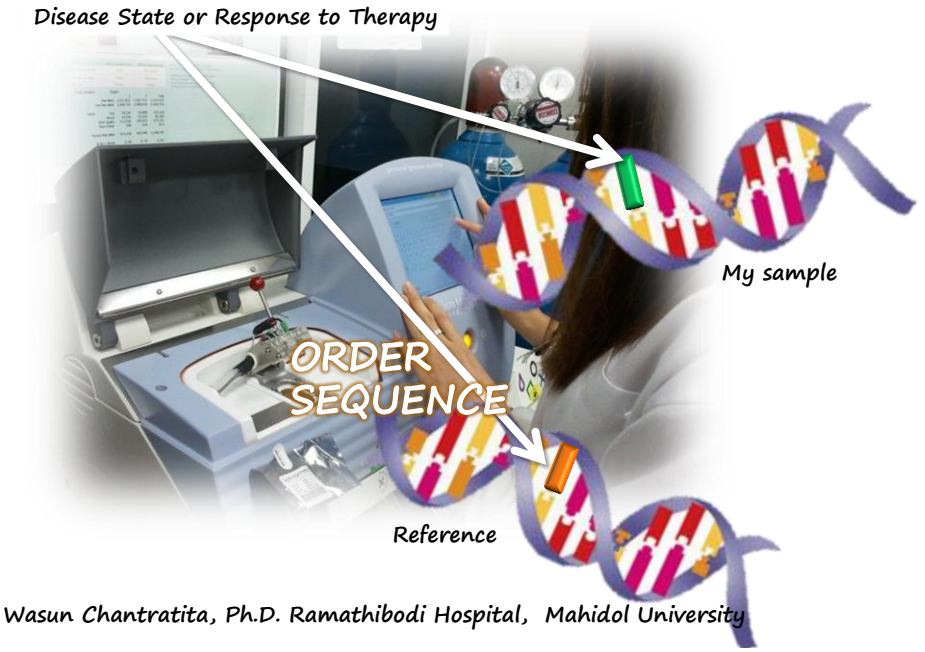
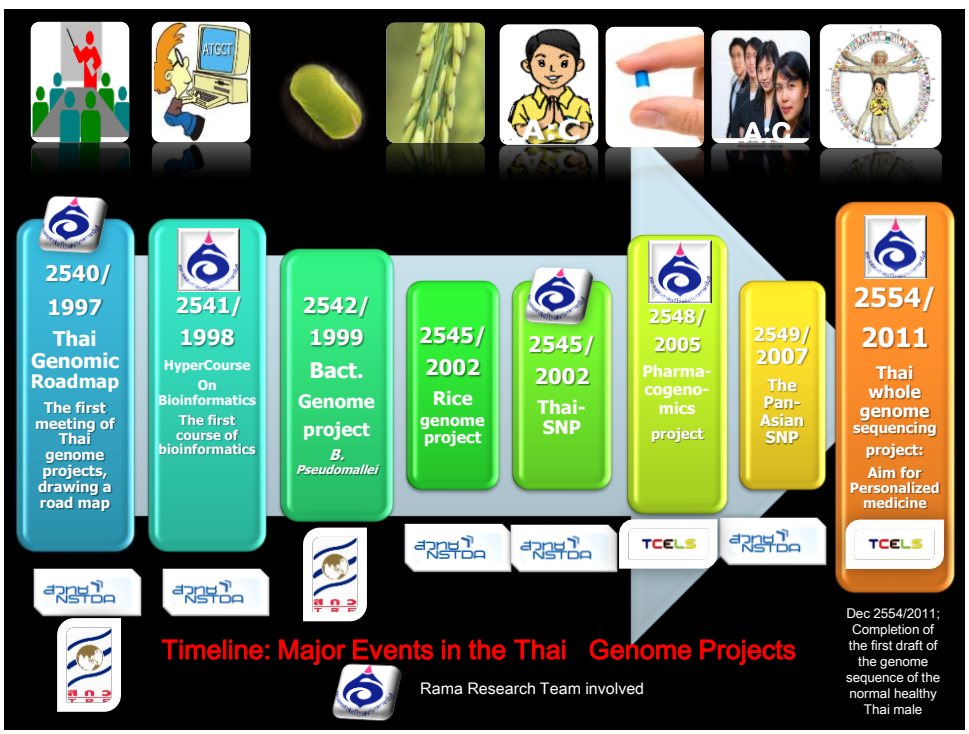
Human genome project and personalized medicine



Wasun Chantratita, Ph.D. Ramathibodi Hospital, Mahidol University



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Decoding the Thai Genome Project

วันที่ 12 พฤษภาคม 2554 08:31 น.
ที่มา TCELS

May 12 2011

SOLiD 5500XL

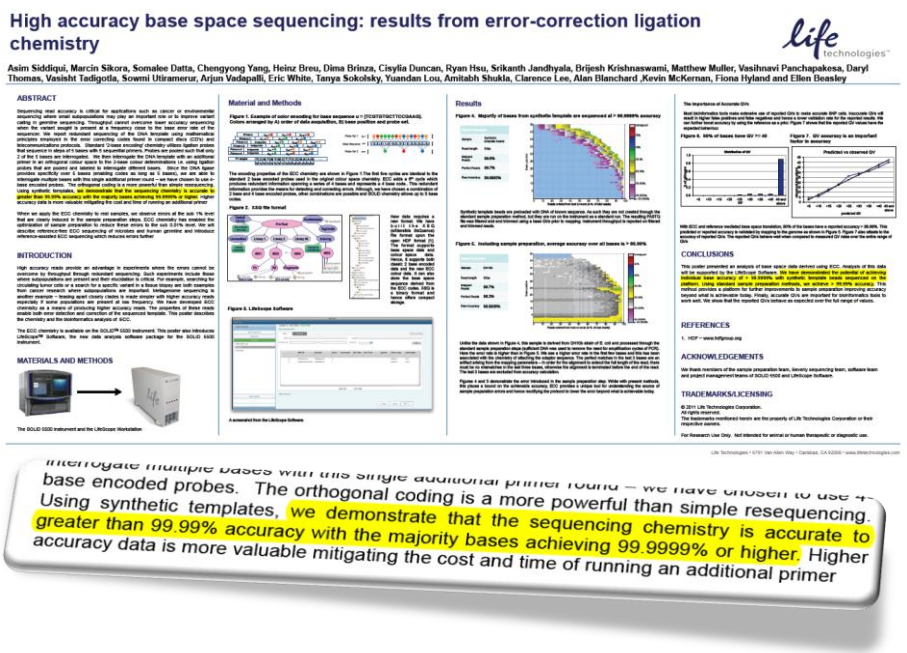
From June 2011, the Virology Unit and Laboratory for Pharmacogenomics and Personalized Medicine, Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, with support from the Thailand Center of Excellence for Life Sciences (TCELS), will collaborate jointly to decode the human genome (whole genome sequencing) of three billion bases of an anonymous, healthy Thai male donor as a model for further study of DNA changes (DNA variant).

Dr. Wasun Chantratita, project leader made the announcement that this genome will be compared latter with genomes of various persons who have different diseases, including those that are common and rare. The two main objectives of this project are, firstly, to locate the DNA variant(s) on the genome, which is associated strongly with disease. That genomic maker can then be developed into a set of genetic screening tests at a low cost. If the test results (from the laboratory) are positive, it will mean that the person is at high risk of the diseases in the future. However, the risk may be reduced if these people get regular medical checkups, change or modify their behavior regarding diet or their environment. In children, they are often given a "failure to thrive" diagnosis for an unknown disorder. "Sequencing those genomes will be a key hint to how to treat them properly.

The second objective is to determine the genome of patients for which current therapy does not work properly (difficult to treat). By sequencing their genomes and submitting the DNA variants to the special computational biology program based on computer simulations developed by Dr. Ram Samudrala and his team from the University of Washington, United States of America to identify all approved drugs that can bind to the disease target protein structures which are caused by DNA variants and somehow malfunction in ways that lead to damage and disease in the body. The drug(s) can be picked up and used to replace the medication that did not work in the first place (personalized medicine).

The outcome of the project will finally help both the government and patients regarding effective treatment and reduction of medical expenditure and unnecessary laboratory diagnostic assays. The development of special computational biology program has been supported by the National Institutes of Health (NIH) fund, United States of America.

90 Gb:1 human genome at 30 x coverage (90,000,000,000/3,000,000,000=30).
One run with a single ship will be needed for the re-sequencing of a human genome.



High accuracy base space sequencing: results from error-correction ligation chemistry

life technologies

Asim Siddiqui, Marcin Sikora, Somalee Datta, Chengyong Yang, Heinz Breu, Dima Brinza, Cisylia Duncan, Ryan Hsu, Srikanth Jandhyala, Brijesh Krishnaswami, Matthew Muller, Vasihnavi Panchapakesa, Daryl Thomas, Vasisht Tadigotla, Sowmi Utiramerur, Arjun Vadapalli, Eric White, Tanya Sokolsky, Yuandan Lou, Amitabh Shukla, Clarence Lee, Alan Blanchard ,Kevin McKernan, Fiona Hyland and Ellen Beasley

ABSTRACT

Material and Methods

Results

INTRODUCTION

MATERIALS AND METHODS

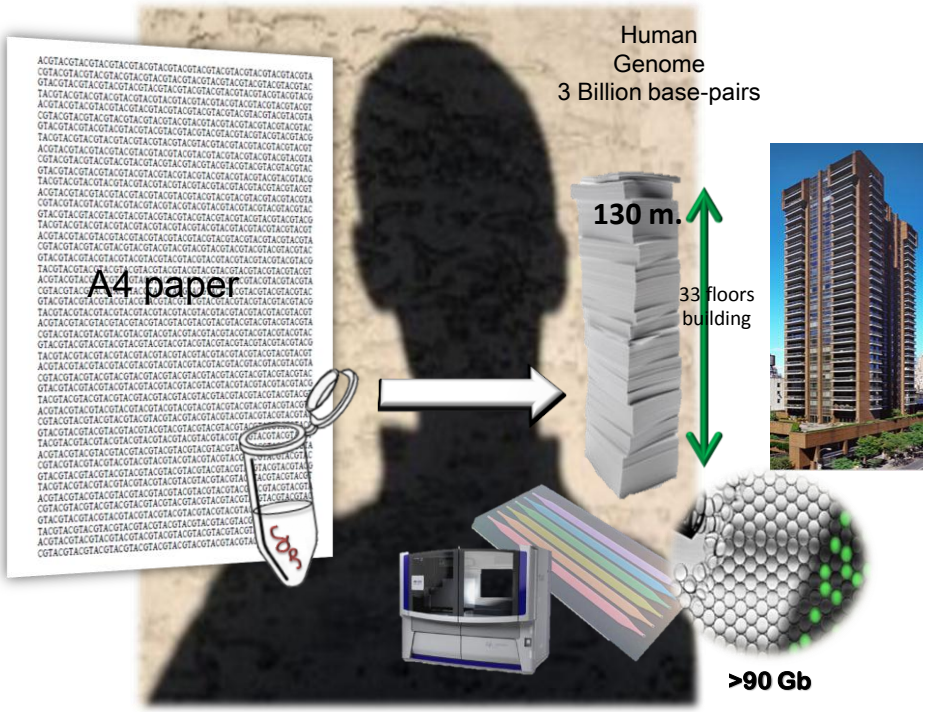
CONCLUSIONS

REFERENCES

ACKNOWLEDGEMENTS

TRADEMARKS/LICENSING

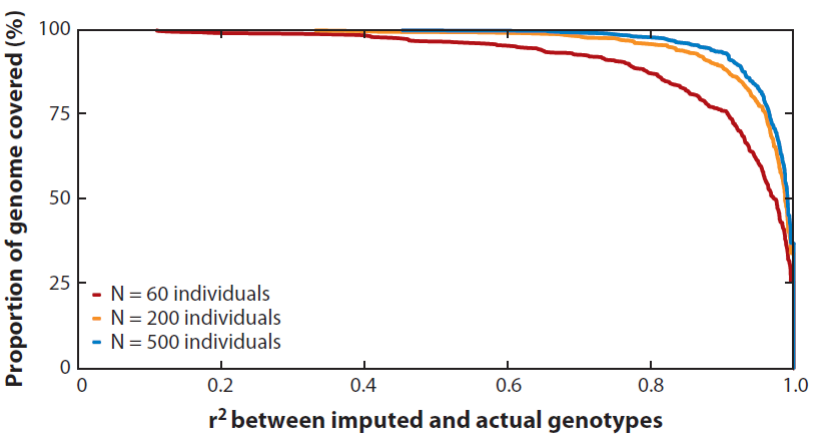
interrogate multiple bases with this single additional primer round – we have chosen to use 4-base encoded probes. The orthogonal coding is a more powerful than simple resequencing. Using synthetic templates, we demonstrate that the sequencing chemistry is accurate to greater than 99.99% accuracy with the majority bases achieving 99.9999% or higher. Higher accuracy data is more valuable mitigating the cost and time of running an additional primer



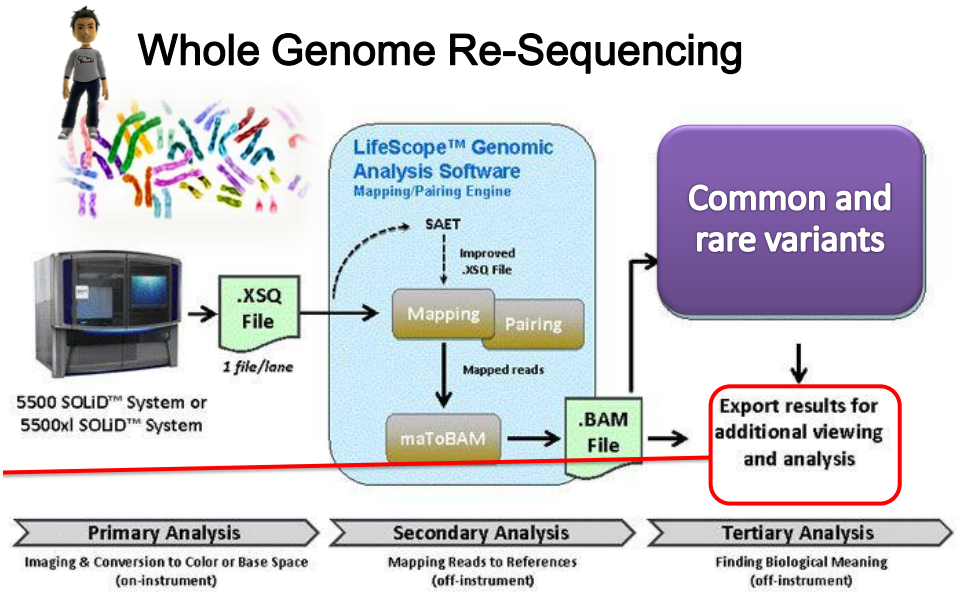
One whole human genome and two whole human exome re-sequencings

Whole human genome re-sequencer in one day @ $1,000

Life Technologies' Ion Torrent business is planning to launch a new sequencing instrument by mid-year (2012) that will enable a whole human genome to be sequenced in hours at a run cost of $1,000.



