

Supplementary Table 1. Diseases/traits associated *CDKN2A/2B* SNPs

SNP ID	P.value	Disease/trait
rs662463	1.54E-04	Acute lymphoblastic leukemia
rs17694572	2.18E-04	Acute lymphoblastic leukemia
rs17694493	3.46E-04	Acute lymphoblastic leukemia
rs2811720	6.80E-03	Acute lymphoblastic leukemia
rs7044859	7.60E-03	Acute lymphoblastic leukemia
rs575427	9.02E-03	Acute lymphoblastic leukemia
rs10965215	9.28E-03	Acute lymphoblastic leukemia
rs10965212	1.87E-02	Acute lymphoblastic leukemia
rs10120688	2.23E-02	Acute lymphoblastic leukemia
rs9657608	2.44E-02	Acute lymphoblastic leukemia
rs10965219	3.43E-02	Acute lymphoblastic leukemia
rs717326	4.79E-02	Acute lymphoblastic leukemia
rs1360137	7.81E-02	Acute lymphoblastic leukemia
rs10757270	9.08E-02	Acute lymphoblastic leukemia
rs1590626	0.107733139	Acute lymphoblastic leukemia
rs1329404	0.117974006	Acute lymphoblastic leukemia
rs12352425	0.118752025	Acute lymphoblastic leukemia
rs7868374	0.120045804	Acute lymphoblastic leukemia
rs10738625	0.126334518	Acute lymphoblastic leukemia
rs6475606	0.129891983	Acute lymphoblastic leukemia
rs1333048	0.137058496	Acute lymphoblastic leukemia
rs10757272	0.13793194	Acute lymphoblastic leukemia
rs4977574	0.142278371	Acute lymphoblastic leukemia
rs7853527	0.148797059	Acute lymphoblastic leukemia
rs1333053	0.153790715	Acute lymphoblastic leukemia
rs2383213	0.157418922	Acute lymphoblastic leukemia
rs1333049	0.161026334	Acute lymphoblastic leukemia
rs17761446	0.165805171	Acute lymphoblastic leukemia
rs7856683	0.166994512	Acute lymphoblastic leukemia

rs10113901	0.168181756	Acute lymphoblastic leukemia
rs2891168	0.177607028	Acute lymphoblastic leukemia
rs12555547	0.188065835	Acute lymphoblastic leukemia
rs7864029	0.192668557	Acute lymphoblastic leukemia
rs16923583	0.192668557	Acute lymphoblastic leukemia
rs7851706	0.197244762	Acute lymphoblastic leukemia
rs7872794	0.197244762	Acute lymphoblastic leukemia
rs7039105	0.199523239	Acute lymphoblastic leukemia
rs4977749	0.208575734	Acute lymphoblastic leukemia
rs1333042	0.209700617	Acute lymphoblastic leukemia
rs10965279	0.215303684	Acute lymphoblastic leukemia
rs1329394	0.217535178	Acute lymphoblastic leukemia
rs10965224	0.230813453	Acute lymphoblastic leukemia
rs2518713	0.240655159	Acute lymphoblastic leukemia
rs7024096	0.240655159	Acute lymphoblastic leukemia
rs828580	0.250404141	Acute lymphoblastic leukemia
rs10757321	0.266462416	Acute lymphoblastic leukemia
rs10965256	0.270707072	Acute lymphoblastic leukemia
rs10811668	0.292754185	Acute lymphoblastic leukemia
rs8181047	0.296911134	Acute lymphoblastic leukemia
rs10757283	0.304155164	Acute lymphoblastic leukemia
rs1409776	0.30930635	Acute lymphoblastic leukemia
rs1327045	0.315463211	Acute lymphoblastic leukemia
rs10757308	0.336813465	Acute lymphoblastic leukemia
rs7850937	0.337822818	Acute lymphoblastic leukemia
rs7864275	0.33983961	Acute lymphoblastic leukemia
rs1679014	0.377706214	Acute lymphoblastic leukemia
rs2383216	0.386558473	Acute lymphoblastic leukemia
rs12003027	0.393415377	Acute lymphoblastic leukemia
rs7851133	0.396346718	Acute lymphoblastic leukemia
rs3731194	0.396346718	Acute lymphoblastic leukemia
rs2383209	0.405115096	Acute lymphoblastic leukemia

