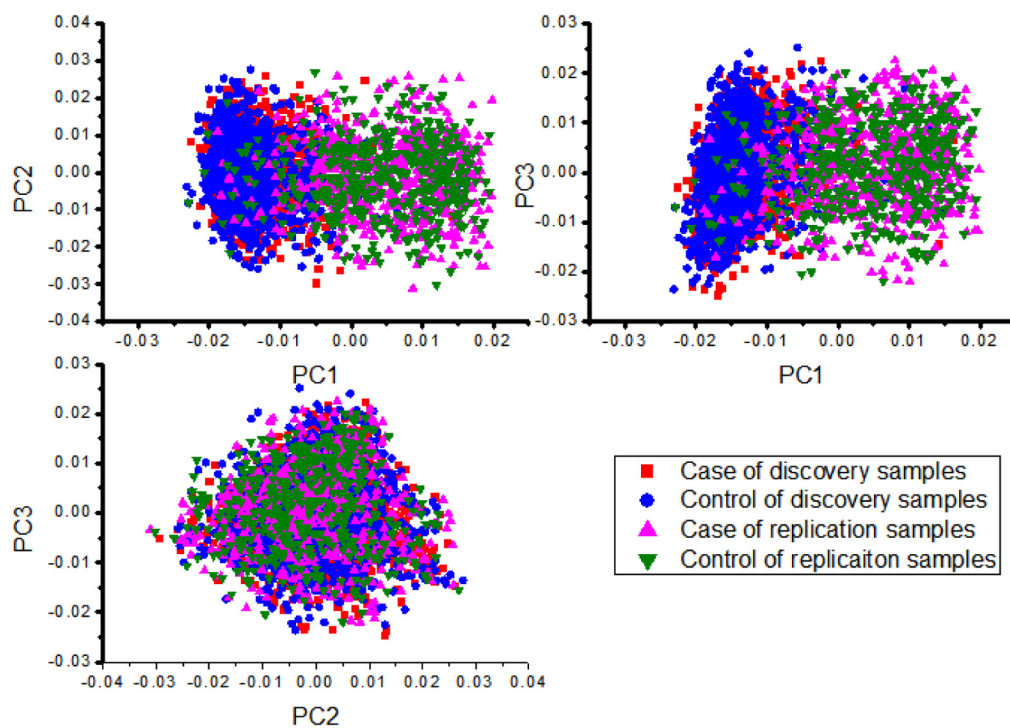


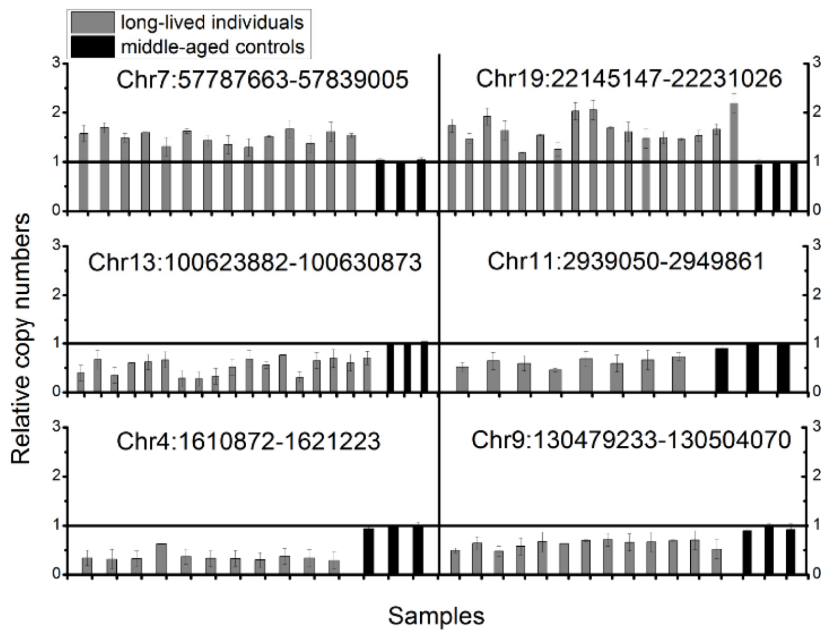
SUPPLEMENTARY MATERIAL



Supplementary Figure 1. Principal component analyses of the discovery and replicate cohorts: different symbol represented different groups: circle: case of discovery samples; square: control of discovery samples; up-triangle: case of replication samples; down-triangle: control of replication samples.



Supplementary Figure 2. The chromosomal display of the longevity-associated CNVRs. Red rectangles represent deletions in cases while blue represent duplications.