100-1,000 Thai genome project (5 years project)



Sequencing, assembly, and annotation of the genomes, then

1) Clinically relevant interpretation of DNA variant(s)
2) Identify potential drug targets for the disease
3) Recommendations (for treatment)

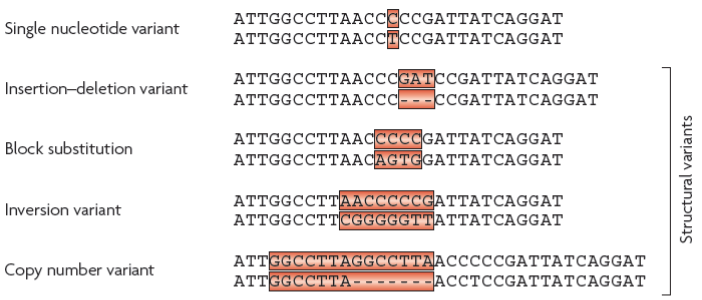
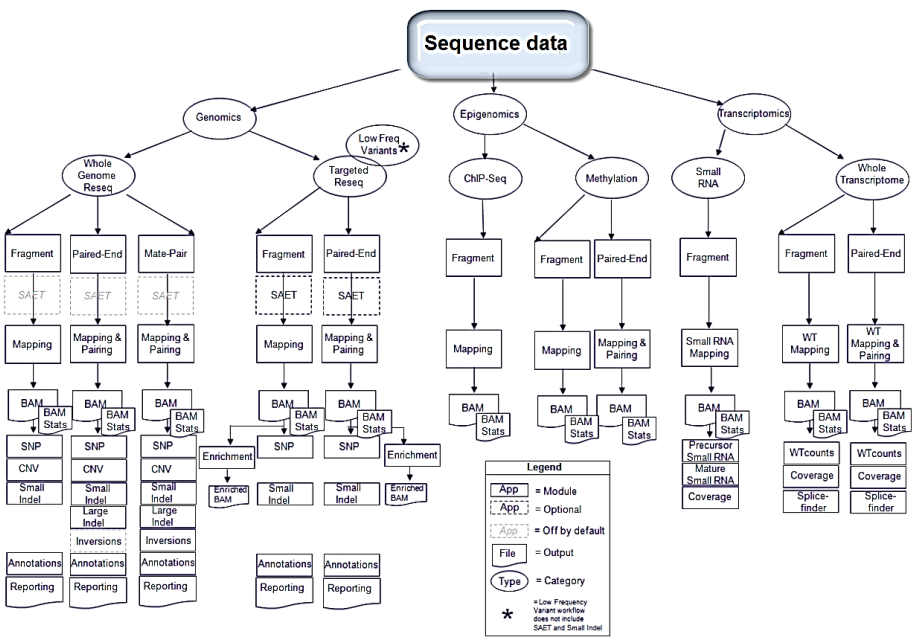
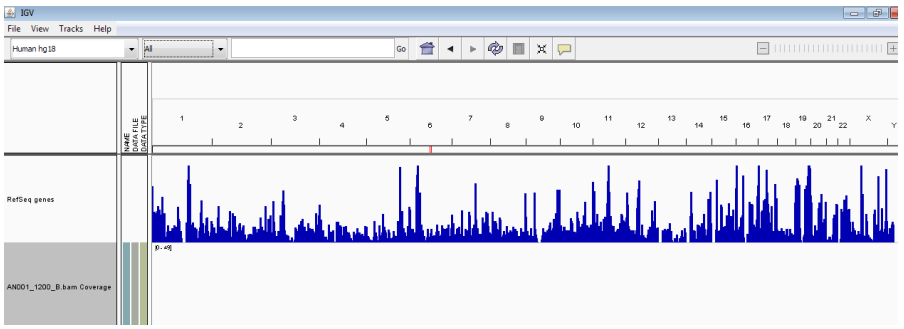


Figure 1 | **Classes of human genetic variants.** The nomenclature used to describe the various types of structural variants is not yet standard[121]. Here, the terminology used aims to describe the nucleotide composition of the variant and distinguish it from other types of variants. Single nucleotide variants are DNA sequence variations in which a single nucleotide (A, T, G or C) is altered. Insertion–deletion variants (indels) occur when one or more base pairs are present in some genomes but absent in others. They are generally composed of only a few bases but can be greater than 80 kb in length[11]. Block substitutions describe cases in which a string of adjacent nucleotides varies between two genomes. An inversion variant is one in which the order of the base pairs is reversed in a defined section of a chromosome. A well-characterized inversion variant that has been described in humans involves a section of chromosome 17 in which a ~900 kb interval is in the reverse order in approximately 20% of individuals with Northern European ancestry[122]. Copy number variants occur when identical or nearly identical sequences are repeated in some chromosomes but not others. The largest copy number variant identified in the Venter genome[11] was almost 2 Mb in length.

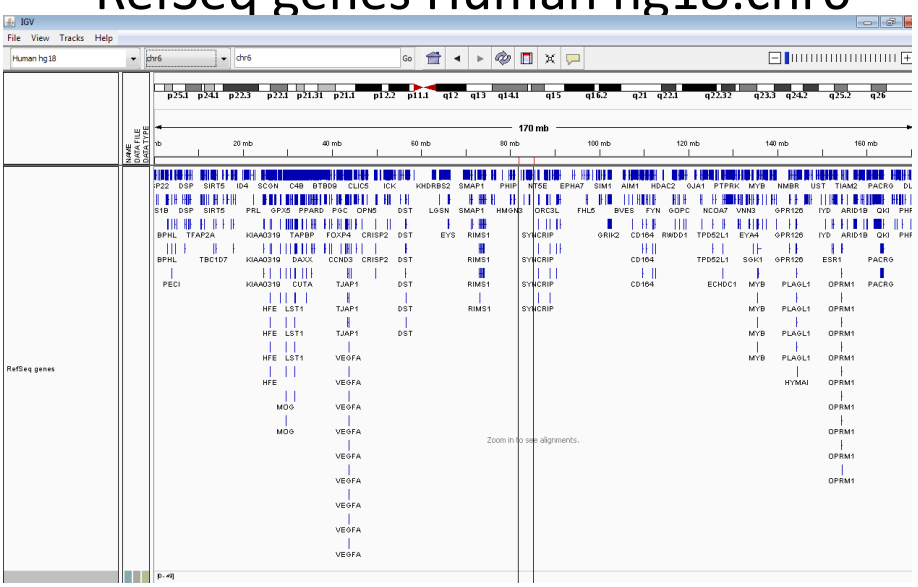
Analysis type	Statistics
All supported modules (SNPs, CNVs, Indels)	Number of variants Number of variants per chromosome Number of heterozygous variants Number of homozygous variants Number of heterozygous SNPs per chromosome Number of homozygous SNPs per chromosome
SNPs	Number of heterozygous SNPs that are transitions, transversions Number of homozygous SNPs that are transitions, transversions (compared to the reference)
Indels	Indel variant length distribution (negative for deletion, positive for insertion)
CNVs	Copy number distribution CNV length distribution
Annotations from dbSNPs	Number of SNPs or indels in dbSNP Number of homozygous SNPs or indels in dbSNP Number of heterozygous SNPs or indels in dbSNP Overall dbSNP concordance (percentage of SNPs or indels in dbSNP) Heterozygous dbSNP concordance (the percentage of heterozygous SNPs or indels found in dbSNP) Homozygous dbSNP concordance (the percentage of homozygous SNPs or indels found in dbSNP)
Annotations from GTF file content	Number of variants in exons, and the percentage of exons that are variant Number of heterozygous variants in exons, and their percentage Number of homozygous variants in exons, and their percentage Number of variants in genes, and the percentage that are variant Number of heterozygous variants in genes, and their percentage Number of homozygous variants in genes, and their percentage



