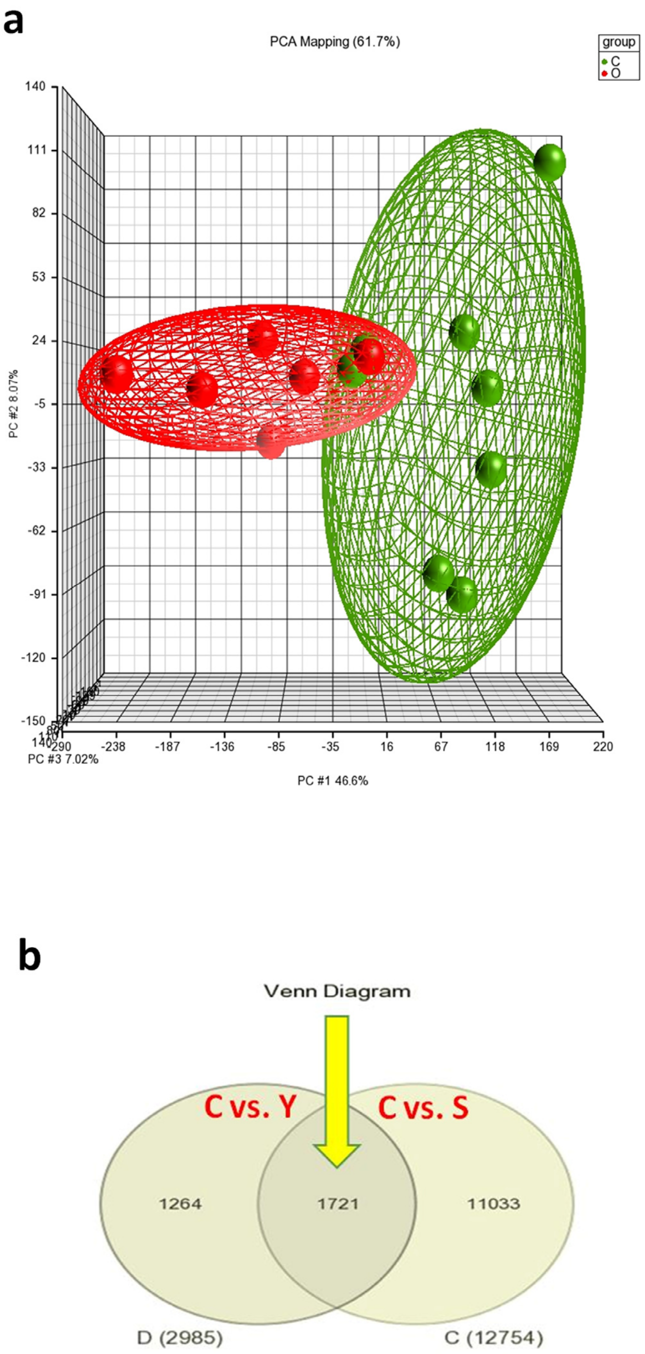
SUPPLEMENTARY MATERIAL

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.

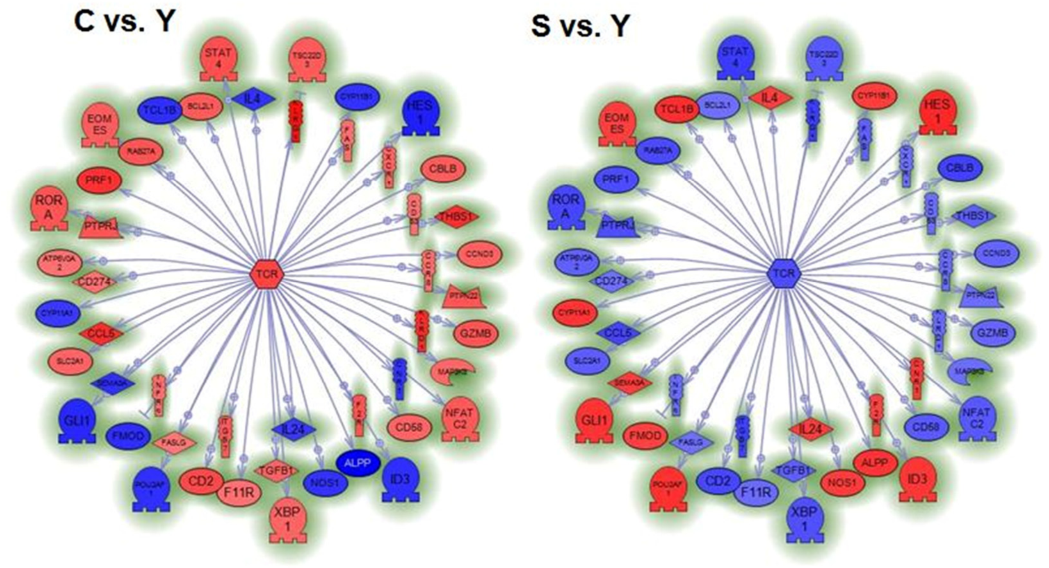
Order according to p value	Name	Number of genes
1	immune response	63
2	cell adhesion	58
3	MHC class I receptor activity	9
4	transport	97
5	antigen processing and presentation of peptide antigen via MHC class I	9
6	cellular defense response	14
7	response to drug	35
8	ion transport	44
9	interspecies interaction 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

