Supplementary Information:

SUPPLEMENTARY MATERIALS AND METHODS

SUPPLEMENTARY TABLE 1: The SNPs and genes under study

SUPPLEMENTARY TABLE 2: The results of all analyses of phenotype intake values in the discovery sample (see Supplementary Table 2.xlsx (separate file)). Notes: *: highlights the SNPs reported to associate to longevity in previous studies of the genotype data (Soerensen et al., 2012 and Soerensen et al., 2013).

SUPPLEMENTARY TABLE 3: Association study of the change in phenotypes during seven years of follow-up in the discovery sample and the five SNPs found to associate to the phenotypes at the beginning of follow-up.

SUPPLEMENTARY TABLE 4: Replication study of the initial findings.

SUPPLEMENTARY FIGURE 1: Average individual decline from 93 to 100 years of age for the phenotypes investigated for association to one of the five SNPs significantly associated to the intake values.

References:

Soerensen, M., Dato, S., Tan, Q., Thinggaard, M., Kleindorp, R., Beekman, M., Jacobsen, R., Suchiman, H.E., de Craen, A.J., Westendorp, R.G., Schreiber, S., Stevnsner, T., Bohr, V.A., Slagboom, P.E., Nebel, A., Vaupel, J.W., Christensen, K., McGue, M., Christiansen, L., 2012. Human longevity and variation in GH/IGF-1/insulin signaling, DNA damage signaling and repair and pro/antioxidant pathway genes: cross sectional and longitudinal studies. Exp. Gerontol. 47 (5), 379-87.

Soerensen, M., Dato, S., Tan, Q., Thinggaard, M., Kleindorp, R., Beekman, M., Suchiman, H.E., Jacobsen, R., McGue, M., Stevnsner, T., Bohr, V.A., de Craen, A.J., Westendorp, R.G., Schreiber, S., Slagboom, P.E., Nebel, A., Vaupel, J.W., Christensen, K., Christiansen, L., 2013. Evidence from case-control and longitudinal studies supports associations of genetic variation in APOE, CETP, and IL6 with human longevity. Age (Dordr) 35 (2), 487-500.

SUPPLEMENTARY MATERIALS AND METHODS

The phenotypes under study

Six phenotypes were investigated here. Briefly, two cognitive state phenotypes were considered: the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), as well as a cognitive composite score (McGue and Christensen, 2002). The latter was included to explore verbal fluency, forward and backward digit span, and immediate and delayed recall. As the MMSE data are not suitable for analysis by linear regression, we produced a categorical variable with three groups: MMSE<18, MMSE ≥18 to <24 and MMSE ≥24, which is compatible to severe cognitive impairment, mild cognitive impairment and no cognitive impairment (Nybo et al., 2003). Handgrip strength was measured using a hand-held dynamometer (SMEDLEY' dynamometer, Scandidact, Kvistgaard, Denmark), using the maximum of three measurements with the strongest hand. Self-rated health was evaluated by asking the participants "How do you consider your health in general?" with five response categories: very poor, poor, acceptable, good, and excellent. For assessment of ADL, we employed a five item ADL disability score, which was based the Katz ADL index on bathing, dressing, toileting, transfer and feeding (Katz et al., 1970); the score was categorized into 'disabled = could do maximum 2 items', 'moderately disabled = could do 3 or 4 items' or 'not disabled = could do all five items'. To enable the depiction of physical functioning and endurance we, moreover, used an 11 item ADL strength score related to among others the ability to walk, run, go upstairs and carrying weights. Each item was categorized into 'could not do', 'could do with difficulty or an aid', 'could do with fatigue' and 'could do without fatigue' and an average over the 11 items was taken (Christensen et al., 2000 and Nybo et al., 2001). For analysing the ADL strength score, the data were split into four groups based on the quartiles, with increasing value corresponding to increased strength score (decreased fatigue).

