

The 3rd Vietnam School of Biology

December 06-08, 2024, ICISE, Quy Nhon

Functional-based analysis of multi-omics data in **Vietnam Genome Program**

Nam Sy Vo, PhD

CTO/Chief Scientist & Co-Founder, GeneStory JSC.

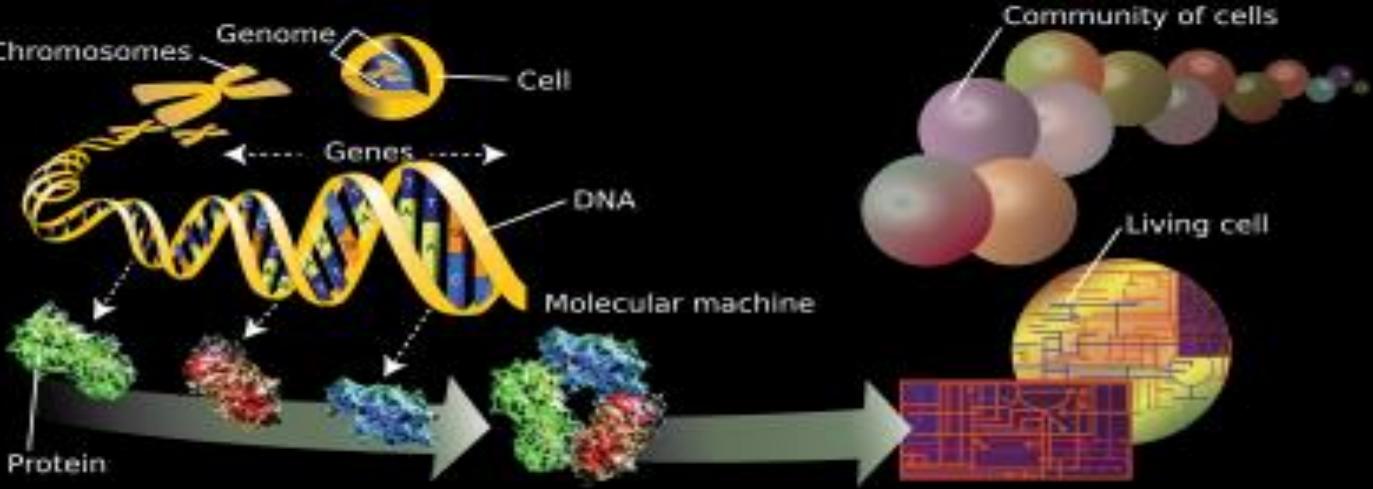
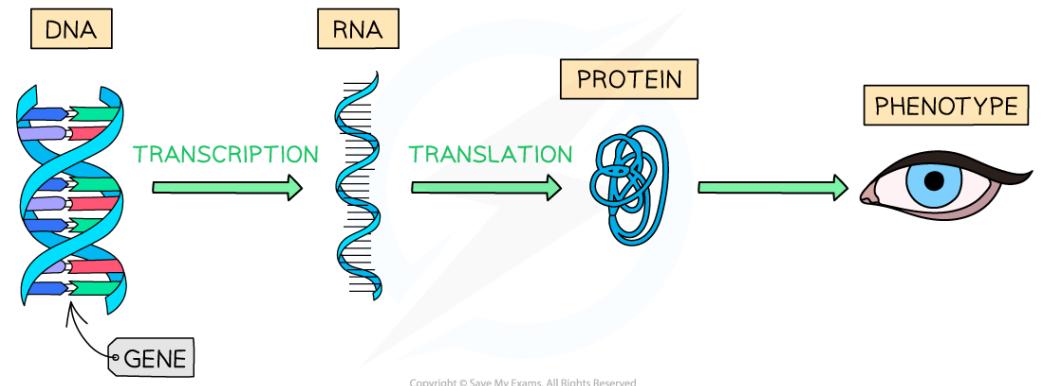
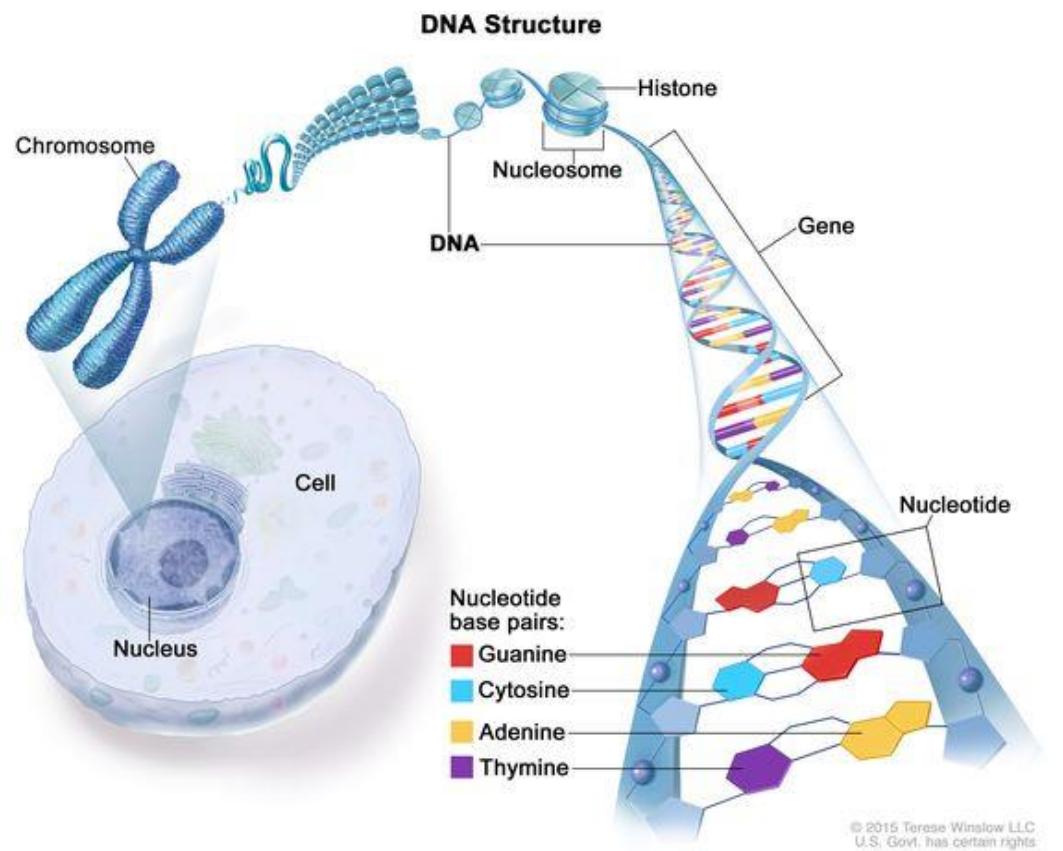
Director, Center for Biomedical Informatics, Vingroup Big Data Institute

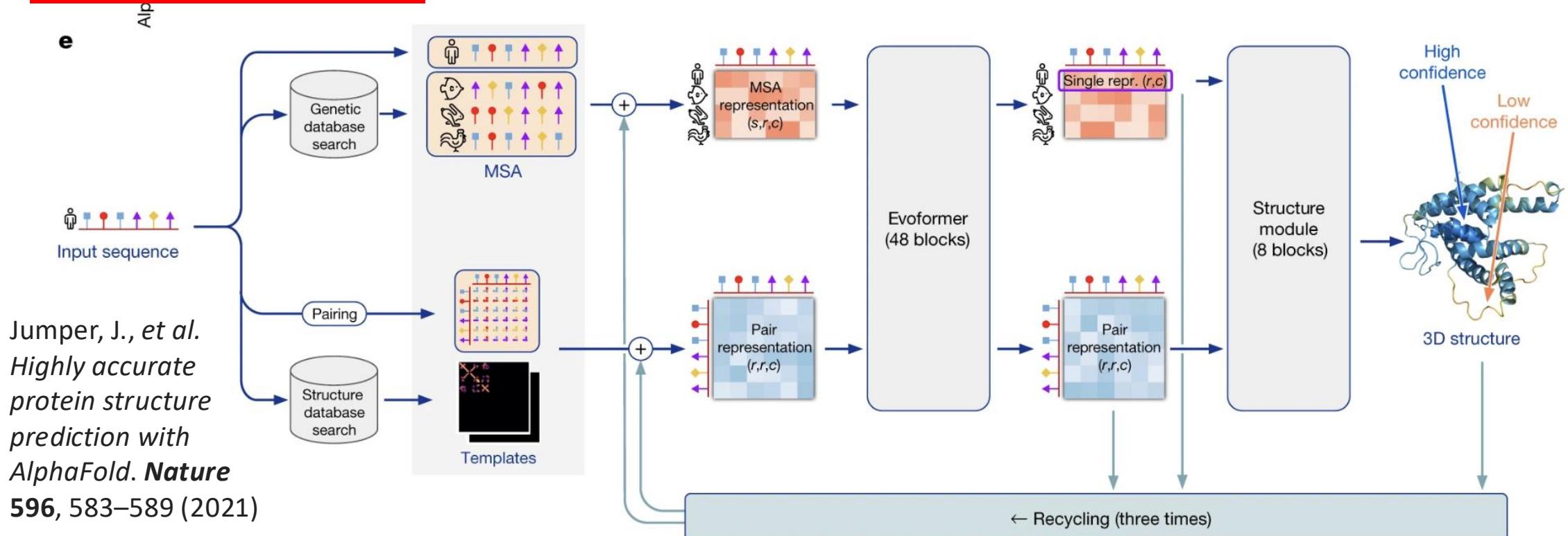
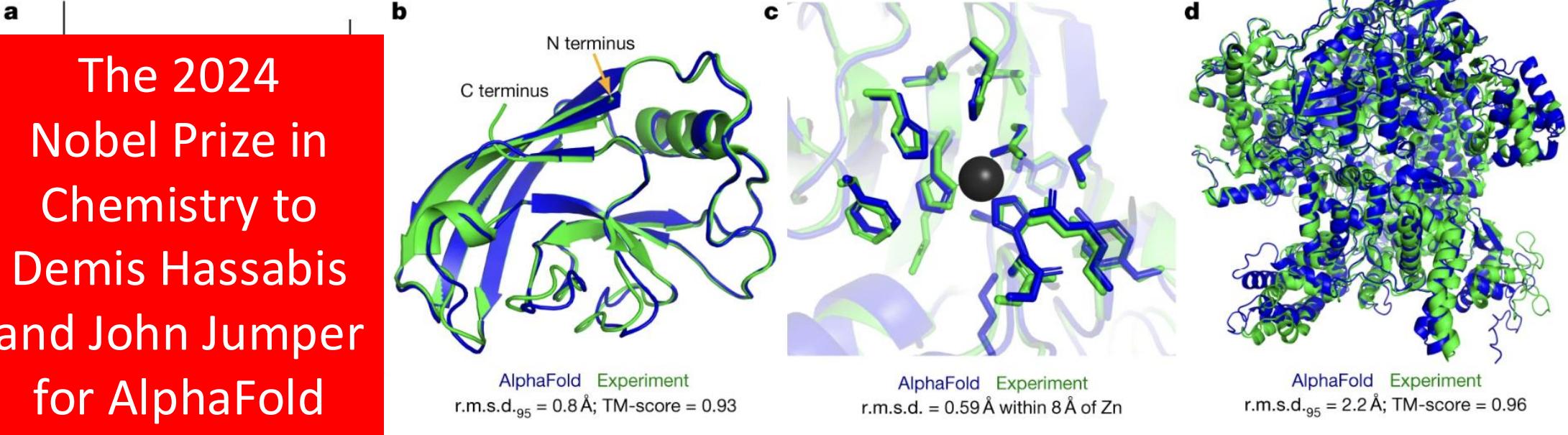


