

The Taiwan Precision Medicine Initiative



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Precision Medicine: Predictions

	Prediction	Action
Before Disease	Risk/Age of Onset	Preventive Measures
Emerging Disease	Symptom Onset	Treatment for Cure
Established Disease	Prognosis	Treatment to Avoid Serious Sequelae
Medication Use	Effectiveness and Adverse Reactions	Optimize Drug Use and Dosage

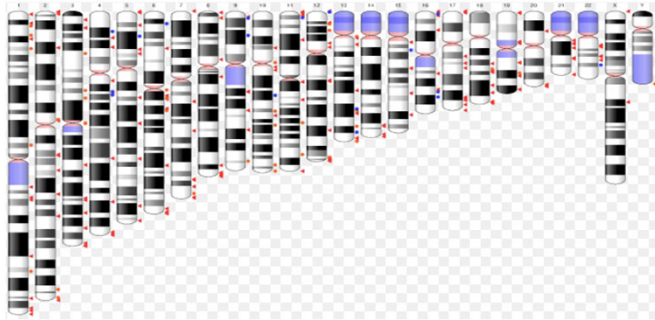
Precision Medicine Common Diseases

- Affect all of us
- Caused by many risk variants
- Risk variants different across populations
- Highly influenced by environment
- DNA sequencing of one person is not useful
- Must study large populations

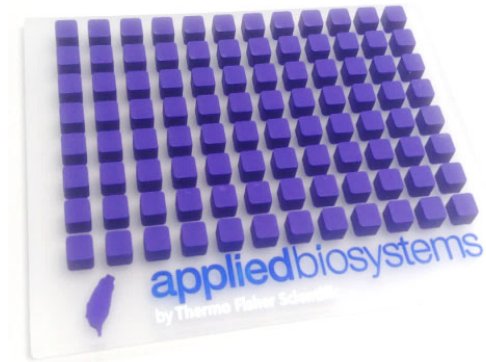


Key: disease risk prediction and risk reduction

Taiwan Precision Medicine Initiative



Taiwan reference genomes



Taiwan Precision Medicine SNP array



Comprehensive clinical record

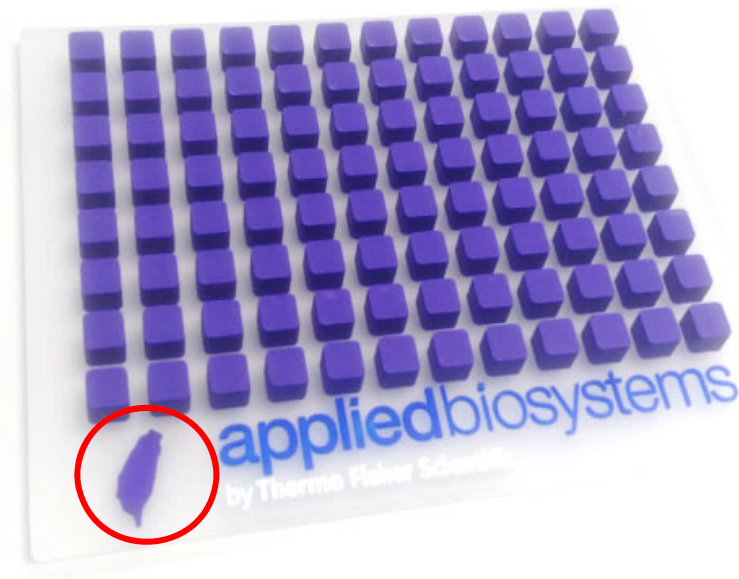


Tailored treatment and health management for all



Genetic profiling of 1 million participants

TPM Array Design



Genetic Testing
124,279 genetic tests

Disease Risk Profiling
578,776 SNPs

Test once in a lifetime

Goals of the TPMI

- Collect sufficient clinical and genetic data from a large (1 million) cohort for common disease risk prediction
- CLINICAL GOALS:
 - Return results to participants for use in their care
 - Establish management guidelines for Han Chinese based on TPMI results
- RESEARCH GOALS:
 - Analyze TPMI data in many studies

Early Genetic Testing Results

ARTICLE OPEN



Genetic profiles of 103,106 individuals in the Taiwan Biobank provide insights into the health and history of Han Chinese

Chun-Yu Wei^{1,4}, Jenn-Hwai Yang^{1,4}, Erh-Chan Yeh¹, Ming-Fang Tsai¹, Hsiao-Jung Kao¹, Chen-Zen Lo¹, Lung-Pao Chang¹, Wan-Jia Lin¹, Feng-Jen Hsieh¹, Saurabh Belsare^{1,2}, Anand Bhaskar^{1,3}, Ming-Wei Su¹, Te-Chang Lee¹, Yi-Ling Lin¹, Fu-Tong Liu¹, Chen-Yang Shen¹, Ling-Hui Li¹, Chien-Hsiun Chen¹, Jeffrey D. Wall², Jer-Yuarn Wu¹ and Pui-Yan Kwok^{1,2}✉