Selection of candidate genes and variants, genotyping and data cleaning in the discovery sample

The selection of genes and gene variants, and the generation of genotype data are described in detail in (Soerensen et al., 2012 and Soerensen et al., 2013). In short, first comprehensive literature and data base searches, applying the search terms 'human longevity', 'human aging', 'age related disease' (including specific diseases e.g. myocardial infarction), 'premature aging syndromes' and 'model organisms of aging and longevity', were performed for identifying candidate genes and SNPs. Secondly, the chromosomal regions of each candidate gene plus 5,000 bp upstream and 1,000 bp downstream were determined, so were tagging SNPs and potential functional SNPs (i.e. coding non-synonymous SNPs, SNPs in potential splice sites or transcription factor binding sites and SNPs potentially causing frame shifts or nonsense-mediated mRNA decay) within the gene regions. The tagging SNPs were recovered via the HapMap consortium database for the CEU population. Finally, the QIAamp DNA Mini and Micro Kits (Qiagen, Düsseldorf, Germany) were employed for purification of DNA from blood spot cards, while the Illumina GoldenGate platform (Illumina Inc., San Diego, CA, USA) was used for SNP genotyping. Data cleaning was accomplished according to the manufacturers' recommendations; after data cleaning the final sample size was 1,088 oldest-olds.

References

Christensen, K., McGue, M., Yashin, A., Iachine, I., Holm, N.V., Vaupel, J.W., 2000. Genetic and environmental influences on functional abilities in Danish twins aged 75 years and older. J. Gerontol. A. Biol. Sci. Med. Sci. 55 (8), M446-M452.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12 (3), 189-98.

Katz, S., Downs, T.D., Cash, H.R., Grotz, R.C., 1970. Progress in development of the index of ADL. Gerontologist 10 (1), 20-30.

McGue, M., Christensen, K., 2002. The heritability of level and rate-of-change in cognitive functioning in Danish twins aged 70 years and older. Exp. Aging. Res. 28 (4), 435-451.

Nybo, H., Gaist, D., Jeune, B., McGue, M., Vaupel, J.W., Christensen, K., 2001. Functional status and self-rated health in 2,262 nonagenarians: the Danish 1905 Cohort Survey. J. Am. Geriatr. Soc. 49 (5), 601-609.

Nybo, H., Petersen, H.C., Gaist, D., Jeune, B., Andersen, K., McGue, M., Vaupel, J.W., Christensen, K., 2003. Predictors of mortality in 2,249 nonagenarians--the Danish 1905-Cohort Survey. J. Am. Geriatr. Soc. 51 (10), 1365-1373.

Soerensen, M., Dato, S., Tan, Q., Thinggaard, M., Kleindorp, R., Beekman, M., Jacobsen, R., Suchiman, H.E., de Craen, A.J., Westendorp, R.G., Schreiber, S., Stevnsner, T., Bohr, V.A., Slagboom, P.E., Nebel, A., Vaupel, J.W., Christensen, K., McGue, M., Christiansen, L., 2012. Human longevity and variation in GH/IGF-1/insulin signaling, DNA damage signaling and repair and pro/antioxidant pathway genes: cross sectional and longitudinal studies. Exp. Gerontol. 47 (5), 379-87.

Soerensen, M., Dato, S., Tan, Q., Thinggaard, M., Kleindorp, R., Beekman, M., Suchiman, H.E., Jacobsen, R., McGue, M., Stevnsner, T., Bohr, V.A., de Craen, A.J., Westendorp, R.G., Schreiber,

S., Slagboom, P.E., Nebel, A., Vaupel, J.W., Christensen, K., Christiansen, L., 2013. Evidence from case-control and longitudinal studies supports associations of genetic variation in APOE, CETP, and IL6 with human longevity. Age (Dordr) 35 (2), 487-500.