rs1410979	0.418681225	Acute lymphoblastic leukemia
rs2891170	0.421577038	Acute lymphoblastic leukemia
rs6475641	0.434081753	Acute lymphoblastic leukemia
rs7045889	0.443654071	Acute lymphoblastic leukemia
rs505447	0.456040347	Acute lymphoblastic leukemia
rs4478654	0.456990522	Acute lymphoblastic leukemia
rs7863846	0.465525795	Acute lymphoblastic leukemia
rs4977761	0.470255188	Acute lymphoblastic leukemia
rs3903983	0.481570747	Acute lymphoblastic leukemia
rs10811688	0.482511533	Acute lymphoblastic leukemia
rs4977772	0.486271402	Acute lymphoblastic leukemia
rs1575964	0.495648583	Acute lymphoblastic leukemia
rs10811685	0.499390666	Acute lymphoblastic leukemia
rs1410976	0.503127841	Acute lymphoblastic leukemia
rs1333051	0.511518923	Acute lymphoblastic leukemia
rs10121530	0.513380368	Acute lymphoblastic leukemia
rs10811687	0.520814645	Acute lymphoblastic leukemia
rs1327046	0.521742653	Acute lymphoblastic leukemia
rs510901	0.526378514	Acute lymphoblastic leukemia
rs7871143	0.529156724	Acute lymphoblastic leukemia
rs1359740	0.539322765	Acute lymphoblastic leukemia
rs16906084	0.551296558	Acute lymphoblastic leukemia
rs3218022	0.584241245	Acute lymphoblastic leukemia
rs2811710	0.594249505	Acute lymphoblastic leukemia
rs7869004	0.603325881	Acute lymphoblastic leukemia
rs10811659	0.605138707	Acute lymphoblastic leukemia
rs12341394	0.620515886	Acute lymphoblastic leukemia
rs10965290	0.621418694	Acute lymphoblastic leukemia
rs564398	0.623223747	Acute lymphoblastic leukemia
rs6475620	0.625028053	Acute lymphoblastic leukemia
rs2188126	0.633138335	Acute lymphoblastic leukemia
rs2891169	0.641234091	Acute lymphoblastic leukemia

rs3935920	0.64392953	Acute lymphoblastic leukemia
rs10733377	0.661860456	Acute lymphoblastic leukemia
rs7042832	0.674373874	Acute lymphoblastic leukemia
rs10965267	0.679727598	Acute lymphoblastic leukemia
rs7047631	0.693978493	Acute lymphoblastic leukemia
rs9406787	0.699313276	Acute lymphoblastic leukemia
rs693370	0.709081082	Acute lymphoblastic leukemia
rs1547704	0.718833129	Acute lymphoblastic leukemia
rs1537377	0.74358996	Acute lymphoblastic leukemia
rs10757292	0.744472459	Acute lymphoblastic leukemia
rs6475619	0.747119293	Acute lymphoblastic leukemia
rs3218003	0.796359402	Acute lymphoblastic leukemia
rs10965266	0.805122136	Acute lymphoblastic leukemia
rs1359739	0.805122136	Acute lymphoblastic leukemia
rs4977736	0.806873702	Acute lymphoblastic leukemia
rs7018475	0.832237114	Acute lymphoblastic leukemia
rs16905988	0.852311551	Acute lymphoblastic leukemia
rs3802394	0.853183604	Acute lymphoblastic leukemia
rs518394	0.85579941	Acute lymphoblastic leukemia
rs1679023	0.856671229	Acute lymphoblastic leukemia
rs523096	0.85928634	Acute lymphoblastic leukemia
rs11791416	0.864515045	Acute lymphoblastic leukemia
rs10965245	0.869741793	Acute lymphoblastic leukemia
rs10811661	0.870612733	Acute lymphoblastic leukemia
rs7022662	0.872354458	Acute lymphoblastic leukemia
rs7865618	0.873225243	Acute lymphoblastic leukemia
rs4545183	0.881060078	Acute lymphoblastic leukemia
rs10120722	0.894109733	Acute lymphoblastic leukemia
rs4977569	0.921918917	Acute lymphoblastic leukemia
rs10757282	0.932338632	Acute lymphoblastic leukemia
rs10965278	0.979188582	Acute lymphoblastic leukemia
rs944031	0.983524524	Acute lymphoblastic leukemia

rs7024703	0.99826578	Acute lymphoblastic leukemia
rs116150891	NA	Acute lymphoblastic leukemia
rs146179135	0.653	Acute lymphoblastic leukemia
rs45456595	0.107	Acute lymphoblastic leukemia
rs7865618	0.447	Acute lymphoblastic leukemia
rs1011970	0.0308	Acute lymphoblastic leukemia
rs1333040	0.782	Acute lymphoblastic leukemia
rs4977574	0.41	Acute lymphoblastic leukemia
rs10965235	0.551	Acute lymphoblastic leukemia
rs2383207	0.102	Acute lymphoblastic leukemia
rs3731217	2.00E-08	Acute lymphoblastic leukemia
rs17756311	1.40E-05	Acute lymphoblastic leukemia
rs7033598	8.00E-26	Macular thickness
rs970987	3.00E-12	Autoimmune traits
rs970987	6.00E-17	Hypothyroidism
rs970987	2.00E-16	Medication use (thyroid preparations)
rs116945318	8.00E-06	Refractive astigmatism
rs7868228	3.00E-06	Gut microbiome composition (winter)
rs12686364	6.00E-09	Familial squamous cell lung carcinoma
rs184042824	2.00E-06	Time to smoke first cigarette in the morning
rs11999970	5.00E-07	Pediatric bone mineral content (radius)
rs7035284	1.00E-08	Pediatric bone mineral content (radius)
rs896655	2.00E-12	Coronary artery disease
rs2004627	7.00E-06	Interleukin-6 levels
rs12336169	2.00E-06	Lung cancer in never smokers
rs10811609	2.00E-06	Lung cancer
rs4636294	3.00E-15	Cutaneous nevi
rs11496368	4.00E-06	Familial lung adenocarcinoma
rs17755650	6.00E-06	Diastolic blood pressure response to hydrochlorothiazide in hypertension
rs10429489	8.00E-06	Non-small cell lung cancer
rs10429489	5.00E-07	Lung adenocarcinoma
rs10429489	7.00E-10	Non-small cell lung cancer