- 21% with Mutations in Autosomal Recessive Disease Genes
- 5% with Mutations for Autosomal Dominant Traits
- 3.1% with Cancer Risk Variants
- 87.3% with Variants that Affect Drug Response

Colon Cancer Incidence in Taiwan

	Male		Female	
	0-49	50-85	0-49	50-85
2019	812 (10.8%)	6700 (89.2%)	677 (12%)	4980 (88.0%)
2018	731 (10.3%)	6386 (89.7%)	638 (11.9%)	4708 (88.1%)
2017	757 (11.1%)	6058 (88.9%)	625 (12.1%)	4529 (87.9%)
2016	626 (10.0%)	5650 (90.0%)	553 (11.7%)	4156 (88.3%)
2015	585 (9.6%)	5536 (90.4%)	588 (12.7%)	4040 (87.3%)

Identify these two group and screen them early

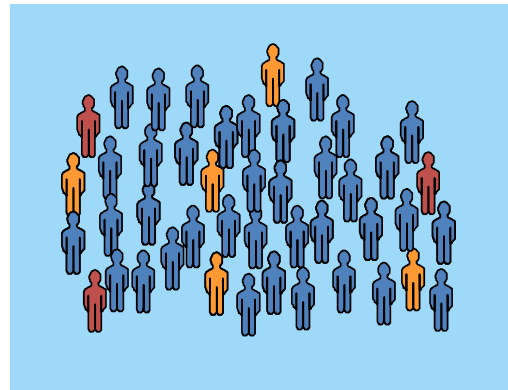
Breast Cancer Incidence

	Female		
	0-39	40-44	≥45
2019	1254 (7.4%)	1674 (9.9%)	14057 (82.8%)
2018	1253 (7.7%)	1563 (9.6%)	13449 (82.7%)
2017	1212 (7.7%)	1566 (9.9%)	13056 (82.4%)
2016	1140 (8.2%)	1360 (9.8%)	11332 (81.9%)
2015	1237 (9.1%)	1352 (10.0%)	10954 (80.9%)

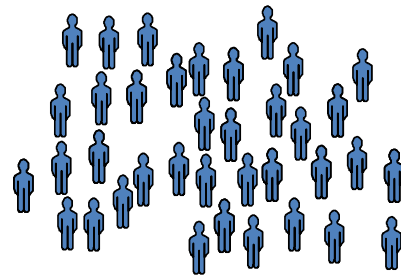
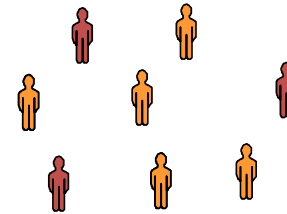
Identify this group and screen them early

Drug	Gene(s)	# Subjects	%
Tacrolimus	CYP3A5	75,111	52.4%
Atazanavir, Irinotecan, Nilotinib, Pazopanib	UGT1A1	70,726	49.3%
Efavirenz	CYP2B6	52,880	36.9%
Warfarin	CYP2C9, VKORC1	38,372	26.8%
Isoniazid, Sulfamethoxazole and Trimethoprim, Sulfasalazine	NAT2	34,005	23.7%
Simvastatin	SLCO1B1	32,240	22.5%
Allopurinol	HLA-B*5801	30,936	21.6%
Carisoprodol, Citalopram, Clobazam, Clopidogrel, Escitalopram, Sertraline	CYP2C19	21,849	15.2%
Peginterferon Alfa-2a & Alfa-2b, Ribavirin	IFNL3	17,770	12.4%
Carbamazepine, Oxcarbazepine, Phenytoin	HLA-B*1502	12,472	8.7%
Celecoxib, Flurbiprofen, Ibuprofen, Lornoxicam, Meloxicam, Phenytoin	CYP2C9	9,809	6.8%
Amikacin, Gentamicin, Neomycin, Paromomycin, Streptomycin, Tobramycin	MT-RNR1	7,207	5.0%
Azathioprine	TPMT	4,313	3.0%
Carbamazepine	HLA-A*3101	5,715	4.0%
Ceftriaxone, Hydroxychloroquine, Lidocaine, Ropivacaine, Sulfamethoxazole and Trimethoprim, Sulfasalazine	G6PD	3,561	2.5%