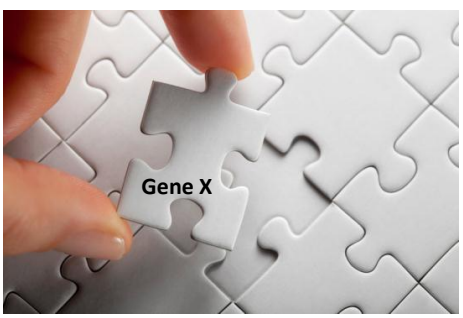
Show RefSeq genes Human hg18

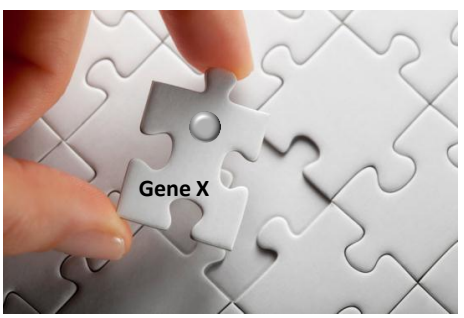


RefSeq genes Human hg18:chr6



show all bases ,show coverage track

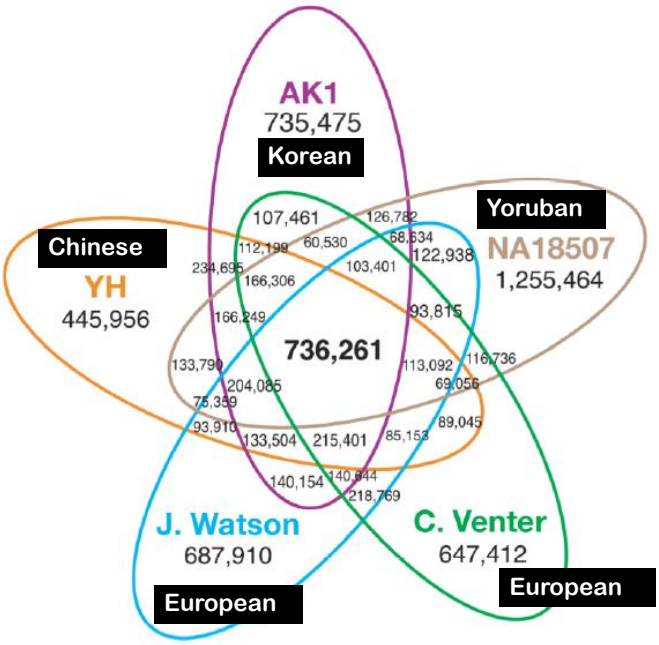




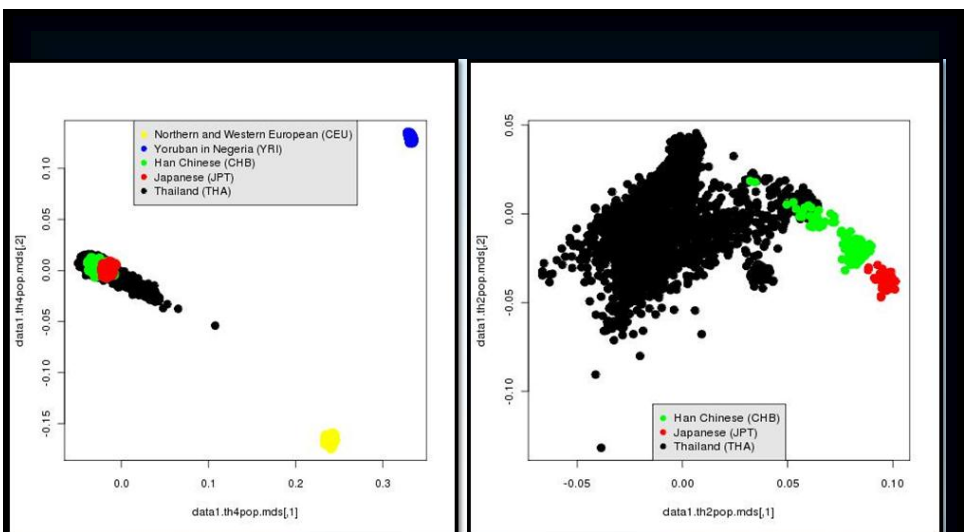
Mr. A

Mr. B

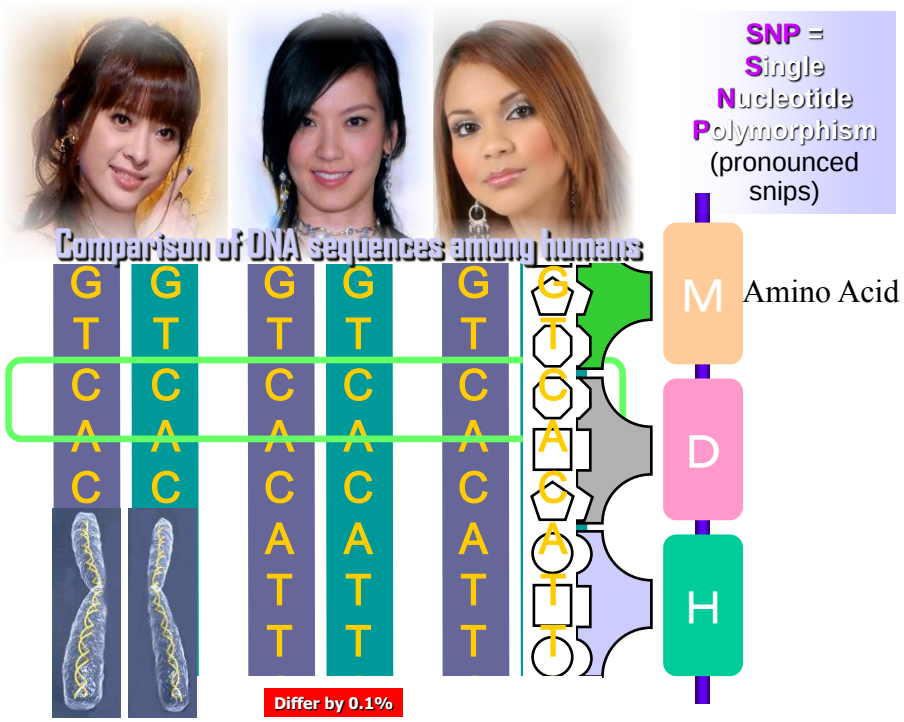
Differ by 0.1% or 3,000,000 bases

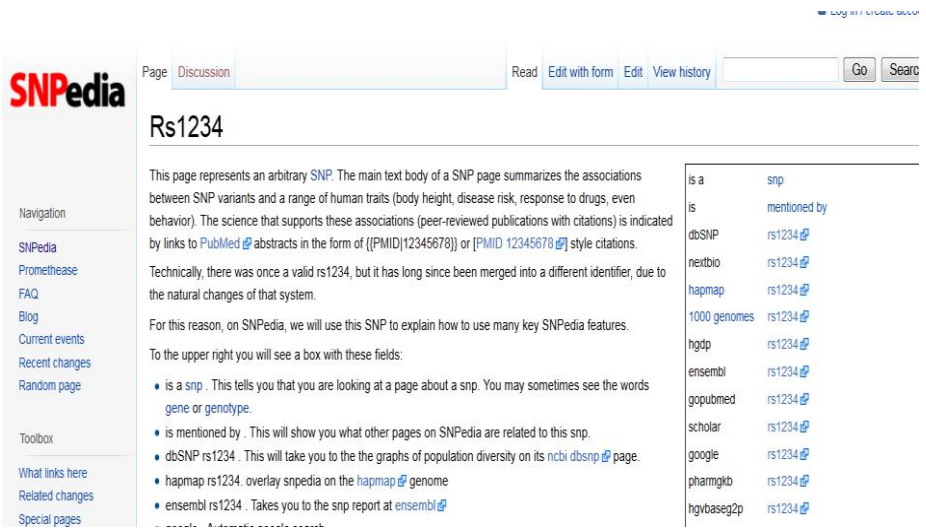


The number of SNPs overlapping between five genomes

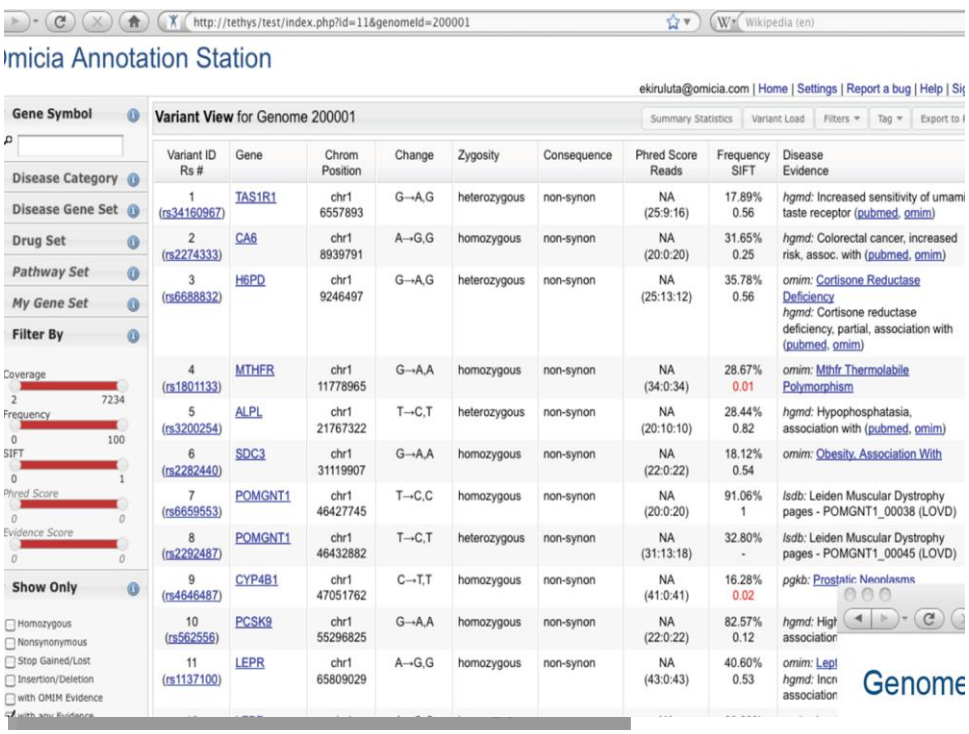


Tag SNPs (610K) from TCELS-Thai MOPH- PGx 6 projects (2805 samples) – THAI VS 4 populations


SNP =
Single
Nucleotide
Polymorphism
(pronounced
snips)
Comparison of DNA sequences among humans
G T C A C
G T C A C
G T C A C A T T
G T C A C A T T
G T C A C A T T
Differ by 0.1%
M
D
H
Amino Acid

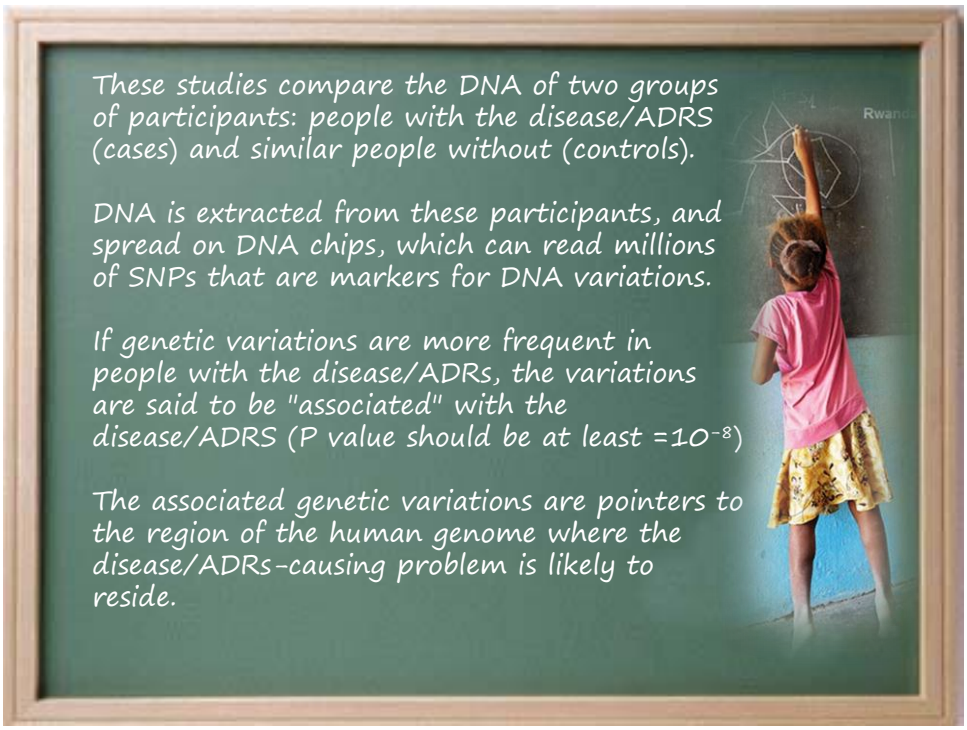

SNPedia
Page
Discussion
Read
Edit with form
Edit
View history
Go
Search
Rs1234
This page represents an arbitrary SNP. The main text body of a SNP page summarizes the associations between SNP variants and a range of human traits (body height, disease risk, response to drugs, even behavior). The science that supports these associations (peer-reviewed publications with citations) is indicated by links to PubMed abstracts in the form of {{PMID|12345678}} or [PMID 12345678] style citations.
Technically, there was once a valid rs1234, but it has long since been merged into a different identifier, due to the natural changes of that system.
For this reason, on SNPedia, we will use this SNP to explain how to use many key SNPedia features.
To the upper right you will see a box with these fields:
• is a snp . This tells you that you are looking at a page about a snp. You may sometimes see the words gene or genotype.
• is mentioned by . This will show you what other pages on SNPedia are related to this snp.
• dbSNP rs1234 . This will take you to the the graphs of population diversity on its ncbi dbsnp page.
• hapmap rs1234. overlay snpedia on the hapmap genome
• ensembl rs1234 . Takes you to the snp report at ensembl
Navigation
SNPedia
Promethease
FAQ
Blog
Current events
Recent changes
Random page
Toolbox
What links here
Related changes
Special pages
is a snp
is mentioned by
dbSNP rs1234
nextbio rs1234
hapmap rs1234
1000 genomes rs1234
hgdp rs1234
ensembl rs1234
gopubmed rs1234
scholar rs1234
google rs1234
pharmgkb rs1234
hgvbaseg2p rs1234

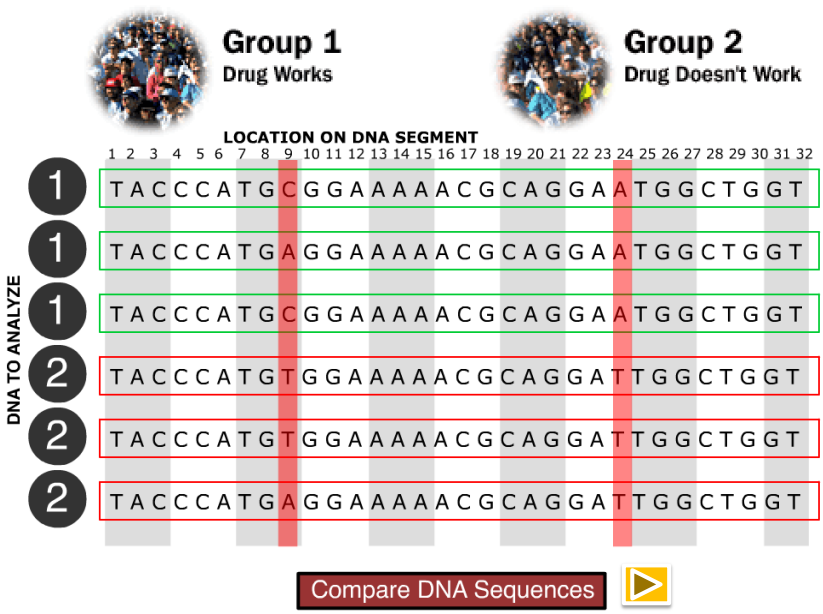

The human genome interpretation company™
Finding the genetic basis of human disease and drug response
Rare Disease
Identify the variants that underlie rare disease.
Common Disease
Unravel the complex basis of common disease.
Cancer
Find and understand the drivers of tumor growth.
Drug Response
Pinpoint the genetic variants that govern drug response.

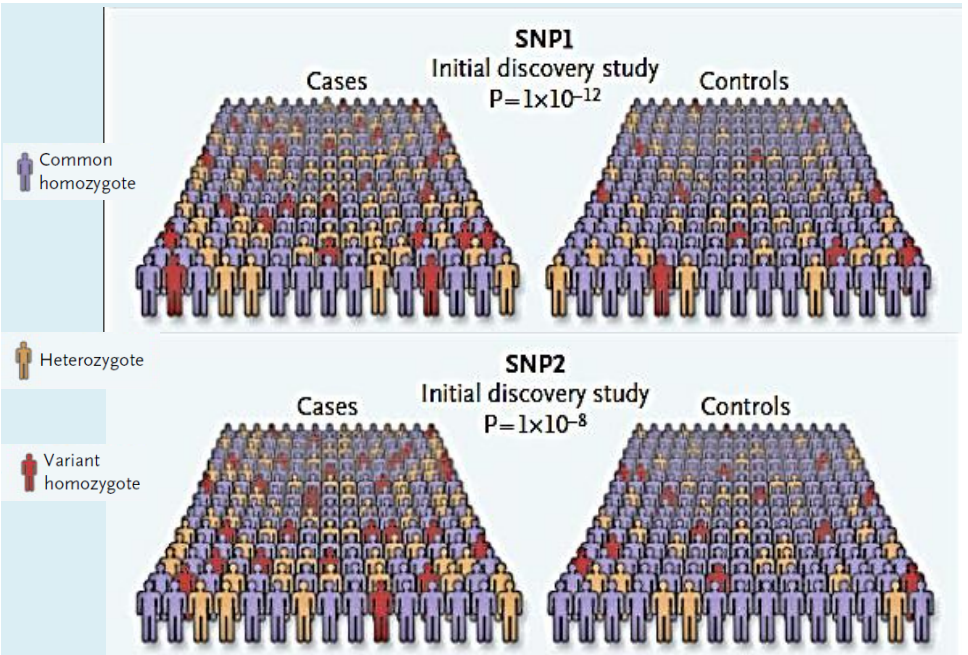

http://tethys/test/index.php?id=11&genomeId=200001
Wikipedia (en)
micia Annotation Station
ekiruluta@omicia.com | Home | Settings | Report a bug | Help | Sig
Gene Symbol
Disease Category
Disease Gene Set
Drug Set
Pathway Set
My Gene Set
Filter By
Coverage
2 7234
Frequency
0 100
SIFT
0 1
Phred Score
0 0
Evidence Score
0 0
Show Only
Homozygous
Nonsynonymous
Stop Gained/Lost
Insertion/Deletion
with OMIM Evidence
Variant View for Genome 200001
Summary Statistics
Variant Load
Filters
Tag
Export to
Variant ID Rs #
Gene
Chrom Position
Change
Zygosity
Consequence
Phred Score Reads
Frequency SIFT
Disease Evidence
1 (rs34160967) TAS1R1 chr1 6557893 G→A,G heterozygous non-synon NA (25:9:16) 17.89% 0.56 hgmd: Increased sensitivity of umami taste receptor (pubmed, omim)
2 (rs2274333) CA6 chr1 8939791 A→G,G homozygous non-synon NA (20:0:20) 31.65% 0.25 hgmd: Colorectal cancer, increased risk, assoc. with (pubmed, omim)
3 (rs6688832) H6PD chr1 9246497 G→A,G heterozygous non-synon NA (25:13:12) 35.78% 0.56 omim: Cortisone Reductase Deficiency hgmd: Cortisone reductase deficiency, partial, association with (pubmed, omim)
4 (rs1801133) MTHFR chr1 11778965 G→A,A homozygous non-synon NA (34:0:34) 28.67% 0.01 omim: Mthfr Thermolabile Polymorphism
5 (rs3200254) ALPL chr1 21767322 T→C,T heterozygous non-synon NA (20:10:10) 28.44% 0.82 hgmd: Hypophosphatasia, association with (pubmed, omim)
6 (rs2282440) SDC3 chr1 31119907 G→A,A homozygous non-synon NA (22:0:22) 18.12% 0.54 omim: Obesity, Association With
7 (rs6659553) POMGNT1 chr1 46427745 T→C,C homozygous non-synon NA (20:0:20) 91.06% 1 lsdb: Leiden Muscular Dystrophy pages - POMGNT1_00038 (LOVD)
8 (rs2292487) POMGNT1 chr1 46432882 T→C,T heterozygous non-synon NA (31:13:18) 32.80% - lsdb: Leiden Muscular Dystrophy pages - POMGNT1_00045 (LOVD)
9 (rs4646487) CYP4B1 chr1 47051762 C→T,T homozygous non-synon NA (41:0:41) 16.28% 0.02 pgkb: Prostatic Neoplasms
10 (rs562556) PCSK9 chr1 55296825 G→A,A homozygous non-synon NA (22:0:22) 82.57% 0.12 hgmd: High association
11 (rs1137100) LEPR chr1 65809029 A→G,G homozygous non-synon NA (43:0:43) 40.60% 0.53 omim: Lep hgmd: Incr association
Genome