rs4364717	1.00E-10	Diastolic blood pressure
rs871024	3.00E-65	Cutaneous malignant melanoma
rs869330	6.00E-113	Nevus count or cutaneous melanoma
rs869329	7.00E-67	Nevus count or cutaneous melanoma
rs869329	2.00E-37	Nevus count
rs201131773	3.00E-17	Melanoma
rs7023329	4.00E-07	Melanoma
rs7023329	7.00E-09	Melanoma
rs7023329	7.00E-09	Melanoma
rs885518	1.00E-09	Lung adenocarcinoma
rs11532907	2.00E-34	Nevus count or cutaneous melanoma
rs67134687	7.00E-07	Adverse response to drug
rs7026112	9.00E-06	Lung cancer
rs185224597	2.00E-07	Lung function in heavy smokers (low FEV1 vs high FEV1)
rs10811635	9.00E-06	Depressive symptoms x dependent stressful life events interaction (2df test)
rs142754775	4.00E-06	Coronary artery calcified atherosclerotic plaque (130 HU threshold) in type 2 diabetes
rs12349081	6.00E-06	Cancer
rs145542470	6.00E-10	Coronary artery disease
rs2027939	3.00E-09	Cutaneous malignant melanoma
rs3057314	7.00E-25	Breast cancer
rs3731257	5.00E-08	Inflammatory bowel disease
rs3731249	1.00E-27	Acute lymphoblastic leukemia in childhood (B cell precursor)
rs3731239	1.00E-06	Nasopharyngeal carcinoma
rs113650570	8.00E-35	B-cell acute lymphoblastic leukaemia
rs3731217	2.00E-08	Acute lymphoblastic leukemia (B-cell precursor)
rs3731217	7.00E-14	Acute lymphoblastic leukemia in childhood (B cell precursor)
rs3731211	6.00E-14	Platelet count
rs3731211	5.00E-24	Platelet count
rs3731211	6.00E-29	Plateletcrit
rs3731211	6.00E-13	Monocyte count
rs3731211	4.00E-23	Lymphocyte counts
rs3731211	3.00E-13	Red cell distribution width

rs3731211	3.00E-15	Eosinophil counts
rs7036656	3.00E-12	White blood cell count
rs7036656	8.00E-37	White blood cell count
rs2811710	2.00E-13	Multiple myeloma
rs55797833	3.00E-19	Cutaneous malignant melanoma
rs78545330	3.00E-06	BRCA1/2-negative high-risk breast cancer
rs61271866	7.00E-07	Esophageal squamous cell carcinoma
rs35720900	4.00E-09	White matter microstructure (radial diffusivities)
rs3217992	4.00E-06	Psychosis proneness (hypomanic personality scale and revised social anhedonia scale)
rs3217992	7.00E-07	Psychosis proneness (hypomanic personality scale)
rs3217992	4.00E-06	Psychosis proneness (hypomanic personality scale and perceptual aberration scale)
rs3217992	4.00E-06	Psychosis proneness (hypomanic personality scale and revised physical anhedonia scale)
rs1063192	5.00E-11	Glaucoma (primary open-angle)
rs1063192	4.00E-15	Vertical cup-disc ratio
rs1063192	8.00E-07	Nasopharyngeal carcinoma
rs1063192	3.00E-18	Type 2 diabetes
rs3217986	4.00E-22	Cutaneous malignant melanoma
rs2069426	4.00E-09	Acute lymphoblastic leukemia (childhood)
rs3217978	2.00E-10	Coronary artery disease
rs2069418	5.00E-10	White matter microstructure (fractional anisotropy)
rs2069416	3.00E-08	White matter microstructure (radial diffusivities)
rs79356439	9.00E-13	Cutaneous malignant melanoma
rs1101330	9.00E-09	White matter microstructure (mean diffusivities)
rs523096	5.00E-11	Glaucoma
rs518394	2.00E-10	White matter microstructure (radial diffusivities)
rs615552	4.00E-06	Migraine without aura
rs62560774	7.00E-09	White matter microstructure (fractional anisotropy)
rs564398	1.00E-06	Type 2 diabetes
rs564398	2.00E-07	Coronary heart disease
rs7865618	9.00E-11	Glaucoma (primary open-angle)
rs7865618	1.00E-21	Optic cup area
rs7865618	9.00E-20	Optic cup area

