

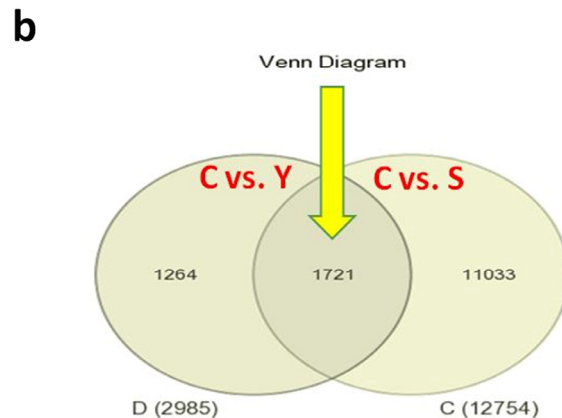
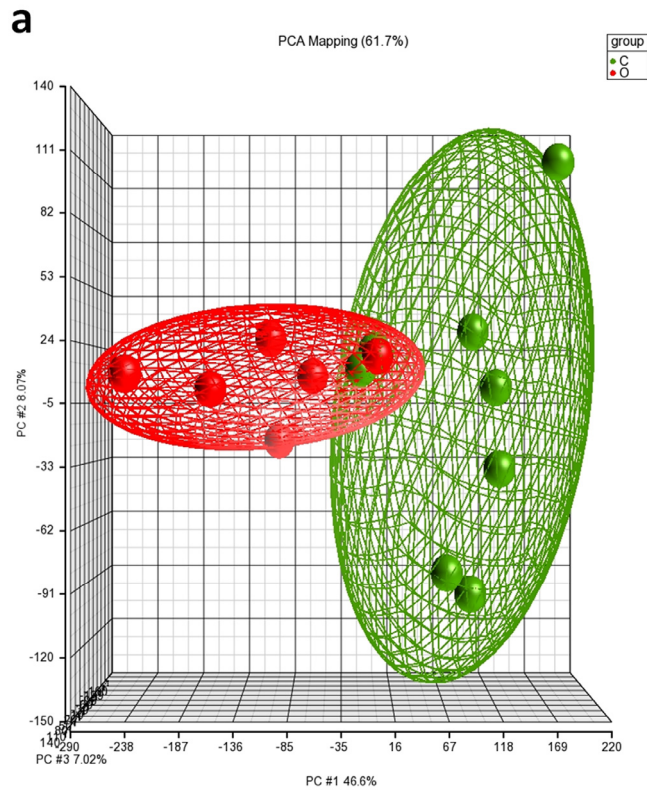
SUPPLEMENTARY MATERIAL

Supplementary Table 1. List of the hundred processes that are more involved in exceptional longevity. These processes are ordered by p value from the highest to the lowest.

| Order according to p value | Name | Number of genes |
|----------------------------|--|-----------------|
| 1 | immune response | 63 |
| 2 | cell adhesion | 58 |
| 3 | MHC class I receptor activity | 9 |
| 4 | transport | 97 |
| 5 | antigen processing and presentation of peptide antigen via MHC class I | 9 |
| 6 | cellular defense response | 14 |
| 7 | response to drug | 35 |
| 8 | ion transport | 44 |
| 9 | interspecies interaction between organisms | 27 |
| 10 | signal transduction | 129 |
| 11 | cell surface receptor linked signaling pathway | 24 |
| 12 | small GTPase mediated signal transduction | 26 |
| 13 | intracellular signaling pathway | 30 |
| 14 | response to wounding | 13 |
| 15 | Presentation of endogenous peptide antigen | 5 |
| 16 | response to hypoxia | 21 |
| 17 | apoptosis | 40 |
| 18 | protein transport | 36 |
| 19 | T cell activation | 9 |
| 20 | integral to plasma membrane | 79 |
| 21 | response to lipopolysaccharide | 17 |
| 22 | actin binding | 30 |
| 23 | myoblast fusion | 5 |
| 24 | GTPase activator activity | 21 |
| 25 | regulation of blood volume by renal aldosterone | 3 |
| 26 | nucleotide binding | 113 |
| 27 | cytoskeleton | 60 |
| 28 | post-Golgi vesicle-mediated transport | 8 |
| 29 | positive regulation of T cell mediated cytotoxicity | 5 |
| 30 | membrane raft | 18 |
| 31 | GTP binding | 34 |
| 32 | Oncogenes | 27 |
| 33 | cellular response to growth factor stimulus | 7 |
| 34 | cell surface | 28 |

