

## Supplementary Material

### Supplementary Tables

**Supplementary Table S1: Clinical information for the 2 selected GWAS datasets of RA.**

	Year	Population	nCase	ncontrol	Sample size	Number of SNPs
ieu-a-832	2014	European	14361	43923	58284	8747963
GCST90132223	2022	European	22350	74823	97173	8218396

**Supplementary Table S2: Summary of the SNPs associated with mTOR-related proteins**

Name	SNP	CHR	Position	Effect allele	Other allele	P.value	SE	Beta	EAF	F-statistic	R <sup>2</sup>
AKT	rs11751659	6	33081632	G	A	0.00000275	0.0364	-0.1705	0.13083	21.94047367	0.00661136
	rs11789587	9	3088740	T	C	0.000000398	0.0263	0.1332	0.43254	25.65056601	0.008709635
	rs2319337	3	147362224	A	G	0.0000055	0.071	0.3227	0.96843	20.65766515	0.006367526
	rs56227739	19	57675575	G	A	0.00000501	0.039	-0.1781	0.12417	20.85444444	0.00689913
	rs9755696	3	23333557	G	A	0.00000115	0.0842	-0.4095	0.02871	23.65285826	0.009352332
RPS6KA	rs1381968	5	101423444	C	T	0.00000355	0.0746	-0.3462	0.02868	21.53656678	0.00667768
	rs17035713	1	10840905	G	A	0.00000813	0.0545	0.243	0.06214	19.88014477	0.006882589
	rs35747952	4	145934089	C	T	0.00000389	0.0809	-0.3736	0.02474	21.32635783	0.006735407
	rs482759	6	32195017	G	A	0.00000851	0.0316	-0.1406	0.194	19.79686749	0.00618212
	rs58565824	3	22584610	T	C	0.000000891	0.0937	0.4607	0.02192	24.17448566	0.009100837
	rs62143197	19	54320716	A	G	8.13E-76	0.029	0.5347	0.22311	339.9573008	0.099112614
	rs62398809	5	152488248	G	A	0.0000049	0.0247	-0.1129	0.48004	20.89267157	0.006363049
	rs7017005	8	56752146	G	A	0.00000214	0.0256	-0.1213	0.63078	22.4513092	0.006853537
	rs72881486	6	68218559	A	G	0.00000107	0.0745	0.3633	0.03313	23.78035043	0.008455715
rs9833044	3	27587457	T	C	0.000000513	0.0635	-0.319	0.03925	25.23677847	0.0076747	
EIF4EBP2	rs10733789	10	64948684	C	T	0.00000407	0.0272	0.1254	0.31231	21.25481185	0.006754663
	rs10864412	1	9425722	A	G	0.000000158	0.0254	-0.1334	0.38487	27.58317317	0.008426023
	rs13120502	4	67609904	T	G	0.00000631	0.0546	0.2463	0.06048	20.34902186	0.006894085
	rs17003636	21	21934726	C	T	0.00000288	0.0984	0.4607	0.01618	21.92028658	0.006757104
	rs2552108	8	3925098	T	C	0.00000646	0.0325	0.1467	0.81859	20.3748071	0.006391722
	rs2745108	16	1547477	C	T	0.00000158	0.0402	-0.1927	0.11306	22.97795228	0.007447262
	rs60862477	17	53296188	G	A	0.00000646	0.0312	0.1408	0.19168	20.36554898	0.006143211
	rs67506762	11	128896222	A	G	0.00000525	0.0365	-0.1661	0.13618	20.70873335	0.006490914
	rs72743058	15	58881788	A	G	0.00000347	0.0827	-0.3839	0.02963	21.54890493	0.008474913
	rs9289950	3	154545552	G	A	0.00000617	0.0371	-0.168	0.1241	20.50551798	0.006135852
EIF4B	rs10956734	8	134959835	G	A	0.00000363	0.0253	0.117	0.59765	21.38605509	0.006583436
	rs10968642	9	28525868	A	G	0.0000049	0.0661	0.302	0.0405	20.87425416	0.007088329
	rs11021718	11	11261045	A	G	0.00000257	0.0261	0.1229	0.3718	22.1729129	0.007055716
	rs13282034	8	5581368	T	C	0.00000776	0.0277	0.124	0.2995	20.0393593	0.006451762
	rs1474470	2	123244252	G	A	0.00000417	0.0351	0.1615	0.14995	21.17048563	0.006649148
	rs16941339	16	86515652	T	C	0.00000661	0.1092	0.4921	0.01429	20.3077334	0.006822101
	rs2275132	9	133911598	G	A	0.00000741	0.0334	0.1499	0.81476	20.14235899	0.006782624
	rs4573743	12	17908887	A	G	0.00000347	0.0269	-0.1248	0.31113	21.52408065	0.006676338

