PRECISE-SG100K Flagship Projects

S/N	Project Title	Team	Aims of Project
1	The SG100K cognitive health programme Topic: Mental Health	Lead PI: Dr Max Lam, Lee Kong Chian School of Medicine, Institute of Mental Health Co-Lead PI: Dr Jimmy Lee, Institute of Mental Health Co-Lead PI: Prof Liu Jianjun, Acting Executive Director, Genome Institute of Singapore	1. Establish the biological underpinnings for cognitive function in diverse Asian and global populations, 2. Establish the biological convergence between cognitive function and disease traits, and 3. Establish epidemiological and genomic risk predictors of cognitive health.
	Institutions involved: Lee Kong Chian School of Medicine, Nanyang Technological University, Institute of Mental Health, National Neuroscience Institute, A*STAR Genome Institute of Singapore		
2	The SG100K_Med Alliance - clinical genetics researchers united for the analysis of mendelian disease variation in SG100K Topic: Mendelian Diseases	Lead PI: Dr Lim Weng Khong, Duke-NUS Medical School Co-Lead PI: Dr Joanne Ngeow, Lee Kong Chian School of Medicine Co-Lead PI: Dr Saumya Jamuar, KK Women's and Children's Hospital	1. Seek a deeper understanding of genetic disease burden in major Asian populations through a comprehensive analysis of structural variation and short tandem repeat expansions, 2. Demonstrate how SG100K data can resolve variants of uncertain significance, and 3. Explore impact of polygenic backgrounds on penetrance in autosomal dominant conditions for under-represented Asian populations.
	Institutions involved: Duke-NUS Medical School, Lee Kong Chian School of Medicine, KK Women's and Children's Hospital, A*STAR Genome Institute of Singapore, Singapore National Eye Centre, Tan Tock Seng Hospital, National University of Singapore, National Heart Centre Singapore, National Neuroscience Institute, Khoo Teck Puat Hospital, Nanyang Technological University		
3	Identification of Asian-specific genetic association with fat and	Lead PI: Dr Liu Boxiang, National University of Singapore	1. Perform multi-ethnic meta-analysis of fat and lean muscle mass using SG100K and UKBB datasets,

	lean muscle mass distribution Topic: Fat and Lean Muscle Mass	Co-Lead PI: A/P Sim Xueling, National University of Singapore Co-Lead PI: Prof Tai E Shyong, National University of Singapore	2. Mendelian randomisation analysis to identify the contribution of fat and lean muscle mass to cardiometabolic diseases, 3. Colocalisation analysis to identify risk genes affecting fat and lean muscle mass, and 4. Conduct functional validation studies of identified genetic loci.
	Institutions involved: National University of Singapore		
4	HLA alleles and its association with auto-immune diseases and pharmacogenomics in multi-ancestral Asian populations Topic: Human leukocyte antigen	Lead PI: A/P Sim Xueling, National University of Singapore Co-Lead PI: Dr Leong Khai Pang, Tan Tock Seng Hospital Co-Lead PI: Dr Wharton Chan, Duke-NUS Medical School	1. Generate a high-resolution human leukocyte antigen (HLA) reference panel in Asian populations, 2. Generate frequencies of HLA alleles and haplotypes in Asian populations for local reference and for global population comparisons, and 3. Conduct association analyses of HLA alleles in outcomes including auto-immune diseases and pharmacogenomic responses.
	Institutions involved: National University of Singapore, Tan Tock Seng Hospital, Duke-NUS Medical School		
5	Unravelling the determinants of kidney health in a multi-ethnic Asian population Topic: Kidney Disease	Lead PI: Dr Yeo See Cheng, Tan Tock Seng Hospital Co-Lead PI: Prof John Chambers, Lee Kong Chian School of Medicine	1. Determine prevalence of chronic kidney disease (CKD) among adults 2. Examine association of CKD with genetic, clinical and socio-behavioural predictors, 3. Examine relative contribution of key predictors driving differences in CKD risks

			across different sub-population, and 4. Develop and validate an integrated risk score for the development of CKD in a representative multi-ethnic Asian population-based cohort in Singapore.
	Institutions involved: Tan Tock Seng Hospital, Lee Kong Chian School of Medicine		
6	The high variability of tandem repeats offers insights into population diversity and may explain the missing heritability of complex neurological and neurocognitive disorders in Asian populations Topic: Tandem Repeats	Lead PI: Prof Liu Jianjun, A*STAR Genome Institute of Singapore Co-Lead PI: Dr Nicolas Bertin, A*STAR Genome Institute of Singapore Co-Lead PI: Dr Lim Weng Khong, Duke-NUS Medical School	1. Generate SG100K genome wide tandem repeats (TR) variation catalogue and characterisation their respective prevalence in Asian populations, and 2. Characterise contributions of TR variations to the aetiology of complex neurological and neurocognitive disorders.
	Institutions involved: A*STAR Genome Institute of Singapore, Duke-NUS Medical School, National Neuroscience Institute		
7	An integrated pharmacoeconomic-pharmacokinetic framework for prioritising and testing clinically important drug-gene interactions Topic: Pharmacogenomics	Lead PI: Dr Janice Goh, A*STAR Bioinformatics Institute Co-Lead PI: A/P Wee Hwee Lin, National University of Singapore Co-Lead PI: Dr Nicolas Bertin, A*STAR Genome Institute of Singapore	1. Evaluate the occurrence of known drug-gene interactions based on EHR data and its impact on efficacy and toxicity, 2. Explore genotype-drug response associations using SG100K and linked EHR datasets augmented by a dedicated pipeline for haplotyping highly polymorphic drug metabolising enzyme CYP2D6, and 3. Develop a pharmacokinetics-informed framework for evaluating and ranking both known and novel drug-gene sets for clinical