WGS>GWAS

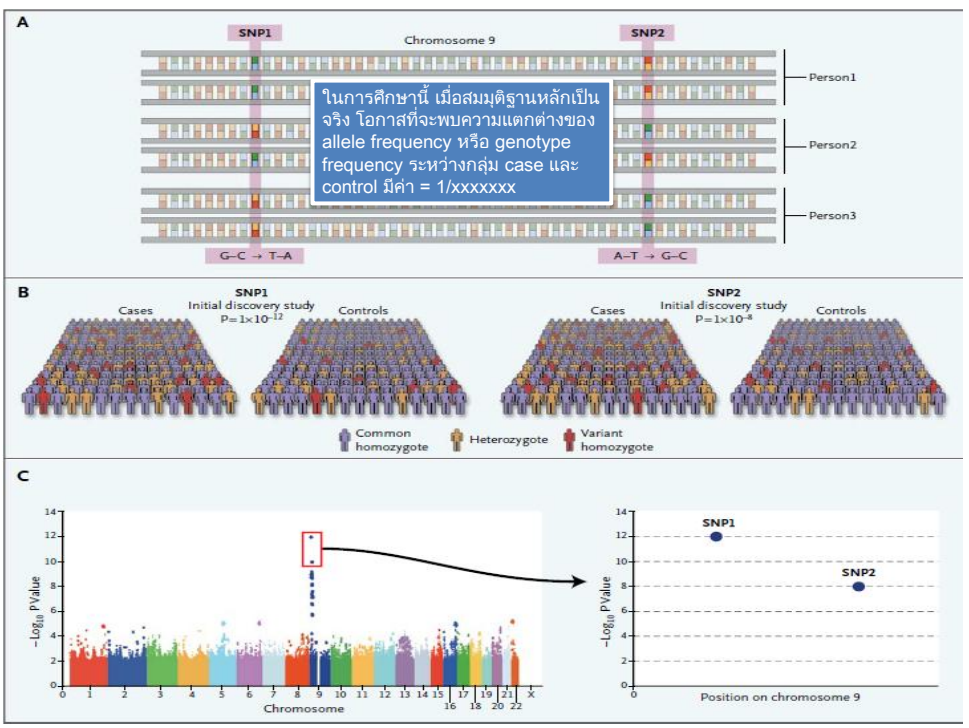

www.Thaigov.go.th
TCELS
Thailand Center of Excellence for Life Sciences
Prime Minister's Office
Thailand Center of Excellence for Life Sciences (TCELS)
HIV-1 Pharmacogenomics (Nevirapine-rash)
อ. ศศิโสภิณ เกียรติบูรณกุล
Drug allergy: Allopurinol, Carbamazepine
อ.ทิชา ลิ่มสุวรรณ, อ. วสุ ก่าชัยเสถียร
Pharmacogenomics in Childhood acute lymphoblastic leukemia
อ สุรเดช หงส์ยิง
Pharmacogenomics in oncology-chemotherapy
อ. เอกภพ สีระชัยนันท์
Pharmacogenomics in Thalassemia
อ. ธันยชัย สุระ
Pharmacogenomic study of aspirin responsiveness
อ. วัลยา จงเจริญประเสริฐ
Posttraumatic Stress Disorder (PTSD)
Pharmacogenomics in Psychiatric Diseases
(Tsunami victims and relatives)
Chunlalongkorn Hospital
Rajanukul Institute
Wasun Chantratita
Project director
Individualized medicine
Pharmacogenomics projects: Ramathibodi hospital, Mahidol University &
Thailand Center of Excellence for Life Sciences


These studies compare the DNA of two groups of participants: people with the disease/ADRS (cases) and similar people without (controls).
DNA is extracted from these participants, and spread on DNA chips, which can read millions of SNPs that are markers for DNA variations.
If genetic variations are more frequent in people with the disease/ADRs, the variations are said to be "associated" with the disease/ADRS (P value should be at least =10-8)
The associated genetic variations are pointers to the region of the human genome where the disease/ADRs-causing problem is likely to reside.


Group 1
Drug Works
Group 2
Drug Doesn't Work
LOCATION ON DNA SEGMENT
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32
DNA TO ANALYZE
1 TACCCATGCGGAAAAACGCAGGAATGGCTGGT
1 TACCCATGAGGAAAAACGCAGGAATGGCTGGT
1 TACCCATGCGGAAAAACGCAGGAATGGCTGGT
2 TACCCATGTGGAAAAACGCAGGATTGGCTGGT
2 TACCCATGTGGAAAAACGCAGGATTGGCTGGT
2 TACCCATGAGGAAAAACGCAGGATTGGCTGGT
Compare DNA Sequences



ในการศึกษานี้ เมื่อสมมุติฐานหลักเป็นจริง โอกาสที่จะพบความแตกต่างของ allele frequency หรือ genotype frequency ระหว่างกลุ่ม case และ control มีค่า = 1/xxxxxxx



ในการศึกษานี้ เมื่อสมมุติฐานหลักเป็นจริง โอกาสที่จะพบความแตกต่างของ allele frequency หรือ genotype frequency ระหว่างกลุ่ม case และ control มีค่า = 1/xxxxxxx

Figure 1. The Genomewide Association Study.

The genomewide association study is typically based on a case–control design in which single-nucleotide polymorphisms (SNPs) across the human genome are genotyped. Panel A depicts a small locus on chromosome 9, and thus a very small fragment of the genome. In Panel B, the strength of association between each SNP and disease is calculated on the basis of the prevalence of each SNP in cases and controls. In this example, SNPs 1 and 2 on chromosome 9 are associated with disease, with P values of 10^{-12} and 10^{-8}, respectively. The plot in Panel C shows the P values for all genotyped SNPs that have survived a quality-control screen, with each chromosome shown in a different color. The results implicate a locus on chromosome 9, marked by SNPs 1 and 2, which are adjacent to each other (graph at right), and other neighboring SNPs.

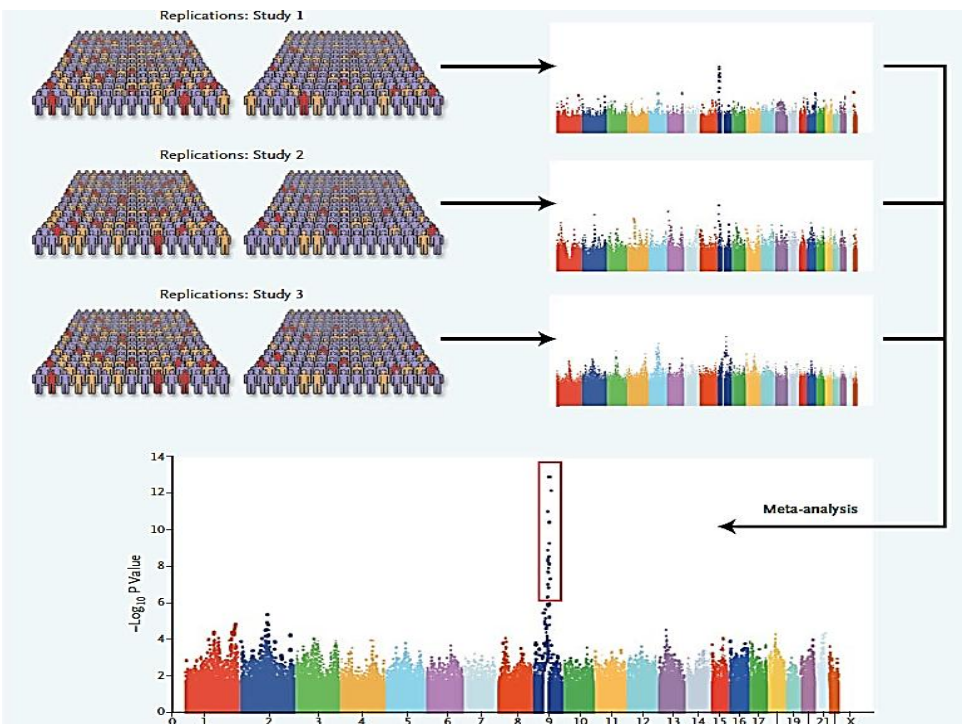


Figure 2. Meta-Analysis of Genomewide Association Studies.

The results of genomewide association studies can be evaluated in a meta-analysis, which combines the results of multiple studies to improve the power for detecting associations. In this example, the results of three studies, none of which may show genomewide significance individually, are combined in a meta-analysis to reveal a strong, significant signal on chromosome 9.

Genomewide Associations Reported through March 2010.

Circles indicate the chromosomal location of nearly 800 single-nucleotide polymorphisms (SNPs) significantly associated ($P<5\times10^{-8}$) with a disease or trait and reported in the literature (545 studies published through March 2010 yielded the associations depicted). Each disease type or trait is coded by color. Adapted from the National Human Genome Research Institute.[4]

Science News

Genetic Variant Increases Risk of Common Type Stroke

ScienceDaily (Feb. 5, 2012) — A genetic variant that increases the risk of a common type of stroke has been identified by scientists in a study funded by the Wellcome Trust and published online in *Nature Genetics*. This is one of the few genetic variants to date to be associated with the risk of stroke, and the discovery opens up new possibilities for treatment.

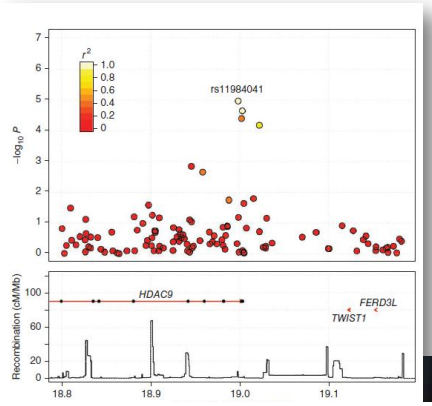
nature genetics

Received 26 May 2011; accepted 15 December 2011; publish

Genome-wide association study identifies a variant in *HDAC9* associated with large vessel ischemic stroke

The International Stroke Genetics Consortium (ISGC)[1] & the Wellcome Trust Case Control Consortium 2 (WTCCC2)[1]

Genetic factors have been implicated in stroke risk, but few replicated associations have been reported. We conducted a genome-wide association study (GWAS) for ischemic stroke and its subtypes in 3,548 affected individuals and 5,972 controls, all of European ancestry. Replication of potential signals was performed in 5,859 affected individuals and 6,281 controls. We replicated previous associations for cardioembolic stroke near *PITX2* and *ZFHX3* and for large vessel stroke at a 9p21 locus. We identified a new association for large vessel stroke within *HDAC9* (encoding histone deacetylase 9) on chromosome 7p21.1 (including further replication in an additional 735 affected individuals and 28,583 controls) (rs11984041; combined $P = 1.87 \times 10^{-11}$; odds ratio (OR) = 1.42, 95% confidence interval (CI) = 1.28–1.57). All four loci exhibited evidence for heterogeneity of effect across the stroke subtypes, with some and possibly all affecting risk for only one subtype. This suggests distinct genetic architectures for different stroke subtypes.



Science News

Colorectal Cancer Risk Increased By Single-Base Change In The Human Genome

ScienceDaily (June 29, 2009) — Finnish Academy Professors Lauri Aaltonen and Jussi Taipale have identified and described a mechanism whereby a single-base change in the human genome increases the risk of colorectal cancer.

ARTICLES

nature genetics

VOLUME 41 | NUMBER 8 | AUGUST 2009 NATURE GENETICS

The common colorectal cancer predisposition SNP rs6983267 at chromosome 8q24 confers potential to enhanced Wnt signaling

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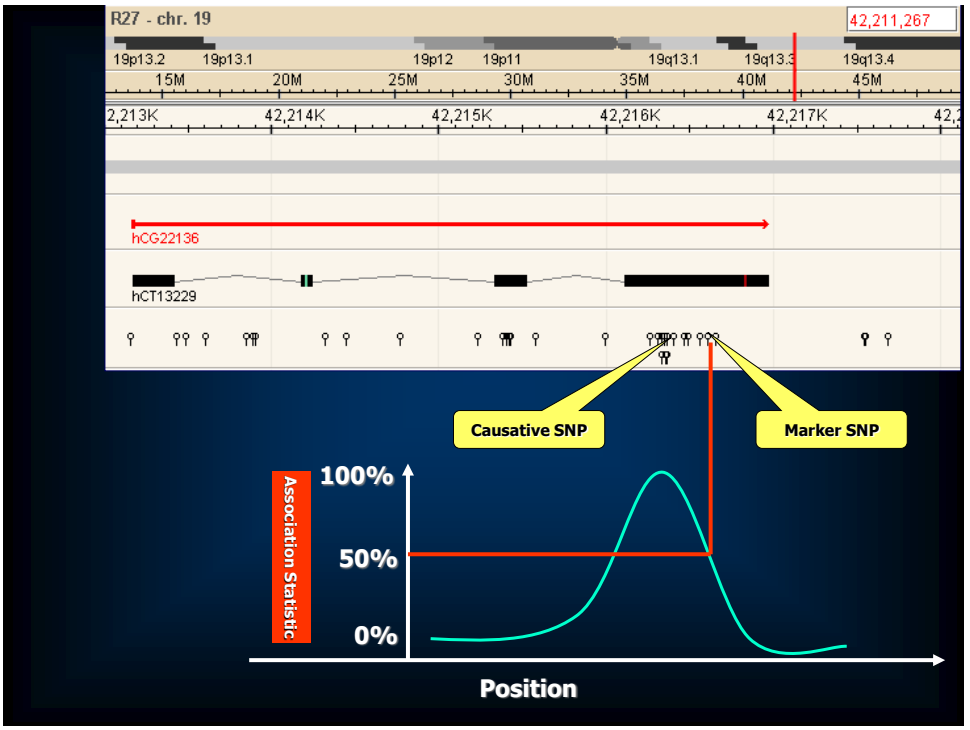
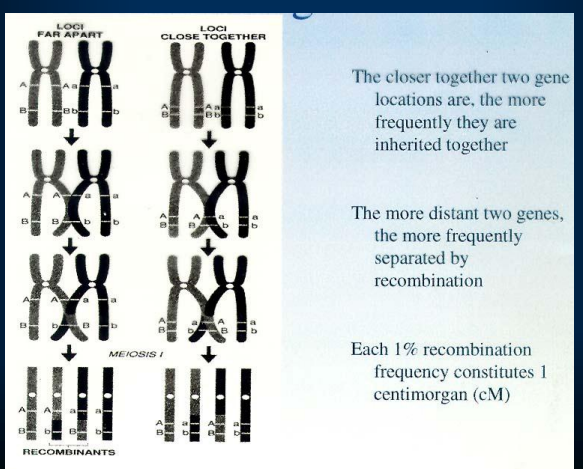
Homozygosity for the G allele of rs6983267 at 8q24 increases colorectal cancer (CRC) risk ~1.5 fold. We report here that the risk allele G shows copy number increase during CRC development. Our computer algorithm, Enhancer Element Locator (EEL), identified an enhancer element that contains rs6983267. The element drove expression of a reporter gene in a pattern that is consistent with regulation by the key CRC pathway Wnt. rs6983267 affects a binding site for the Wnt-regulated transcription factor TCF4, with the risk allele G showing stronger binding *in vitro* and *in vivo*. Genome-wide ChIP assay revealed the element as the strongest TCF4 binding site within 1 Mb of *MYC*. An unambiguous correlation between rs6983267 genotype and *MYC* expression was not detected, and additional work is required to scrutinize all possible targets of the enhancer. Our work provides evidence that the common CRC predisposition associated with 8q24 arises from enhanced responsiveness to Wnt signaling.