Content

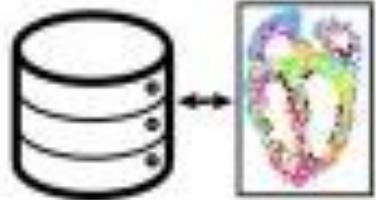
- 1 Why functional multi-omics?**
- 2 VGP: Vietnam Genome Program**
- 3 VGP: What next?**

01 Why functional multi-omics?

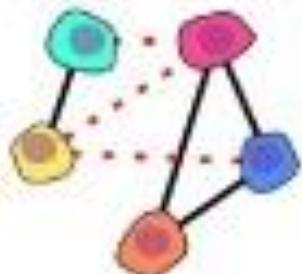




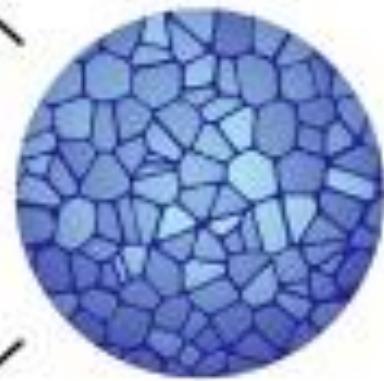
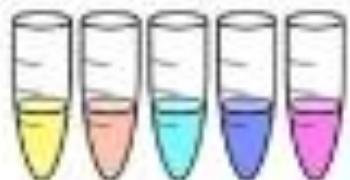
Reference for spatial and molecular cell characteristics



Disease mechanisms



Diagnostics

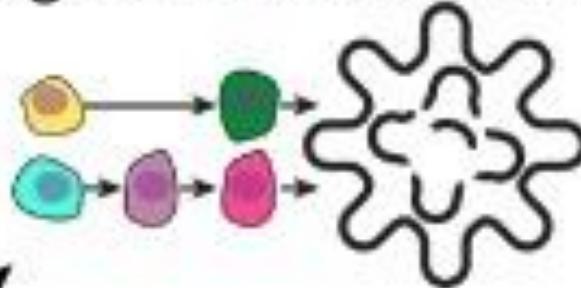


Towards a Human Cell Atlas:
Taking Notes from the Past

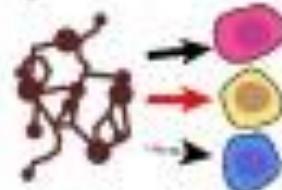
Lindeboom et al., Trends in Genetics, 37(7), 625-630, 2021

HUMAN CELL ATLAS

Regenerative medicine

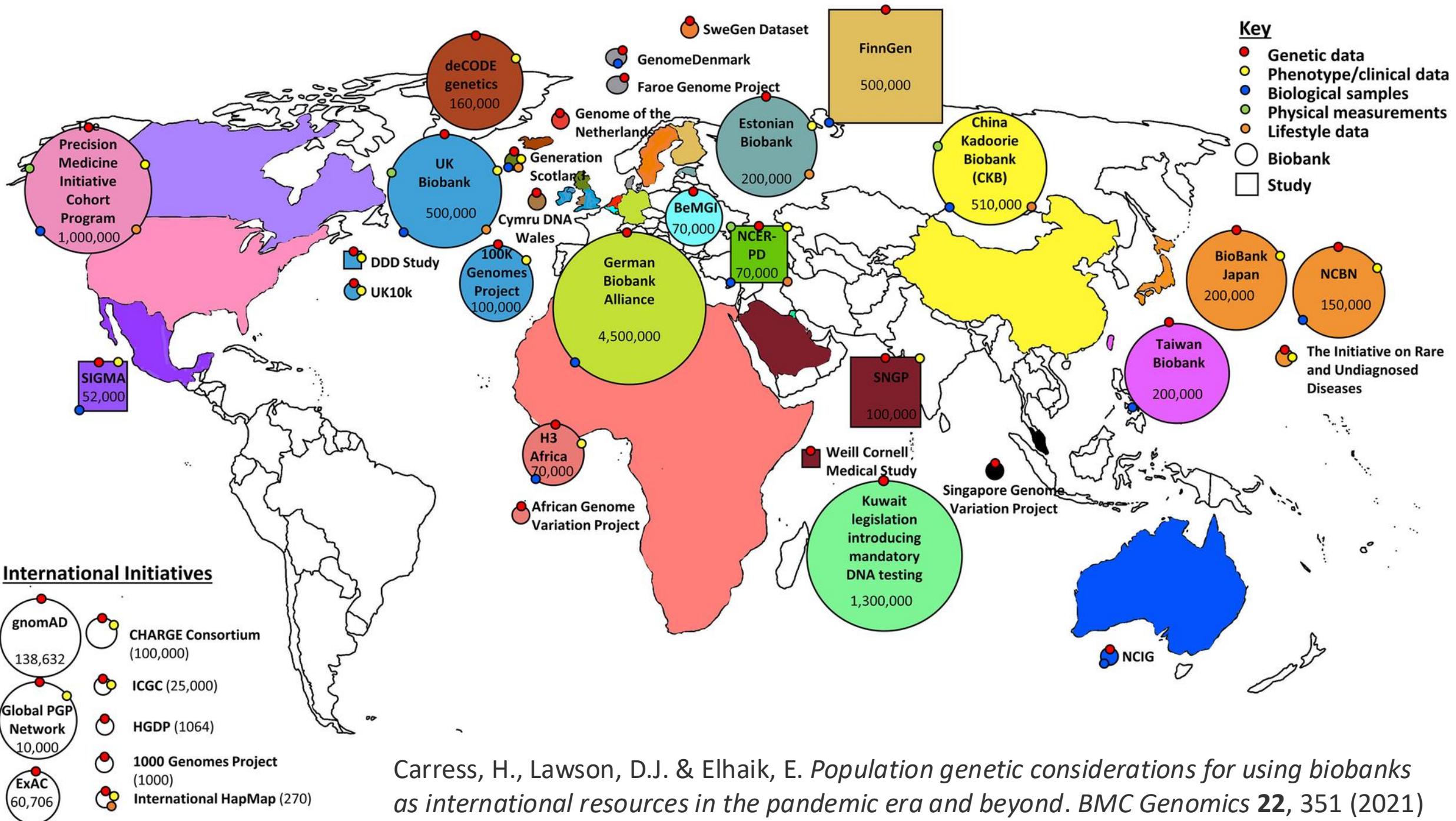


Drug development



Foundation for future consortia







Approved by Thailand Cabinet in 2019

GDP: \$500B (VN: \$400B)

Per capita: \$7K (VN: \$4K)

- 150M USD

- 50k Thai

- 33k samples done

- 20k sequencing done

- 11 sites

- 05 domains:

+ Cancer

+ Rare Diseases

+ Infectious Diseases

+ NCDs

+ Pharmacogenomics

Vietnamese Genomics?

- Opportunities?

- Gaps: samples, data, lab, infrastructure
- Problems: bioinfo, biostats, biomed, clinical
- Demands: universities, institutions, hospitals

- Challenges?

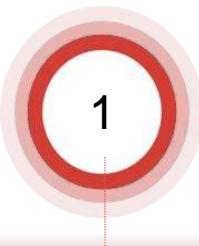
- Human resources
- Scientific standard
- Scientific community & network
- Research management & funding

Top-down or
Bottom-up?
“Khoán 10”

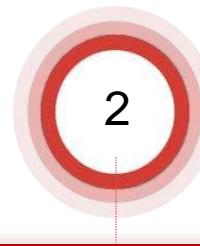
02 Vietnam Genome Program

-
- 1000 Vietnamese Genomes Project
 - Vietnamese-specific SNP Chips
 - Disease Risk & Adverse Drug Reaction

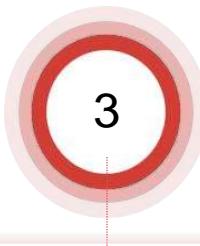
VGP: Vietnam Genome Program



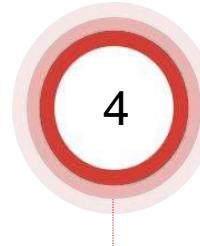
Large-scale biomed databases for Vietnamese population



Platform for large-scale biomed data management & sharing



Methods for large-scale biomed data analysis & interpretation



Solutions for disease risk and adverse drug reaction prediction

Highlighted Projects:

- * VN1K: Vietnamese Whole Genomes Sequencing
- * VGR: Vietnamese Genome Reference
- * VGC: Vietnamese-specific Genotyping Arrays
- * DRP: Type 2 Diabetes & Common Diseases
- * ADR: SCAR, NSAID hypersensitivity, DILI

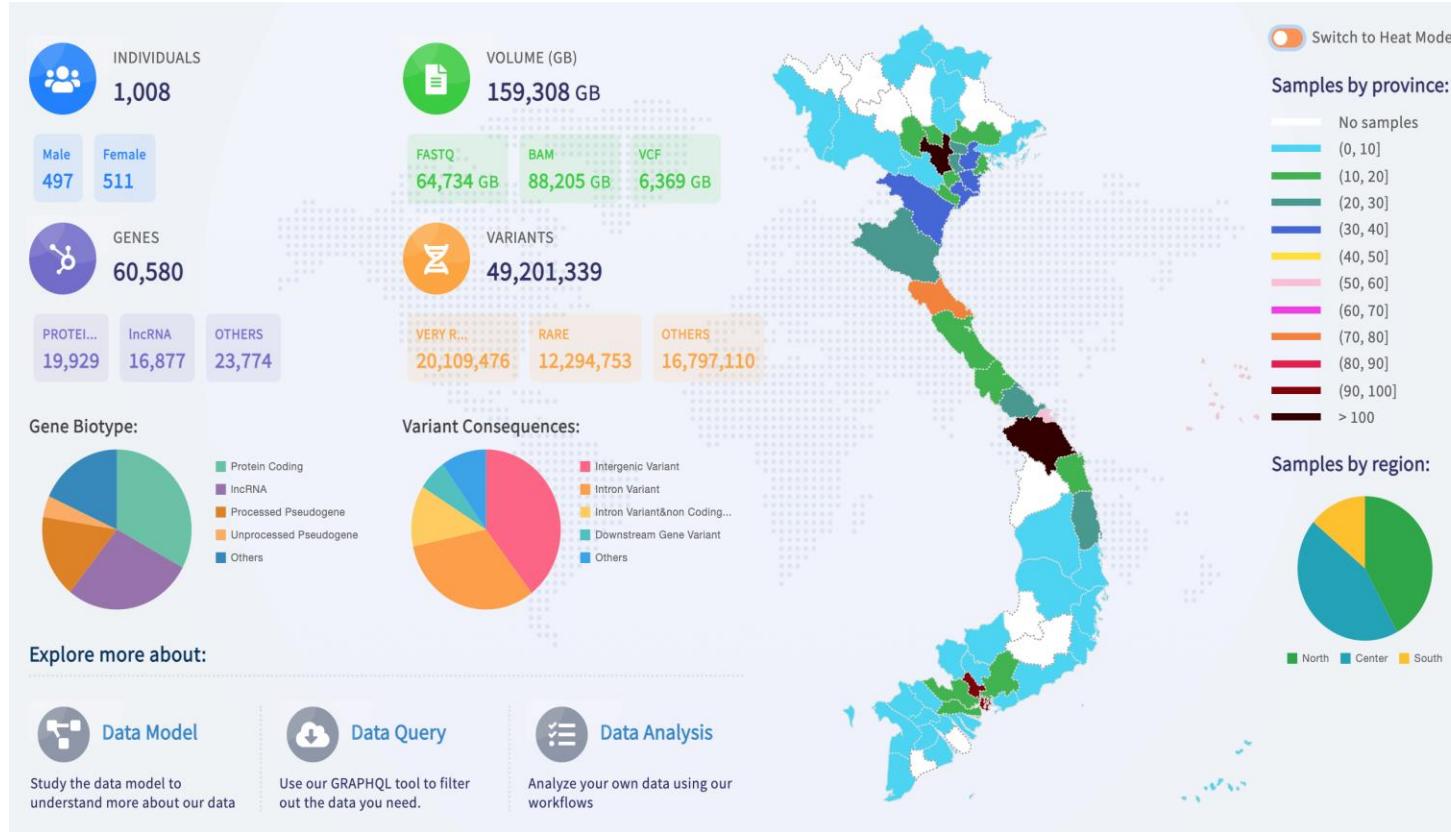


<https://vingen.vinbigdata.org>

VN1K: 1000 Vietnamese Genomes Project

Ilmn WGS short-read, Pacbio & ONT WGS long-read, DNA-Methyl, DNA microarray, RNA-Seq

