_0000115* RNAi knockdown on *ifc-2* expression in GO exposed wild-type nematodes. GO concentration is 100  $\mu$ g L<sup>-1</sup>. Prolonged exposure to GO was performed from L1-lavae to adult day-1. Bars represent means  $\pm$  SD. \*\**p* < 0.01 *vs* control or VP303(GO).



**Fig. S5.** Effect of intestine-specific RNAi knockdown of *ifc-2* on intestinal permeability and defecation behavior. (a) Effect of intestine-specific RNAi knockdown of *ifc-2* on intestinal permeability and defecation behavior. The nematodes were suspended in blue food dye (erioglaucine disodium, 5.0% wt/vol) for 3 h, and then analyzed the distribution of blue food dye in the body using a microscope. Twenty nematodes were examined per treatment. The blue dye was distributed in the intestinal lumen of both VP303 and *ifc-2(RNAi)* nematodes. (b) Effect of intestine-specific RNAi knockdown of *ifc-2* on mean defecation cycle length. Individual animal was examined for a fixed number of cycles, and a cycle period was defined as the interval between the initiations of two successive posterior body-wall muscle contraction steps. Thirty replicates were performed. Bars represent means  $\pm$  SD.



**Fig. S6.** Effect of RNAi knockdown of seven genes on GO toxicity in inducing ROS production. GO concentration is 100  $\mu$ g L<sup>-1</sup>. Prolonged exposure to GO was performed from L1-lavae to adult day-1. Bars represent means  $\pm$  SD. \*\*p < 0.01 vs control (if not specially indicated).

| Gene                | Forward primer (5'-3') | Reverse primer (5'-3') | Primer type      |
|---------------------|------------------------|------------------------|------------------|
| circ_0000032        | TTAAGCTGGCTGCTCCAAG    | ATCCATTGAGGAGAGGGGG    | Divergent Primer |
| circ_0000035        | TGGAAAGAGTGTTGGCTGAC   | CGGCATTGCAGTTGAACTTG   | Divergent Primer |
| circ_0000097        | AACGAAACCAGCTACTTCAACA | AGAATCGCTTTGAGAACGTTC  | Divergent Primer |
| <i>circ_0000107</i> | TGATCTACAAACTGGAAAACCC | GCCGATTTTCAGATTTTCCAGT | Divergent Primer |
| circ_0000115        | GTGGATGGGGAAAGACACTG   | ATTAAGAGCGGCAAGCAGAA   | Divergent Primer |
| circ_0000119        | ACAAAGGCTGCGCATTTCTC   | CCAAATTGCTCAAATAGGTG   | Divergent Primer |
| circ_0000132        | GCTAAATTCTGTGCGATACCAA | TTTCGAATGTTTTCAACGCC   | Divergent Primer |
| circ_0000155        | CACCGTGTACCTACAGCCTTCA | GTTTTACACTTGGCGCATTC   | Divergent Primer |
| circ_0000160        | GCGTATTGTGGATCCTTATGGC | CAAACGACGCGTAGAAATGGAC | Divergent Primer |
| circ_0000201        | TTTACGCATATTTCTGCCGC   | GGAAGTTGTCGTATCAGCCA   | Divergent Primer |
| <i>circ_0000247</i> | TTGTCTCAAATCCAGCAGCC   | TCGCACTTAAACCGAACCTC   | Divergent Primer |
| circ_0000281        | ATTACACGACGACGACCTTG   | AATCGATGCTCCGAACGAAA   | Divergent Primer |
| circ_0000304        | GAACTTCTCGACCGTGGATT   | TACTTGGACCATCCGTCTCG   | Divergent Primer |
| circ_0000308        | CATCTCTTGACGCCTACATTCA | TCTTTGCGTGATACATTGTGG  | Divergent Primer |
| circ_0000311        | GGGACGCCGTCACAGATTAA   | GCAGCACATAAACCACTCGAT  | Divergent Primer |
| circ_0000313        | GCCGACTGGATTCGAGACAA   | GCTGAATCGCTTCGAGACCT   | Divergent Primer |
| circ_0000315        | GCTGTTCGAGTGGTGCTGAC   | TGAGTCGGCTCCAATCTCAT   | Divergent Primer |
| circ_0000329        | GAATTGCCGACACCATCAGT   | GATTTCCCGCTCCTCACAAG   | Divergent Primer |
| circ_0000333        | ACGCAGAGATTACAGTCGGA   | TGATTTTCACGTTTCGGGGT   | Divergent Primer |
| circ_0000342        | ATTCCACGTCGAATTTCTCTC  | GACCACCTTGAACCCAACAA   | Divergent Primer |
| circ_0000352        | CGTCGCTAAGCAAGTCTGAA   | CTGGTTTCTGTGATCGGGTG   | Divergent Primer |
| circ_0000356        | TTCGCTTTTTCGTTGGGAAT   | GGTCGAGAATTTGGGATTGT   | Divergent Primer |
| circ_0000363        | CCACATTCGTCATTCTTGCC   | ATAGGTGAGCCAGTTGGTGA   | Divergent Primer |
| circ_0000364        | GGAATGTTTGACGGGGTTGA   | CGTGGATTCGACAGGGTTAC   | Divergent Primer |
| circ_0000451        | CGACATCATAAATACTTTGCCG | TTTCCAATCGGCTGCATTTT   | Divergent Primer |
| <i>circ_0000488</i> | GTGTGGTAACATGCGTTCGG   | AACACTTGCAACCCATGACA   | Divergent Primer |
| circ_0000558        | CCACAACACTGGAACAACAAC  | AGTCCTTCCGATCCCATCAG   | Divergent Primer |