SUPPLEMENTARY TABLE 1: The SNPs and Genes under Study													
	Gene	Number of SNPs											
DNA repair genes	ACD	2	rs14920	rs6979									
	APEX1	2	rs1048945	rs3136817									
	APTX	8	rs1016674	rs10813916	rs10971264	rs1125479	rs1197774	rs13296038	rs3780476	rs3824457			
	ATM	8	rs170548	rs17503908	rs1800058	rs1800889	rs1801516	rs611646	rs639923	rs664677			
	ATR	8	rs10804682	rs11920625	rs1802904	rs2227928	rs2229032	rs6805118	rs7630115	rs9856772			
	BLM	15	rs2270132	rs2518967	rs2518968	rs2532105	rs3784782	rs3815003	rs389480	rs401549	rs414634	rs4932365	rs7162960
			rs7165117	rs7165790	rs7179346	rs7184015							
	BRIP1	13	rs11652980	rs16945628	rs16945643	rs2048718	rs2191248	rs2378908	rs4986764	rs4988340	rs4988357	rs6504063	rs8076746
			rs8077088	rs9908659									
	C10orf2	1	rs3740487										
	DCLRE1C	12	rs10128350	rs10796227	rs10906777	rs11259405	rs11593133	rs12572872	rs3814176	rs4237441	rs7900814	rs7906952	rs7916722
			rs7920514										
	DDB1	3	rs17549396	rs2230356	rs9651726								
	DDB2	6	rs1685404	rs2013867	rs2291120	rs3824866	rs4567413	rs4647709					
	ERCC1	6	rs11615	rs3212948	rs3212955	rs3212961	rs3212964	rs762562					
	ERCC2	9	rs13181	rs1799788	rs238404	rs238407	rs238415	rs3810366	rs3916874	rs50871	rs50872		
	ERCC3	4	rs4150403	rs4150454	rs4150459	rs4150506							
	ERCC4	4	rs1364362	rs1799802	rs1800067	rs3136202							
	ERCC5	13	rs17655	rs2227869	rs2296147	rs3759500	rs4150350	rs4150351	rs4150355	rs4150383	rs4150386	rs4150393	rs7325708
			rs876430	rs9514065									
	ERCC6	11	rs1012553	rs1018603	rs1964145	rs2228527	rs2228528	rs2228529	rs3793784	rs4253079	rs4253164	rs4253200	rs4838519
	ERCC8	8	rs1021005	rs12522154	rs158931	rs158937	rs17332991	rs2306350	rs4647068	rs7726671			
	EXO1	16	rs1047840	rs11581448	rs12118937	rs12564134	rs1635518	rs1776131	rs1776177	rs2797604	rs4149855	rs4149867	rs4149965
			rs4150018	rs4150027	rs4408133	rs735943	rs9350						
	FANCA	11	rs1006548	rs12924101	rs16966142	rs17226075	rs1800339	rs2238526	rs3743860	rs7187436	rs7190823	rs8046872	rs9282681
	FANCD2	7	rs2075310	rs3172417	rs6775725	rs6792811	rs6807485	rs803335	rs9875081				
	FEN1	2	rs412334	rs695867									
	H2AFX	2	rs2509049	rs640603									
	HMGB1	1	rs3742305										
	LIG1	8	rs156640	rs156641	rs20580	rs2304136	rs274860	rs3731037	rs7246512	rs8100261			
	LIG3	4	rs1052536	rs2074516	rs3135989	rs3135998							