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rs56181691	10	7195123	A	G	0.00000575	0.0704	0.3194	0.03182	20.58375032	0.006285735
rs62143197	19	54320716	A	G	1.1E-36	0.0298	0.3766	0.22311	159.7085266	0.049166489
rs73173693	3	171176148	G	T	0.000000339	0.0764	-0.3895	0.02738	25.99131226	0.00808019
rs9987128	8	2980123	G	A	0.00000355	0.0496	-0.2302	0.06758	21.54007869	0.006678369
EIF4G3										
rs10883933	10	83688822	A	G	0.00000661	0.0437	0.1969	0.09874	20.30152014	0.006900247
rs10928832	2	129516214	G	A	0.00000832	0.042	-0.1869	0.09868	19.8025	0.006213793
rs11022626	11	13086274	A	C	0.00000589	0.0359	-0.1625	0.14557	20.48886182	0.006568786
rs12578287	12	99556447	C	T	0.00000933	0.1223	-0.542	0.01185	19.64018883	0.006879705
rs13194494	6	4950866	T	C	0.00000525	0.0663	-0.3017	0.03803	20.7073042	0.006659912
rs1411879	9	3762150	A	G	0.00000427	0.089	0.4092	0.97398	21.13933089	0.008487085
rs704	17	26694861	A	G	4.27E-11	0.0245	0.1618	0.46665	43.61389421	0.013031386
rs746860	4	40857194	C	T	0.00000724	0.0267	-0.1197	0.66546	20.09859866	0.006379524
rs7955609	12	116387486	A	G	0.000002	0.0263	0.1251	0.37973	22.6257572	0.007372254
rs9817294	3	177712676	C	T	0.00000912	0.0287	0.1275	0.23874	19.73588365	0.005908926
EIF4A3										
rs2462049	7	85099898	T	G	0.00000331	0.0249	0.1159	0.47898	21.66547314	0.006704535
rs34131899	2	29058128	A	G	0.0000017	0.0591	-0.2829	0.05209	22.91347368	0.007903462
rs57716901	17	3483421	T	C	0.00000741	0.026	0.1163	0.34994	20.00841716	0.006153702
rs6792693	3	27245225	G	A	0.00000282	0.0286	0.134	0.252	21.9521737	0.006769268
EIF4E2										
rs12640699	4	167757172	A	C	0.00000407	0.0341	0.1574	0.82721	21.30593992	0.007082292
rs12686565	9	107739152	C	A	0.00000832	0.0257	0.1144	0.37576	19.81462248	0.006139658
rs2209485	10	20905192	T	C	0.00000151	0.034	0.1637	0.15317	23.18139273	0.006951801
rs3111529	5	179643117	T	C	0.00000955	0.0346	0.1533	0.15158	19.63053393	0.006044594
rs62007370	15	62325956	G	T	0.00000912	0.1379	0.612	0.00869	19.69583113	0.006453007
rs62130614	2	29505824	T	G	0.00000398	0.0999	0.4606	0.01552	21.2577302	0.006483007
rs62143198	19	54320939	A	G	6.76E-56	0.0296	0.4669	0.21453	248.8079917	0.07346752
rs741454	19	29350614	C	T	0.00000417	0.031	0.1426	0.19622	21.16	0.006414304
rs7874966	9	6674246	A	G	0.00000617	0.036	0.1627	0.13653	20.42537809	0.006241377