Table S1. Primer information for qRT-PCR of circRNAs

| <i>circ_0000603</i> | GCCGAGACTAGACTTTGAGC   | CCGGCTGAAATCCGTGATAC   | Divergent Primer  |
|---------------------|------------------------|------------------------|-------------------|
| <i>circ_0000653</i> | AGCAATTAATGGTTATGCGGAG | ATTCGGCGGCTTTCAGTAGA   | Divergent Primer  |
| <i>circ_0000665</i> | AAAAGCATAGCCTGAGACGG   | TCCAGCGGAATGTGAATGTT   | Divergent Primer  |
| <i>circ_0000672</i> | TTGAAAAGTGGCACGGATACA  | GTGCATCCATTCCTAGCCAA   | Divergent Primer  |
| circ_0000699        | CTGCTGGCAGAGTTGAAAGA   | GCTCATTTTCGGAGACTTCTGC | Divergent Primer  |
| <i>circ_0000713</i> | TCGATGAAGTGTGCGTGAG    | TCCCTACGTGGATTCATGGTT  | Divergent Primer  |
| <i>circ_0000115</i> | AATTGTTTCGGGGCTTCTGC   | CGGTCGATCCATAGTATTTTCA | Convergent Primer |
| tba-1               | TCAACACTGCCATCGCCGCC   | TCCAAGCGAGACCAGGCTTCAG | Convergent Primer |