DNA repair genes	LIG4	6	rs10131	rs1151402	rs1805386	rs1805388	rs3093748	rs3093772					
	LONP1	5	rs2436508	rs2436509	rs2436514	rs3818815	rs3892355						
	MLH1	5	rs13320360	rs1540354	rs1799977	rs1800734	rs3774335						
	MLH3	3	rs175076	rs175080	rs7156586								
	MRE11A	12	rs10831227	rs13447717	rs13447720	rs16920467	rs1805363	rs500558	rs512150	rs533984	rs569143	rs592068	rs604845
			rs680695										
	MSH2	11	rs10183143	rs12999145	rs17036577	rs1863332	rs1981929	rs2347794	rs3732183	rs4638843	rs4952887	rs6741393	rs6753135
	MSH3	25	rs10075024	rs12522474	rs1650649	rs1650737	rs1677645	rs17206221	rs181747	rs184967	rs1979005	rs245011	rs245378
			rs245397	rs249633	rs26279	rs26784	rs27385	rs33003	rs397628	rs40139	rs6151616	rs6151627	rs6151735
			rs6151792	rs6151816	rs7712332								
	MSH6	9	rs2020911	rs2348244	rs3136228	rs3136245	rs3136284	rs3136329	rs3136337	rs3136367	rs330792		
	NBN	12	rs1235369	rs12680687	rs13312954	rs16893166	rs1805794	rs1805810	rs1805812	rs2735385	rs3026271	rs6470522	rs6999227
			rs7010210										
	NEIL1	1	rs4462560										
	NEIL2	14	rs1043180	rs1466785	rs1874546	rs2686211	rs4840583	rs4841593	rs804269	rs8191529	rs8191534	rs8191542	rs8191589
			rs8191605	rs8191663	rs904009								
	NTHL1	2	rs2516739	rs3211994									
	OGG1	7	rs159153	rs17252807	rs2304277	rs2472037	rs293794	rs293796	rs3218997				
	PARP1	8	rs1136410	rs1805401	rs1805410	rs1805414	rs2271347	rs3219110	rs3219142	rs7542788			
	PCNA	4	rs17349	rs25406	rs3729558	rs8125170							
	PIF1	3	rs11631663	rs17802279	rs3743046								
	PMS1	6	rs1233255	rs1233258	rs1233284	rs17806132	rs256552	rs5743100					
	PMS2	5	rs11769380	rs12112229	rs2286680	rs2345060	rs7811924						
	PNKP	1	rs2257103										
	POLB	3	rs2953983	rs3136717	rs3136797								
	POLD1	6	rs1673026	rs1673041	rs2445837	rs2546551	rs3219281	rs3219337					
	POLE	10	rs4883539	rs4883617	rs5744761	rs5744807	rs5744873	rs5744897	rs5744934	rs5744941	rs5744990	rs5745066	
	POLG	6	rs2072266	rs2074885	rs2351000	rs3087374	rs3176205	rs3176208					
	POLRMT	2	rs2283575	rs9304924									
	POT1	5	rs10228682	rs10271646	rs11768553	rs11972248	rs929365						
	PRKDC	10	rs10109984	rs2213178	rs4278157	rs4521758	rs4873772	rs7003908	rs8178017	rs8178068	rs8178071	rs8178179	
	RAD23B	14	rs10119641	rs10739239	rs10816492	rs10978792	rs11573631	rs11573709	rs11573711	rs1323808	rs13299620	rs1805329	rs1805330
			rs4978820	rs7023656	rs7030169								

DNA repair genes	RAD50	3	rs17772583	rs2237060	rs2706370								
	RAD51	5	rs11633269	rs1801320	rs2619681	rs5030783	rs7177265						
	RAD52	11	rs10744729	rs11064598	rs11064613	rs11571461	rs12822733	rs12827646	rs4766377	rs6413436	rs7311151	rs7311263	rs7962050
	RAD54L	7	rs10789488	rs12146051	rs12410307	rs17102086	rs17102087	rs2295465	rs9793263				
	RecQL1	17	rs10492116	rs1061627	rs10841830	rs10841833	rs11835261	rs12231436	rs17627175	rs1860947	rs2110159	rs2192170	rs2284392
			rs2284393	rs2300211	rs3213212	rs6487233	rs7307519	rs917855					
	RECQL4	2	rs4244612	rs4251689									
	RecQL5	1	rs820157										
	RFC1	10	rs12644680	rs13147094	rs16995255	rs17584703	rs2066789	rs2306596	rs2306597	rs3733282	rs6829064	rs6851075	
	RPA1	15	rs11656253	rs11867830	rs16951710	rs17292175	rs17339284	rs17734	rs2230931	rs2270412	rs2287320	rs4790830	rs4790838
			rs5030740	rs5030755	rs8067195	rs9909163							
	SUPV3L1	4	rs2063047	rs4746821	rs6480392	rs7893492							
	TERF1	5	rs10095169	rs10098931	rs2929586	rs2975842	rs6982126						
	TERF2	8	rs13337258	rs153045	rs251796	rs34295116	rs34415214	rs35439397	rs8061352	rs9925619			
	TERF2IP	4	rs11639771	rs1865493	rs4888444	rs7186790							
	TERT	11	rs10069690	rs13167280	rs2735940	rs2736100	rs2736114	rs2736122	rs2853668	rs2853676	rs33954691	rs3891054	rs4246742
	TFAM	8	rs10826176	rs10826179	rs11006127	rs11006132	rs12355138	rs16912200	rs2279339	rs3876			
	TP53	7	rs12951053	rs17880604	rs2078486	rs2909430	rs8079544	rs9894946	rs9903378				
	UNG	5	rs246079	rs2541886	rs2569987	rs3219243	rs759561						
	WRN	17	rs11574214	rs11574218	rs11574304	rs11574309	rs13251813	rs13269094	rs1346044	rs1800389	rs1800391	rs1882928	rs2113950
			rs2230009	rs2725344	rs2725351	rs4733220	rs6982140	rs6982948					
	XPA	8	rs2805835	rs2808667	rs2808668	rs3176658	rs3176683	rs3176689	rs3176748	rs3176757			
	XPC	8	rs13099160	rs2228000	rs2228001	rs2733534	rs2733537	rs3731108	rs3731143	rs9653966			
	XRCC1	12	rs1001581	rs1799782	rs2023614	rs25487	rs2682585	rs2682587	rs2854501	rs2854508	rs2854510	rs3213266	rs3213282
			rs3213403										
	XRRC4	17	rs1011980	rs10474079	rs1056503	rs1193695	rs13178127	rs1478483	rs1478486	rs16900340	rs177297	rs2075685	rs2731852
			rs301275	rs301287	rs6452524	rs7711825	rs7720588	rs7735781					
	XRCC5	20	rs10166817	rs11685387	rs13006837	rs1364726	rs16855458	rs16855489	rs207905	rs207910	rs207924	rs207929	rs207943
			rs2303400	rs3770500	rs3821107	rs3834	rs4674066	rs668844	rs705649	rs828704	rs828910		
	YBX1	8	rs10493112	rs10493113	rs11210696	rs11210698	rs12030724	rs3895305	rs6659400	rs7556150			
GH/IGF-1/INS genes	AKT1	6	rs1130214	rs2494731	rs2494732	rs2494738	rs2494748	rs2498796					
	FOXO1	12	rs10507486	rs12854161	rs12876443	rs2180961	rs2701858	rs2721068	rs2755209	rs2755213	rs2951787	rs2984121	rs4581585
			rs9603776										