rs7926858	11	21384100	T	C	0.00000891	0.0284	0.1263	0.55187	19.77743751	0.007890009
rs9458439	6	162465203	T	C	0.00000525	0.0248	0.1129	0.47789	20.72452198	0.006360743
PKC-A										
rs4149991	1	242047847	G	A	1.26E-06	0.0414	0.2005	0.10903	23.45460221	0.007810302
rs754864	3	191843818	A	G	2.88E-06	0.0264	-0.1233	0.47327	21.81314566	0.00757972
rs3857001	4	161618784	A	C	2.09E-06	0.0242	-0.1146	0.52218	22.42531248	0.006553658
rs11098538	4	80025236	G	A	7.76E-06	0.0249	-0.1115	0.43687	20.05169271	0.00611703
rs2984440	6	39894628	G	A	3.98E-06	0.0255	0.1177	0.39578	21.30455978	0.006625701
rs10102315	8	12686511	T	C	7.59E-06	0.0246	0.1101	0.49244	20.03108269	0.006059619
rs7865382	9	85380695	T	C	6.03E-06	0.1129	0.5108	0.01286	20.46981385	0.006624475
rs3935950	17	7974179	T	G	3.55E-07	0.1048	0.5337	0.0146	25.93413936	0.008195771
rs28638450	18	44874456	G	A	7.08E-06	0.0352	0.1583	0.14521	20.22443989	0.006220822
rs62143197	19	54320716	A	G	4.79E-09	0.0303	0.1775	0.22311	34.31716934	0.010922078
BECN1										
rs12028627	1	67829890	A	G	8.32E-06	0.0585	0.2607	0.04774	19.85959237	0.006179453
rs34796515	3	22138738	C	T	5.62E-06	0.0347	-0.1574	0.16277	20.57550515	0.006752407
rs62527483	8	141248922	A	G	5.75E-06	0.0909	0.4121	0.01906	20.55310603	0.006350392
rs61871597	10	127156277	C	T	4.79E-06	0.0535	0.2446	0.0581	20.90284217	0.006548229
rs12432766	14	34036007	G	A	5.89E-07	0.0291	0.1452	0.23855	24.8970135	0.007659211
rs8106983	19	23879679	A	G	8.91E-06	0.0299	0.1326	0.25535	19.66729679	0.006686596
rs416255	19	40213503	T	C	3.39E-06	0.0259	-0.1202	0.66566	21.53820009	0.006431018
rs13050833	21	42093041	C	T	6.31E-06	0.0393	0.1774	0.1128	20.37615006	0.006298946
ATG7										
rs10808045	7	140180177	C	T	0.00000263	0.0271	-0.1272	0.61994	22.03107256	0.007624406
rs17084612	4	55533654	A	G	0.00000794	0.072	0.3214	0.03418	19.92630401	0.006820088
rs17260076	9	15978131	G	A	0.0000024	0.0889	-0.4193	0.0239	22.24570649	0.008202985
rs229842	14	83871553	C	T	0.00000617	0.0259	-0.1168	0.38686	20.33696576	0.006471861
rs6072493	20	40478270	T	C	0.000000257	0.0584	0.301	0.05039	26.56484566	0.008670669
rs62248536	3	34344814	T	C	0.00000851	0.1214	0.5401	0.01138	19.79297067	0.006563719
rs9400346	6	110244389	A	G	0.00000204	0.0263	-0.1251	0.65729	22.6257572	0.007050638