Tailored Medication Use



Remove
Non-Responders
and Toxic Responders



Treat
Responders Not
Predisposed to Toxicity

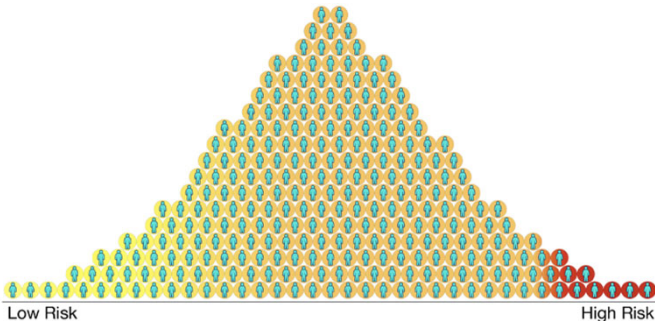
Disease Risk Calculator



Clinical data/genetic profiles



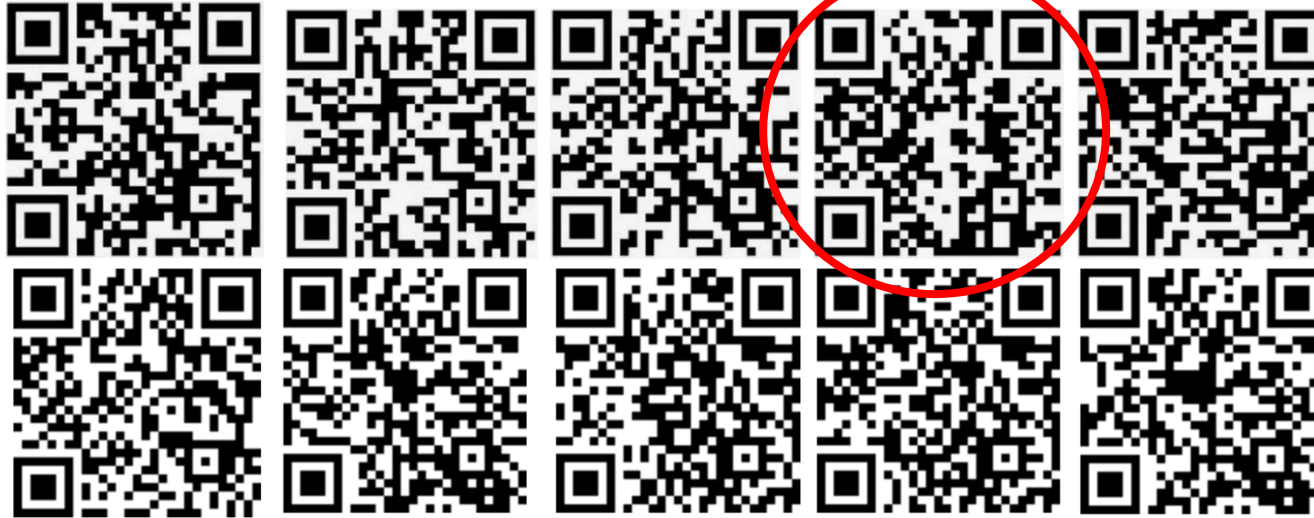
Disease Risk Calculator



Polygenic risk scores



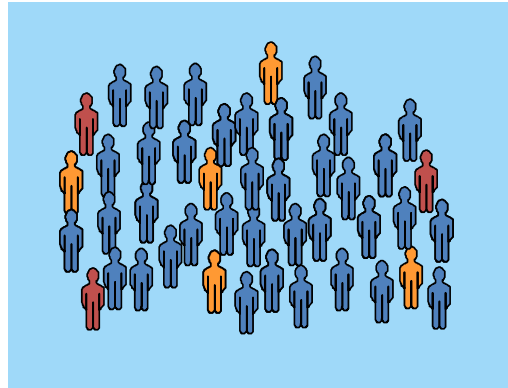
Health Prediction & Management



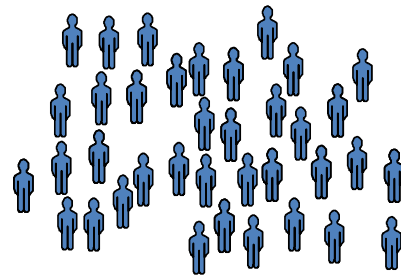
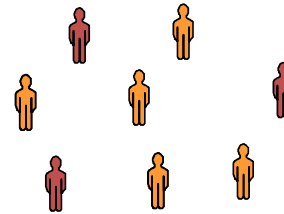
Each has unique risk profile and optimal health management plan



Tailored Disease Management



High Risk Patients
Change life-style
Screening tests early
Treat before symptomatic



Low Risk Patients
Screening tests late

TPMI Status (3/22/2022)

- Subjects enrolled = 452,693
- Samples collected = 353,162
- Samples genotyped = 297,683
- EMR uploaded = 275,309
- Return of results = launched Oct 2021
- Data analysis/research = 22 working groups
(106 projects)

Conclusions

- Taiwan is the perfect place to implement precision medicine for **COMMON DISEASES**
- Polygenic risk scores from the TPMI will predict a person's risk for all major diseases
- Disease risk can be lowered by life-style changes or early intervention
- Early screening of high-risk group increases cure rate of cancer and reduces morbidity of serious diseases
- **Data useful for disease risk prediction of 1.5 billion Han Chinese in the world**



<https://tpmi.ibms.sinica.edu.tw>