GH/IGF-1/INS genes	FOXO4	2	rs5980741	rs5980742									
	GH1	3	rs2854184	rs3020619	rs3744287								
	GHR	20	rs11739840	rs11744988	rs12153009	rs12187996	rs12233949	rs13182117	rs1509453	rs17230998	rs17574650	rs2940918	rs2972418
			rs4130113	rs4410646	rs4547964	rs6180	rs6451620	rs6451634	rs6883523	rs7702524	rs7703713		
	GHRH	2	rs1073768	rs6032470									
	GHRHR	11	rs10225302	rs11761979	rs2267723	rs4723038	rs4988494	rs4988496	rs4988498	rs4988501	rs4988504	rs4988505	rs6954044
	GHRL	10	rs10490815	rs1617161	rs26802	rs27498	rs27647	rs35682	rs3755777	rs42451	rs4684677	rs696217	
	GHSR	4	rs495225	rs512692	rs572169	rs9819506							
	IDE	10	rs11187033	rs11187065	rs17445328	rs1887922	rs2275218	rs2421943	rs4646957	rs6583820	rs7078413	rs7899603	
	IGF1	13	rs1019731	rs10735380	rs10778176	rs10860865	rs11111262	rs11831436	rs12821878	rs1520220	rs17727841	rs2033178	rs5742632
			rs6214	rs7136446									
	IGF1R	57	rs1058696	rs11247367	rs11630259	rs11630479	rs12437963	rs12440962	rs12442093	rs12592205	rs12910200	rs12916884	rs1464430
			rs1521483	rs1546713	rs1815009	rs1879613	rs2017500	rs2139924	rs2684787	rs2684788	rs2684790	rs2684792	rs2684796
			rs2684799	rs2684802	rs2684806	rs2684807	rs2684811	rs2715416	rs2715419	rs3743254	rs3743258	rs3784605	rs4284619
			rs4305005	rs4965438	rs4966008	rs4966013	rs4966014	rs4966015	rs4966038	rs4966039	rs4966042	rs4966046	rs7162336
			rs7166348	rs7168671	rs7173191	rs8025801	rs8026157	rs8032477	rs8038056	rs867431	rs871335	rs939626	rs9672254
			rs9672965	rs9920651									
	IGF2	10	rs1004446	rs10770125	rs17885652	rs2239681	rs2585	rs3168310	rs3213216	rs3741211	rs734351	rs7481173	
	IGF2BP2	15	rs11705701	rs11708719	rs11925694	rs12635769	rs1447890	rs17293846	rs2290066	rs4402960	rs4686692	rs6770227	rs6778126
			rs6794209	rs6799330	rs7634540	rs7648605							
	IGF2R	28	rs1003737	rs10945647	rs10945649	rs17200966	rs1805075	rs2282140	rs2297370	rs3734181	rs3798176	rs3798186	rs3798187
			rs3798189	rs3798201	rs3798207	rs4709395	rs633863	rs6917747	rs7755435	rs8191745	rs8191772	rs8191811	rs8191824
			rs8191829	rs9295119	rs9347380	rs9456490	rs9456497	rs9457795					
	IGFALS	1	rs344352										
	IGFBP2	12	rs1525608	rs2270360	rs3770473	rs6413492	rs7603372	rs9341105	rs9341130	rs9341134	rs9341145	rs9341156	rs9341191
			rs9341201										
	IGFBP3	9	rs13223993	rs2132571	rs2453836	rs2453839	rs2471551	rs3110697	rs6670	rs924140	rs9282734		
	INS	2	rs3842748	rs3842755									
	INSR	29	rs1035939	rs10401628	rs1052371	rs11667110	rs11672739	rs11880337	rs12979424	rs1549616	rs17253937	rs1799817	rs2059807
			rs2252673	rs2860175	rs2860183	rs2860184	rs2963	rs6510949	rs6510956	rs6510959	rs7248939	rs7254060	rs7254487
			rs7254921	rs7258382	rs8103483	rs8110428	rs8111710	rs8112883	rs891087				
	IRS1	10	rs10179720	rs1025333	rs1560251	rs17208239	rs17208470	rs17347714	rs17508368	rs6436635	rs6725330	rs9282766	