rs7865618	2.00E-27	Coronary heart disease
rs7865618	5.00E-24	Vertical cup-disc ratio
rs634537	1.00E-15	Non-glioblastoma glioma
rs634537	1.00E-45	Glioma
rs634537	7.00E-45	Glioblastoma
rs634537	2.00E-21	Glioma
rs634537	7.00E-14	Glioma
rs634537	1.00E-20	Glioblastoma
rs634537	2.00E-16	Glioblastoma
rs634537	3.00E-08	Non-glioblastoma glioma
rs634537	4.00E-19	Glioblastoma (age-stratified)
rs634537	3.00E-15	Glioblastoma (age-stratified)
rs634537	1.00E-16	Glioblastoma (age-stratified)
rs2157719	1.00E-12	Glaucoma (primary open-angle)
rs2157719	2.00E-18	Glaucoma (primary open-angle)
rs2157719	5.00E-16	Glioma
rs2157719	2.00E-11	Non-glioblastoma glioma
rs2157719	3.00E-17	Glioma
rs2157719	6.00E-33	Vertical cup-disc ratio
rs2157719	4.00E-35	Vertical cup-disc ratio
rs2157719	3.00E-33	Glaucoma (primary open-angle)
rs2151280	3.00E-10	Basal cell carcinoma
rs2151280	9.00E-11	Basal cell carcinoma
rs1333037	1.00E-12	Glaucoma (low intraocular pressure)
rs1333037	2.00E-23	Glaucoma (primary open-angle)
rs17694493	4.00E-08	Prostate cancer
rs17694493	1.00E-06	Prostate cancer
rs17694493	2.00E-10	Prostate cancer
rs17694493	1.00E-06	Adolescent idiopathic scoliosis
rs1412830	9.00E-08	Type 2 diabetes
rs1412829	2.00E-10	Glioma (high-grade)
rs1412829	5.00E-07	Nasopharyngeal carcinoma

rs1412829	3.00E-08	Nasopharyngeal carcinoma
rs1360589	3.00E-28	Optic cup area
rs1360589	3.00E-27	Optic cup area
rs1360589	5.00E-30	Vertical cup-disc ratio
rs1360589	1.00E-31	Optic cup area
rs1360589	2.00E-13	Medication use (antiglaucoma preparations and miotics)
rs10738605	6.00E-10	Non-melanoma skin cancer
rs10811645	1.00E-18	Glaucoma (primary open-angle)
rs944800	4.00E-14	Glaucoma (primary open-angle)
rs944800	3.00E-09	White matter microstructure (radial diffusivities)
rs944801	1.00E-11	Type 2 diabetes
rs944801	5.00E-91	Vertical cup-disc ratio (multi-trait analysis)
rs944801	2.00E-38	Glaucoma (multi-trait analysis)
rs944801	3.00E-21	Glaucoma
rs944801	2.00E-49	Glaucoma (primary open-angle)
rs944801	8.00E-36	Glaucoma
rs62560775	2.00E-09	Lung adenocarcinoma
rs62560775	6.00E-07	Lung cancer
rs6475604	3.00E-15	Glaucoma
rs7874604	6.00E-27	Keratinocyte cancer (MTAG)
rs7874604	4.00E-36	Basal cell carcinoma
rs7874604	5.00E-13	Basal cell carcinoma
rs7039467	2.00E-07	Longevity (age >99th survival percentile)
rs7039467	3.00E-54	Vertical cup-disc ratio (multi-trait analysis)
rs7039467	2.00E-37	Vertical cup-disc ratio (adjusted for vertical disc diameter)
rs7866783	4.00E-08	Glaucoma (primary open-angle)
rs7866783	5.00E-64	Vertical cup-disc ratio (adjusted for vertical disc diameter)
rs10120688	1.00E-08	White matter microstructure (mean diffusivities)
rs10120688	1.00E-08	White matter microstructure (radial diffusivities)
rs10120688	2.00E-12	White matter microstructure (radial diffusivities)
rs10120688	1.00E-08	White matter microstructure (mean diffusivities)
rs10120688	5.00E-12	White matter microstructure (fractional anisotropy)

rs1011970	3.00E-08	Breast cancer
rs1011970	6.00E-08	Breast cancer
rs1011970	2.00E-06	Breast cancer (estrogen-receptor negative)
rs1011970	5.00E-06	Cancer (pleiotropy)
rs1011970	2.00E-07	Cancer
rs1011970	5.00E-07	Breast cancer (estrogen-receptor negative)
rs1011970	1.00E-15	Breast cancer
rs1011970	4.00E-09	Breast cancer
rs8181047	4.00E-09	Oral cavity cancer
rs145929329	5.00E-12	Glioblastoma
rs10811650	2.00E-13	Breast cancer
rs10811650	2.00E-18	Cutaneous melanoma or hair colour
rs10811650	2.00E-15	Hair color
rs75883022	7.00E-13	Cutaneous malignant melanoma
rs4977756	7.00E-15	Glioma
rs4977756	1.00E-08	Glioma
rs4977756	1.00E-14	Glaucoma
rs4977756	7.00E-30	Glaucoma (primary open-angle)
rs4977756	7.00E-07	Nasopharyngeal carcinoma
rs4645630	2.00E-08	Macular thickness
rs10757269	9.00E-09	Ankle-brachial index
rs9632884	5.00E-12	Carotid plaque
rs1831733	4.00E-18	Medication use (antithrombotic agents)
rs1831733	9.00E-09	Medication use (salicylic acid and derivatives)
rs10811652	6.00E-11	Coronary artery disease in diabetes
rs6475606	4.00E-08	Intracranial aneurysm
rs6475606	2.00E-22	LDL cholesterol levels
rs6475606	6.00E-17	Apolipoprotein B levels
rs1333040	2.00E-22	Intracranial aneurysm
rs1333040	1.00E-10	Intracranial aneurysm
rs1333040	7.00E-07	Squamous cell lung carcinoma
rs1333040	3.00E-06	Interleukin-6 levels