1000 TB data; North: 37%; Central: 22%; South: 41%



Accessed 10/2021

Country	Acquisition		
	Users	New Users	Sessions
	7,492 % of Total: 100.00% (7,492)	7,487 % of Total: 100.04% (7,484)	16,581 % of Total: 100.00% (16,581)
1. Vietnam	6,038 (80.07%)	6,005 (80.21%)	14,695 (88.63%)
2. United States	533 (7.07%)	530 (7.08%)	629 (3.79%)
3. South Korea	130 (1.72%)	129 (1.72%)	160 (0.96%)
4. Japan	99 (1.31%)	99 (1.32%)	122 (0.74%)
5. Australia	80 (1.06%)	80 (1.07%)	102 (0.62%)
6. Taiwan	77 (1.02%)	77 (1.03%)	120 (0.72%)
7. France	72 (0.95%)	72 (0.96%)	91 (0.55%)

genome.vinbigdata.org

Represent variants: Genome graphs

a

Reference sequence: ACCTCCAGACGTTAGGGACCCCATTGAGTG

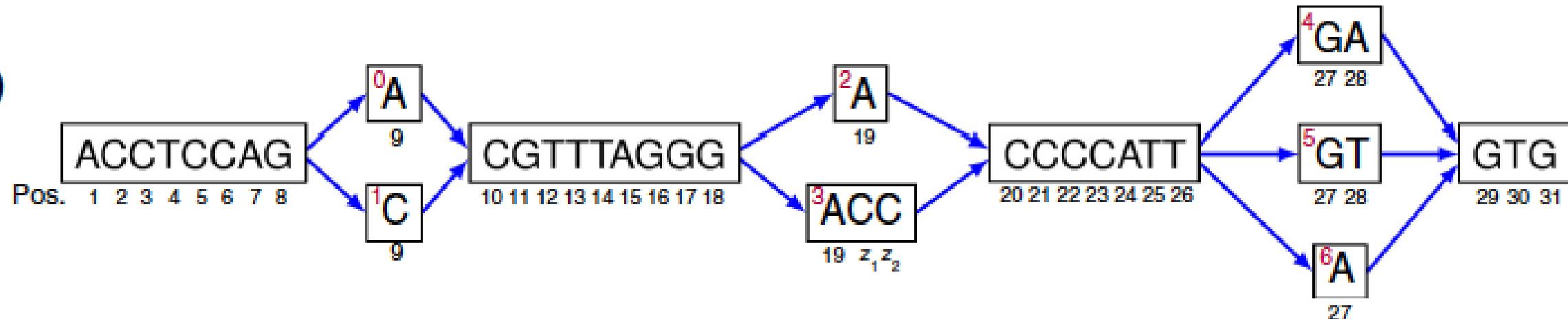
Known variants

Position	Reference	Alternative
9	A	C
19	A	ACC
27	GA	A
28	A	T

Known variants after merge

Position	Reference	Alternative
9	A	C
19	A	ACC
27	GA	GT,A

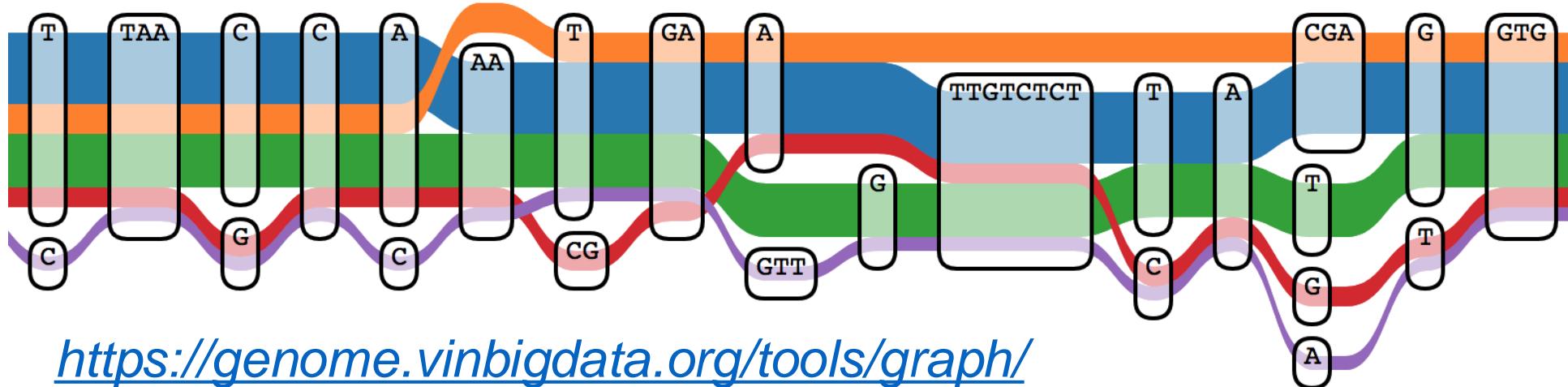
b



Eggertsson et al. *Nature Genetics* (49), pp. 1654–1660 (2017)

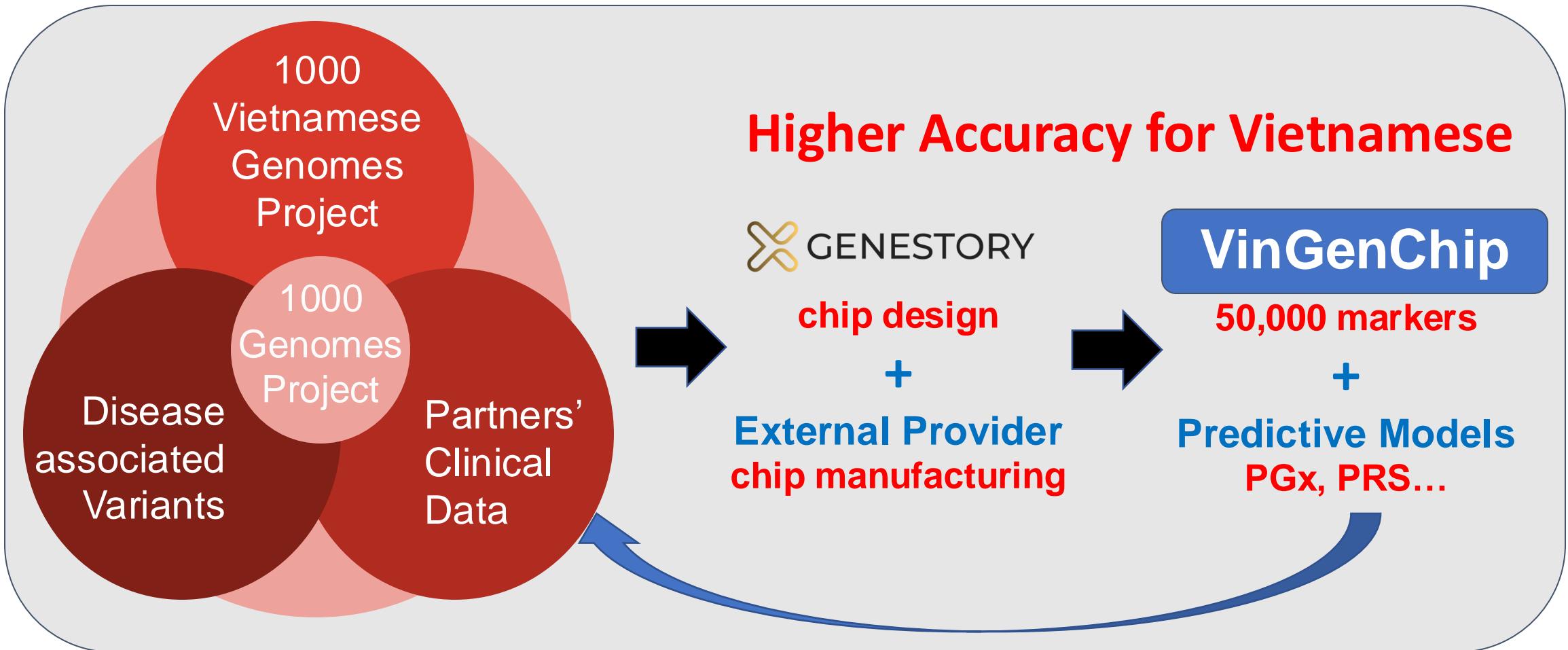
VGR: Vietnamese Genome Reference

- The first comprehensive Vietnamese Genome Reference
 - Employ both second and third-generation sequencing technologies
- A graph-based genome reference
 - More difficult to construct but facilitate dealing with complex variants