| Cono                | Formand and (52, 32)                          | D                       | Restriction       |  |
|---------------------|---|-------------------------|-------------------|--|
| Gene                | Forward primer (5 -5 )                        | Reverse primer (5 -5')  | enzyme site       |  |
| circ_0000115        | CAGTCTAGAGATCATGTGGTTG GTCAAGCTTGAAACAATTGGCC |                         | Vhol/IIindIII     |  |
| RNAi                | ACG CA A                                      |                         | Abai/minum        |  |
| <i>circ_0000201</i> | GCACTGCAGATCCAATTTATTA                        | ATCAAGCTTCGTTCTTCTTCTTA | Det // Lin di II  |  |
| RNAi                | AGAC TCC                                      |                         | PSu/mindin        |  |
| <i>circ_0000247</i> | TATCCATGGTTGTCTCAAATCC                        | ATAAAGCTTCGGTCGTTGACCA  | Nacl/HindH        |  |
| RNAi                | AGCA GTT                                      |                         | NCOI/ HIIIdIII    |  |
| <i>circ_0000308</i> | CTGCCATGGAGTTCTTTCCACA CGCCTGCAGCGAAATCTAGTGA |                         | Na a I/Dati       |  |
| RNAi                | GCT   | CAA                     | NCOI/PSu          |  |
| <i>circ_0000665</i> | ACGCCATGGAAAGGAAAAGCA                         | ACTCTGCAGCGCCAAAAATCCC  | Na a I/Dati       |  |
| RNAi                | TAGCC   | TTT                     | NC01/PSti         |  |
|                     | ATATCTAGAACATTGTCCAGCG                        | TATAAGCTTGAGCCTTGAACAC  | N/1 - 1/11 - 4111 |  |
| png-1 KNAi          | GT  | СТ                      | Xbai/Hindiii      |  |
|                     | ATACCATGGGCTCTAAACACTC                        | TAGCTGCAGTTCCAATAAATCC  |                   |  |
| F 54A3.2 RNA1       | AA  | AG                      | Ncol/Pstl         |  |
| 1. D.V. (.          | GCGTCTAGAATGATGGATCGTG                        | ATACCATGGGTTGCCGACACTT  | 371 T/ST T        |  |
| cam-1 RNAi          | GA TT   |                         | Xbal/Ncol         |  |
| · 2 D.1.4           | ATACCATGGGGAAAATCCACGT                        | ATGCTGCAGTGTAGTCCTCGAC  |                   |  |
| zıp-2 RNAi          | CATCG TTG                                     |                         | Ncol/Pstl         |  |
| 1 10 D. 14          | TACTCTAGATGGACACCGACAA                        | AGTCCATGGGGTGATCACAGTC  | 371 TAT T         |  |
| ubc-19 RNAi         | GTGCA ATC                                     |                         | Xbal/Ncol         |  |
|                     | CGATCTAGAAGCAAACAACCG                         | ATACCATGGACGGAGGGTCGCA  |                   |  |
| ıfc-2 RNA1          | CTCACCG                                       | АТСТ                    | Xbal/Ncol         |  |
|                     | ATACTGCAGCCAAAACTTCCAT                        | ATAGGTACCTTGCATAGGCCTT  |                   |  |
| nep-17 RNAi         | CCG   | CTG                     | Pstl/Kpnl         |  |
|                     | GAGTCTAGATTCCCTTCAGTTC                        | ATACCATGGGATCCACCGAATC  |                   |  |
| hrpk-1 RNAi         | CGTG  | GTTC                    | Xbal/Ncol         |  |
|                     | AGATCTAGAATCATCAATTGGA                        | ATACTGCAGTTGGTTGCTCCTG  |                   |  |
| unc-87 RNAi         | CCACCAC                                       | CCACCAC ATT             |                   |  |
|                     | CGATCTAGATGGAGTCAAGCA                         | ATACTGCAGTTCTTCTTTGGTGC |                   |  |
| eft-3 RNAi          | АСТС  | AGC                     | Xbal/Pstl         |  |
| nap-1 RNAi          | TGATCTAGATCAGGCTTTGCCT                        | ATAGGTACCCTGACACATCATC  | 2                 |  |
|                     | СТС   | ACC                     | Xbal/Kpnl         |  |
|                     | CGACCATGGCAATCAATGTTGA                        | ATAGGTACCCTCCTCCATTTGT  | NcoI/KpnI         |  |
| vit-6 RNAi          | ACC   | GGT                     |                   |  |

Table S2. Primer information for RNAi of certain circRNA or gene

| Table S3. Primer information | for vector construction |
|------------------------------|-------------------------|
|------------------------------|-------------------------|

|             | Forward primer (5'-3')  | Reverse primer (5'-3') | Restriction     |
|-------------|-------------------------|------------------------|-----------------|
|             | forward printer (5 -5 ) | Keverse primer (5-5 )  | enzyme site     |
| Pages 1     | ATATCTAGAAGCCACTCAGCCA  | ATAGGATCCCATCTGAATTCAA | YhaI/BamHI      |
| Pges-1      | СТТСА                   | AGATA                  | Abal/ Dalli II  |
| ife 2/M6.1d | ATAGGATCCATGTCGACTTACG  | TAACCCGGGGTCAAGGTAGACA | BamHI/Smal      |
| ıjc-2/M0.1a | CGGCCT                  | AACCA                  | Baiiiffi/Sillai |