rs1537370	2.00E-11	Coronary artery calcification
rs10738607	2.00E-13	Coronary artery disease
rs10738607	7.00E-13	Myocardial infarction
rs10738607	2.00E-09	Total cholesterol levels
rs10757272	2.00E-07	Intracranial aneurysm
rs10757272	3.00E-07	Endometriosis
rs10757272	6.00E-06	Endometriosis
rs9644861	5.00E-08	Diastolic blood pressure
rs9644862	9.00E-12	Carotid plaque burden
rs7866503	2.00E-13	Intracranial, abdominal aortic or thoracic aortic aneurysm (pleiotropy)
rs10757274	8.00E-45	Coronary heart disease
rs10757274	2.00E-33	Abdominal aortic aneurysm
rs4977574	5.00E-14	Coronary artery disease
rs4977574	3.00E-44	Myocardial infarction (early onset)
rs4977574	1.00E-22	Coronary heart disease
rs4977574	2.00E-25	Coronary heart disease
rs4977574	8.00E-06	Myocardial infarction
rs4977574	9.00E-223	Coronary artery disease
rs4977574	1.00E-07	Coronary artery disease
rs2891168	2.00E-98	Coronary artery disease
rs2891168	5.00E-75	Myocardial infarction
rs2891168	1.00E-101	Coronary artery disease (myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, angina or chronic ischemic heart disease)
rs2891168	5.00E-204	Coronary artery disease
rs2891168	4.00E-18	Medication use (beta blocking agents)
rs1537371	3.00E-25	Medication use (HMG CoA reductase inhibitors)
rs1556516	5.00E-16	Parental longevity (combined parental attained age, Martingale residuals)
rs1556516	7.00E-09	Parental longevity (father's age at death)
rs1556516	1.00E-20	Parental longevity (father's attained age)
rs1556516	2.00E-10	Parental longevity (combined parental age at death)
rs1556516	2.00E-15	Heart failure
rs1556516	7.00E-11	Parental lifespan

rs7859727	4.00E-10	Stroke
rs7859727	2.00E-07	Ischemic stroke
rs7859727	7.00E-08	Stroke
rs7859727	1.00E-09	Ischemic stroke
rs7859727	3.00E-10	Healthspan
rs1537372	1.00E-08	Colorectal cancer or advanced adenoma
rs1537372	4.00E-39	Peripheral artery disease
rs1537373	4.00E-11	Coronary artery calcification
rs1537373	7.00E-07	Coronary artery calcification
rs1333042	1.00E-09	Coronary heart disease
rs1333042	3.00E-07	Parental longevity (mother's age at death or mother's attained age)
rs1333042	7.00E-15	Parental longevity (father's age at death)
rs1333042	2.00E-08	Parental longevity (both parents in top 10%)
rs1333042	2.00E-72	Coronary artery disease
rs1412834	4.00E-14	Colorectal cancer
rs10733376	4.00E-12	Intracranial aneurysm
rs10965235	6.00E-12	Endometriosis
rs944797	6.00E-16	Coronary heart disease
rs2383207	2.00E-08	Abdominal aortic aneurysm
rs1333045	6.00E-06	Parental longevity (mother's age at death)
rs1333045	8.00E-09	Minimum ankle-brachial index
rs1333045	3.00E-12	Pulse pressure
rs1333045	3.00E-07	Serum total cholesterol levels
rs1333045	1.00E-09	Systolic blood pressure
rs10217586	2.00E-06	Colorectal or endometrial cancer
rs10217586	1.00E-17	Medication use (agents acting on the renin-angiotensin system)
rs10757278	1.00E-20	Myocardial infarction
rs1333047	2.00E-07	Large artery stroke
rs1333047	2.00E-10	Pulse pressure
rs1333047	5.00E-08	Hypertension
rs1333047	5.00E-18	Medication use (vasodilators used in cardiac diseases)
rs4977575	1.00E-07	Pulse pressure

rs4977575	5.00E-23	Coronary artery disease
rs1333048	1.00E-06	Age-related diseases and mortality
rs1333049	1.00E-13	Coronary heart disease
rs1333049	3.00E-19	Coronary heart disease
rs1333049	3.00E-24	Coronary artery calcification
rs1333049	1.00E-59	Coronary artery disease or large artery stroke
rs1333049	1.00E-56	Coronary artery disease or ischemic stroke
rs1333049	3.00E-56	Coronary artery disease
rs1333049	7.00E-58	Coronary heart disease
rs1333049	9.00E-08	Age-related diseases, mortality and associated endophenotypes
rs1333049	1.00E-25	Coronary artery disease
rs1333049	2.00E-192	Coronary artery disease
rs7020996	2.00E-07	Type 2 diabetes
rs7020996	6.00E-18	Body mass index
rs10965243	1.00E-15	Hemoglobin A1c levels
rs10965245	7.00E-07	Hematological and biochemical traits
rs2383208	2.00E-29	Type 2 diabetes
rs2383208	3.00E-06	Type 2 diabetes
rs2383208	5.00E-33	Type 2 diabetes
rs2383208	3.00E-17	Type 2 diabetes
rs2383208	7.00E-12	Glycated hemoglobin levels
rs10965246	2.00E-16	Blood sugar levels
rs10965246	7.00E-21	Medication use (drugs used in diabetes)
rs10965247	1.00E-87	Type 2 diabetes
rs10965248	4.00E-164	Type 2 diabetes
rs10965250	1.00E-10	Type 2 diabetes
rs10965250	6.00E-16	Type 2 diabetes
rs10965250	9.00E-15	Type 2 diabetes
rs10965250	4.00E-07	Multiple sclerosis
rs10965250	7.00E-07	Type 2 diabetes
rs76011118	1.00E-07	Type 2 diabetes
rs10811660	1.00E-115	Type 2 diabetes