ATF6	rs10945552	6	158992610	G	A	3.24E-06	0.0286	-0.1332	0.2728	21.69084063	0.007039417
	rs11875725	18	59557628	C	A	2.40E-06	0.0272	0.1284	0.32753	22.28395329	0.007262465
	rs13107325	4	103188709	T	C	1.35E-06	0.0469	-0.2263	0.07631	23.2821682	0.007219495
	rs1818818	5	162099186	T	C	3.98E-06	0.0286	-0.1321	0.24693	21.33406279	0.006490002
	rs2722176	12	104313943	C	T	1.20E-07	0.0262	0.1385	0.66747	27.94453995	0.008515147
	rs4577047	15	84484166	G	T	7.76E-06	0.0428	0.1916	0.09299	20.04026553	0.006192547
	rs4951597	1	212600327	C	A	5.01E-06	0.0309	-0.1412	0.20257	20.88105487	0.006441204
	rs6089232	20	61082940	T	G	8.51E-09	0.0255	0.1467	0.59664	33.09633218	0.010358465
	rs7431380	3	57450988	G	T	2.82E-06	0.025	-0.1171	0.49787	21.939856	0.006856081
	rs9625595	22	29238913	T	C	4.47E-06	0.0347	0.1591	0.14624	21.02235713	0.006320804
	rs9660390	1	93745535	T	C	2.40E-06	0.0258	0.1217	0.36431	22.25060093	0.006860055
	rs9822805	3	16597814	C	T	6.03E-06	0.0265	0.1197	0.65963	20.40311855	0.006433836
ULK3	rs72964195	2	208691978	T	C	4.17E-06	0.0525	-0.2419	0.06141	21.23015329	0.00674554
	rs10223014	4	116545941	C	T	7.94E-06	0.0253	0.113	0.61964	19.94875721	0.006018956
	rs11760327	7	879301	C	T	9.33E-06	0.0311	0.1378	0.19976	19.63259272	0.006070958
	rs56113811	9	83742030	C	T	4.90E-06	0.028	0.1278	0.27141	20.83270408	0.006459528
	rs2393469	10	60461322	T	C	7.24E-07	0.0314	-0.1557	0.80501	24.58770133	0.007610634
	rs11252949	10	5147208	G	T	9.55E-07	0.0309	-0.1512	0.21417	23.94344425	0.007695216
	rs695821	22	26271505	G	A	5.37E-06	0.0277	0.1262	0.71159	20.75674126	0.006537156
HIF1A	rs10750581	11	134669679	G	A	0.00000407	0.027	0.1242	0.66241	21.16	0.006899056
	rs16831952	1	44864216	G	A	0.00000204	0.1006	-0.4775	0.01613	22.52946041	0.007236838
	rs6506265	18	4945127	G	T	0.00000955	0.0568	-0.2513	0.95119	19.5743931	0.005863961
	rs72821519	17	37096739	T	C	0.00000832	0.0596	-0.2657	0.05015	19.87424271	0.006725724
	rs73147904	7	77105173	T	C	0.00000631	0.0284	0.1285	0.26213	20.4724385	0.006387528
	rs752937	2	67311244	C	T	0.00000269	0.0325	0.1524	0.18114	21.98888521	0.006890075
	rs9791261	6	62284928	C	T	0.000000776	0.0619	0.3059	0.04212	24.42179919	0.007550721
LST1	rs10107851	8	11703002	C	T	9.55E-10	0.0792	0.4843	0.02576	37.39198966	0.011772556
	rs10417813	19	32802077	G	T	0.00000191	0.0249	-0.1188	0.45348	22.76324575	0.006995634
	rs1473794	1	34057453	C	A	0.000000112	0.0313	-0.1663	0.21311	28.22902143	0.009275394
	rs17751216	1	218239234	A	G	0.00000339	0.0872	0.4049	0.0223	21.56068644	0.007148847
	rs2017681	10	21758244	T	C	0.00000891	0.0756	-0.3357	0.02854	19.7178288	0.006249015
	rs56111434	8	30907657	C	T	0.00000676	0.0527	0.2375	0.05988	20.3098164	0.00635071
	rs5762048	22	27661989	T	C	0.00000525	0.0455	0.2071	0.1043	20.71750272	0.008013774
	rs593213	18	75369629	G	A	0.00000295	0.0431	-0.2014	0.09037	21.8355629	0.006668651
	rs706018	7	27138754	G	T	0.00000295	0.0449	-0.2097	0.91807	21.81243645	0.00661524
	rs7217343	17	79113322	C	T	0.000000871	0.0326	0.1602	0.82565	24.14848131	0.007388784
rs9268199	6	32278635	A	G	0.00000331	0.0326	-0.1516	0.82568	21.62535285	0.006615876	