Improve Vietnamese genomic analysis

VGC: Vietnamese-specific SNP chips

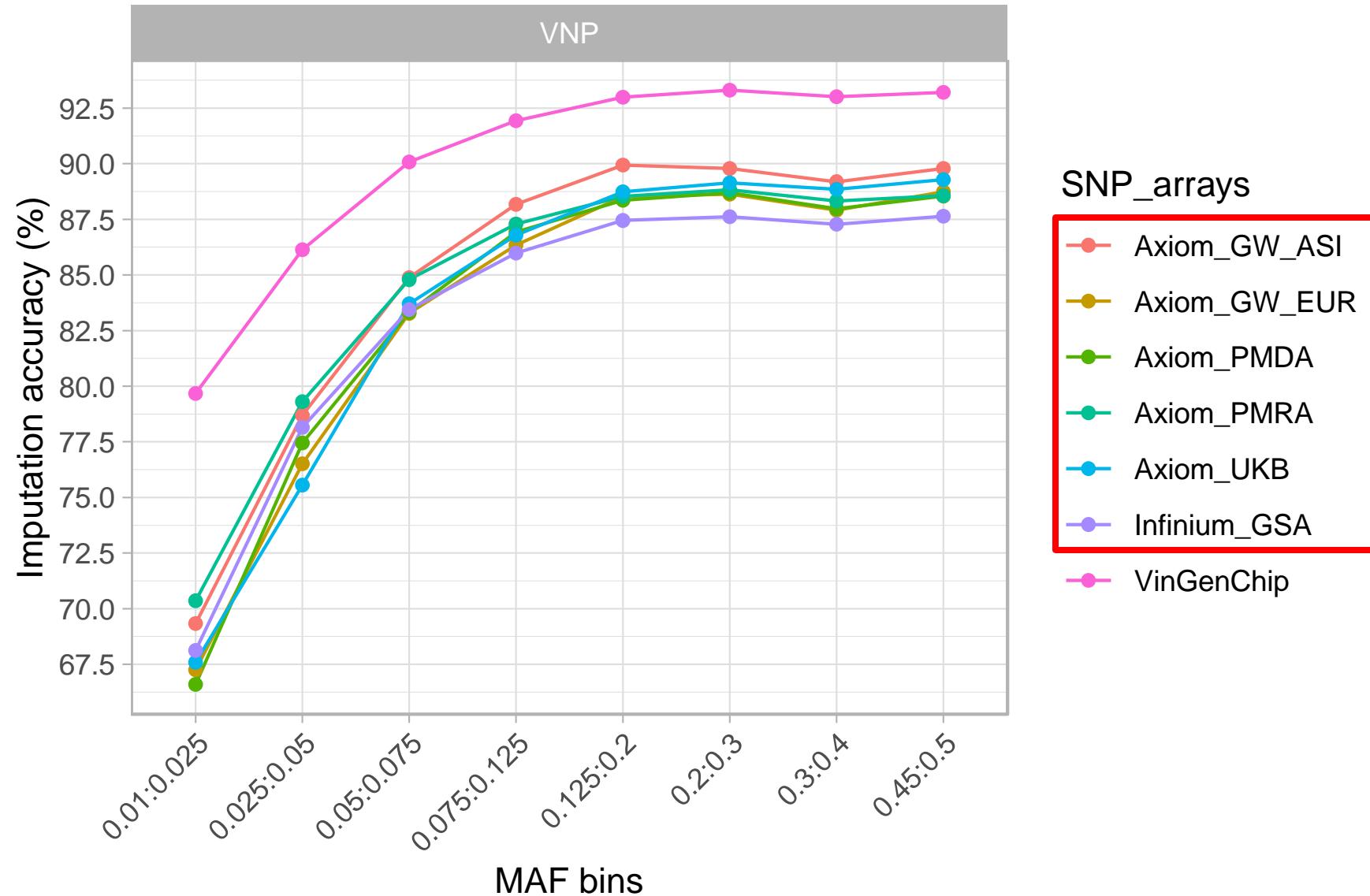


Affordable for genotyping millions of people

VGC: Super-sensitive for Vietnamese

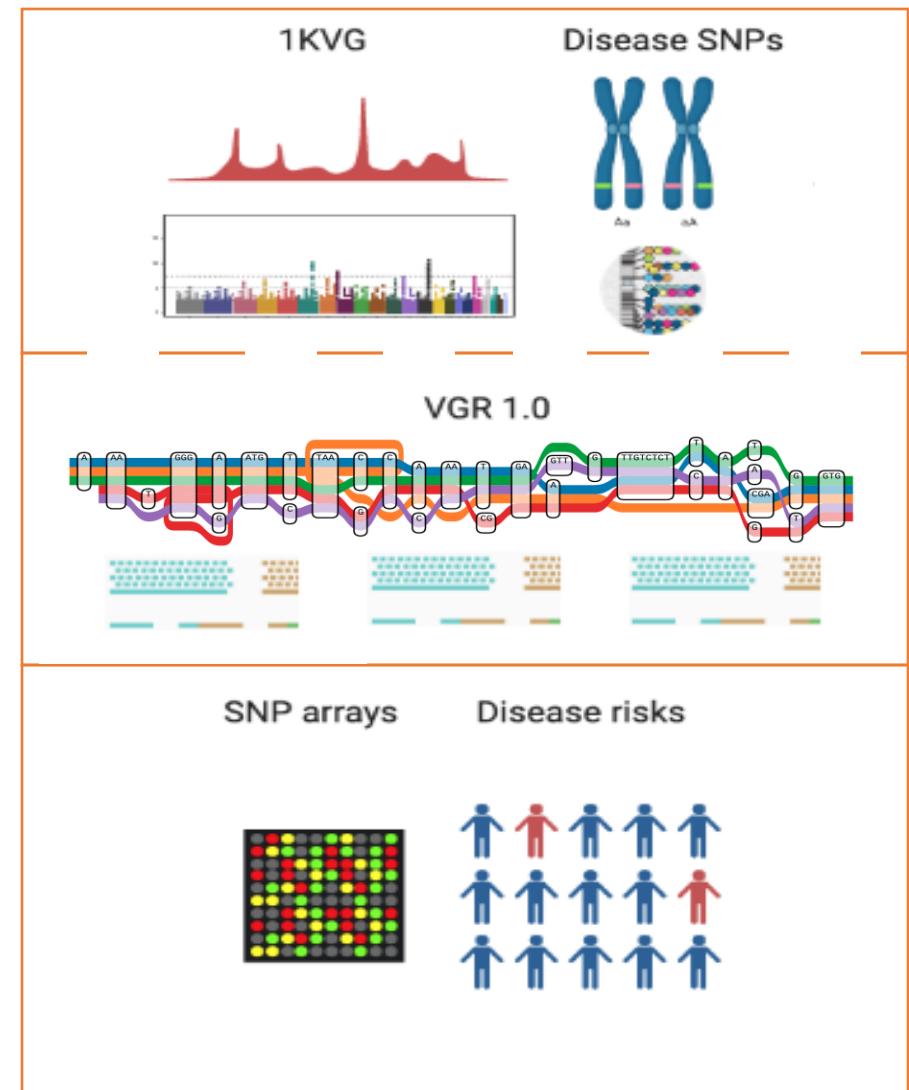
Genome-wide studies for Vietnamese may need to consider VGC instead of popular chips

Dat T. Nguyen et al., LmTag: functional-enrichment and imputation-aware tag SNP selection for population-specific genotyping arrays
Briefings in Bioinfo, 23(4) 2022



DRP: Disease Risk Prediction for Vietnamese

- Sequencing and genotyping of **3500+** samples
 - Vietnamese-specific disease-associated variants
 - **Common diseases:** type 2 diabetes, cancer, cardiovascular, Alzheimer/Parkinson, gout...
- Developing **SNP chips/PRS/TRS models**
 - Trans-ethnic genome-wide analysis
 - DNA-methyl and RNA-Seq analysis



ADR: Adverse Drug Reaction in Vietnamese

- Sequencing and genotyping **1500+** samples
 - WGS/RNA-Seq/SNP microarray
 - Vietnamese-specific ADR-associated variants
 - SCAR, DILI, NSAID hyper.
- Developing predictive models (PRS, ML)
- Broader impacts of PGx research in Vietnam
 - Revise National List of Essential Medicines of Vietnam
 - Increase ADR awareness in clinical practice in Vietnam

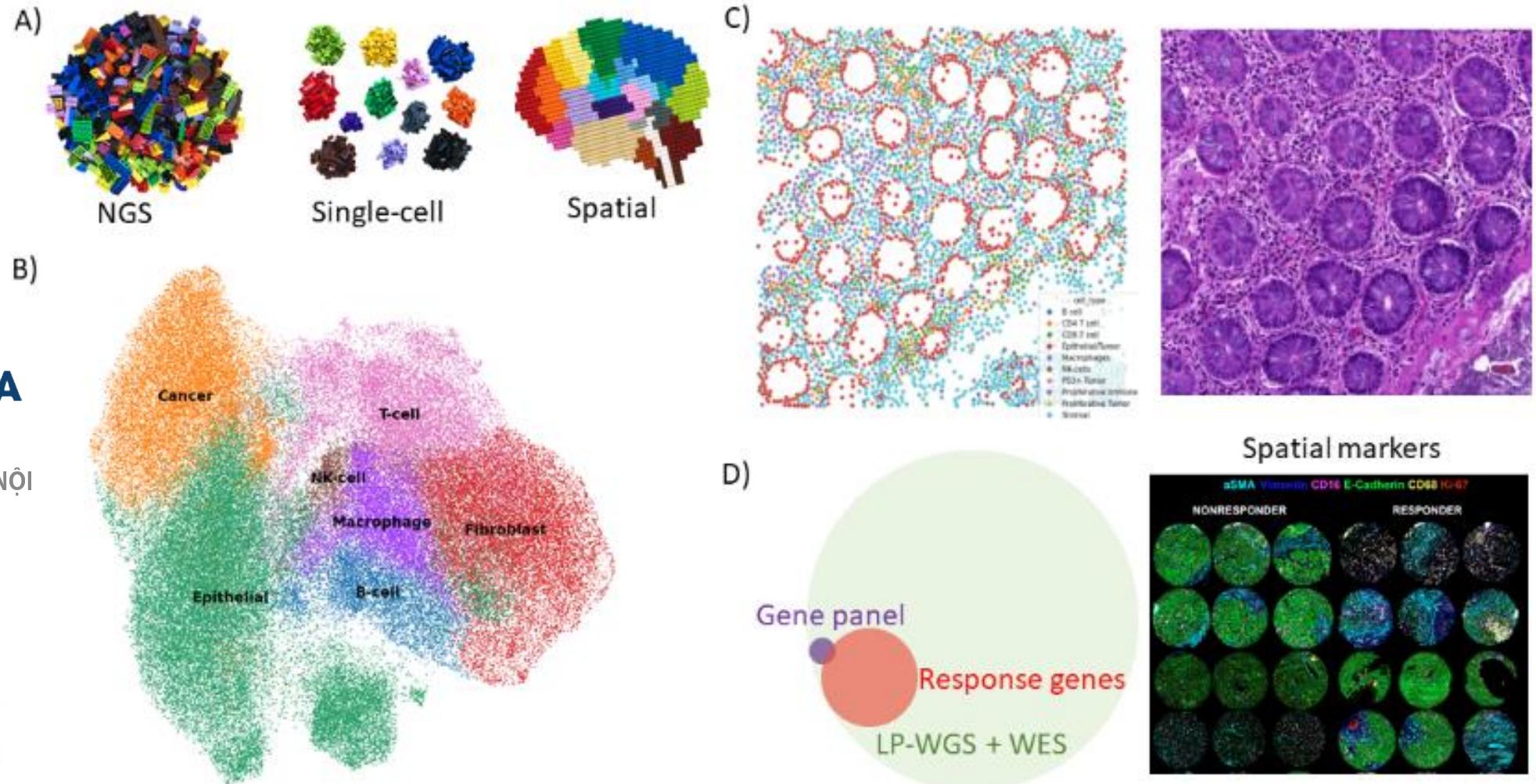


VCB: Single-cell & Spatial Transcriptomics

- ❖ HCA Asia community
- ❖ SEAPharm network



THE UNIVERSITY
OF QUEENSLAND
AUSTRALIA
CREATE CHANGE



VCB: Vietnam Cancer Biobank Project

Pasa: leveraging population pangenome graph to scaffold prokaryote genome assemblies ⚡

Van Hoan Do ✉, Son Hoang Nguyen, Duc Quang Le, Tam Thi Nguyen, Canh Hao Nguyen, Tho Huu Ho, Nam S Vo, Trang Nguyen, Hoang Anh Nguyen
Minh Duc Cao ✉ Author Notes

Nucleic Acids Research, Volume 52, Issue 3, 9 February 2024, Page e15,
<https://doi.org/10.1093/nar/gkad1170>