| | | |
|----|---|----|
| 35 | embryonic digit morphogenesis | 7 |
| 36 | calmodulin binding | 16 |
| 37 | metabolic process | 43 |
| 38 | skeletal system development | 14 |
| 39 | positive regulation of transcription from RNA polymerase II promoter | 27 |
| 40 | NK Cell Activation | 50 |
| 41 | vesicle-mediated transport | 18 |
| 42 | integrin binding | 11 |
| 43 | protein amino acid phosphorylation | 38 |
| 44 | Golgi apparatus | 61 |
| 45 | negative regulation of epithelial cell migration | 3 |
| 46 | cytoskeletal anchoring at nuclear membrane | 3 |
| 47 | endoplasmic reticulum | 67 |
| 48 | hydrolase activity | 85 |
| 49 | cellular component movement | 12 |
| 50 | induction of apoptosis by extracellular signals | 11 |
| 51 | regulation of transcription | 81 |
| 52 | wound healing | 10 |
| 53 | microtubule | 26 |
| 54 | negative regulation of T cell activation | 4 |
| 55 | response to stress | 18 |
| 56 | regulation of G-protein coupled receptor protein signaling pathway | 7 |
| 57 | T cell receptor signaling pathway | 6 |
| 58 | peptide antigen binding | 6 |
| 59 | NAD+ ADP-ribosyltransferase activity | 6 |
| 60 | endosome | 26 |
| 61 | hematopoietin-interferon-class (D200-domain) cytokine receptor signal transducer activity | 3 |
| 62 | chemotaxis | 13 |
| 63 | SH3-SH2 adaptor activity | 8 |
| 64 | positive regulation of triglyceride biosynthetic process | 3 |
| 65 | thrombin receptor signaling pathway | 3 |
| 66 | integral to membrane of membrane fraction | 6 |
| 67 | activation of pro-apoptotic gene products | 5 |
| 68 | regulation of smoothened signaling pathway | 4 |
| 69 | mitochondrion | 89 |
| 70 | positive regulation of T cell proliferation | 6 |
| 71 | response to organic cyclic substance | 16 |
| 72 | antigen processing and presentation | 10 |
| 73 | platelet dense granule membrane | 3 |
| 74 | SUN-KASH complex | 3 |

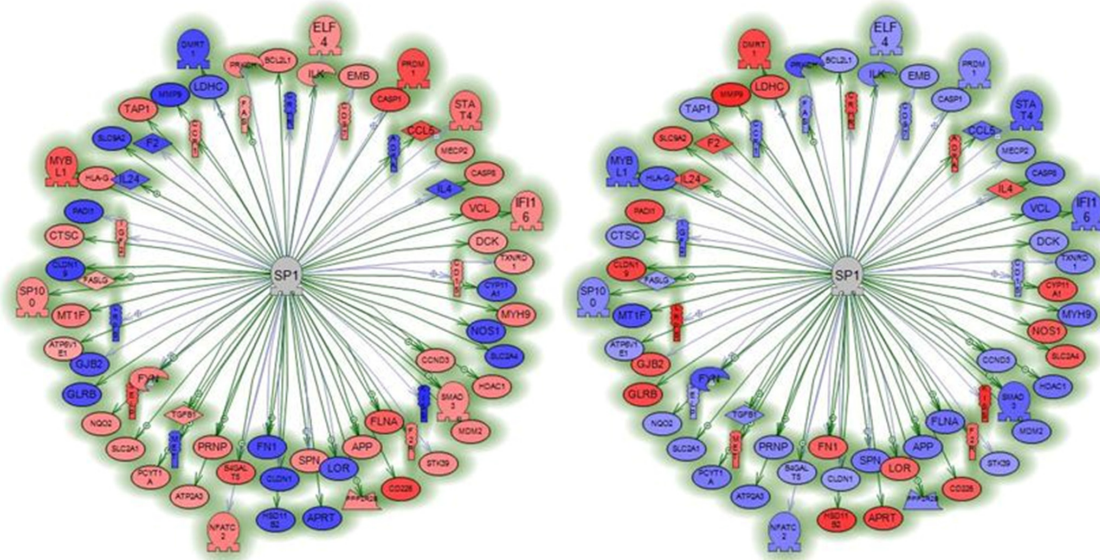
| | | |
|-----|--|-----|
| 75 | eukaryotic cell surface binding | 5 |
| 76 | myelination | 7 |
| 77 | C21-steroid hormone biosynthetic process | 3 |
| 78 | regulation of ARF GTPase activity | 6 |
| 79 | MHC class I protein complex | 9 |
| 80 | ruffle | 10 |
| 81 | cytokine-mediated signaling pathway | 9 |
| 82 | evasion of host defenses by virus | 2 |
| 83 | negative regulation of calcium-mediated signaling | 2 |
| 84 | interleukin-2 secretion | 2 |
| 85 | cortisol biosynthetic process | 2 |
| 86 | cellular response to antibiotic | 2 |
| 87 | positive regulation of plasma membrane long-chain fatty acid transport | 2 |
| 88 | PAS domain | 5 |
| 89 | cell proliferation | 24 |
| 90 | cellular response to insulin stimulus | 8 |
| 91 | Transcytosis | 4 |
| 92 | CCR1 -> STAT signaling | 5 |
| 93 | metal ion binding | 150 |
| 94 | actin cytoskeleton reorganization | 5 |
| 95 | NAD or NADH binding | 9 |
| 96 | protein ubiquitination | 12 |
| 97 | protein kinase activity | 34 |
| 98 | lipopolysaccharide-mediated signaling pathway | 4 |
| 99 | negative regulation of T cell receptor signaling pathway | 3 |
| 100 | chemokine receptor activity | 5 |