Supplementary Figure 3. qPCR validation of CNVR. Two independent primers were designed and used for the validation; better results were shown in Supplement Figure 3. Relative copy number (CN) was calculated with the CT value of each sample. The relative copy number for the control was 1. More or less than 1 was regarded as the duplications or deletions.

Supplementary Table 1. Deletions and duplications commonly identified in the discovery, discovery replicate, and their combined cohorts.

| CNVR | Discovery samples | | | | | Replication samples | | | | Combined samples | | | |
|---------------------------|-------------------|-----------------------|-------|-------|----------|-----------------------|----------|-------|-----------|-----------------------|-------|-------|-----------|
| | Type | P | OR | Case% | Control% | P | OR | Case% | Control % | P | OR | Case% | Control % |
| chr9:130479233-130504070 | DEL | 6.11×10^{-6} | 22.25 | 1.80 | 0.08 | NA | NA | NA | NA | NA* | NA* | NA* | NA* |
| chr4:1610872-1621223 | DEL | 1.30×10^{-5} | 20.99 | 1.70 | 0.08 | NA | NA | NA | NA | NA* | NA* | NA* | NA* |
| chr7:57787663-57839005 | DUP | 5.28×10^{-5} | 1.69 | 16.0 | 5.6 | 1.77×10^{-3} | 1.68 | 11.79 | 7.36 | 8.68×10^{-7} | 1.59 | 15.89 | 5.74 |
| chr20:60900481-60927412 | DEL | 5.73×10^{-5} | 18.49 | 1.60 | 0.08 | NA | NA | NA | NA | NA* | NA* | NA* | NA* |
| chr11:2939050-2949861 | DEL | 1.25×10^{-4} | 4.61 | 2.60 | 0.58 | 1.30×10^{-2} | 8.95 | 1.05 | 0.12 | 6.25×10^{-6} | 4.81 | 1.84 | 0.39 |
| chr15:96898166-96909819 | DEL | 4.2×10^{-4} | 5.86 | 1.90 | 0.33 | NA | NA | NA | NA | NA* | NA* | NA* | NA* |
| chr8:1789006-1799964 | DEL | 1.24×10^{-3} | 7.99 | 1.30 | 0.25 | 1.66×10^{-2} | infinity | 1.04 | 0 | 4.45×10^{-5} | 10.65 | 1.02 | 0.15 |
| chr19:22145147-22231026 | DUP | 2.07×10^{-3} | 3.9 | 1.90 | 0.58 | 4.13×10^{-4} | 4.71 | 2.74 | 0.59 | 1.89×10^{-6} | 4.11 | 2.35 | 0.63 |
| chr13:100620882-100630973 | DEL | 2.94×10^{-3} | 2.96 | 2.40 | 0.82 | 2.06×10^{-4} | 6.94 | 2.42 | 0.36 | 2.89×10^{-6} | 3.88 | 2.41 | 0.63 |
| chr21:38442208-38453183 | DEL | 3.95×10^{-3} | 4.19 | 1.80 | 0.41 | 4.01×10^{-3} | 10.76 | 1.26 | 0.12 | 4.90×10^{-5} | 5.16 | 1.53 | 0.29 |
| chr14:38058065-38081005 | DEL | 1.29×10^{-2} | 2.98 | 1.70 | 0.58 | 3.03×10^{-4} | infinity | 1.37 | 0 | 8.43×10^{-5} | 4.57 | 1.53 | 0.34 |

Copy number variant region (CNVR), The discovery samples CNV position with information about chromosome and start and stop base pair positions based on the GRCh37 hg19 genome build; DEL, deletion; DUP, duplication; Case%, case frequency; Control%, control frequency; OR, odds ratio; P, P-value obtained from a fisher's exact test for longevity and middle aged subjects. NA, not applicable due to a frequency lower than 1% in the replication study; NA*, not applicable due to a frequency lower than 1% in the replication samples, but get a frequency higher than 1% in the combined samples.

Supplementary Table 2. Association between specific deletions and duplications among nonagenarians, centenarians and middle-aged control.