Haplotype

ความหมายเดิมจะหมายถึงกลุ่มของหน่วยพันธุกรรม บนโครโมโซมข้างเดียวกัน ที่มีการถ่ายทอดทางพันธุกรรมไปสู่รุ่นลูกรุ่นหลานโดยไม่แตกกลุ่มเนื่องจากกลุ่ม marker เหล่านี้จะอยู่ใกล้กันมาก จึงมีโอกาสน้อยที่จะถูกแบ่งแยกจากกันด้วยกระบวนการ crossing over ต่างจาก genetic marker ที่อยู่บนโครโมโซมข้างเดียวกันแต่อยู่ห่างกัน จะมีโอกาศสูงที่จะถูกตัดแยกจากกันโดยกระบวนการ crossing over ในระยะ meiosis ถ่ายทอดไปสู่รุ่นลูกรุ่นหลานบน chromatid ต่างเส้นกัน




We thought that we are so close.


An attempt to use common SNPs that show association with diseases, as "a tool for screening assay" mostly fail

- However, the bad news is GWAS are not useful in finding genes or genomic markers that predict risks of disease.
- Therefore, general, screening tests, based on most SNPs detected in GWAS to date, are likely to have low positive (and negative) predictive value for disease and limited usefulness in a diagnostic setting.
- This observation has led many to question of the common disease-common variant hypothesis and has contributed to growing interest in evaluating the roles of rare genetic variants in common diseases.
- However, the good news is GWAS have discovered pharmacogenomic related genes for some traits, such as severe adverse reactions to certain drugs, which are essentially monogenic and already used clinically.

Original Paper

Human Heredity

Hum Hered 2012;73:18–25
DOI: 10.1159/000334084

Received: April 20, 2011
Accepted after revision: September 24, 2011
Published online: December 30, 2011

Performance of Genotype Imputations Using Data from the 1000 Genomes Project

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Genotype imputations based on 1000 Genomes (1KG) Project data have the advantage of imputing many more SNPs than imputations based on HapMap data. It also provides an opportunity to discover associations with relatively rare variants.

Our findings suggest that 1KG-based imputation can increase the opportunity to discover significant associations for SNPs across the allele frequency spectrum.

Imputation of SNPs

What is imputation in genetics?

- In genetics, imputation usually refers to the substitution of missing SNP values

Why should we use imputation?

- Missing SNP data is fairly common in association studies, sometimes with rates as high as 5-10% [J. Dai, et al 2006].
- Re-genotyping is usually not possible due to financial constraints.
- Individuals with missing SNP data are usually thrown out, decreasing the effective sample size.
- Recovery of SNP values can keep costs down and restore some of the power lost by errors in data

http://stsnyder.com/wp-content/uploads/2011/08/imputationtalk.pdf

How do we use SNP imputation?

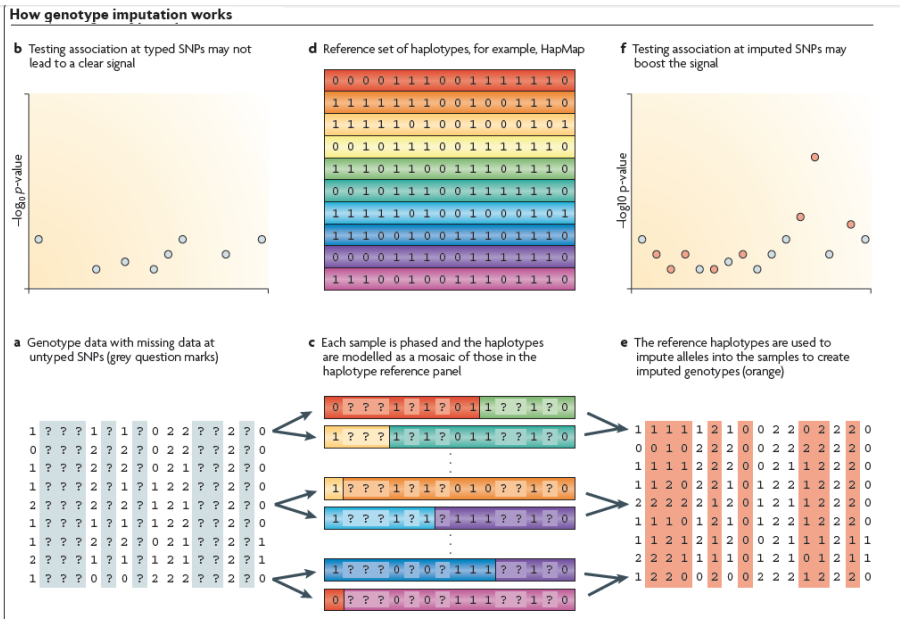
Example:
We measured 16 SNPs from an individual, but the value of one SNP was missing due to lab equipment problems.

- Suppose we measured and phased the following sequence of SNPs for one of the individual's haplotypes:

A G A T T ? T G C A T G C A C G

missing SNP

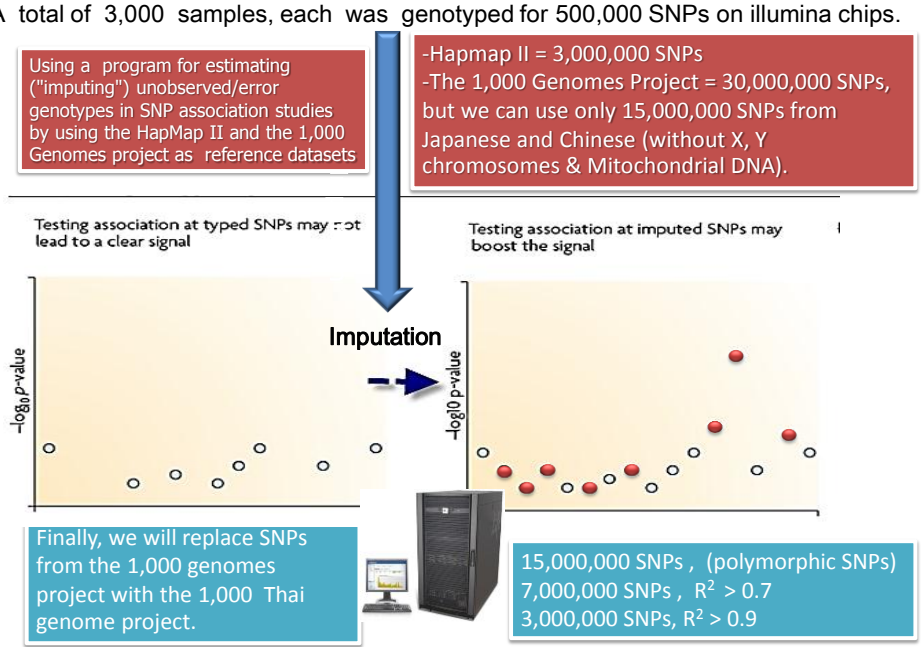
- If we could impute the value of the missing SNP, we wouldn't have to re-sequence the individual.

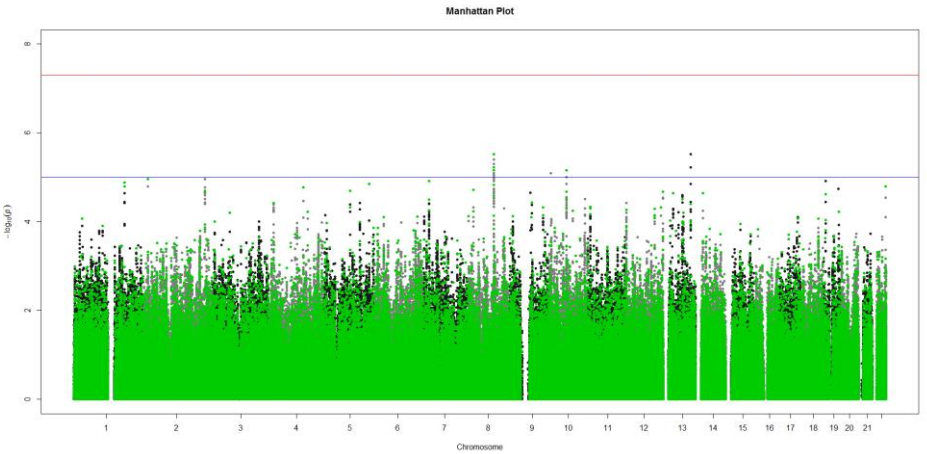


http://www.nature.com/nrg/journal/v11/n7/pdf/nrg2796.pdf

From Thai-MOPH & TCELs' PGx Studies,

A total of 3,000 samples, each was genotyped for 500,000 SNPs on illumina chips.



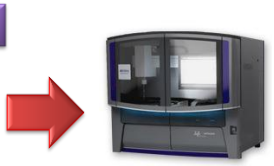


Black or gray is imputed data (take out GWAS data) and green is GWAS data.
chr1 = black, chr2 = gray, chr3 = black and so on .....

Total GWAS data around 500,000 SNPs and imputed data around 7,000,000 SNPs (with RSQ > 0.7)

Decoding the Thai Genome Project

An anonymous, healthy Thai male donor



Next generation sequencer

2-4 weeks

3,000,000,000 bases

>8-12 months

20,000 genes (annotation),

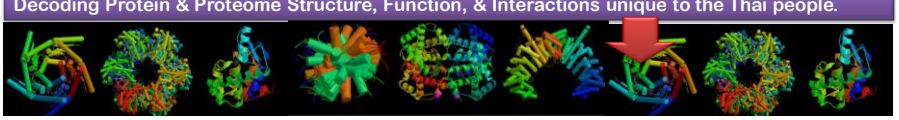
>12 months

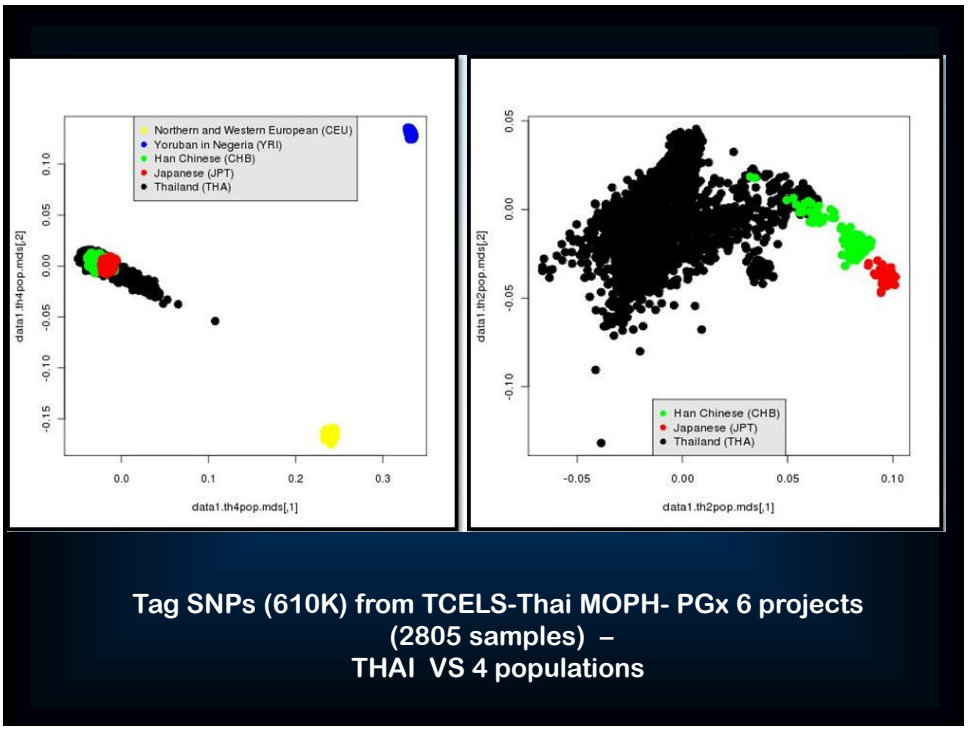
60,000 different kinds of proteins

Making Protein 3D structure based on DNA sequence

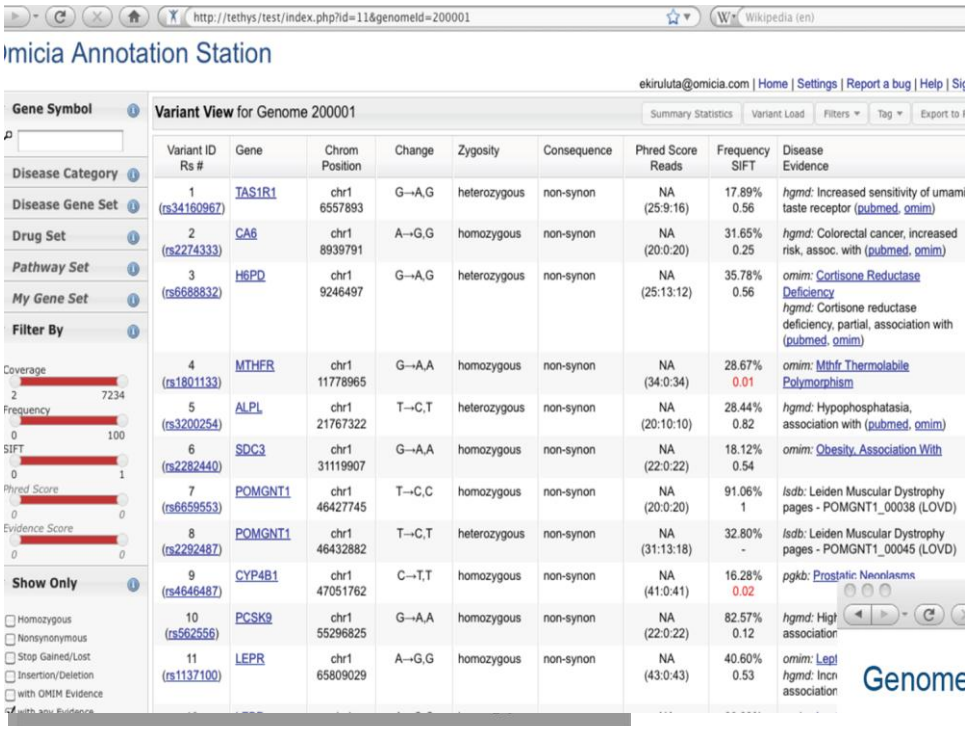
Samudrala Computational Biology Group

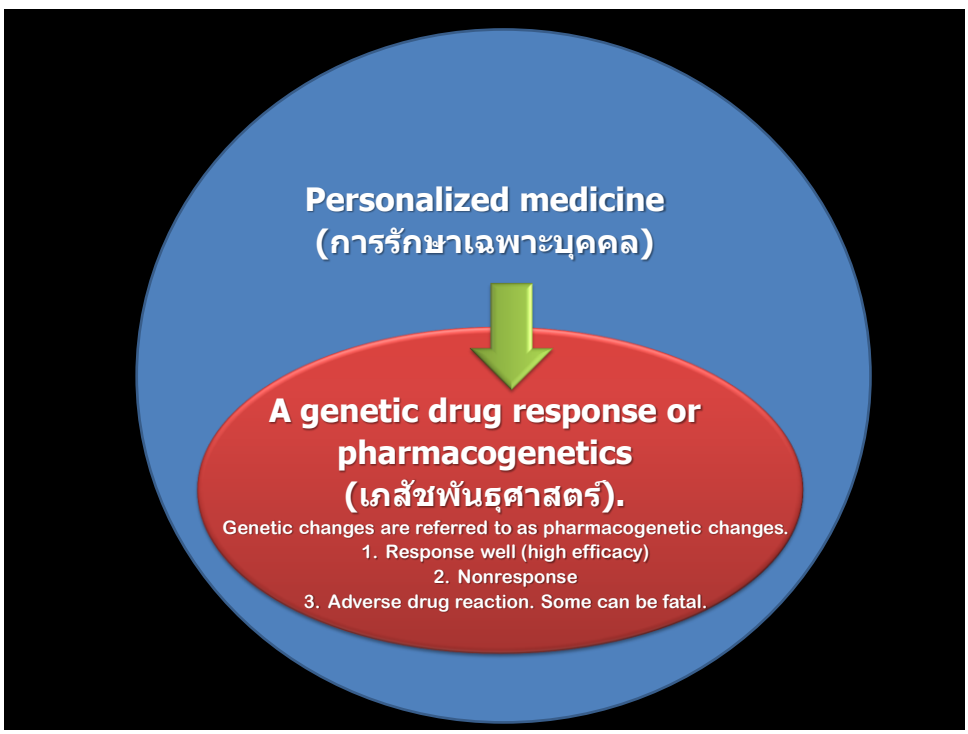
Decoding Protein & Proteome Structure, Function, & Interactions unique to the Thai people.