rs10811660	3.00E-31	Type 2 diabetes
rs10811661	5.00E-06	Type 2 diabetes
rs10811661	8.00E-15	Type 2 diabetes
rs10811661	8.00E-15	Type 2 diabetes
rs10811661	7.00E-07	Type 2 diabetes
rs10811661	1.00E-18	Type 2 diabetes
rs10811661	9.00E-12	Fasting plasma glucose
rs10811661	1.00E-06	Fasting blood glucose
rs10811661	7.00E-06	Fasting blood glucose (BMI interaction)
rs10811661	1.00E-27	Type 2 diabetes
rs10811661	4.00E-27	Type 2 diabetes
rs10811661	5.00E-13	Body mass index
rs10811661	1.00E-30	Type 2 diabetes
rs10811661	2.00E-10	Type 2 diabetes
rs10811661	2.00E-68	Type 2 diabetes
rs10811661	9.00E-11	Type 2 diabetes
rs10811661	1.00E-09	Type 2 diabetes
rs10811661	4.00E-58	Type 2 diabetes
rs10811661	2.00E-07	Fasting blood glucose
rs10757283	2.00E-41	Type 2 diabetes
rs10811662	1.00E-13	Type 2 diabetes
rs10811662	6.00E-09	Triglyceride levels
rs1333051	6.00E-10	Type 2 diabetes
rs7018475	3.00E-08	Type 2 diabetes
rs7018475	5.00E-06	Glucose homeostasis traits
rs7018475	1.00E-08	Hemoglobin A1c levels
rs7018475	5.00E-14	Medication use (drugs used in diabetes)
rs2065504	3.00E-09	Monocyte percentage of white cells
rs10811664	2.00E-31	Platelet count
rs10757287	4.00E-10	Granulocyte percentage of myeloid white cells
rs10757287	8.00E-19	Platelet count
rs2065500	1.00E-10	Neutrophil percentage of white cells

rs6475611	1.00E-36	Plateletcrit
rs6475611	3.00E-21	Monocyte count
rs6475611	3.00E-25	Lymphocyte counts
rs6475611	9.00E-11	Red cell distribution width
rs6475611	2.00E-27	White blood cell count
rs944802	2.00E-11	White blood cell count
rs137893140	8.00E-07	Type 2 diabetes
rs1333052	6.00E-07	Type 2 diabetes
rs12238587	9.00E-16	Height
rs72658409	1.00E-10	Lung cancer
rs72658409	2.00E-09	Adenocarcinoma
rs7864275	9.00E-06	Trauma exposure in major depressive disorder-negative individuals
rs7041895	1.00E-07	Deep ovarian and/or rectovaginal disease with dense adhesions
rs7041895	4.00E-16	Monocyte count
rs17694933	2.00E-12	White blood cell count
rs1333054	5.00E-17	Lymphocyte counts
rs1537377	2.00E-09	Endometriosis
rs1537377	1.00E-10	Endometriosis
rs1537377	2.00E-08	Endometriosis
rs861189	8.00E-06	Exploratory eye movement dysfunction in schizophrenia (responsive search score)
rs861189	3.00E-06	Exploratory eye movement dysfunction in schizophrenia (number of eye fixations)
rs1679013	1.00E-08	Chronic lymphocytic leukemia
rs1679013	2.00E-08	Chronic lymphocytic leukemia
rs1679013	1.00E-14	Cataracts (operation)
rs1679014	4.00E-06	Endometrial cancer (endometrioid histology)
rs1679014	6.00E-09	Endometrial cancer
rs1575972	2.00E-09	Type 2 diabetes
rs1575972	6.00E-15	Type 2 diabetes
rs1575972	3.00E-07	Type 2 diabetes
rs1575972	5.00E-13	Type 2 diabetes
rs1359742	7.00E-09	Chronic lymphocytic leukemia
rs961831	7.00E-06	Personality dimensions