| 90-99 case enrich vs 100+ control | | | | | | |
|------------------------------------|----------|-------|----------|--|------------|-------------|
| CNVR(hg19) | P | case% | control% | Gene | Length(kb) | CNVtype |
| chr16:60082486-60100445 | 9.74E-03 | 12.64 | 8.66 | LOC644649 | 17.96 | Deletion |
| chr19:22142930-22237629 | 1.21E-03 | 2.83 | 0.77 | ZNF208,ZNF257 | 94.70 | Duplication |
| chr11:89319607-89397819 | 1.57E-03 | 1.89 | 0.35 | AB231784,FOLH1B,NOX4 | 78.21 | Duplication |
| chr13:102315051-102326456 | 3.84E-02 | 3.02 | 1.48 | ITGBL1 | 11.41 | Duplication |
| 100+ case enrich vs 90-99 control | | | | | | |
| CNVR(hg19) | P | case% | control% | Gene | Length(kb) | CNVtype |
| chr14:22755575-22767645 | 5.93E-05 | 4.08 | 0.75 | AV4S1,T-Cell Receptor V-alpha region,TCR-alpha,TCRA,TRA,TRA@,TRAC,TRD | 12.07 | Deletion |
| chr9:130489558-130513469 | 3.67E-03 | 1.41 | 0.00 | SH2D3C,TOR2A,TTC16 | 23.91 | Deletion |
| chr21:46936423-46952750 | 5.68E-03 | 1.20 | 0.00 | SLC19A1 | 16.33 | Deletion |
| chr20:60881330-60909832 | 2.20E-02 | 1.41 | 0.19 | ADRM1,LAMA5,MIR4758 | 28.50 | Deletion |
| chr16:1858888-2074219 | 3.49E-02 | 1.27 | 0.19 | C16orf73,FAHD1,GFER,HAGH,HS3ST6,NDUFB10,NOXO1,NPW,RNF151,RPL3L,RPS2,SEPX1,SNHG9,SYNGR3,TBL3,ZNF598 | 215.33 | Deletion |
| chr2:25835636-25886631 | 4.21E-02 | 1.13 | 0.00 | DTNB | 51.00 | Deletion |
| <65 case enrich vs 100-120 control | | | | | | |
| CNVR(hg19) | P | case% | control% | Gene | length(kb) | CNVtype |
| chr11:2939050-2949861 | 6.25E-06 | 1.75 | 0.56 | PHLDA2,SLC22A18 | 10.81 | Deletion |
| chr4:1610872-1621223 | 6.51E-06 | 1.12 | 0.14 | FAM53A | 10.35 | Deletion |
| chr20:60900481-60927412 | 4.42E-05 | 1.02 | 0.14 | LAMA5,MIR4758 | 26.93 | Deletion |
| chr21:38442208-38453183 | 4.90E-05 | 1.46 | 0.42 | PIGP,TTC3 | 10.98 | Deletion |
| chr14:38058065-38081005 | 8.43E-05 | 1.46 | 0.49 | C14orf25,FOXA1 | 22.94 | Deletion |
| chr1:1151232-1191870 | 1.99E-04 | 1.02 | 0.21 | B3GALT6,FAM132A,SDF4,UBE2J2 | 40.64 | Deletion |
| chr16:88786245-88806348 | 2.27E-04 | 1.07 | 0.35 | AK294743,PIEZO1 | 20.10 | Deletion |
| chr17:80367353-80391684 | 2.40E-04 | 1.17 | 0.35 | C17orf101,HEXDC | 24.33 | Deletion |
| chr2:176985696-177011655 | 2.40E-04 | 1.17 | 0.35 | AX747372,BC047605,HOXD8,HOXD9,LOC100506783 | 25.96 | Deletion |
| chr6:158634175-158655732 | 6.53E-03 | 1.46 | 0.99 | GTF2H5 | 21.56 | Deletion |
| chr2:239047020-239064760 | 1.76E-02 | 1.07 | 0.63 | KLHL30 | 17.74 | Deletion |
| chr7:57787663-57839005 | 8.68E-07 | 15.07 | 15.35 | ZNF716 | 51.34 | Duplication |
| chr19:22145147-22231026 | 1.89E-06 | 2.24 | 0.92 | ZNF208 | 85.88 | Duplication |
| chr4:190801108-190894359 | 1.03E-02 | 2.77 | 2.46 | BC087857,FRG1 | 93.25 | Duplication |
| 100-120 case enrich vs <65 control | | | | | | |
| CNVR(hg19) | P | case% | control% | Gene | length(kb) | CNVtype |
| chr1:1151232-1191870 | 4.47E-05 | 1.34 | 0.15 | B3GALT6,FAM132A,SDF4,UBE2J2 | 40.64 | Deletion |
| chr11:2939050-2949861 | 3.79E-07 | 2.32 | 0.39 | PHLDA2,SLC22A18 | 10.81 | Deletion |
| chr12:132923159-132956191 | 1.50E-05 | 1.20 | 0.10 | GALNT9 | 33.03 | Deletion |
| chr14:38057334-38081005 | 5.47E-05 | 1.69 | 0.34 | C14orf25,FOXA1 | 23.67 | Deletion |
| chr16:2065666-2079393 | 8.81E-05 | 1.27 | 0.15 | NPW,SLC9A3R2,TCRBV20S1 | 13.73 | Deletion |
| chr2:128387937-128403997 | 3.31E-05 | 1.13 | 0.10 | GPR17,LIMS2,MYO7B | 16.06 | Deletion |
| chr2:176992220-177011655 | 3.74E-04 | 1.27 | 0.24 | AX747372,BC047605,HOXD8,LOC100506783 | 19.44 | Deletion |
| chr2:239047020-239066379 | 5.92E-03 | 1.48 | 0.53 | KLHL30 | 19.36 | Deletion |
| chr20:60900481-60927412 | 2.97E-06 | 1.41 | 0.10 | LAMA5,MIR4758 | 26.93 | Deletion |
| chr21:38442208-38453183 | 4.23E-06 | 1.90 | 0.29 | PIGP,TTC3 | 10.98 | Deletion |
| chr3:103079255-103096303 | 3.26E-03 | 1.20 | 0.34 | DD413615 | 17.05 | Deletion |
| chr6:158634175-158647999 | 1.47E-02 | 1.48 | 0.73 | GTF2H5 | 13.82 | Deletion |