Published: 12 December 2023 Article history ▾

Software | [Open access](#) | Published: 06 August 2024

Efficient inference of large prokaryotic pangenomes with PanTA

Duc Quang Le, Tien Anh Nguyen, Son Hoang Nguyen, Tam Thi Nguyen, Canh Hao Nguyen, Huong Thanh Phung, Tho Huu Ho, Nam S. Vo, Trang Nguyen, Hoang Anh Nguyen & Minh Duc Cao ✉

[Genome Biology](#) 25, Article number: 209 (2024) | [Cite this article](#)

Article | [Open access](#) | Published: 27 December 2023

A rapid and reference-free imputation method for low-cost genotyping platforms

Vinh Chi Duong, Giang Minh Vu, Thien Khac Nguyen, Hung Tran The Nguyen, Luong Pham, Nam S. Vo ✉ & Tham Hong Hoang ✉

[Scientific Reports](#) 13, Article number: 23083 (2023) | [Cite this article](#)

Article | [Open access](#) | Published: 20 October 2022

A comprehensive evaluation of polygenic score and genotype imputation performances of human SNP arrays in diverse populations

Dat Thanh Nguyen ✉, Trang T. H. Tran, Mai Hoang Tran, Khai Tran, Duy Pham, Nguyen Thuy Duong, Quan Nguyen ✉ & Nam S. Vo ✉

[Scientific Reports](#) 12, Article number: 17556 (2022) | [Cite this article](#)

JOURNAL ARTICLE

LmTag: functional-enrichment and imputation-aware tag SNP selection for population-specific genotyping arrays FREE

Dat Thanh Nguyen ✉, Quan Hoang Nguyen, Nguyen Thuy Duong, Nam S Vo ✉

Briefings in Bioinformatics, Volume 23, Issue 4, July 2022, bbac252,
<https://doi.org/10.1093/bib/bbac252>

Published: 02 July 2022 Article history ▾

JOURNAL ARTICLE

Assessing polygenic risk score models for applications in populations with under-represented genomics data: an example of Vietnam ⓘ

Duy Pham ✉, Buu Truong, Khai Tran, Guiyan Ni, Dat Nguyen, Trang T H Tran, Mai H Tran, Duong Nguyen Thuy, Nam S Vo ✉, Quan Nguyen ✉

Briefings in Bioinformatics, Volume 23, Issue 6, November 2022, bbac459,
<https://doi.org/10.1093/bib/bbac459>

Published: 02 November 2022 Article history ▾

US20230335218A1

United States

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Similar

Inventor: Tham Hong Hoang, Giang Minh Vu, Dat Thanh Nguyen, Trang Thi Ha Tran, Vinh Chi Duong, Nam Sy Vo

Current Assignee : Genestory Joint Stock , Genestory Joint Stock Co

Worldwide applications

2023 • US

Application US18/213,157 events ⓘ

2023-06-22 • Application filed by Genestory Joint Stock Co

2023-06-22 • Assigned to GENESTORY JOINT STOCK ⓘ

2023-10-19 • Publication of US20230335218A1

Status • Pending

Research | [Open access](#) | Published: 11 January 2024

A study of genetic variants associated with skin traits in the Vietnamese population

Tham Hong Hoang, Duc Minh Vu, Giang Minh Vu, Thien Khac Nguyen, Nguyet Minh Do, Vinh Chi Duong, Thang Luong Pham, Mai Hoang Tran, Ly Thi Khanh Nguyen, Han Thi Tuong Han, Thu-Thuy Can, Thai Hong Pham, Tho Duc Pham, Thanh Hong Nguyen, Huy Phuoc Do, Nam S. Vo ✉ & Xuan Hung Nguyen ✉

[BMC Genomics](#) 25, Article number: 52 (2024) | [Cite this article](#)

Data Report | [Open access](#) | Published: 04 February 2021

Prevalence of pharmacogenomic variants in 100 pharmacogenes among Southeast Asian populations under the collaboration of the Southeast Asian Pharmacogenomics Research Network (SEAPharm)

Chakkaphan Runcharoen, Koya Fukunaga, Insee Sensorn, Nareenart Iemwimangsa, Sommon Klumsathian, Hang Tong, Nam Sy Vo, Ly Le, Tin Maung Hlaing, Myo Thant, Shamsul Mohd Zain, Zahurin Mohamed, Yuh-Fen Pung, Francis Capule, Jose Nevado Jr., Catherine Lynn Silao, Zeina N. Al-Mahayri, Bassam R. Ali, Rika Yuliwulandari, Kinasih Prayuni, Hilyatuz Zahroh, Dzul Azri Mohamed Noor, Phonepadith Xangsayarath, Dalouny Xayavong, ... Wasun Chanratita ✉ + Show authors

[Human Genome Variation](#) 8, Article number: 7 (2021) | [Cite this article](#)



ABSTRACT ONLY · Volume 153, Issue 2, Supplement , AB157, February 2024

Polygenic Risk Score of Common Genetic Variants for NSAIDS Hypersensitivity Prediction in Vietnamese

Dinh Nguyen, MD, PhD¹ · Trang Tran Thi Ha² · Mai Tran Hoang² · Nam Nguyen Le² · Nam Nguyen Ngoc³ · Tien Pham Minh³ · Quang Vu Thanh³ · Anh Nguyen Quynh⁴ · Mai Vu Thi⁴ · Yen Pham Thi Hai⁴ · Thang Nguyen Van⁴ · Lan Phan Quynh⁴ · Nguyet Nguyen Thi Minh⁵ · Oanh Hoang Thi⁵ · Thuy Can Thi Thu⁴ · Anh Duong Thuy⁴ · Nguyet Nguyen Nhu⁶ · Hang Vu Thi⁶ · Sheryl Nunen Van⁴ · Timothy Craig John⁴ · Nam Vo Sy² · Hieu Chu Chi⁴



Log in

CORRESPONDENCE · Volume 10, Issue 6, e27043, March 30, 2024
Open Access

The therapeutic landscape for COVID-19 and post-COVID-19 medications from genetic profiling of the Vietnamese population and a predictive model of drug-drug interaction for comorbid COVID-19 patients

Thien Khac Nguyen^b · Giang Minh Vu^{a,b} · Vinh Chi Duong^{a,b} · Thang Luong Pham^b · Nguyen Thanh Nguyen^b · Trang Thi Ha Tran^{a,b} · Mai Hoang Tran^{a,b} · Duong Thuy Nguyen^{a,b} · Nam S. Vo^{a,b} ✉ · Huong Thanh Phung^{a,c} ✉ · Tham Hong Hoang^{a,b} ✉ Show less

Genome-wide Polygenic Risk Score

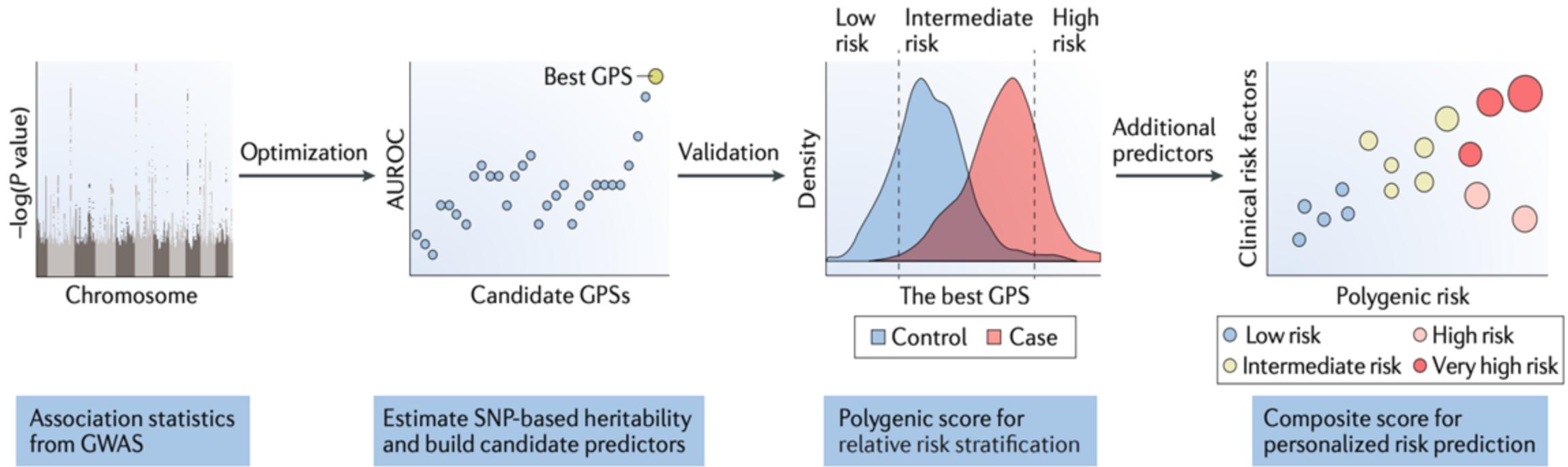


Fig. 1 | Construction of a GPS. A genome-wide polygenic risk score (GPS) is based on genome-wide association study (GWAS) summary statistics. The optimization step enables selection of the best method according to the genetic architecture of a disease under study. The validation step requires an external cohort and is critical to obtaining reliable metrics of performance. Clinical predictors of absolute risk will require incorporation of additional demographic, clinical or lifestyle factors into composite risk models. AUROC, area under receiver operating characteristic. SNP, single-nucleotide polymorphism.

Polygenic Risk Score calculation

- PRS: A quantitative measure of the cumulative genetic risk or vulnerability that an individual possesses for a trait
- The traditional approach to calculating PRS is to construct a weighted sum of the betas (or other effect size measure) for a set of independent loci thresholded at different significance levels

https://ibg.colorado.edu/cdrom2019/medland/Tuesday/PRS_Medland.pdf

$$PRS_i = \sum_{j=1}^p \beta_j \times SNP_{ij}$$

PRS based on p SNPs

β_j : beta coefficient for the j th SNP

SNP_{ij} : value of j th SNP for the i th individual

Population Bias in PRS Models

- Most training data are European
 - Disease risk prediction accuracy in other populations is not clear
- Usage of training data is typically one way
 - European (large sample size) or target population (small sample size)
- Prediction accuracy reduces from European to the others
 - Due to different causal effects, patterns of LD, etc.
- Model parameters are transferable
 - Factors: LD, AF, genetic architecture/selection, gene-env. interactions

PRS models for under-represented populations (URP)