rs10738626	1.00E-08	Atopic dermatitis
rs34254072	3.00E-09	Brain region volumes
rs1999124	3.00E-15	Adolescent idiopathic scoliosis
rs586716	8.00E-06	Tuberculosis
rs1032687	5.00E-08	Educational attainment (years of education)
rs62572328	8.00E-09	Lung function (FVC)
rs10811723	3.00E-11	Number of decayed, missing and filled tooth surfaces or use of dentures
rs10811723	2.00E-11	Dentures
rs1499555	1.00E-06	Crohn's disease (indolent vs progressive)
rs34864022	1.00E-06	Driving (hours per day)
rs34864022	1.00E-09	Leisure sedentary behaviour (television watching)
rs1448792	2.00E-07	Endometriosis
rs1448792	1.00E-07	Endometriosis
rs1020463	3.00E-06	Hip circumference
rs2210865	2.00E-06	Post bronchodilator FEV1/FVC ratio in smoking
rs613391	5.00E-06	Quantitative traits
rs687184	2.00E-07	Moderate-to-late spontaneous preterm birth
rs9695226	4.00E-07	Schizophrenia
rs9695226	2.00E-07	Schizophrenia
rs9695226	7.00E-08	Schizophrenia
rs9695226	9.00E-08	Schizophrenia
rs10811771	8.00E-07	Response to antipsychotic therapy (extrapyramidal side effects)
rs10811772	2.00E-06	Metabolite levels
rs7852363	2.00E-09	Subclinical trait of interstitial lung disease (basilar peel-core ratio of high attenuation areas on CT scan)
rs1823289	1.00E-09	Refractive error
rs7031401	6.00E-06	Periodontitis
rs7849973	8.00E-06	Autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder, and schizophrenia (combined)
rs12554707	2.00E-06	Response to amphetamines
rs760063500	7.00E-06	Trunk fat mass
rs13286845	4.00E-09	Adventurousness
rs13286845	4.00E-08	General risk tolerance (MTAG)
rs13286845	4.00E-08	Systolic blood pressure

rs9886665	3.00E-09	Systolic blood pressure
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Supplementary Table 2. CDKN2A coding mutations in GWCMC cohorts based on CCCG-ALL-2015 protocol

	SNP ID	Chr	Position*	Ref	Alt	Nucleotide alternation	Amino Acid Change	Variant type	# Patients	Allele frequency (%)
CDKN2A:p16 ^{INK4A} NM_000077	rs764362225	9	21974777	C	A	c. 51C>A	p. Ala17Ala	silent	1	0.3
	-	9	21974766	C	T	c. 62C>T	p. Ala21Val	missense	1	0.3
	rs1328708469	9	21974695	G	C	c. 133G>C	p. Gly45Arg	missense	1	0.3
	rs762397298	9	21971134	C	G	c. 225C>G	p. Pro75Pro	silent	1	0.3
	-	9	21971016	G	T	c. 343G>T	p. Val115Leu	missense	1	0.3
	-	9	21970972	C	A	c. 387C>A	p. Ser129X	missense	1	0.3
CDKN2A:p14 ^{ARF} NM_058195	-	9	21994240	C	G	c. 92C>G	p. Thr31Arg	missense	2	0.6
	-	9	21994164	G	A	c. 168G>A	p. Gly56Gly	silent	1	0.3
	rs762397298	9	21971134	C	G	c. 268C>G	p. Arg90Gly	missense	1	0.3
	-	9	21971016	G	T	c. 386G>T	p. Arg129Leu	missense	1	0.3
CDKN2A:smARF NM_058195	-	9	21971016	G	T	c. 245G>T	p. Arg82Leu	missense	1	0.3

Supplementary Table 3. Summary of current clinical trials of CDK4/6 inhibitors for R/R-ALL treatment

Study Identifier	Study Name	Interventions	Age Population	Outcome Measures	Phases	Enrollment	Locations	Study Start	Estimated Completion	Status
NCT03472573	Palbociclib and Dexamethasone in Treating Participants With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia	Palbociclib , Dexamethasone	>=18 years old	Safety, DLT	Phase I	24	USA	2018	2022	Recruiting
NCT03515200	Treatment With Combination Chemotherapy for Relapsed or Refractory Acute Lymphoblastic Leukemia	Palbociclib , Bortezomib, <i>et al</i>	<=21 years old	Safety, efficacy	Phase I	12	USA	2018	2020	Terminated
NCT02310243	Study of Palbociclib in MLL-rearranged Acute Leukemias	Palbociclib	>=18 years old	Safety, DLT	Phase I, II	50	Germany	2015	2019	Recruiting
NCT03792256	Palbociclib in Combination With Chemotherapy in Treating Children With Relapsed Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LL)	Palbociclib , Cytarabine, <i>et al</i>	1-31 years old	Safety, DLT	Phase I	15	USA	2019	2021	Recruiting
NCT03132454	Palbociclib and Sorafenib, Decitabine, or Dexamethasone in Treating Patients With Recurrent or Refractory Leukemia	Palbociclib , Decitabine, <i>et al</i>	>=15 years old	Safety, DLT	Phase I	54	USA	2017	2021	Recruiting
NCT03878524	Serial Measurements of Molecular and Architectural Responses to Therapy (SMMART) PRIME Trial	Palbociclib , Abemaciclib , <i>et al</i>	>=21 years old	Safety, efficacy	Phase I	40	USA	2020	2025	Recruiting
NCT03740334	Ribociclib in Combination With Everolimus and Dexamethasone in Relapsed ALL	Ribociclib , Dexamethasone, <i>et al</i>	1-30 years old	Safety, DLT	Phase I	45	USA	2019	2023	Recruiting