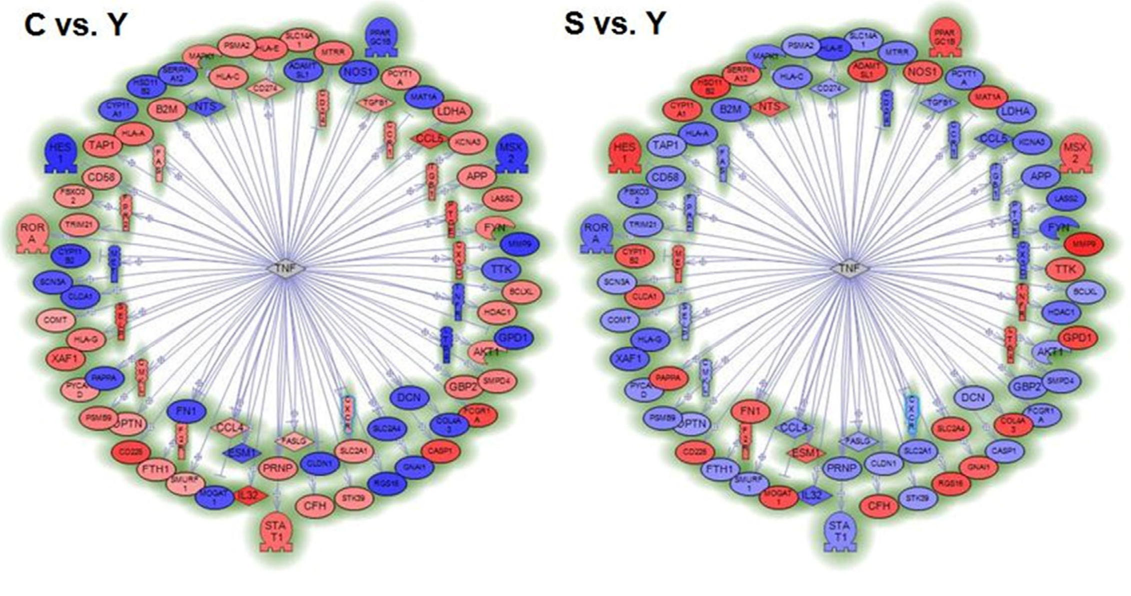
75	eukaryotic cell surface binding	**5**
76	myelination	7
77	C21-steroid hormone biosynthetic process	3
78	regulation of ARF GTPase activity	6
79	MHC class I protein complex	9
80	ruffle	10
81	cytokine-mediated signaling pathway	9
82	evasion of host defenses by virus	2
83	negative regulation of calcium-mediated 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