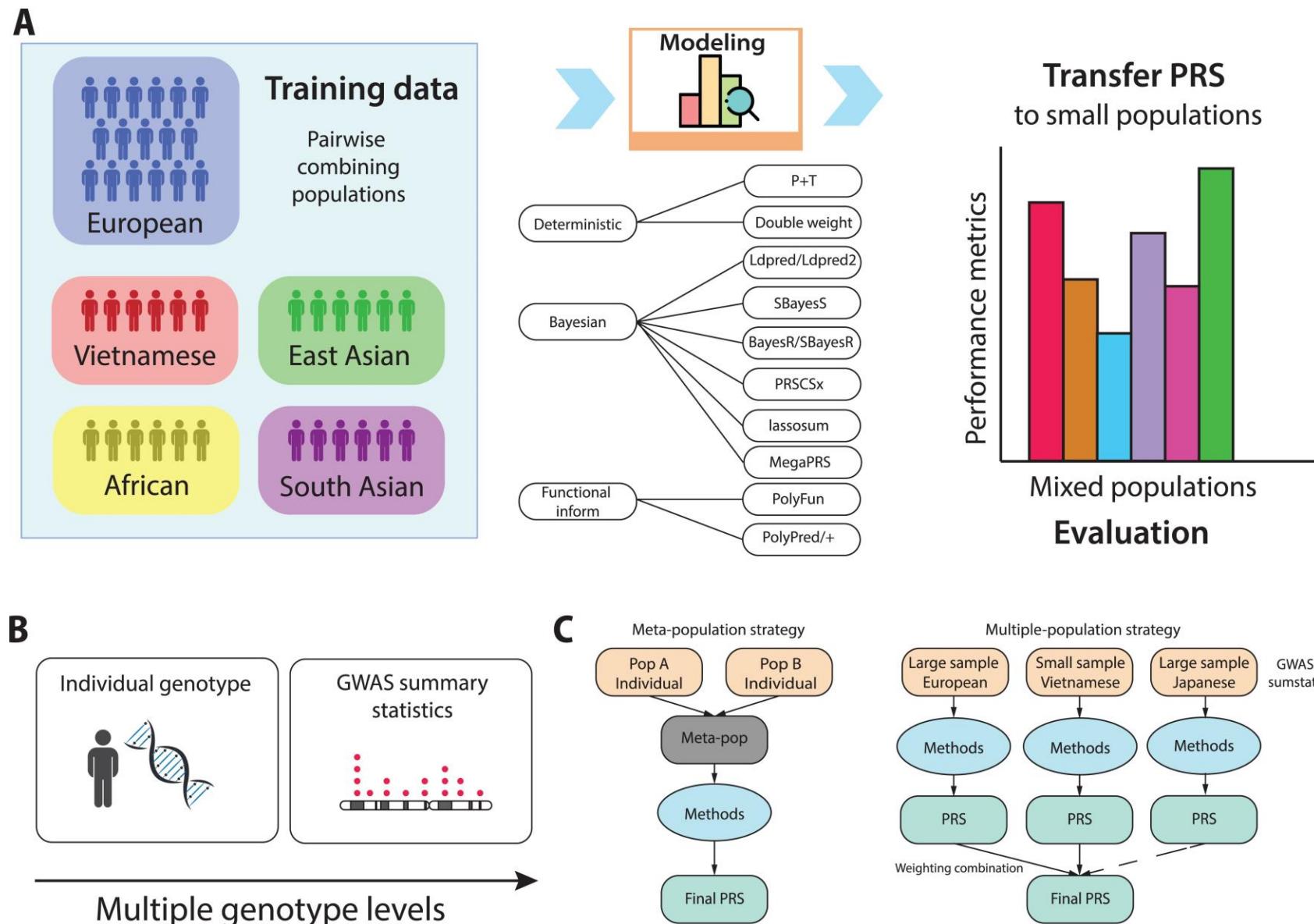
Benchmarking framework PRS-URP

(A) Assess perf. of PRS transferring for an URP

(B) Apply the framework for multi-genotype levels

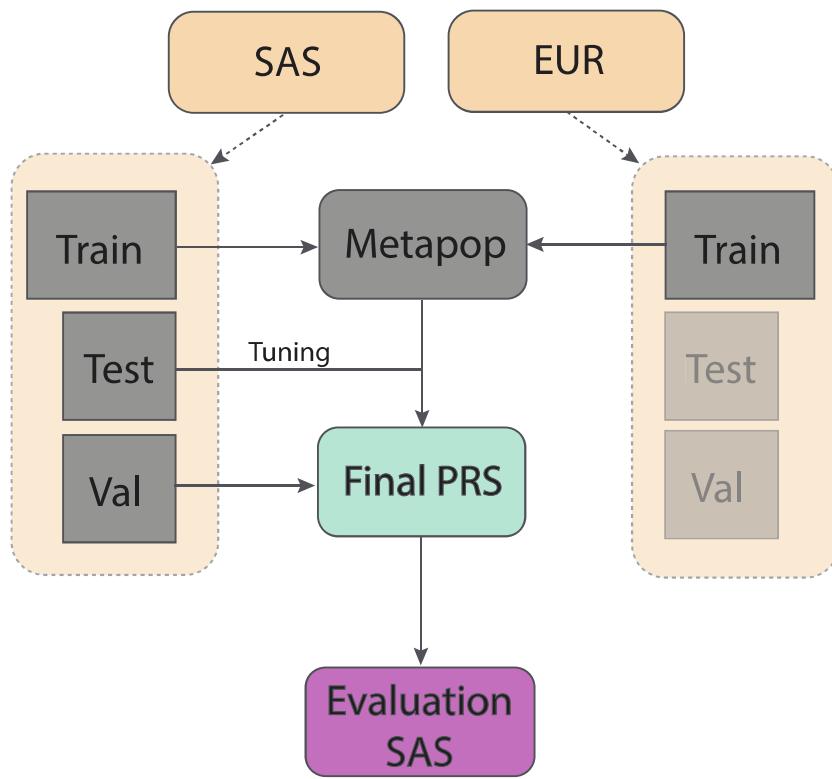
(C) Benchmark with 2 main strategies: meta-pop. and multiple-pop.

Duy Pham et al., Assessing polygenic risk score models for applications in populations with under-represented genomics data: an example of Vietnam
Briefings in Bioinfo., 23(6) 2022