GH/IGF-1/INS genes	IRS2	14	rs11618950	rs12584136	rs2099435	rs4771644	rs4773094	rs7323191	rs754204	rs7997595	rs7999797	rs913949	rs9515119
			rs9521512	rs9559648	rs9559656								
	KL	19	rs1207362	rs1888057	rs2283368	rs2320762	rs385564	rs397703	rs398655	rs495392	rs522796	rs562020	rs564481
			rs575536	rs576404	rs648202	rs657049	rs687045	rs9526984	rs9527026	rs9536314			
	PAPPA	18	rs10122701	rs10513270	rs10817866	rs12236532	rs12344396	rs1998499	rs3761843	rs3789280	rs3789303	rs398400	rs449807
			rs4837525	rs7020782	rs7025886	rs731146	rs7469968	rs7869550	rs978201				
	PDPK1	1	rs1005273										
	PI3KCB	2	rs10513055	rs361072									
	POU1F1	7	rs10511134	rs12486159	rs177292	rs2633674	rs300982	rs300994	rs9824592				
	PROP1	5	rs4431364	rs4604209	rs4610479	rs6883364	rs6890425						
	PTEN	7	rs11202596	rs11202600	rs1234220	rs17431184	rs1903858	rs1903860	rs2736627				
	PTPN1	7	rs13045716	rs2038526	rs2426164	rs6063534	rs6067484	rs6126033	rs6512652				
	SST	4	rs10513819	rs17796004	rs2162189	rs7624906							
	SSTR2	5	rs11077670	rs1466113	rs7210080	rs7224362	rs728291						
Additional genes	ACE	11	rs1055086	rs1800764	rs4291	rs4295	rs4309	rs4311	rs4331	rs4335	rs4343	rs4344	rs4351
	APOA4	1	rs2849174										
	APOC3	2	rs5128	rs595049									
	APOE	3	rs405509	rs440446	rs769449								
	CETP	20	rs11076175	rs12708967	rs12708974	rs1800774	rs1800775	rs1800777	rs1801706	rs289714	rs289742	rs3764261	rs4783961
			rs4783962	rs4784744	rs5882	rs5883	rs6499863	rs7205804	rs9923854	rs9929488	rs9930761		
	HFE	6	rs1572982	rs1800708	rs2858993	rs707889	rs9295687	rs9379825					
	HSPA14	6	rs10906772	rs12770830	rs17155992	rs17268499	rs7905174	rs9787671					
	HSPA1A	1	rs1043618										
	HSPA1L	4	rs2075799	rs2075800	rs2227955	rs2227956							
	IL6	2	rs12700386	rs2069827									
	IL6R	8	rs12083537	rs2229238	rs4075015	rs4240872	rs4601580	rs4845626	rs6684439	rs6689393			
	MTHFR	13	rs11121832	rs12121543	rs1476413	rs17037390	rs17421462	rs1801131	rs1801133	rs2066471	rs3737964	rs3737967	rs4846048
			rs4846052	rs9651118									
	SIRT1	5	rs12778366	rs2236319	rs2273773	rs3758391	rs3818291						
	SIRT3	10	rs1023430	rs11246009	rs11246020	rs12226697	rs3782116	rs3825075	rs4758633	rs535716	rs536715	rs7104764	
	SIRT6	3	rs107251	rs352492	rs7260071								
	TGFB1	7	rs11466321	rs11466338	rs11466359	rs1800469	rs4803455	rs8105161	rs8110090				