Tag SNPs (610K) from TCELS-Thai MOPH- PGx 6 projects (2805 samples) – THAI VS 4 populations


http://tethys/test/index.php?id=11&genomeId=200001
Wikipedia (en)
micia Annotation Station
ekiruluta@omicia.com | Home | Settings | Report a bug | Help
Gene Symbol
Disease Category
Disease Gene Set
Drug Set
Pathway Set
My Gene Set
Filter By
Coverage
2
7234
Frequency
0
100
SIFT
0
1
Phred Score
0
0
Evidence Score
0
0
Show Only
Homozygous
Nonsynonymous
Stop Gained/Lost
Insertion/Deletion
with OMIM Evidence
Variant View for Genome 200001
Summary Statistics
Variant Load
Filters
Tag
Export to
Variant ID Rs #
Gene
Chrom Position
Change
Zygosity
Consequence
Phred Score Reads
Frequency SIFT
Disease Evidence
1 (rs34160967) TAS1R1 chr1 6557893 G→A,G heterozygous non-synon NA (25:9:16) 17.89% 0.56 hgmd: Increased sensitivity of umami taste receptor (pubmed, omim)
2 (rs2274333) CA6 chr1 8939791 A→G,G homozygous non-synon NA (20:0:20) 31.65% 0.25 hgmd: Colorectal cancer, increased risk, assoc. with (pubmed, omim)
3 (rs6688832) H6PD chr1 9246497 G→A,G heterozygous non-synon NA (25:13:12) 35.78% 0.56 omim: Cortisone Reductase Deficiency hgmd: Cortisone reductase deficiency, partial, association with (pubmed, omim)
4 (rs1801133) MTHFR chr1 11778965 G→A,A homozygous non-synon NA (34:0:34) 28.67% 0.01 omim: Mthfr Thermolabile Polymorphism
5 (rs3200254) ALPL chr1 21767322 T→C,T heterozygous non-synon NA (20:10:10) 28.44% 0.82 hgmd: Hypophosphatasia, association with (pubmed, omim)
6 (rs2282440) SDC3 chr1 31119907 G→A,A homozygous non-synon NA (22:0:22) 18.12% 0.54 omim: Obesity, Association With
7 (rs6659553) POMGNT1 chr1 46427745 T→C,C homozygous non-synon NA (20:0:20) 91.06% 1 lsdb: Leiden Muscular Dystrophy pages - POMGNT1_00038 (LOVD)
8 (rs2292487) POMGNT1 chr1 46432882 T→C,T heterozygous non-synon NA (31:13:18) 32.80% - lsdb: Leiden Muscular Dystrophy pages - POMGNT1_00045 (LOVD)
9 (rs4646487) CYP4B1 chr1 47051762 C→T,T homozygous non-synon NA (41:0:41) 16.28% 0.02 pgkb: Prostatic Neoplasms
10 (rs562556) PCSK9 chr1 55296825 G→A,A homozygous non-synon NA (22:0:22) 82.57% 0.12
11 (rs1137100) LEPR chr1 65809029 A→G,G homozygous non-synon NA (43:0:43) 40.60% 0.53
Genome


Personalized medicine
(การรักษาเฉพาะบุคคล)
A genetic drug response or pharmacogenetics
(เภสัชพันธุศาสตร์).
Genetic changes are referred to as pharmacogenetic changes.
1. Response well (high efficacy)
2. Nonresponse
3. Adverse drug reaction. Some can be fatal.

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Pharmacogenomics can play an important role in identifying;

1. Responders,
2. Non-responders to medications,
3. Avoiding adverse events, and
4. Optimizing drug dose.

The table below lists FDA-approved drugs with pharmacogenomic information in their labels.

Drug	Therapeutic Area	Biomarker	Label Sections 1/8
Abacavir	Antivirals	HLA-B*5701	Boxed Warning, Contradindications, Warnings and Precautions, Patient Counseling Information
Aripiprazole	Psychiatry	CYP2D6	Clinical Pharmacology, Dosage and Administration
Arsenic Trioxide	Oncology	PML/RARα	Boxed Warning, Clinical Pharmacology, Indications and Usage, Warnings
Atomoxetine	Psychiatry	CYP2D6	Dosage and Administration, Warnings and Precautions, Drug Interactions, Clinical Pharmacology
Atorvastatin	Metabolic and Endocrinology	LDL receptor	Indications and Usage, Dosage and Administration, Warnings and Precautions, Clinical Pharmacology, Clinical Studies
Azathioprine	Rheumatology	TPMT	Dosage and Administration, Warnings and Precautions, Drug Interactions, Adverse Reactions, Clinical Pharmacology
Boceprevir	Antivirals	IL28B	Clinical Pharmacology
Brentuximab Vedotin	Oncology	CD30	Indications and Usage, Description, Clinical Pharmacology
Busulfan	Oncology	Ph Chromosome	Clinical Studies
Capecitabine	Oncology	DPD	Contraindications, Precautions, Patient Information
Carbamazepine	Neurology	HLA-B*1502	Boxed Warning, Warnings and Precautions
Carisoprodol	Musculoskeletal	CYP2C19	Clinical Pharmacology, Special Populations

Drug	Therapeutic Area	Biomarker	Label Sections 2/8
Carvedilol	Cardiovascular	CYP2D6	Drug Interactions, Clinical Pharmacology
Celecoxib	Analgesics	CYP2C9	Dosage and Administration, Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Cetuximab (1)	Oncology	EGFR	Indications and Usage, Warnings and Precautions, Description, Clinical Pharmacology, Clinical Studies
Cetuximab (2)	Oncology	KRAS	Indications and Usage, Clinical Pharmacology, Clinical Studies
Cevimeline	Dermatology and Dental	CYP2D6	Drug Interactions
Chlordiazepoxide and Amitriptyline	Psychiatry	CYP2D6	Precautions
Chloroquine	Antiinfectives	G6PD	Precautions
Cisplatin	Oncology	TPMT	Clinical Pharmacology, Warnings, Precautions
Citalopram (1)	Psychiatry	CYP2C19	Drug Interactions, Warnings
Citalopram (2)	Psychiatry	CYP2D6	Drug Interactions
Clobazam	Neurology	CYP2C19	Clinical Pharmacology, Dosage and Administration, Use in Specific Populations
Clomiphene	Reproductive and Urologic	Rh genotype	Precautions
Clomipramine	Psychiatry	CYP2D6	Drug Interactions
Clopidogrel	Cardiovascular	CYP2C19	Boxed Warning, Dosage and Administration, Warnings and Precautions, Drug Interactions, Clinical Pharmacology
Clozapine	Psychiatry	CYP2D6	Drug Interactions, Clinical Pharmacology

Drug	Therapeutic Area	Biomarker	Label Sections 3/8
Clozapine	Psychiatry	CYP2D6	Drug Interactions, Clinical Pharmacology
Codeine	Analgesics	CYP2D6	Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Crizotinib	Oncology	ALK	Indications and Usage, Warnings and Precautions, Adverse Reactions, Clinical Pharmacology, Clinical Studies
Dapsone	Dermatology and Dental	G6PD	Indications and Usage, Precautions, Adverse Reactions, Patient Counseling Information
Dasatinib	Oncology	Ph Chromosome	Indications and Usage, Clinical Studies, Patient Counseling Information
Desipramine	Psychiatry	CYP2D6	Drug Interactions
Desloratadine and Pseudoephedrine	Allergy	CYP2D6	Clinical Pharmacology
Dexlansoprazole (1)	Gastroenterology	CYP2C19	Clinical Pharmacology, Drug Interactions
Dexlansoprazole (2)	Gastroenterology	CYP1A2	Clinical Pharmacology
Dextromethorphan and Quinidine	Neurology	CYP2D6	Clinical Pharmacology, Warnings and Precautions
Diazepam	Psychiatry	CYP2C19	Drug Interactions, Clinical Pharmacology
Doxepin	Psychiatry	CYP2D6	Precautions
Drospirenone and Ethinyl Estradiol	Reproductive	CYP2C19	Precautions, Drug Interactions
Erlotinib	Oncology	EGFR	Clinical Pharmacology
Esomeprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology

Drug	Therapeutic Area	Biomarker	Label Sections 4/8
Exemestane	Oncology	ER &/ PgR receptor	Indications and Usage, Dosage and Administration, Clinical Studies, Clinical Pharmacology
Fluorouracil	Dermatology and Dental	DPD	Contraindications, Warnings
Fluoxetine	Psychiatry	CYP2D6	Warnings, Precautions, Clinical Pharmacology
Fluoxetine and Olanzapine	Psychiatry	CYP2D6	Drug Interactions, Clinical Pharmacology
Flurbiprofen	Rheumatology	CYP2C9	Clinical Pharmacology, Special Populations
Fluvoxamine (1)	Psychiatry	CYP2C9	Drug Interactions
Fluvoxamine (2)	Psychiatry	CYP2C19	Drug Interactions
Fluvoxamine (3)	Psychiatry	CYP2D6	Drug Interactions
Fulvestrant	Oncology	ER receptor	Indications and Usage, Patient Counseling Information
Galantamine	Neurology	CYP2D6	Special Populations
Gefitinib (1)	Oncology	CYP2D6	Drug Interactions
Gefitinib (2)	Oncology	EGFR	Clinical Pharmacology
Iloperidone	Psychiatry	CYP2D6	Clinical Pharmacology, Dosage and Administration, Drug Interactions, Specific Populations, Warnings and Precautions
Imatinib (1)	Oncology	C-Kit	Indications and Usage, Dosage and Administration Clinical Pharmacology, Clinical Studies
Imatinib (2)	Oncology	Ph Chromosome	Indications and Usage, Dosage and Administration, Clinical Pharmacology, Clinical Studies

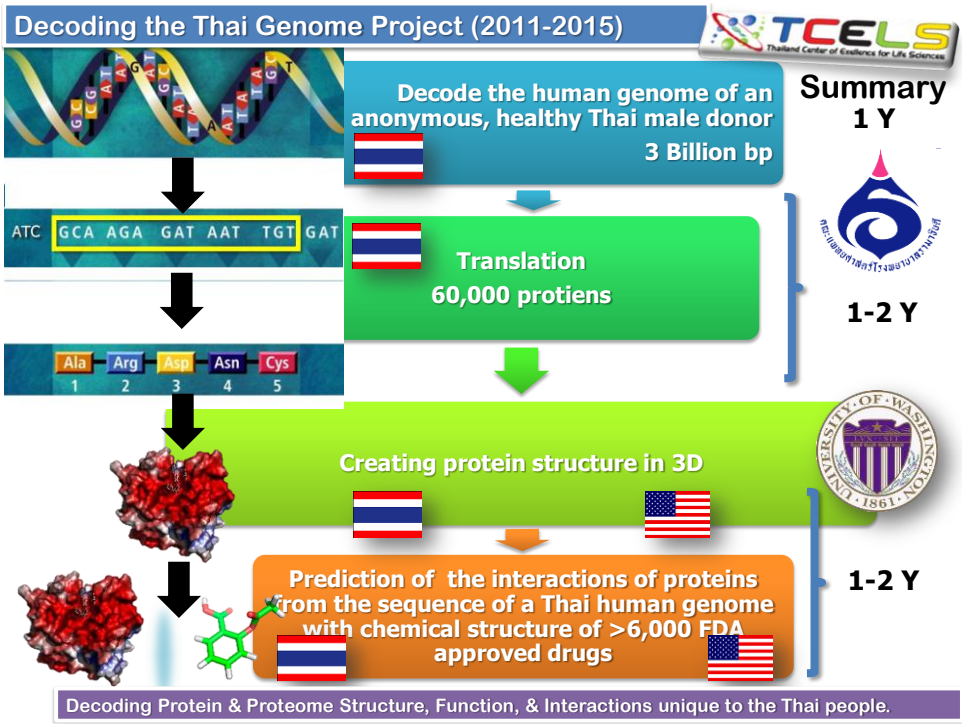
Drug	Therapeutic Area	Biomarker	Label Sections 5/8
Imatinib (3)	Oncology	PDGFR	Indications and Usage, Dosage and Administration, Clincal Studies
Imatinib (4)	Oncology	FIP1L1-PDGFRα	Indications and Usage, Dosage and Administration, Clinical Studies
Imipramine	Psychiatry	CYP2D6	Drug Interactions
Indacaterol	Pulmonary	UGT1A1	Clinical Pharmacology
Irinotecan	Oncology	UGT1A1	Dosage and Administration, Warnings, Clinical Pharmacology
Isosorbide and Hydralazine	Cardiovascular	NAT1; NAT2	Clinical Pharmacology
Ivacaftor	Pulmonary	CFTR (G551D)	Indications and Usage, Adverse Reactions, Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Lapatinib	Oncology	Her2/neu	Indications and Usage, Clinical Pharmacology, Patient Counseling Information
Lenalidomide	Hematology	Chromosome 5q	Boxed Warning, Indications and Usage, Clinical Studies, Patient Counseling
Letrozole	Oncology	ER &/ PgR receptor	Indications and Usage, Adverse Reactions, Clinical Studies, Clinical Pharmacology
Maraviroc	Antivirals	CCR5	Indications and Usage, Warnings and Precautions, Clinical Pharmacology, Clinical Studies, Patient Counseling Information
Mercaptopurine	Oncology	TPMT	Dosage and Administration, Contraindications, Precautions, Adverse Reactions, Clinical Pharmacology