| CircRN              |        |                           |                | -           |           |  |
|---------------------|--------|---------------------------|----------------|-------------|-----------|--|
| CircRNA ID          | A type | Chromosome location       | Gene ID        | Gene        | logFC     |  |
| circ_0000032        | exon   | I :1817301:1817613        | WBGene00022142 | Y71G12B.2   | -7.451958 |  |
| circ_0000304        | exon   | Ⅲ:730585:731798           | WBGene00003936 | gei-16      | -7.039664 |  |
| circ_0000035        | exon   | I :1999954:2001195        | WBGene00021238 | Y51F10.9    | -6.558617 |  |
| circ_0000247        | exon   | ∎:9304008:9304745         | WBGene00000289 | cam-1       | -6.354519 |  |
| circ_0000097        | exon   | I :9548218:9548654        | WBGene00007985 | C36F7.2     | -6.116712 |  |
| <i>circ_0000558</i> | exon   | ₩:11722489:1172305<br>5   | WBGene00010444 | magi-1      | -6.110452 |  |
| circ_0000315        | exon   | Ⅲ:1187295:1187741         | WBGene00022491 | Y119D3B.14  | -5.981286 |  |
| circ_0000313        | exon   | Ⅲ:1074167:1076543         | WBGene00006697 | Y92C3B.2a.1 | -5.834821 |  |
| circ_0000311        | exon   | Ⅲ:987238:987508           | WBGene00019915 | tbc-10      | -5.831819 |  |
| circ_0000160        | exon   | I:14427055:14428997       | WBGene00013670 | Y105E8A.10  | -5.831819 |  |
| circ_0000653        | exon   | V:18065061:1806546<br>3   | WBGene00013345 | Y59A8B.8    | -5.831801 |  |
| circ_0000713        | exon   | X:9510459:9511097         | WBGene00001516 | gap-2       | -5.733819 |  |
| circ_0000132        | exon   | I :12878627:1287958<br>2  | WBGene00003905 | pad-1       | -5.476467 |  |
| <i>circ_0000342</i> | exon   | Ⅲ:2140079:2140320         | WBGene00021698 | frl-1       | -5.466567 |  |
| circ_0000356        | exon   | Ⅲ:3088300:3088575         | WBGene00004787 | sft-1       | -5.446967 |  |
| <i>circ_0000488</i> | exon   | <b>Ⅳ</b> :2229794:2230105 | WBGene00020208 | T04C4.1     | -5.476467 |  |
| <i>circ_0000107</i> | exon   | I :10977642:1097804<br>9  | WBGene00013123 | Y52B11A.3   | -5.259465 |  |
| circ_0000119        | exon   | I :11593916:1159429<br>4  | WBGene00006807 | unc-75      | -5.239265 |  |
| circ_0000155        | exon   | I :13944636:1394639<br>1  | WBGene00013506 | usp-3       | -5.229495 |  |
| circ_0000451        | exon   | Ⅲ:12631806:1263480        | WBGene00004161 | Y111B2A.14. | -5.219665 |  |

Table S4. Information for dysregulated known circRNAs

|                     |      | 9                               |                | 2         |           |
|---------------------|------|---------------------------------|----------------|-----------|-----------|
| <i>circ_0000352</i> | exon | Ⅲ:2482724:2483108               | WBGene00004884 | smg-6     | -2.795358 |
| circ_0000364        | exon | Ⅲ:3299365:3299857               | WBGene00021812 | Y53G8AR.5 | -2.775752 |
| circ_0000281        | exon | II:14870599:1487100             | WBGene00011044 | R05H10.3  | -2.739129 |
| circ_0000672        | exon | <b>V</b> :18956093:1895642<br>3 | WBGene00013587 | Y80D3A.9  | -2.253039 |
| circ_0000665        | exon | <b>V</b> :18688227:1868846<br>9 | WBGene00006714 | ubc-19    | -2.174839 |
| circ_0000329        | exon | Ⅲ:1675421:1675681               | WBGene00021260 | Y22D7AR.6 | -2.124374 |
| circ_0000201        | exon | Ⅱ :2246478:2246959              | WBGene00018781 | F54A3.2   | -2.031746 |
| circ_0000603        | exon | <b>V</b> :4571714:4572374       | WBGene00022015 | Y61A9LA.3 | -1.837405 |
| circ_0000115        | exon | I :11384076:1138435<br>6        | WBGene00010160 | png-1     | -1.796724 |
| circ_0000333        | exon | Ⅲ:1927665:1927938               | WBGene00004128 | F53A3.6   | -1.196125 |
| circ_0000363        | exon | Ⅲ:3113760:3114033               | WBGene00021820 | nipa-1    | -1.14193  |
| circ_0000699        | exon | X:344165:345275                 | WBGene00015430 | C04E7.3   | 5.8348208 |
| <i>circ_0000308</i> | exon | Ⅲ:834296:835205                 | WBGene00019327 | zip-2     | 6.0936363 |