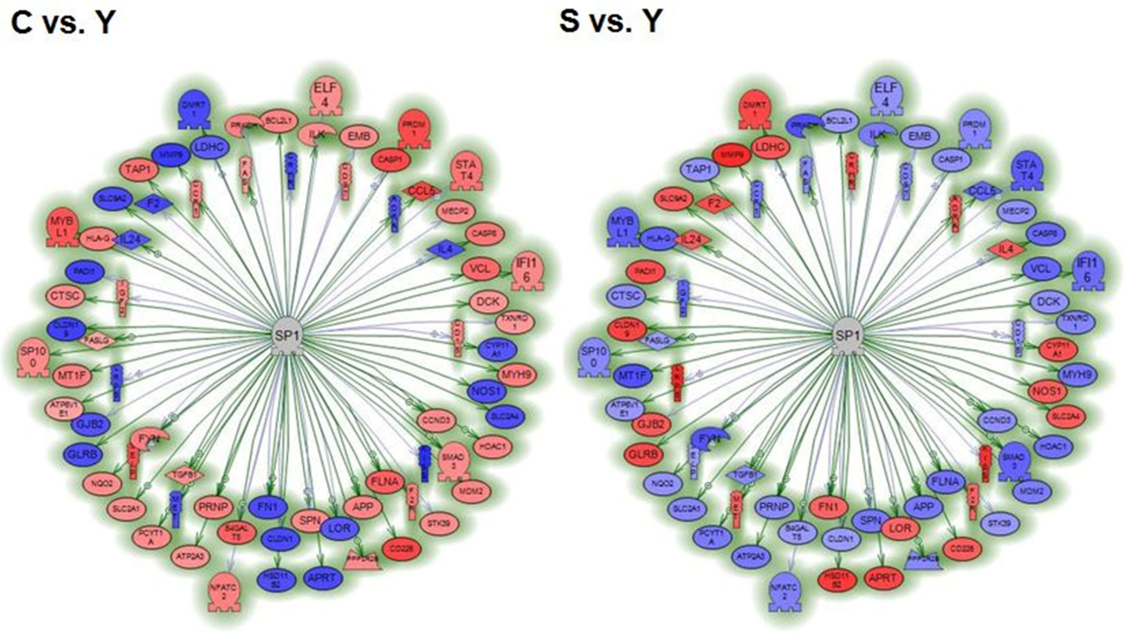
Supplementary Figure 1. (**a**) Principal component analysis (PCA) of mRNA profiles in mononuclear cells from septuagenarians and centenarians. Each sample was assayed by GeneChip Human Gene 1.0ST Array. The ellipsoids (red, septuagenarians; n=6; green, centenarians; n=8) show distinct directionalities. 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 6.4software. Statistically significant mRNAs were filtered by applying P-value <0.05 and fold change ≥ |1.8|.



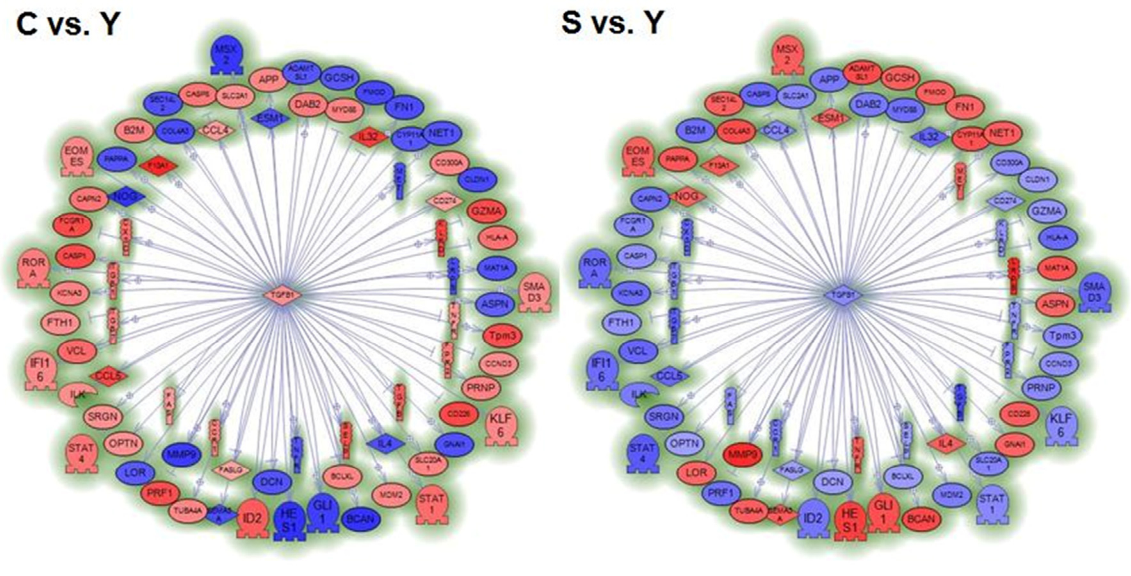
Supplementary Figure 2. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of T cell receptor (TCR). Sub-network of genes regulated by TCR in mononuclear cells obtained from centenarians (**a**) or septuagenarians (**b**) 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.