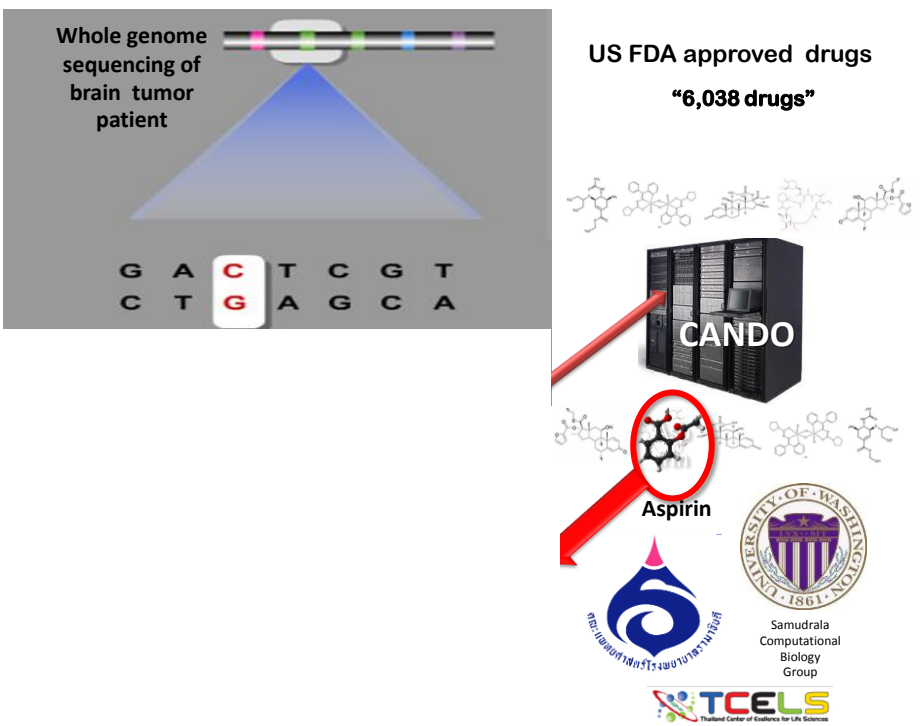
Drug	Therapeutic Area	Biomarker	Label Sections 6/8
Prasugrel	Cardiovascular	CYP2C19	Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Pravastatin	Cardiovascular	ApoE2	Clinical Studies, Use in Specific Populations
Propafenone	Cardiovascular	CYP2D6	Clinical Pharmacology
Propranolol	Cardiovascular	CYP2D6	Precautions, Drug Interactions, Clinical Pharmacology
Protriptyline	Psychiatry	CYP2D6	Precautions
Quinidine	Antiarrhythmics	CYP2D6	Precautions
Rabeprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology
Rasburicase	Oncology	G6PD	Boxed Warning, Contraindications
Rifampin, Isoniazid, and Pyrazinamide	Antiinfectives	NAT1; NAT2	Adverse Reactions, Clinical Pharmacology
Risperidone	Psychiatry	CYP2D6	Drug Interactions, Clinical Pharmacology
Sodium Phenylacetate and Sodium Benzoate	Gastroenterology	UCD (NAGS; CPS; ASS; OTC; ASL; ARG)	Indications and Usage, Description, Clinical Pharmacology
Sodium Phenylbutyrate	Gastroenterology	UCD (NAGS; CPS; ASS; OTC; ASL; ARG)	Indications and Usage, Dosage and Administration, Nutritional Management
Tamoxifen	Oncology	ER receptor	Indications and Usage, Precautions, Medication Guide
Telaprevir	Antivirals	IL28B	Clinical Pharmacology
Terbinafine	Antifungals	CYP2D6	Drug Interactions
Tetrabenazine	Neurology	CYP2D6	Dosage and Administration, Warnings, Clinical Pharmacology

Drug	Therapeutic Area	Biomarker	Label Sections 7/8
Thioguanine	Oncology	TPMT	Dosage and Administration, Precautions, Warnings
Thioridazine	Psychiatry	CYP2D6	Precautions, Warnings, Contraindications
Ticagrelor	Cardiovascular	CYP2C19	Clinical Studies
Tolterodine	Reproductive and Urologic	CYP2D6	Clinical Pharmacology, Drug Interactions, Warnings and Precautions
Tositumomab	Oncology	CD20 antigen	Indications and Usage, Clinical Pharmacology
Tramadol and Acetaminophen	Analgesics	CYP2D6	Clinical Pharmacology
Trastuzumab	Oncology	Her2/neu	Indications and Usage, Precautions, Clinical Pharmacology
Tretinoin	Dermatology and Dental	PML/RARα	Boxed Warning, Dosage and Administration, Precautions
Trimipramine	Psychiatry	CYP2D6	Drug Interactions
Valproic Acid	Psychiatry	UCD (NAGS; CPS; ASS; OTC; ASL; ARG)	Contraindications, Precautions, Adverse Reactions
Vemurafenib	Oncology	BRAF	Indications and Usage, Warning and Precautions, Clinical Pharmacology, Clinical Studies, Patient Counseling Information
Venlafaxine	Psychiatry	CYP2D6	Drug Interactions
Voriconazole	Antifungals	CYP2C19	Clinical Pharmacology, Drug Interactions
Warfarin (1)	Hematology	CYP2C9	Dosage and Administration, Precautions, Clinical Pharmacology
Warfarin (2)	Hematology	VKORC1	Dosage and Administration, Precautions, Clinical Pharmacology

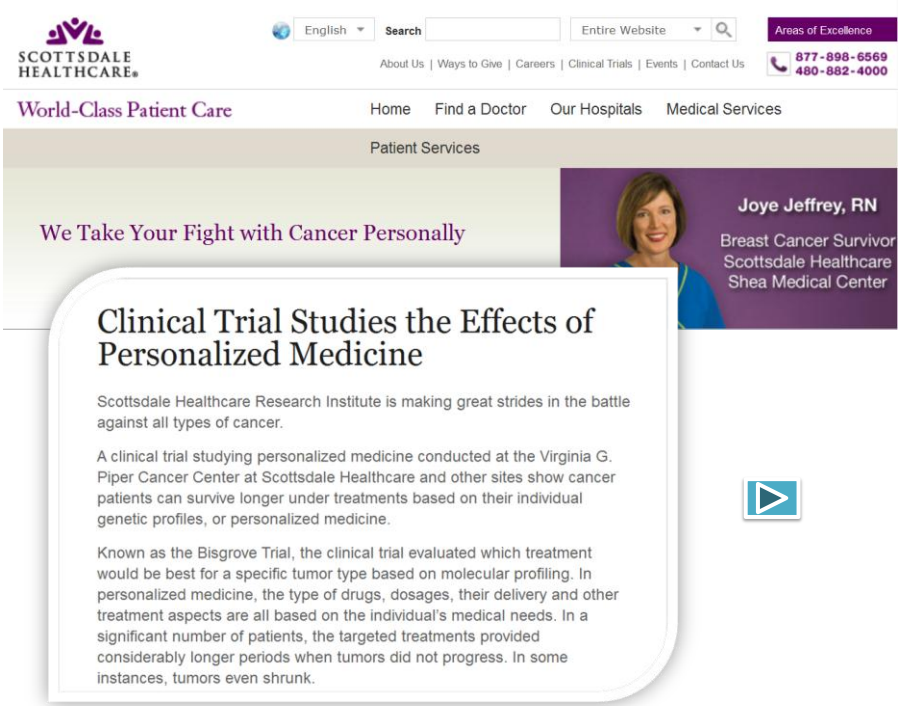
Drug	Therapeutic Area	Biomarker	Label Sections 8/8

Page Last Updated: 02/29/2012
U.S. Food and Drug Administration


Decoding the Thai Genome Project (2011-2015)
TCELS
Thailand Center of Excellence for Life Sciences
Summary
1 Y
Decode the human genome of an anonymous, healthy Thai male donor
3 Billion bp
ATC GCA AGA GAT AAT TGT GAT
Translation
60,000 protiens
1-2 Y
Ala Arg Asp Asn Cys
1 2 3 4 5
Creating protein structure in 3D
Prediction of the interactions of proteins from the sequence of a Thai human genome with chemical structure of >6,000 FDA approved drugs
1-2 Y
Decoding Protein & Proteome Structure, Function, & Interactions unique to the Thai people.


Whole genome sequencing of brain tumor patient
G A C T C G T
C T G A G C A
US FDA approved drugs
"6,038 drugs"
CANDO
Aspirin
Samudrala Computational Biology Group
TCELS
Thailand Center of Excellence for Life Sciences


WGS>Personalized medicine
Target therapy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877-898-6569
480-882-4000
World-Class Patient Care
Home
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Our Hospitals
Medical Services
Patient Services
We Take Your Fight with Cancer Personally
Joye Jeffrey, RN
Breast Cancer Survivor
Scottsdale Healthcare
Shea Medical Center
Clinical Trial Studies the Effects of Personalized Medicine
Scottsdale Healthcare Research Institute is making great strides in the battle against all types of cancer.
A clinical trial studying personalized medicine conducted at the Virginia G. Piper Cancer Center at Scottsdale Healthcare and other sites show cancer patients can survive longer under treatments based on their individual genetic profiles, or personalized medicine.
Known as the Bisgrove Trial, the clinical trial evaluated which treatment would be best for a specific tumor type based on molecular profiling. In personalized medicine, the type of drugs, dosages, their delivery and other treatment aspects are all based on the individual's medical needs. In a significant number of patients, the targeted treatments provided considerably longer periods when tumors did not progress. In some instances, tumors even shrunk.

TGen: Pioneering Translational Medicine

TGen

Founded in 2002
Phoenix, AZ

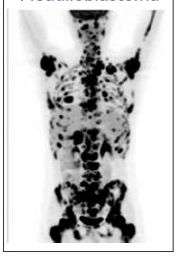
- Translational Genomics Research Institute (TGen) translates basic science discoveries to the clinic
- Research is focused in the areas of oncology, neurology and metabolic disease

Example of success: Bisgrove Trial

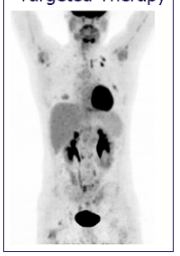
- Patients unresponsive to typical therapies
- Key mutations identified in patients by using 1990's technology: gene expression arrays and IHC
- Mutations identified drugs personalized to patient's cancer
- Successful treatment in 30% of patients

Molecular medicine has huge potential – will only improve as science improves

Metastatic Medulloblastoma

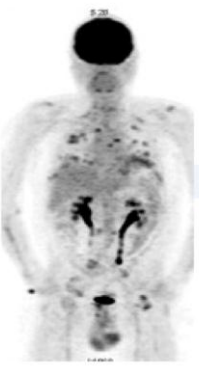


2 Months Later w/ Targeted Therapy

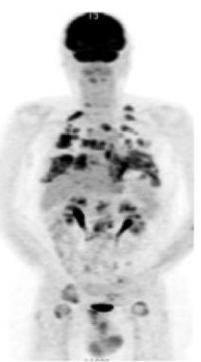


Source: Bisgrove trial, April 2009

The Cost Of A Wrong Answer

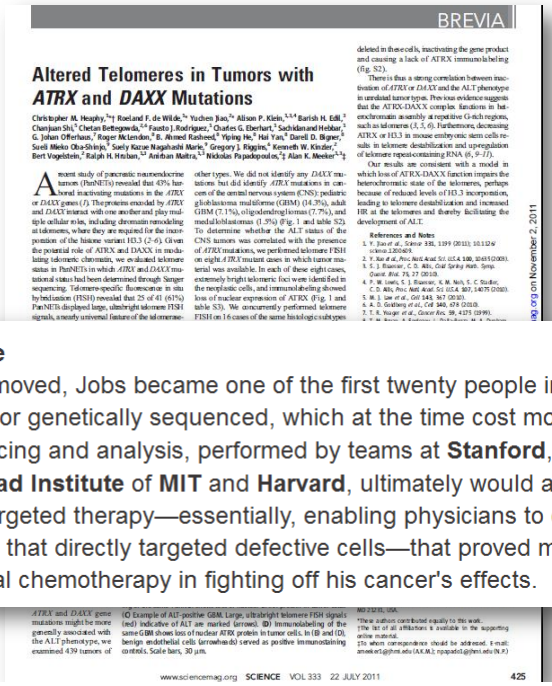


Wrong drug selected
Find out
6 months later



Note: metastatic basal cell carcinoma

Before translational medicine



BREVIA

Altered Telomeres in Tumors with *ATRX* and *DAXX* Mutations

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A recent study of pancreatic neuroendocrine tumors (PanNETs) revealed that 43% harbored inactivating mutations in the *ATRX* or *DAXX* genes (*1*). The proteins encoded by *ATRX* and *DAXX* interact with one another and play multiple cellular roles, including chromatin remodeling at telomeres, where they are required for the incorporation of the histone variant H3.3 (*2*–*6*). Given the potential role of ATRX and DAXX in modulating telomeric chromatin, we evaluated telomere status in PanNETs in which *ATRX* and *DAXX* mutational status had been determined through Sanger sequencing. Telomere-specific fluorescence in situ hybridization (FISH) revealed that 25 of 41 (61%) PanNETs displayed large, ultrabright telomere FISH signals, a nearly universal feature of the telomerase-other types. We did not identify any *DAXX* mutations but did identify *ATRX* mutations in cancers of the central nervous system (CNS): pediatric glioblastoma multiforme (GBM) (14.3%), adult GBM (7.1%), oligodendroglial tumors (7.7%), and medulloblastomas (1.5%) (Fig. 1 and table S2). To determine whether the ALT status of the CNS tumors was correlated with the presence of *ATRX* mutations, we performed telomere FISH on eight *ATRX* mutant cases in which tumor material was available. In each of these eight cases, extremely bright telomeric foci were identified in the neoplastic cells, and immunolabeling showed loss of nuclear expression of ATRX (Fig. 1 and table S3). We concurrently performed telomere FISH on 16 cases of the same histologic subtypes

deleted in these cells, inactivating the gene product and causing a lack of ATRX immunolabeling (fig. S2).

There is thus a strong correlation between inactivation of *ATRX* or *DAXX* and the ALT phenotype in unrelated tumor types. Previous evidence suggests that the ATRX-DAXX complex functions in heterochromatin assembly at repetitive G-rich regions, such as telomeres (*3*, *5*, *6*). Furthermore, decreasing ATRX or H3.3 in mouse embryonic stem cells results in telomere destabilization and upregulation of telomere repeat-containing RNA (*6*, *9*–*11*).

Our results are consistent with a model in which loss of ATRX-DAXX function impairs the heterochromatic state of the telomeres, perhaps because of reduced levels of H3.3 incorporation, leading to telomere destabilization and increased HR at the telomeres and thereby facilitating the development of ALT.

References and Notes

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2. Y. Xue *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **100**, 10635 (2003).
3. S. E. Baumer, C. D. Allis, *Cold Spring Harb. Symp. Quant. Biol.* **71**, 27 (2010).
4. P. M. Lowy, S. E. Baumer, K. M. Neil, S. C. Stuiber, C. D. Allis, *Proc. Natl. Acad. Sci. U.S.A.* **107**, 14075 (2010).
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7. E. R. Yeager *et al.*, *Cancer Res.* **58**, 4175 (1998).

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(C) Example of ALT-positive GBM. Large, ultrabright telomere FISH signals (red) indicative of ALT are marked (arrows). (D) Immunolabeling of the same GBM shows loss of nuclear ATRX protein in tumor cells. In (B and (D), benign endothelial cells (arrowheads) served as positive immunostaining controls. Scale bars, 30 μm.