Supplementary Table S3: Summary of the heterogeneity and pleiotropy for MR analysis.

Outcome	Exposure	SNPs	pleiotropy			heterogeneity			
			egger_intercept	se	pval	MR-Egger		IVW	
						Q	Q_pval	Q	Q_pval
ieu-a-832	AKT	5	0.037	0.047	0.485	4.716	0.194	5.711	0.222
	ATF6	12	0.022	0.056	0.693	146.428	2.022E-26*	326.771	1.973E-63*
	ATG7	7	0.030	0.031	0.378	1.272	0.938	2.207	0.900
	BECN1	8	-0.009	0.035	0.793	3.420	0.755	3.495	0.836
	EIF4A3	4	-0.016	0.067	0.832	5.375	0.068	5.532	0.137
	EIF4B	13	-0.014	0.019	0.479	5.977	0.817	6.516	0.837
	EIF4E2	13	-0.007	0.016	0.683	7.503	0.585	7.681	0.660
	EIF4EBP2	13	0.043	0.059	0.489	16.053	0.066	16.983	0.075
	EIF4G3	11	-0.009	0.031	0.782	9.441	0.307	9.537	0.389
	HIF1A	7	0.017	0.048	0.744	8.867	0.114	9.079	0.169
	ULK3	7	-0.015	0.081	0.863	14.559	0.012*	14.656	0.023*
	LST1	10	-0.148	0.172	0.413	390.070	1.798E-78*	421.954	1.990E-84*
	PKC-A	10	-0.001	0.022	0.974	5.799	0.670	5.800	0.760
	RPS6KA	15	0.056	0.036	0.156	36.917	1.192E-5*	48.247	2.296E-7*
GCST90132223	AKT	21	-0.012	0.018	0.523	25.452	0.113	26.051	0.129
	ATF6	34	0.072	0.049	0.153	501.654	3.076E-88*	540.238	1.491E-95*
	ATG7	18	0.024	0.017	0.178	15.982	0.25	18.472	0.186
	BECN1	26	0.012	0.015	0.435	12.813	0.848	13.449	0.857
	EIF4A3	13	0.008	0.012	0.515	9.8	0.367	10.3	0.415
	EIF4B	26	-0.015	0.013	0.252	9.09	0.993	10.472	0.988
	EIF4E2	24	-0.009	0.011	0.428	11.208	0.917	11.864	0.921
	4EBP2	28	-0.014	0.021	0.491	27.14	0.131	27.809	0.146
	EIF4G3	21	0.011	0.022	0.604	28.568	0.018*	29.103	0.023*
	HIF1A	24	0.008	0.015	0.579	16.069	0.519	16.389	0.565
	ULK3	19	-0.009	0.023	0.71	31.575	0.011*	31.857	0.016*
	LST1	24	-0.009	0.067	0.895	582.77	2.172E-111*	583.32	9.354E-111*
	PKC-A	20	0.0002	0.012	0.981	13.3	0.773	13.301	0.823
	RPS6KA	28	0.037	0.02	0.082	49.492	9.005E-05*	58.819	5.940E-06*

\* $p < 0.05$