Supplementary Figure 1. (a) Principal component analysis (PCA) of mRNA profiles in mononuclear cells from septuagenarians and centenarians. Each sample was assayed by GeneChip Human Gene 1.0ST Array. The ellipsoids (red, septuagenarians; n=6; green, centenarians; n=8) show distinct directionalities. The x-, y-, and z-axes correspond to principal component (PC)1, PC2, and PC3, respectively. (b) Venn diagram displaying no. mRNAs commonly regulated in the different age groups. No. mRNAs that are significantly modified when comparing young (n=8), septuagenarians (n=8), and centenarians (n=8). Data (.CEL files) were analyzed and statistically filtered using Partek Genomic Suite 6.4 software. Statistically significant mRNAs were filtered by applying P-value <0.05 and fold change $\geq |1.8|$.

C vs. Y

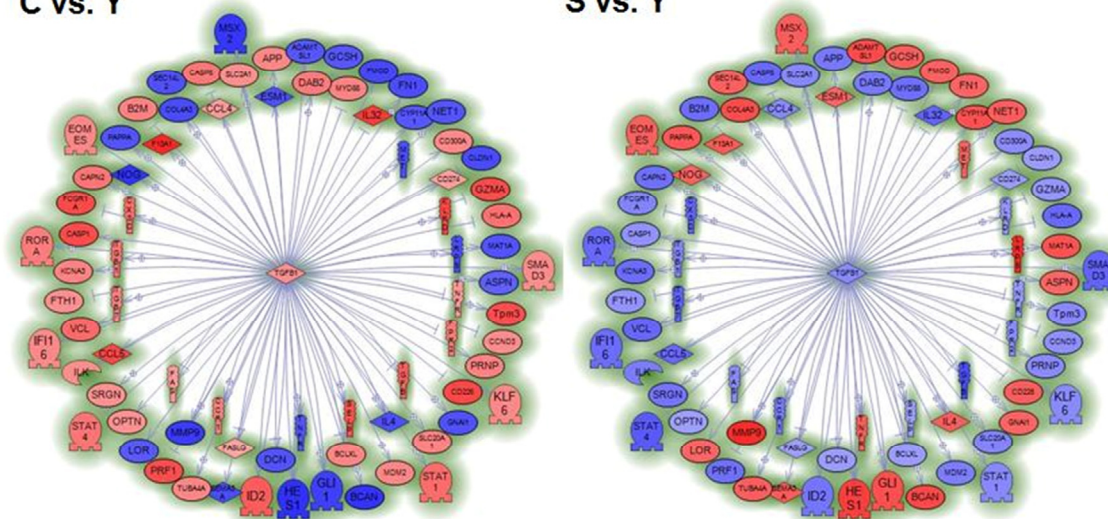
S vs. Y



Supplementary Figure 4. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of SP1. Sub-network of genes regulated by SP1 transcription factor in mononuclear cells obtained from centenarians (a) or septuagenarians (b) versus young subjects. Sub-networks are generated by connecting genes to their neighbors in the database (ResNet 8.0; 2010Q4 Mammal). Sub-networks with enrichment P-value <0.05 cutoff were selected.