| C: DNA ID                   |              | C B            |           | New ID          |
|-----------------------------|--------------|----------------|-----------|-----------------|
| CircRNA ID                  | CircRNA type | Gene ID        | logFC     | (Ivanov 2015)   |
| <b>Ⅳ</b> :17278959:17279168 | exon         | WBGene00002005 | -7.568977 |                 |
| X:8718612:8718907           | exon         | WBGene00018731 | -7.379973 |                 |
| ∎:10013295:10013341         | exon         | WBGene00002265 | -6.650769 |                 |
| I:1670969:1671255           | exon         | WBGene00022158 | -5.981286 | cel_circ_000086 |
| Ⅱ:11133703:11133837         | exon         | WBGene00009578 | -5.971216 |                 |
| Ⅲ:2745138:2745409           | exon         | WBGene00022179 | -5.811319 | cel_circ_000101 |
| V:18857769:18858076         | exon         | WBGene00006945 | -5.476467 | cel_circ_000077 |
| I:1674941:1675386           | exon         | WBGene00185098 | 5.519198  | cel_circ_000121 |
| I:3142042:3142265           | exon         | WBGene00019597 | 5.509298  | cel_circ_000142 |
| ₩:11275681:11276616         | exon         | WBGene00001796 | 5.501128  | cel_circ_000078 |

## **Table S5.** Information for dysregulated novel circRNAs

| No | Score | Name                   | Gene   | Peptides (95%) |
|----|-------|------------------------|--------|----------------|
| 1  | 49.15 | tr Q6LD30 Q6LD30_CAEEL | unc-87 | 47             |
| 2  | 45.08 | tr G8JY94 G8JY94_CAEEL | ifc-2  | 23             |
| 3  | 38.61 | sp P98080 UCR1_CAEEL   | ucr-1  | 21             |
| 4  | 30.46 | sp P53013 EF1A_CAEEL   | eft-3  | 16             |
| 5  | 26.34 | tr Q23050 Q23050_CAEEL | clik-1 | 17             |
| 6  | 25.79 | tr M1Z854 M1Z854_CAEEL | ifb-2  | 14             |
| 7  | 22.56 | tr H2KYS1 H2KYS1_CAEEL | hsp-43 | 16             |
| 8  | 22.12 | tr Q19007 Q19007_CAEEL | nap-1  | 11             |
| 9  | 19.89 | tr Q9XW17 Q9XW17_CAEEL | car-1  | 10             |
| 10 | 19.04 | sp Q19289 IFB1_CAEEL   | ifb-1  | 13             |
| 11 | 18.36 | tr P91277 P91277_CAEEL | hrpk-1 | 11             |
| 12 | 18.17 | tr G4SI07 G4SI07_CAEEL | gei-15 | 10             |
| 13 | 18.11 | sp P10567 MYSP_CAEEL   | unc-15 | 10             |
| 14 | 17.51 | sp P18948 VIT6_CAEEL   | vit-6  | 11             |
| 15 | 16.71 | tr 045569 045569_CAEEL | nep-17 | 10             |

**Table S6.** Information for mass spectrometry result (top 15 proteins)

| No | Gene name | <i>circ_0000115</i> -protein RPIseq |
|----|-----------|-------------------------------------|
| 1  | ifc-2     | 0.8                                 |
| 2  | nep-17    | 0.7                                 |
| 3  | hsp-43    | 0.65                                |
| 4  | hrpk-1    | 0.65                                |
| 5  | unc-87    | 0.6                                 |
| 6  | eft-3     | 0.6                                 |
| 7  | clik-1    | 0.55                                |
| 8  | nap-1     | 0.55                                |
| 9  | vit-6     | 0.55                                |
| 10 | car-1     | 0.5                                 |

 Table S7. RPIseq prediction result of *circ\_0000115*-protein binding capacity