Both genders (n=1,088)				
Phenotype	SNP	Coef.	p-value	95%CI
Cognitive composite score	rs10739239	0.07	0.132	-0.02;0.17
	rs10816492	0.07	0.171	-0.03;0.16
ADL strength score	rs1061627	-0.01	0.699	-0.04;0.02
Females (n=775)				
Phenotype	SNP	Coef.	p-value	95%CI
Grip strength	rs2227869	0.31	0.06	-0.01;0.63
Males (n=313)				
Phenotype	SNP	Coef.	p-value	95%CI
Cognitive composite score	rs10739239	-0.19	0.058	-0.39;-0.01
Self-rated health	rs2849174	-0.03	0.264	-0.09;0.03

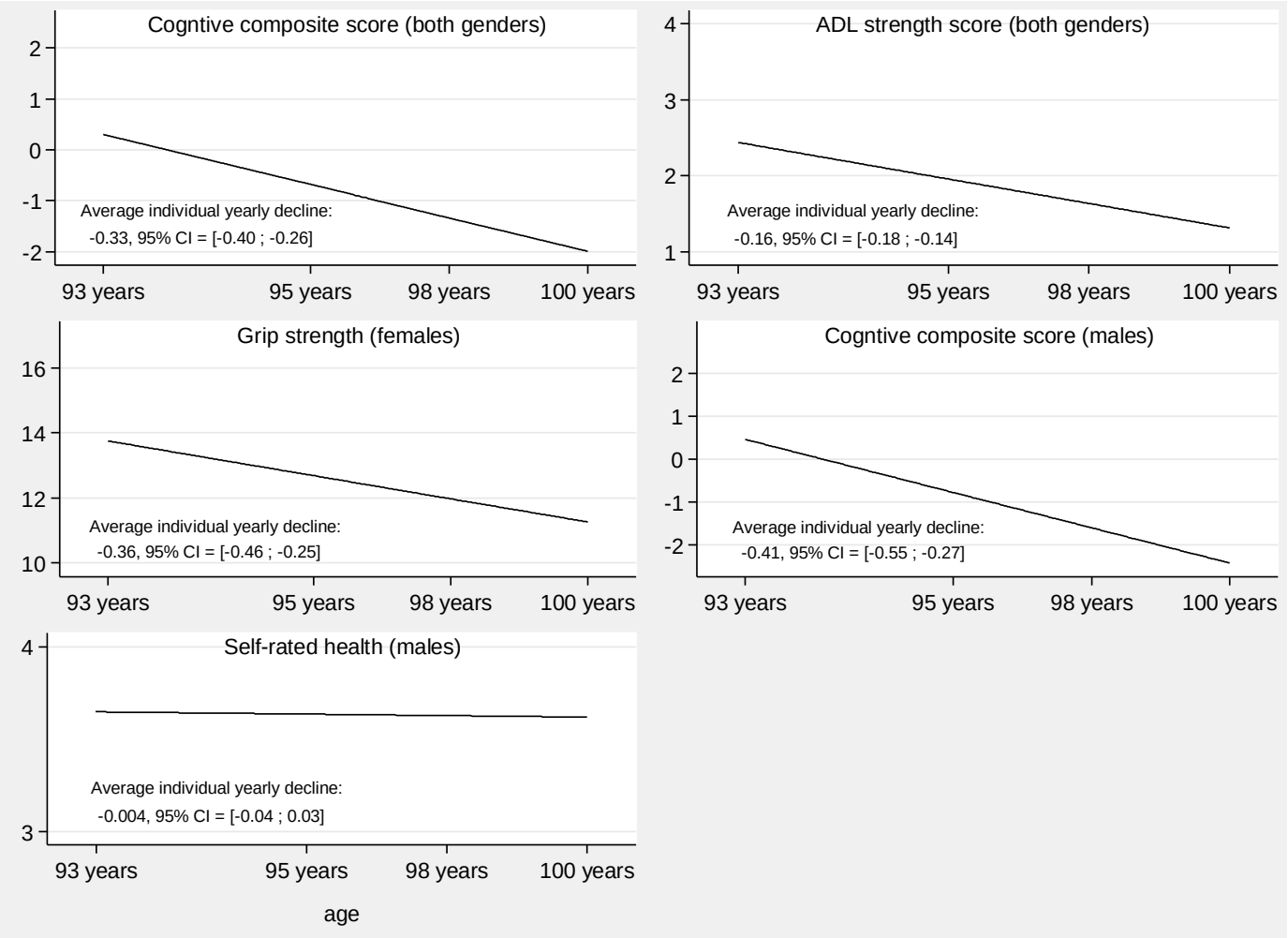
SUPPLEMENTARY TABLE 3: Association study of the change in phenotypes during seven years of follow-up in the discovery sample and the five SNPs found to associate to the phenotypes at the beginning of follow-up.