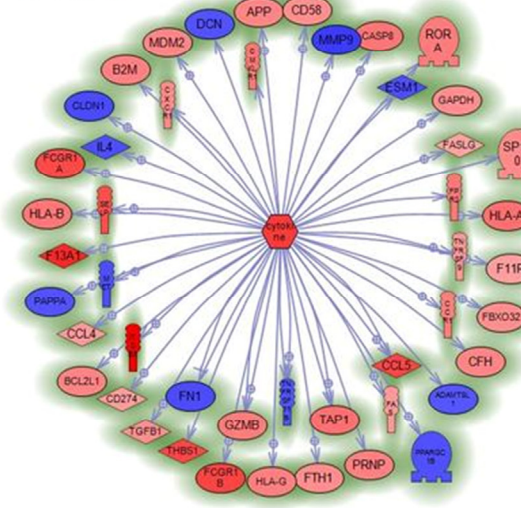
C vs. Y

S vs. Y

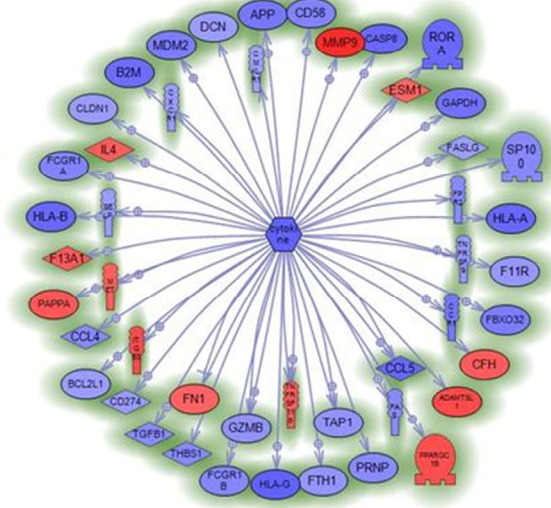


Supplementary Figure 5. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of TGFB1. Sub-network of genes regulated by transforming growth factor(TGF)- β 1 (TGFB1) in mononuclear cells obtained from centenarians (a) or septuagenarians (b) versus young subjects. Sub-networks are generated by connecting genes to their neighbors in the database (ResNet 8.0; 2010Q4 Mammal). Sub-networks with enrichment P-value <0.05 cutoff were selected.

C vs. Y

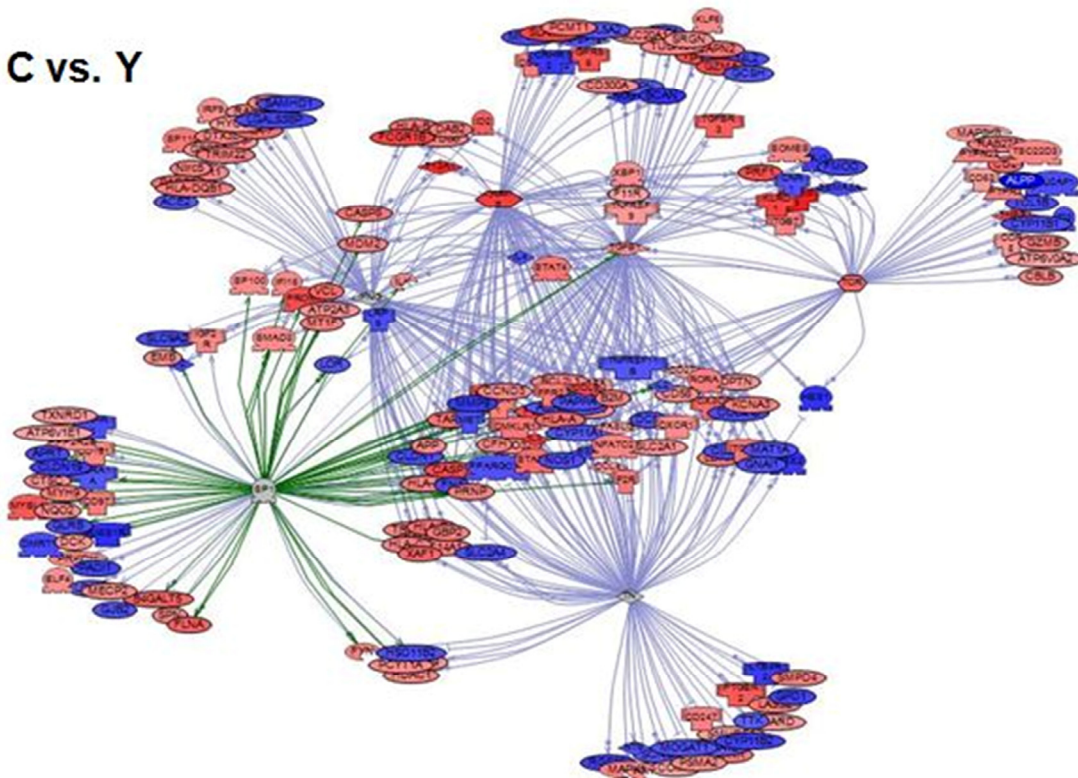


S vs. Y



Supplementary Figure 6. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of cytokine IL-32. Sub-network of genes regulated by IL-32 in mononuclear cells obtained from centenarians (a) or septuagenarians (b) versus young subjects. Sub-networks are generated by connecting genes to their neighbors in the database (ResNet 8.0; 2010Q4 Mammal). Sub-networks with enrichment P-value <0.05 cutoff were selected.

C vs. Y



Supplementary Figure 7. All Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects. Sub-networks are generated by connecting genes to their neighbors in the database (ResNet 8.0; 2010Q4 Mammal). Sub-networks with enrichment P-value <0.05 cutoff were selected.