| | | | | | | |
|--|----------|-------|----------|--------------------------|------------|-------------|
| chr7:27229549-27264337 | 3.49E-04 | 1.06 | 0.15 | HOTTIP,HOXA13 | 34.79 | Deletion |
| chr9:130479233-130504070 | 1.97E-07 | 1.41 | 0.05 | PTRH1,SH2D3C,TOR2A,TTC16 | 24.84 | Deletion |
| chr9:139980385-140028291 | 8.81E-05 | 1.27 | 0.15 | DPP7,LOC100289341,MAN1B1 | 47.91 | Deletion |
| chr19:22145147-22231026 | 1.92E-03 | 1.69 | 0.63 | ZNF208 | 85.88 | Duplication |
| <65 case enrich vs 90-99 control | | | | | | |
| CNVR(hg19) | P | case% | control% | Gene | length(kb) | CNVtype |
| chr1:238930549-238987220 | 4.96E-03 | 1.22 | 0.00 | LOC339535 | 56.67 | Duplication |
| chr10:42406669-42467126 | 3.24E-02 | 2.09 | 0.94 | LOC441666 | 60.46 | Duplication |
| 90-99 case enrich vs <65 control | | | | | | |
| CNVR(hg19) | P | case% | control% | Gene | length(kb) | CNVtype |
| chr13:100624374-100635606 | 4.48E-03 | 2.08 | 0.63 | ZIC2 | 11.23 | Deletion |
| chr9:7017391-7036325 | 7.16E-03 | 1.13 | 0.19 | KDM4C | 18.93 | Deletion |
| chr2:176985696-176999012 | 1.31E-02 | 1.13 | 0.24 | AX747372,HOXD8,HOXD9 | 13.32 | Deletion |
| chr6:158634175-158655732 | 1.84E-02 | 1.89 | 0.68 | GTF2H5 | 21.56 | Deletion |
| chr13:84120973-84157927 | 3.62E-02 | 1.70 | 0.68 | SLITRK1 | 36.95 | Deletion |
| chr5:46128475-46160697 | 3.68E-02 | 1.89 | 1.31 | HCN1 | 32.22 | Deletion |
| chr14:44507227-44533909 | 4.49E-02 | 2.08 | 0.97 | FSCB | 26.68 | Deletion |
| chr19:22145147-22237629 | 2.29E-08 | 4.15 | 0.63 | ZNF208,ZNF257 | 92.48 | Duplication |
| chr11:89319607-89397819 | 5.52E-05 | 1.89 | 0.24 | AB231784,FOLH1B,NOX4 | 78.21 | Duplication |

Supplementary Table 3. The primer sequences used for qPCRs.

| CNVR | Primer-F | Primer-R |
|---------------------------|-----------------------|-----------------------|
| chr7:57787663-57839005 | AGGACAAAACACTTCTGAGCC | TGACCAAAAACATACAGCCAA |
| chr19:22145147-22231026 | GCCGAAAGCAGTTTTTACCA | TTTGTCTGTGCATGTCTTTCC |
| chr13:100620882-100630973 | TTTGAAACGACGAGTCCTT | TTCAGAGAGGAAACGATGACA |
| chr11:2939050-2949861 | TCTGAGTGTCACCACTGCCTT | TCCGTGGCTCGCTATCCTAT |
| chr4:1610872-1621223 | AAGAAGACAGGCAGCTCCTCA | TCTGCTGCTGGCACATGGA |
| chr9:130479233-130504070 | TTCAGATCCTTCTGTAGGGGA | TCTCTGGAAGACCACATCCTT |

Please browse the Full Text version to see the data of **Supplementary Table 4. eQTL functional annotation.**