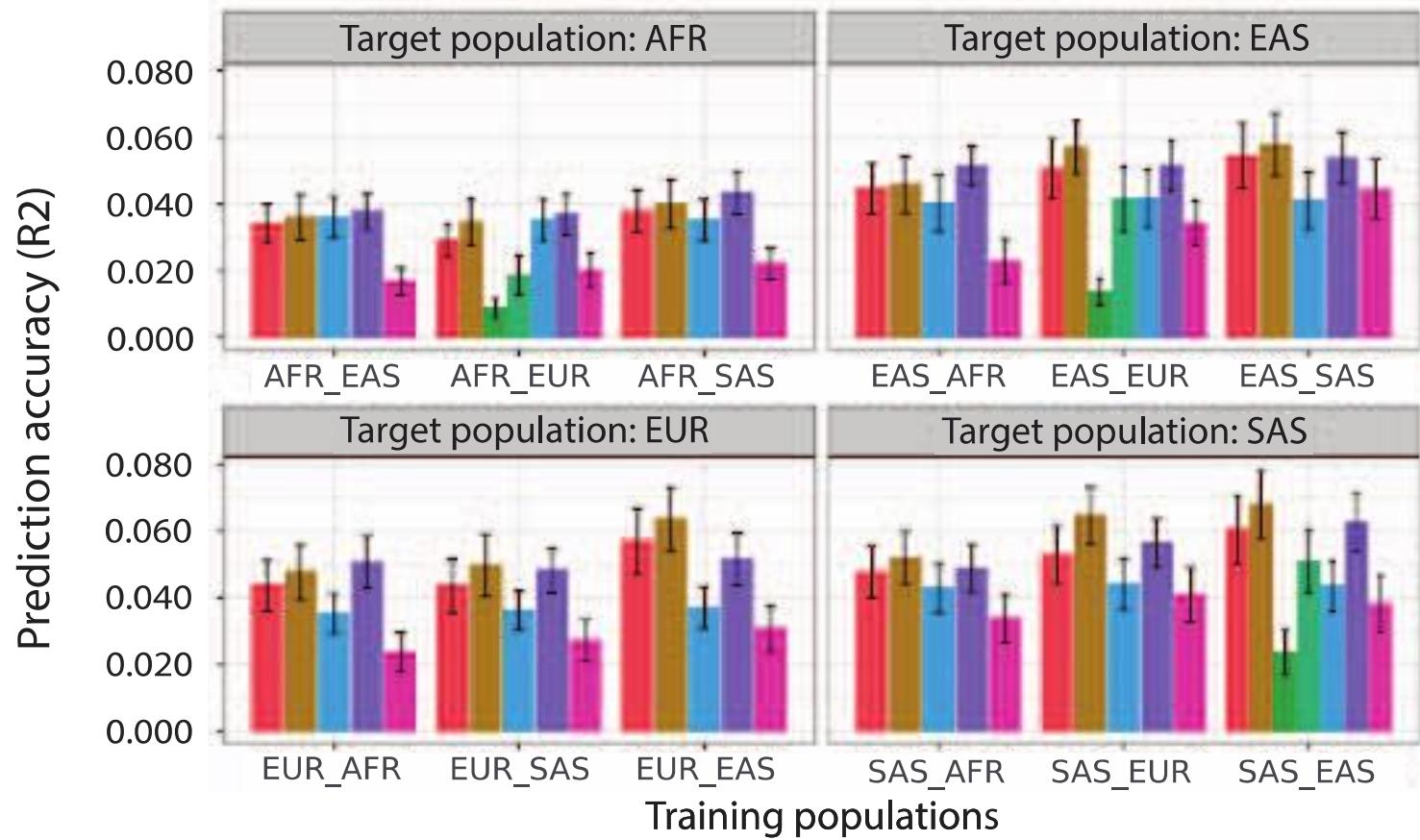


A

Example of experimental design: SAS + EUR to evaluate SAS

**B**

CHR-22 simulation

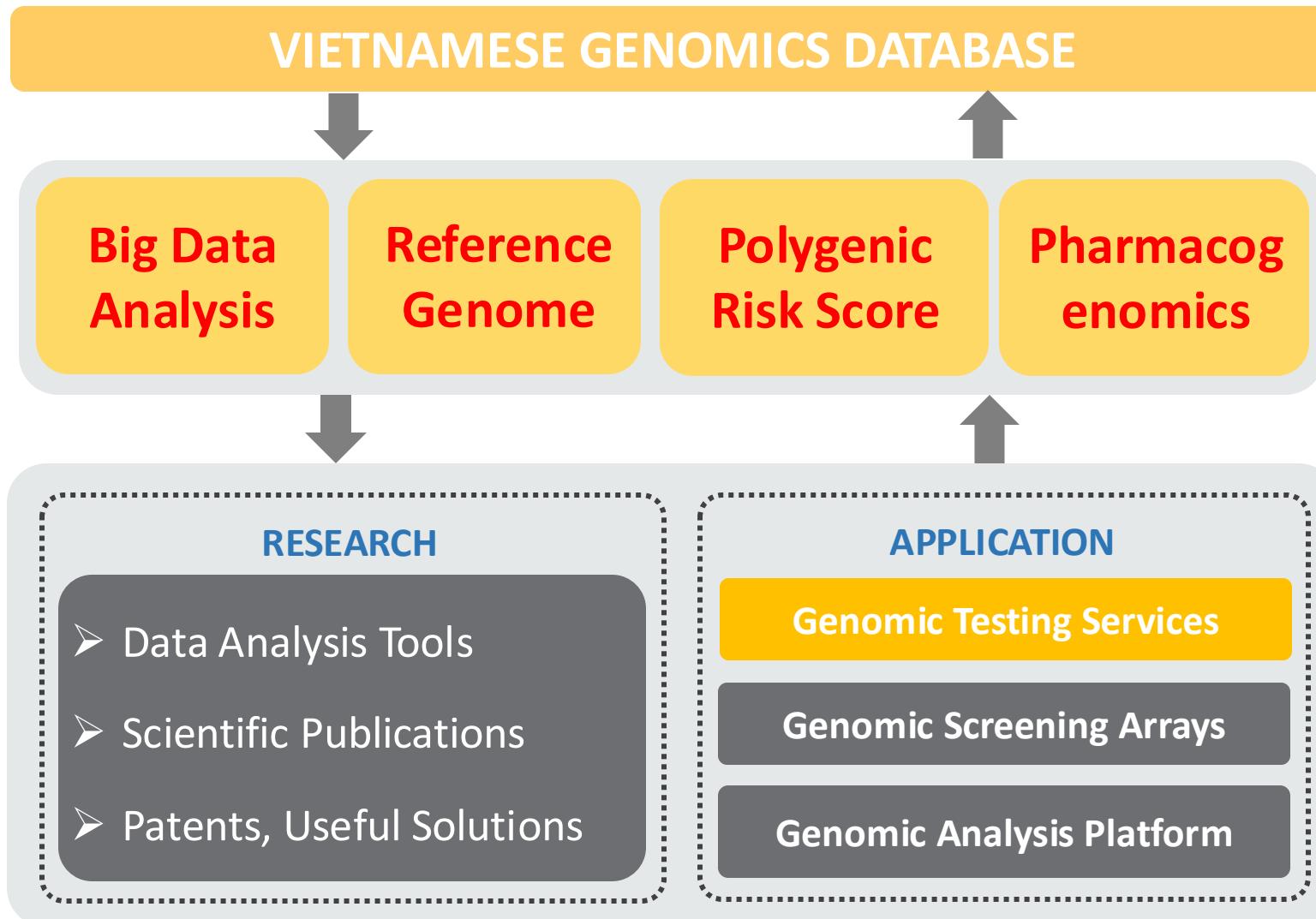


Experimental design and evaluation of the meta-population strategy

2496 random causal SNPs from 24 959 SNPs from real genotype in the 1000 Genomes, effect sizes $N(0, h^2/1000)$; 07 PRS methods: 05 for all combinations of samples and 02 (PolyPred and PolyPred+) leverage the tagging and causal SNP effects of EUR to predict non-EUR. Bars: 100 reps. of random sampling, error bars: 95% conf. intervals

03 VGP: What next?

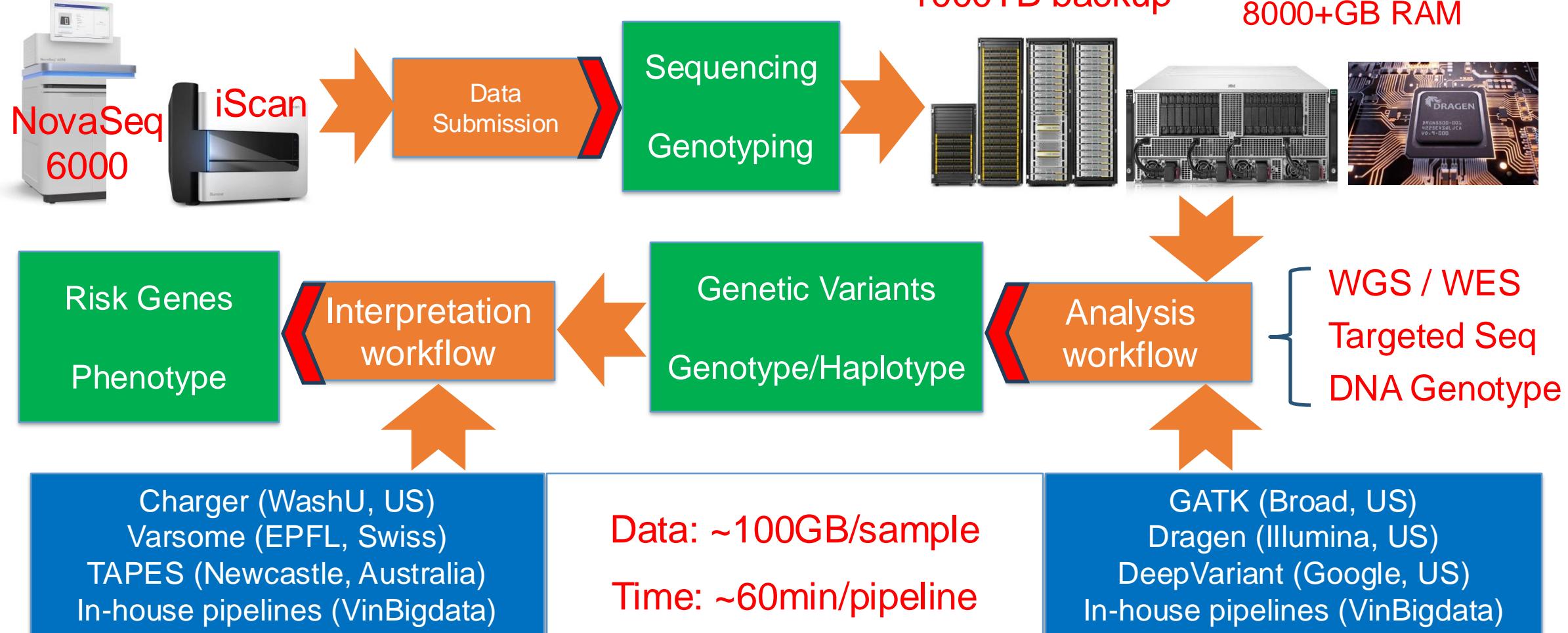
VGP: from 1K to 10K - to 100K



50+ Papers
10+ Patents
1500+ WGS/WES
8500+ Genotype
10000+ Samples
2000+ TB Data

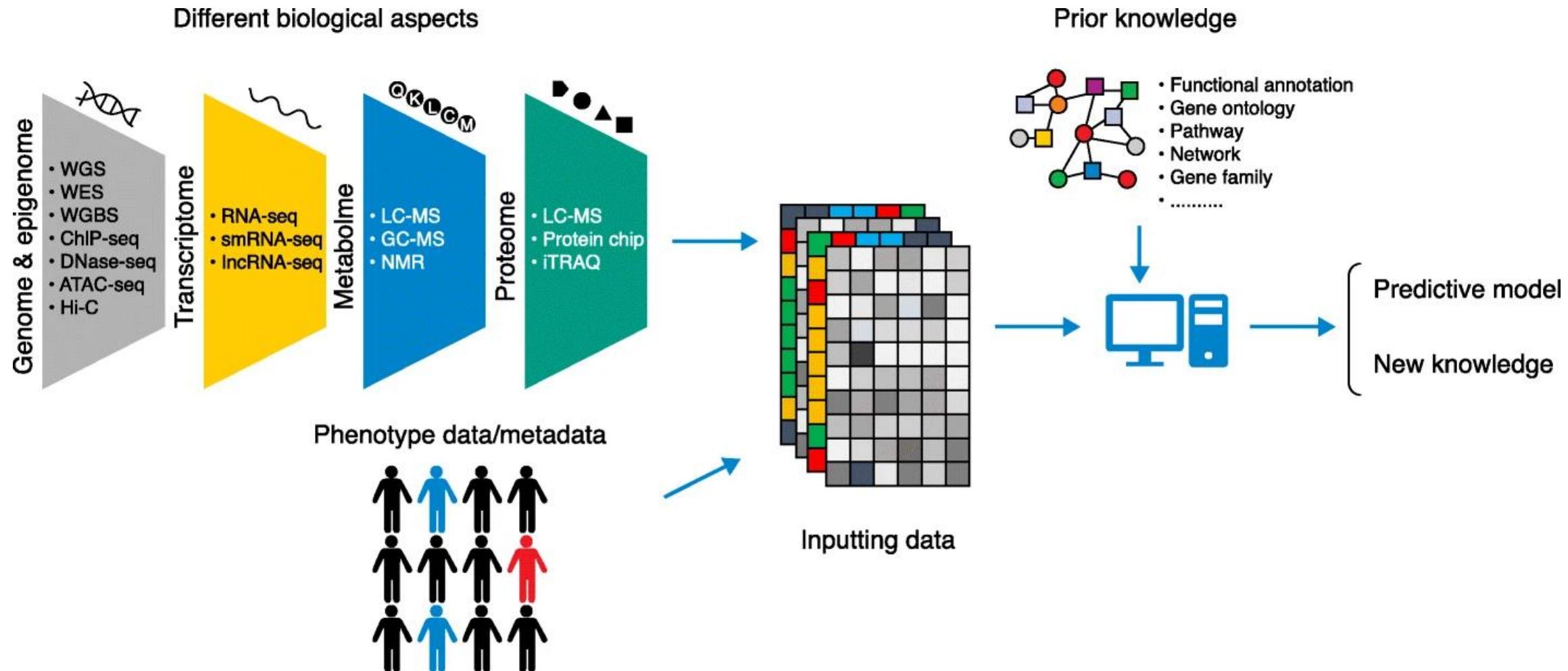
VGP: From wetlab to drylab

How to manage and process PB-scale data?