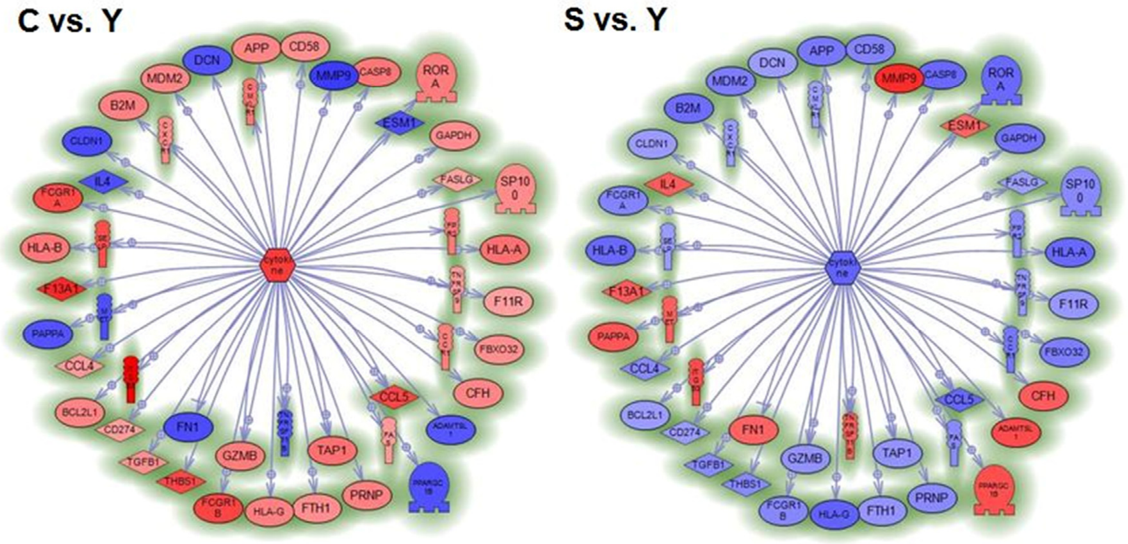
Supplementary Figure 3. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of tumor necrosis factor (TNF). Sub-network of genes regulated by TNF in mononuclear cells obtained from centenarians (**a**) or septuagenarians (**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.



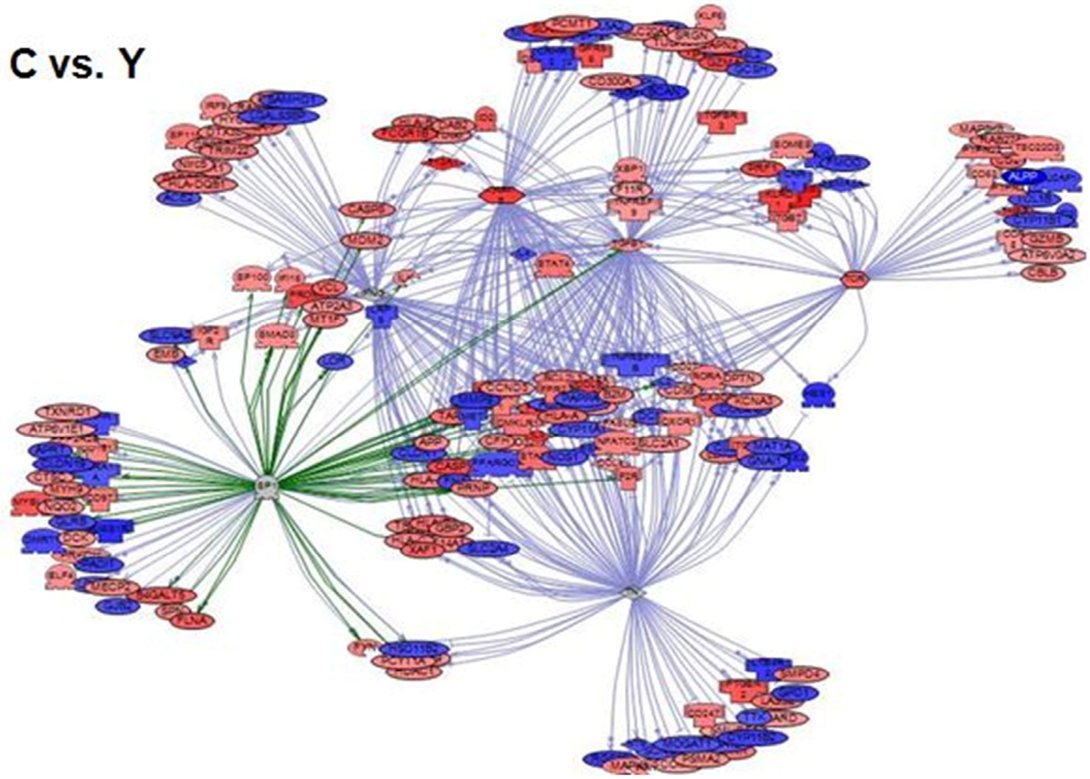
Supplementary Figure 4. Sub-network analysis of genes specifically regulated by centenarians or septuagenarians versus young subjects indicates the relevance of SP1. Sub-network of genes regulated by SP1 transcription factor in mononuclear cells obtained from centenarians (a) or septuagenarians (b) versus 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.



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)-β1 (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.



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-32in 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.



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.