Supplementary Table 4. List of primers used in the study

Primer Name	Primer sequence 5'–3'
CDKN2A PCR primers	
CDKN2A Exon1 forward	GCTGCCTGGAGTTGCGTTC
CDKN2A Exon1 reverse	TGTAACCCGAATGGGAAGC
CDKN2A Exon2 forward	AACGCACTCAAACACGCCT
CDKN2A Exon2 reverse	GAGAATCGAAGCGCTACCTGA
CDKN2A Exon3 forward	GACGACAGCTCCGCAGAAGTT
CDKN2A Exon3 reverse	GGCTGAACTTCTGTGCTGGAA
CDKN2A Exon4 forward	GTGAAGCCATTGCGAGAACTT
CDKN2A Exon4 reverse	TCGATCTTGAGACACGGCTTTT
Sanger Sequencing primers	
CDKN2A Exon1	GCTGCCTGGAGTTGCGTTC
CDKN2A Exon2	AACGCACTCAAACACGCCT
CDKN2A Exon3	GACGACAGCTCCGCAGAAGTT
CDKN2A Exon4	GTGAAGCCATTGCGAGAACTT
Primers for Site-Directed Mutagenesis Substitution	
c120c-p16INK4A-A21V-IRES-GFP-F	ACGGCCGCGGtCCGGGGTCGG
c120c-p16INK4A-A21V-IRES-GFP-R	GGCCAGCCAGTCAGCCGAAGGCTCC
c120c-p16INK4A-A36V-IRES-GFP-F	GAGGCGGGGGtGCTGCCCAAC
c120c-p16INK4A-A36V-IRES-GFP-R	CAGCAGCGCCCGCACCTC
c120c-p16INK4A-G45A-IRES-GFP-F	GAATAGTTACcGTCGGAGGCCGATCCAGGTCATG
c120c-p16INK4A-G45A-IRES-GFP-R	GGTGCCTTGGCAGCGCC
c120c-p16INK4A-A57V-IRES-GFP-F	ATGGGCAGCGtCCGAGTGGCG
c120c-p16INK4A-A57V-IRES-GFP-R	CATCATGACCTGGATCGGCCTCCG
c120c-p16INK4A-R99Q-IRES-GFP-F	GTGCTGCACCgGGCCGGGGCG
c120c-p16INK4A-R99Q-IRES-GFP-R	CACCAGCGTGTCCAGGAAGCC
c120c-p16INK4A-V115L-IRES-GFP-F	CCGTCTGCCCtTGGACCTGGC
c120c-p16INK4A-V115L-IRES-GFP-R	CCCCAGGCATCGCGCACG
c120c-p16INK4A-D125H-IRES-GFP-F	GGGCCATCGCtATGTCGCACG
c120c-p16INK4A-D125H-IRES-GFP-R	AGTCTCTCAGCCAGGTCC

c120c-p16INK4A-A127S-IRES-GFP-F	TCGCGATGTCtCACGGTACCTGC
c120c-p16INK4A-A127S-IRES-GFP-R	TGGCCCAGCTCCTCAGCC
c120c-p16INK4A-S129X-IRES-GFP-F	TCGCACGGTAaCTGCGCGCGG
c120c-p16INK4A-S129X-IRES-GFP-R	CATCGCGATGGCCCAGCTCC
c120c-p16INK4A-R138G-IRES-GFP-F	GGGGGGCACCgGAGGCAGTAAC
c120c-p16INK4A-R138G-IRES-GFP-R	GCAGCCGCGCGCAGGTAC
c120c-p16INK4A-H142R-IRES-GFP-F	GGCAGTAACCgTGCCCGCATAGATGC
c120c-p16INK4A-H142R-IRES-GFP-R	TCTGGTGCCCCCGCAGC
c120c-p16INK4A-A143T-IRES-GFP-F	CAGTAACCATaCCCGCATAGATGCCGC
c120c-p16INK4A-A143T-IRES-GFP-R	CCTCTGGTGCCCCCGCA
c120c-p16INK4A-A148T-IRES-GFP-F	CATAGATGCCaCGGAAGGTCCC
c120c-p16INK4A-A148T-IRES-GFP-R	CGGGCATGGTTACTGCCT

Supplementary Table 5. Reagents used in this study

Product Name	Supplier	LOT number
Propidium Iodide Flow Cytometry Kit	Abcam	ab139418
CloneAmp HiFi PCR Premix	Clontech	639298
CCK8 kit	DOJINDO	CK04
Q5 Site-Directed Mutagenesis Kit	NEB	E0552S
Recombinant Murine IL-3	PeproTech	213-13
Lipofectamine™ 3000 Transfection Reagent	Thermofisher	L3000015
Palbociclib	Selleck	S1116
Ribociclib	TargetMol	T6199
Abemaciclib	TargetMol	T2381
alpha Tubulin Mouse Monoclonal Antibody	Proteintech	66031-1
CDKN2A/p16INK4a antibody [EPR1473]	Abcam	ab108349
p16 INK4A (D3W8G) Rabbit mAb	CST	92803S
GFP (D5.1) XP® Rabbit mAb	CST	2956S
Bcr Antibody	CST	3902S
CDK6 (DCS83) Mouse mAb	CST	3136S
Phospho-CDK4 (Thr172) Polyclonal Antibody	Thermofisher	PA564482
Anti-Cdk4 antibody	Abcam	ab137675
Recombinant Anti-Rb antibody [EPR17512]	Abcam	ab181616
Phospho Rb (S811) antibody [EPR224]	Abcam	ab109399
Recombinant Anti-E2F2 antibody [EPR8622]	Abcam	ab138515