			action to make dose recommendations
	Institutions involved: A*STAR Bioinformatics Institute, National University of Singapore, A*STAR Genome Institute of Singapore		
8	Genetic variants contributing to clonal haematopoiesis across diverse Asian genomes Topic: Clonal haematopoiesis	Lead PI: Prof Ong Sin Tiong, Duke-NUS Medical School Co-Lead PI: Prof Ashok Venkitaraman, National University of Singapore Co-Lead PI: Prof Chng Wee Joo, National University of Singapore Co-Lead PI: Prof John Chambers, Lee Kong Chian School of Medicine Co-Lead PI: Dr Nicolas Bertin, A*STAR Genome Institute of Singapore	1. Determine age-related incidence of clonal haematopoiesis (CH) among our three major ancestry groups, 2. Correlate CH status with clinical metadata, measures of ageing and disease incidence, and disease-related variables including biomarkers, 3. Discover novel genetic associations with CH, 4. Integrate functional genomics for novel Asian CH driver mutation discovery and validation, and 5. Correlate CH status with cell clusters and gene expression signatures in the AIDA scRNA-seq dataset.
	Institutions involved: Duke-NUS Medical School, National University of Singapore, Lee Kong Chian School of Medicine, A*STAR Genome Institute of Singapore, National University Hospital, Singapore General Hospital		

PRECISE-SG100K Driver Projects

S/N	Project Title	Lead PI	Institution
1	Computation of genome-wide LD scores and matrices from the SG100K resource	Li Jingmei	A*STAR Genome Institute of Singapore
2	Chronic liver disease is a significant risk factor for adverse cardiometabolic outcomes	Mark Chan	National University Hospital
3	Nonlinear methods for genomic association analysis of eye diseases	Liu Dianbo	National University of Singapore
4	Advancing the understanding of biological mechanisms influencing chronic inflammatory skin diseases	Yew Yik Weng	National Skin Centre
5	Mood and diet in patients with irritable bowel syndrome (IBS) in Singapore	Kuang Ziyang Jonathan	Tan Tock Seng Hospital
6	The contribution of genetics to dietary habit and its relation to adiposity and cardiometabolic diseases in multiethnic Asian population	Theresia Mina	Lee Kong Chian School of Medicine
7	A structural variation catalogue across three ancestrally diverse Singaporean populations	Joanna Tan Hui Juan	A*STAR Genome Institute of Singapore
8	Genome-wide association study and population-based evaluation of patients with diabetic foot ulcers	Joseph Lo	Woodlands Health
9	The SG100K_cancer and aging workgroup: Developing risk models for cancer associations	Joanne Ngeow	Lee Kong Chian School of Medicine
10	Genetic susceptibility of age-related hearing loss	Liu Jianjun	A*STAR Genome Institute of Singapore
11	Evaluating the promise and perils of glucagon-like peptide-1 (GLP-1) receptor agonist: a deep dive into therapeutic potentials and adverse effects	Huang Jian	A*STAR Singapore Institute for Clinical Sciences
12	Unravelling the pathogenesis of inflammatory bowel disease and associated immune-mediated disorders in the Singaporean population	Sunny Wong	Lee Kong Chian School of Medicine
13	Genetics of allergic diseases and acne vulgaris in the Singapore population: validation and functional characterisation of candidates	Chew Fook Tim	National University of Singapore

14	Modulation of cholesterol 7α-hydroxylase (CYP7A1) activity as an orthogonal approach to the management of hypercholesterolemia	Ho Han Kiat	National University of Singapore
15	Multi-omics data analysis for novel depression mechanisms using deep learning tools	Mu Yuguang	Nanyang Technological University
16	Asian-specific Parkinson's disease-linked genetic risk variants and systemic clinical outcomes	Tan Eng King	National Neuroscience Institute
17	Physiological, environmental and genetic determinants of heterogeneity in Singaporeans' health span	Neerja Karnani	A*STAR Bioinformatics Institute
18	Portability of catalogued polygenic risk scores across ancestrally diverse Singaporean populations	Pierre-Alexis Goy	A*STAR Genome Institute of Singapore
19	Advancing Asian-centric liver disease treatment: machine learning applications in MASLD and MetALD precision medicine	Tan Nguan Soon	Lee Kong Chian School of Medicine
20	Unravelling the correlation between sarcopenia with lifestyle, genetics, and comorbid diseases	Teh Bin Tean	National Cancer Centre Singapore
21	Young-onset obesity and determinants of cancer prevalence	Yusuf Ali	Lee Kong Chian School of Medicine
22	Implications of alternative splicing of voltage-gated calcium channels in schizophrenia	Soong Tuck Wah	National University of Singapore
23	Exploring the impact and origins of somatic mutagenesis in cardiovascular disease	Tan Kar-Tong	National University of Singapore
24	Alport syndrome in the Singapore population: an under-recognised kidney disease?	Ng Kar Hui	National University of Singapore
25	Risk prediction for congenital and early-onset hearing loss	Joshua Tay	National University of Singapore
26	Biological age clocks for multiple organ systems and the lifestyle and genetic risk factors of advanced biological age	Andrea B. Maier	National University of Singapore
27	Identification of risk factors for gastrointestinal cancers through analysis of genetic and phenotypic data	Patrick Tan	Duke-NUS Medical School
28	Genomic associations of COVID-19 susceptibility & severity in Singapore	Kelvin Bryan Tan	Ministry of Health