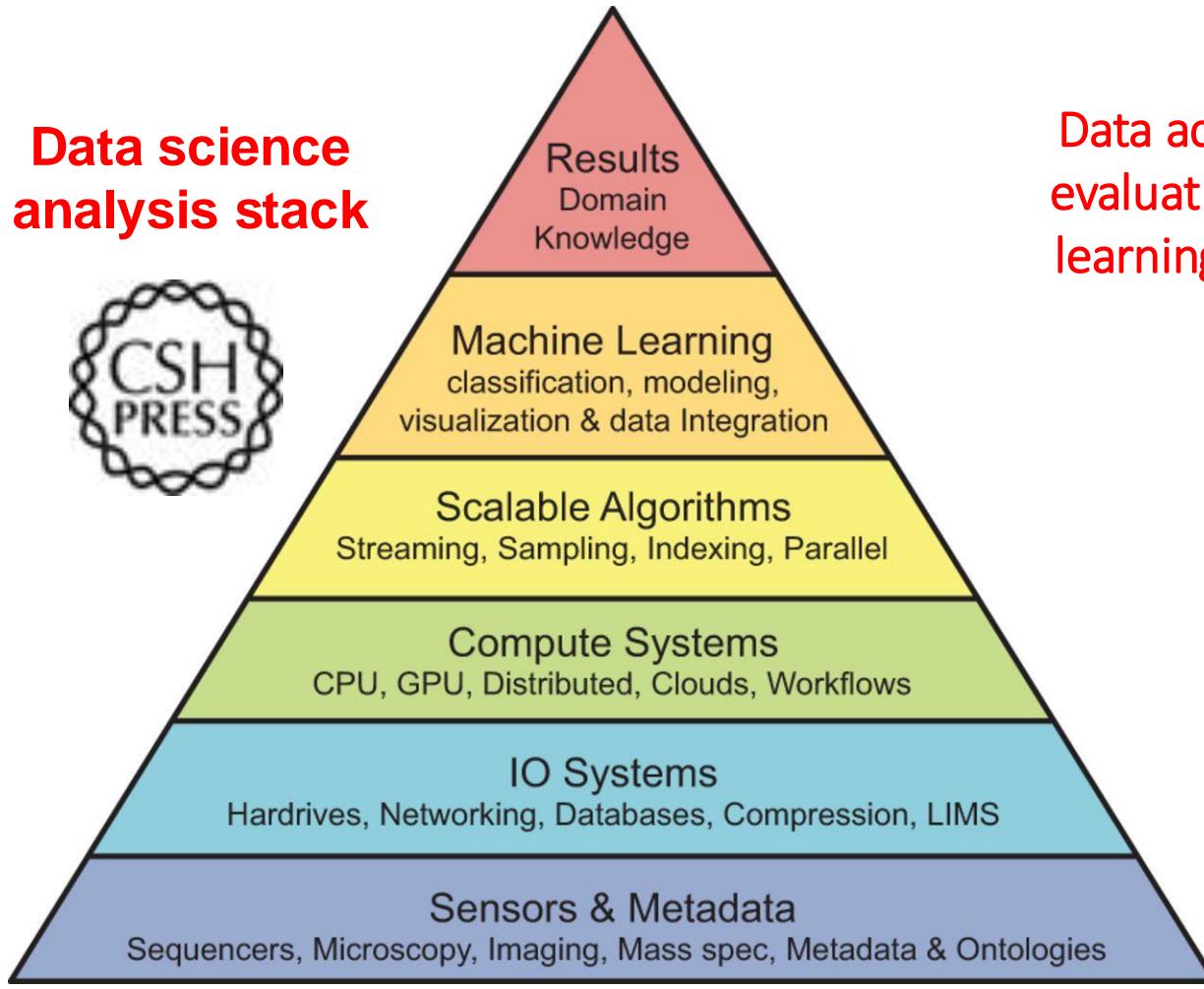


Unraveling information from bio-data

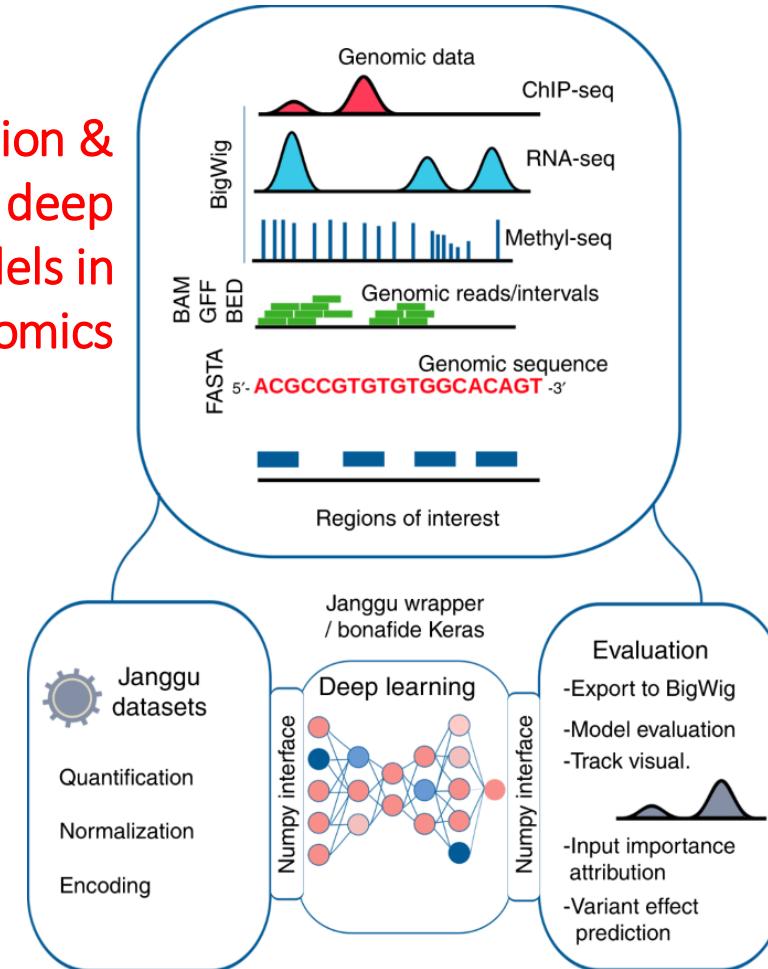
- What knowledge could be inferred?
- How could Machine Learning/Deep Learning help?



Recap: Use DS & ML in Genomics



Data acquisition & evaluation of deep learning models in genomics



Wolfgang Kopp *et al*, Nature Comm.
11(3488) (2020)

Challenges for ML in Biosciences

Explainability x Training efficiency

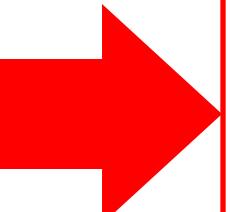
[*Nature Communications*](#) volume 13, Article #: 1728 (2022)

Table 2 Commonly faced challenges in computational biology and potential solution avenues when using DL.

Challenge	Experimental/non-DL solution	DL solution
Biased results	Improve study design	Identify forms and sources of technical bias Fair AI approaches
High infrastructure costs	Optimize code performance Parallelize code Sub-sample analyzed data Statistical analyses	Optimize DL architecture Parallelize to low-cost devices Condense training data (e.g. coresets) Explainable post-hoc methods
Lack of explainability		
Limited training data	Generate and label more data	Data augmentation (e.g. GANs)
Overfitting	Regularization	Dropout Early stopping Smaller models Additional training data Use larger models Analyze generalization potential
Poor performance on novel data	Expand databases	

Take home messages:

Data-driven methodology

- Hypothesis-driven methods:
 - State a hypothesis
 - Collect data
 - Test the hypothesis
 - Data-driven methods:
 - Obtain data
 - Infer information
 - Discover knowledge
- 
- Big data analytics
 - Efficient algorithms
 - Large-scale parallel computation
 - Graph representation, optimization
 - Data science & engineering
 - Heterogeneous data sources
 - Diverse data format
 - Statistical/Machine Learning
 - Interpretable models

Publications & Patents

Pharmacogenomics & Adverse Drug Reaction

[Prevalence of pharmacogenomic variants in 100 pharmacogenes among Southeast Asian populations under the collaboration of the Southeast Asian Pharmacogenomics Research Network \(SEAPharm\)](#)

[Human Genome Variation \(Nature\), 2021](#)

[Review on Databases and Bioinformatics Approaches on Pharmacogenomics of ADR](#)
[Pharmacogenomics and Personalized Medicine, 2021](#)

[Southeast Asian Pharmacogenomics Research Network \(SEAPharm\): Current Status and Perspectives](#)

[Public Health Genomics, 2019](#)

[Autosomal recessive hyper-IgE syndrome due to DOCK8 deficiency: Effectiveness of omalizumab](#)

[Journal of Cutaneous Immunology and Allergy, 2022](#)

[Integrating molecular graph data of drugs and multiple -omics data of cell lines for drug response prediction](#)

[IEEE/ACM Transactions on Computational Biology and Bioinformatics, 2021](#)

[Graph convolutional networks for drug response prediction](#)

[IEEE/ACM Transactions on Computational Biology and Bioinformatics, 2021](#)

[An investigation of cancer cell line-based drug response prediction methods on patient data](#)

[International Conference on Knowledge and Systems Engineering, 2020](#)

Polygenic Risk Score & Genomic Variant Interpretation

[LmTag: functional-enrichment and imputation-aware tag SNP selection for population-specific genotyping arrays](#)

[Briefings in Bioinformatics, 2022](#)

[Assessing polygenic risk score models for applications in populations with under-represented genomics data: an example of Vietnam](#)

[Briefings in Bioinformatics, 2022](#)

[A comprehensive imputation-based evaluation of tag SNP selection strategies](#)
[Scientific Reports, 2022](#)

[A comprehensive and bias-free evaluation of genomic variant clinical interpretation tools](#)
[International Conference on Knowledge and Systems Engineering, 2021](#)

[Development and Implementation of Polygenic Risk Score in Vietnamese Population](#)
[Journal of Research and Development on ICT, 2019](#)

[A comprehensive evaluation of polygenic score and genotype imputation performances of human SNP arrays in diverse populations](#)

[Scientific Reports, 2022](#)

[Polygenic risk scores adaptation for Height in Vietnamese population](#)
[IEEE.org](#)

Cancer Risk Prediction & Stratification

[BRCA1/2 Mutations in Vietnamese Patients with Hereditary Breast and Ovarian Cancer Syndrome](#)

[Genes, 2022](#)

[Integrative Transcriptomic Analysis Identifies Drivers of Squamous Cell Carcinoma Development](#)

[Scientific Reports, 2020](#)

[Improving existing analysis pipeline to identify and analyze cancer driver genes using multi-omics data](#)

[Scientific Reports, 2020](#)

[Multi-Omics Analysis Detects Novel Prognostic Subgroups of Breast Cancer](#)
[Front. Genet., 2020](#)

[Unveiling Prognostics Biomarkers of Tyrosine Metabolism Reprogramming in Liver Cancer by Cross-platform Gene Expression Analyses](#)

[Plos ONE, 2020](#)

[Clinical evaluation of RB1 genetic testing reveals novel mutations in Vietnamese patients with retinoblastoma](#)

[Molecular and Clinical Oncology, 2021](#)

[Meta-analysis of computational methods for breast cancer classification](#)
[Int. J. Intelligent Information and Database Systems, 2019](#)

[Liquid biopsy to characterize cell-free DNA in detecting and monitoring of cancers](#)
[Journal of Research and Development on ICT, 2019](#)

Publications & Patents

Biomedical Data Analysis

[RWRMTN: a tool for predicting disease-associated microRNAs based on a microRNA-target gene network](#)

BMC Bioinformatics, 2020

[UFO: a tool for unifying biomedical ontology-based semantic similarity calculation, enrichment analysis and visualization](#)

PLOS ONE, 2020

[Machine learning-based approaches for disease gene prediction](#)

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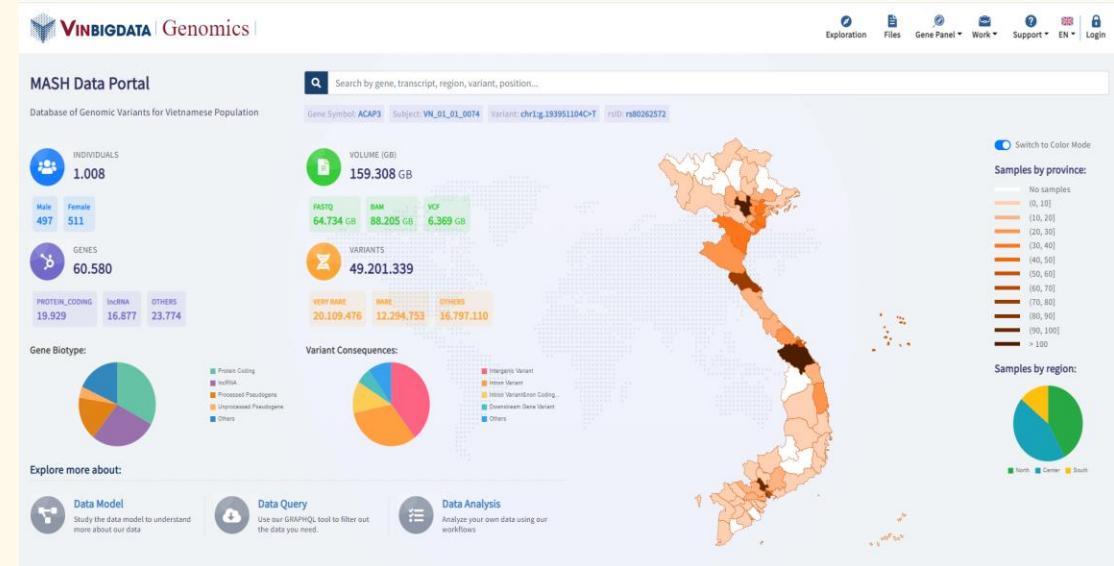
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UNIVERSITY
SINGAPORE**

A photograph of a family meal. A woman in a white shirt is laughing heartily, her hands clasped near her face. In the foreground, a young child is clapping their hands. To the right, a man is smiling warmly at the child. They are all seated around a table with plates of food.

THANK YOU

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