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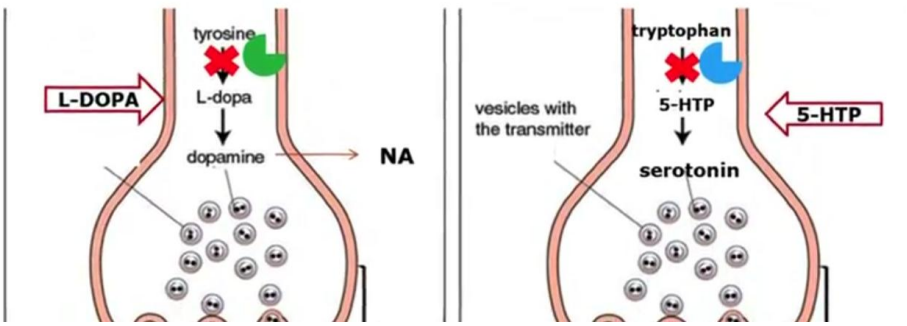
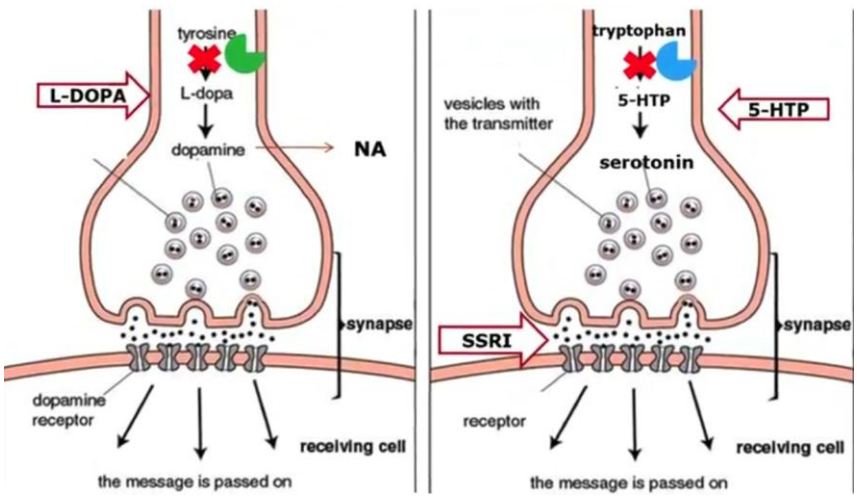
Second medical leave

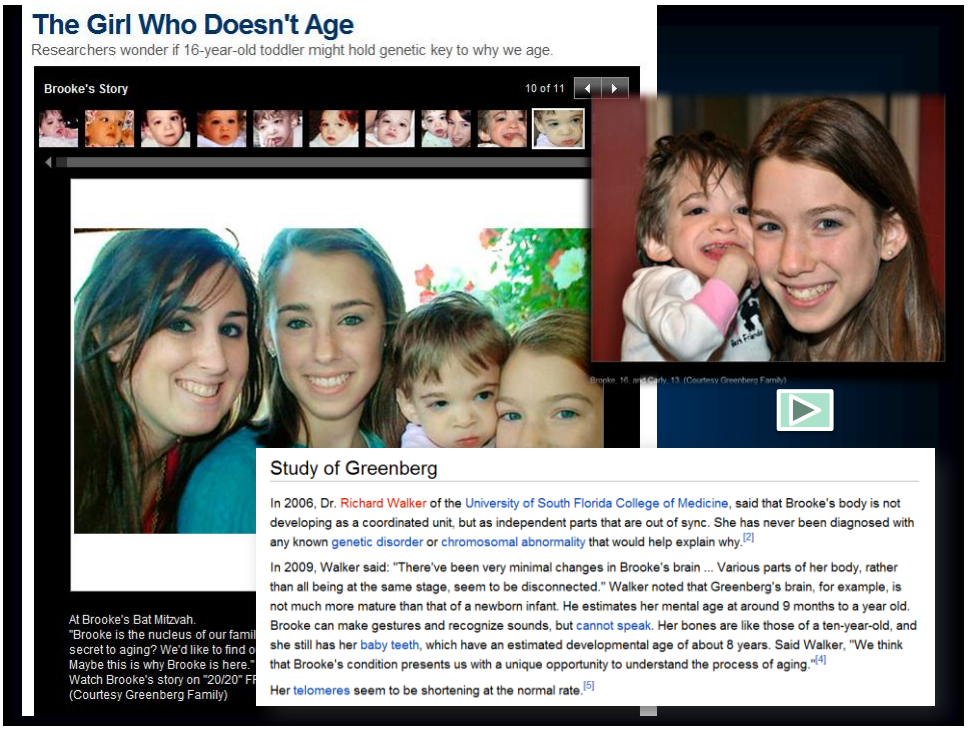
After his tumor was removed, Jobs became one of the first twenty people in the world to have his cancer tumor genetically sequenced, which at the time cost more than $100,000. The sequencing and analysis, performed by teams at **Stanford**, **Johns Hopkins**, and the **Broad Institute** of **MIT** and **Harvard**, ultimately would allow Jobs to receive molecular targeted therapy—essentially, enabling physicians to craft specific drug regimens that directly targeted defective cells—that proved more effective than traditional chemotherapy in fighting off his cancer's effects.

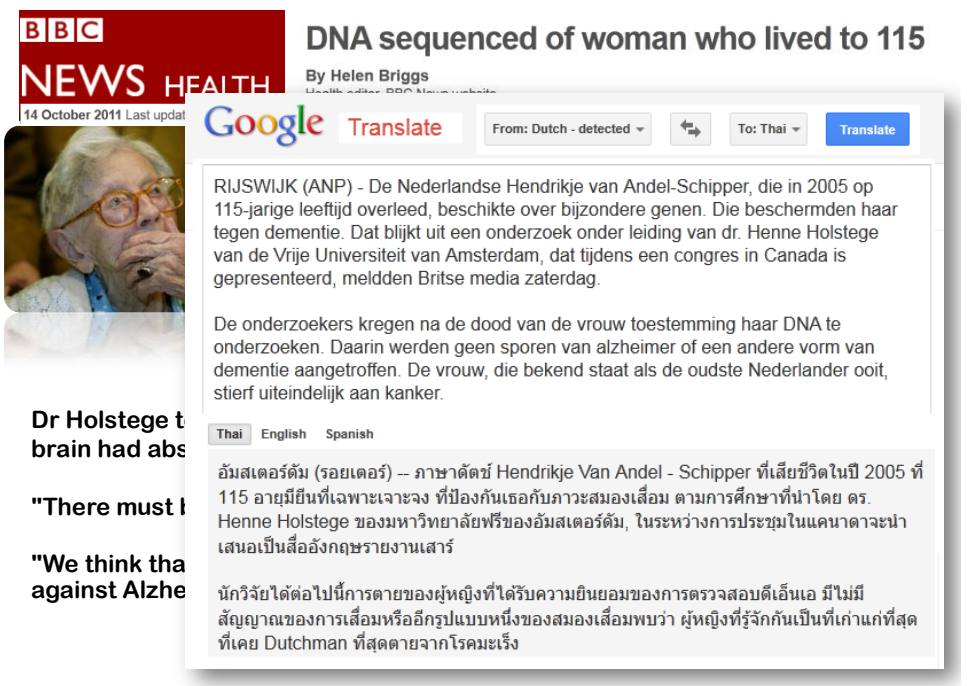
GENETIC FINDINGS

- Dopamine Responsive Dystonia in Beery family is caused by mutations in Sepiopterin Reductase gene
- Two hits (mutations) were found in DNA samples coming from Alexis and Noah: K251X and R150G






The Girl Who Doesn't Age
Researchers wonder if 16-year-old toddler might hold genetic key to why we age.
Brooke's Story
10 of 11
Study of Greenberg
In 2006, Dr. Richard Walker of the University of South Florida College of Medicine, said that Brooke's body is not developing as a coordinated unit, but as independent parts that are out of sync. She has never been diagnosed with any known genetic disorder or chromosomal abnormality that would help explain why.[2]
In 2009, Walker said: "There've been very minimal changes in Brooke's brain ... Various parts of her body, rather than all being at the same stage, seem to be disconnected." Walker noted that Greenberg's brain, for example, is not much more mature than that of a newborn infant. He estimates her mental age at around 9 months to a year old. Brooke can make gestures and recognize sounds, but cannot speak. Her bones are like those of a ten-year-old, and she still has her baby teeth, which have an estimated developmental age of about 8 years. Said Walker, "We think that Brooke's condition presents us with a unique opportunity to understand the process of aging."[4]
Her telomeres seem to be shortening at the normal rate.[5]
At Brooke's Bat Mitzvah:
(Courtesy Greenberg Family)


BBC
NEWS HEALTH
14 October 2011 Last updat
DNA sequenced of woman who lived to 115
By Helen Briggs
Google Translate
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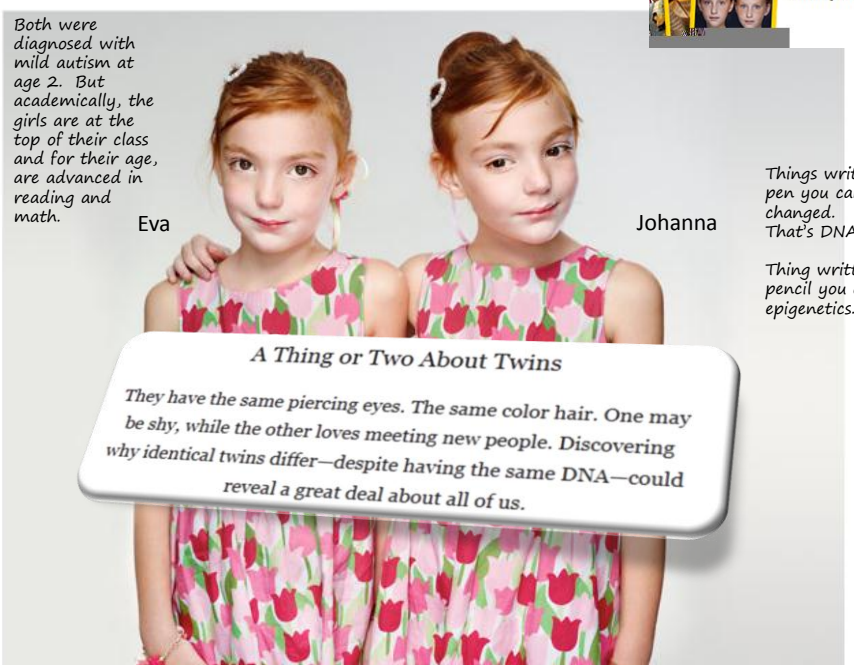
RIJSWIJK (ANP) - De Nederlandse Hendrikje van Andel-Schipper, die in 2005 op 115-jarige leeftijd overleed, beschikte over bijzondere genen. Die beschermden haar tegen dementie. Dat blijkt uit een onderzoek onder leiding van dr. Henne Holstege van de Vrije Universiteit van Amsterdam, dat tijdens een congres in Canada is gepresenteerd, meldden Britse media zaterdag.
De onderzoekers kregen na de dood van de vrouw toestemming haar DNA te onderzoeken. Daarin werden geen sporen van alzheimer of een andere vorm van dementie aangetroffen. De vrouw, die bekend staat als de oudste Nederlander ooit, stierf uiteindelijk aan kanker.
Thai
English
Spanish
อัมสเตอร์ดัม (รอยเตอร์) -- ภาษาดัตช์ Hendrikje Van Andel - Schipper ที่เสียชีวิตในปี 2005 ที่ 115 อายุมียีนที่เฉพาะเจาะจง ที่ป้องกันเธอกับภาวะสมองเสื่อม ตามการศึกษาที่นำโดย ดร. Henne Holstege ของมหาวิทยาลัยฟรีของอัมสเตอร์ดัม, ในระหว่างการประชุมในแคนาดาจะนำเสนอเป็นสื่ออังกฤษรายงานเสาร์
นักวิจัยได้ต่อไปนี้การตายของผู้หญิงที่ได้รับความยินยอมของการตรวจสอบดีเอ็นเอ มีไม่มีสัญญาณของการเสื่อมหรืออีกรูปแบบหนึ่งของสมองเสื่อมพบว่า ผู้หญิงที่รู้จักกันเป็นที่เก่าแก่ที่สุดที่เคย Dutchman ที่สุดตายจากโรคมะเร็ง
Dr Holstege t
brain had abs
"There must
"We think tha
against Alzhe

Twins

Both were diagnosed with mild autism at age 2. But academically, the girls are at the top of their class and for their age, are advanced in reading and math.

Eva

Johanna



Things written in pen you can not changed.
That's DNA.

Thing written in pencil you can. That's epigenetics.

genomeweb Genome Technology

A Large-Scale Twin Study Aims to Elucidate Common Disease

December 2011/January 2012

By Ciara Curtin

A large-scale epigenetic study of common diseases in twins, particularly those discordant for a disease, may provide new targets for therapy.

"Identical twins and epigenetics are the ideal partners because we know there's both genetic effects and environmental effects," says Timothy Spector of King's College London. "In non-twin populations, you'd have to do studies that were perhaps 10 to 20 times as large to find the same results."

TwinsUK, Spector's research group at King's College, is teaming up with BGI to study the epigenetics of common diseases in about 3,000 monozygotic twins and 2,000 dizygotic twins using methylated DNA immunoprecipitation coupled with next-gen sequencing, or MeDIP-seq. This approach gives about 25 million CpG sites, Spector says.

For this project, the team is focusing on age-related diseases like type 2 diabetes, depression, and heart disease, among other common public health issues, and is drawing on DNA and phenotype data collected during the past 20 years by TwinsUK. Spector and his team took a broad approach to their collections over the years. "Anything that's common, we collect — everything from dietary information to personality, behavioral questions to range of diseases, drugs, medications," he says. "We are trying to pick things that are related to generally complex, common age-related traits."

Spector presented the results of the group's pilot project on pain, which was funded by Pfizer, at the International Congress of Human Genetics/American Society of Human Genetics meeting in Montreal, Quebec, in October. "The main finding [was] replicating differentially methylated regions for experimental pain, and some of them are novel regions," he says. "We've identified as proof of concept that three of these regions contain major known pain candidate genes. So we are confident that we are going to find physiologically relevant signals."

The researchers are about halfway through the sequencing phase of the project, and are gearing up for the analysis stage. "Potentially, we have the ability to do a thousand individual studies of each disease or trait. We are prioritizing it depending on where our funding is coming from, or public health interest, or commercial interest," Spector says.

เพิ่มเติม Epigenetics-National Geography

- "Three Million Genomes Projects"- M & M & M Projects

- introduced by Dr Jun Wang, Executive Director of BGI, will consist of

1. "Million Plant and Animal Genomes Project,"
2. "Million Human Genomes Project" and
3. "Million Micro-Ecosystem Project."

- They will provide a clear classification on the studied species, and advance the understanding of the species genome and the application of genome-based research for different objectives.

http://www.bgisequence.com/eu/newsandevents/news/bgi-unveils-significant-new-global-research-collaborations-at-th