Notes: Coef: SNP-time interaction coefficient describing the change in phenotype during follow-up attributed to each copy of the minor allele. 95% CI: 95% confidence interval.

			Both genders discovery sample (n = 1,088)			Both genders replication sample (n=1,281)				Pooled analyses		
Phenotype	Gene	SNP	MAF	β coefficient	p-value	MAF	β coefficient	p-value	95% CI	β coefficient	p-value	95% CI
Cognitive composite score	*RAD23B*	rs10739239	0.42	-0.70	$5.34*10^{-6}$	0.42	-0.05	0.745	-0.33;0.24	-0.34	0.002	-0.55;0.13
	RAD23B	rs10816492	0.47	-0.59	$8.63*10^{-5}$	0.48	0.10	0.481	-0.18;0.38	-0.20	0.054	-0.41;0.01
				OR			OR			OR	p-value	95% CI
ADL strength score	*RECQ1L*	rs1061627	0.17	1.54	$2.65*10^{-5}$	0.18	1.13	0.196	0.94;1.35	1.31	$8.9*10^{-5}$	1.14;1.50
			Females discovery sample (n=775)			Females replication sample (n=936)				Pooled analyses		
Phenotype	Gene	SNP	MAF	β coefficient	p-value	MAF	β coefficient	p-value	95% CI	β coefficient	p-value	95% CI
Handgrip strength	*ERCC5*	rs2227869	0.04	-2.43	$4.55 * 10^{-5}$	0.04	-0.29	0.609	-1.42;0.83	-1.38	0.001	-2.19;-0.56
			Males discovery sample (n=313)			Males replication sample (n=345)				Pooled analyses		
			MAF	β coefficient	p-value	MAF	β coefficient	p-value	95% CI	β coefficient	p-value	95% CI
Cognitive composite score	*RAD23B*	rs10739239	0.42	-1.20	$2.83 * 10^{-5}$	0.42	-0.01	0.961	-0.56;0.53	-0.54	0.007	-0.93;-0.15
				OR			OR			OR	p-value	95% CI
Self-rated health	*APOA4/ APOC3*	rs2849174	0.29	2.10	$4.71*10^{-5}$	0.29	1.30	0.110	0.94;1.79	1.64	$4.05*10^{-5}$	1.30;2.08

SUPPLEMENTARY TABLE 4: Replication study of the initial findings.

Notes: MAF: minor allele frequency, 95% CI: 95% confidence interval and OR: odds ratio.



Supplementary Figure 1: Average individual decline from 93 to 100 years of age for the phenotypes investigated for association one of the 5 SNPs significantly associated to the intake values. The range of the Y-axes is the 25% to the 75% percentile of the phenotypes.