임상 적용 가능한 유전체의학 update

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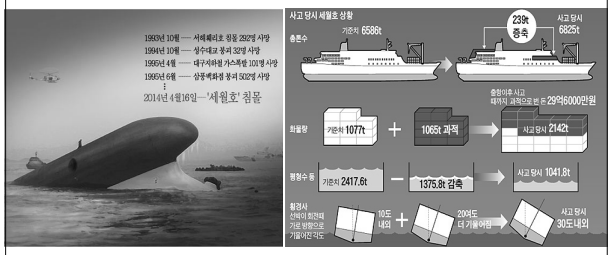
Today's Topic

1. Personalized Medicine 이란 무엇인가?
2. Genomics 의 기본 개념과 발전 상황
3. 유전과 환경의 상호작용에 대한 이해
4. 유전체학의 임상 적용 : 질병예측 및 건강증진

Accidents and Disease should be preventive

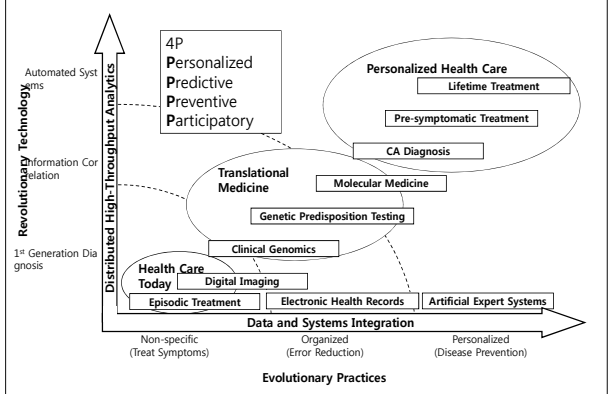


"모든 사고 (질병)은 예방되어야 하며 예방되기 위해서는 예측되어야 한다"

Episodic Treatment → Early Dx & Tx → Preventive Medicine → Predictive Medicine

4P Medicine

This transformation is being accelerated by a combination of revolutionary technologies and evolutionary practices



What's Personalized Medicine

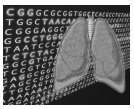
VS

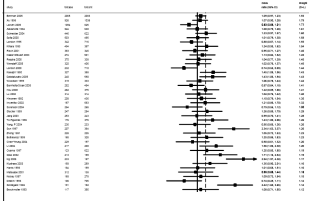
Procrustes (Προκρούστης)

Tailored medicine

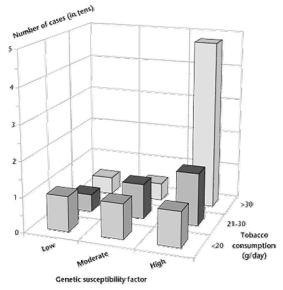
Personalized medicine is a medical model that proposes the **customization** of healthcare, with all decisions and practices being **tailored** to the individual patient by use of genetic or other information.

Smoking vs Gene of Lung Cancer



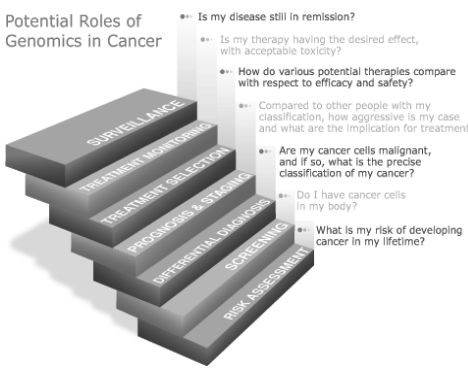


GSTM1) Polymorphisms and Lung Cancer

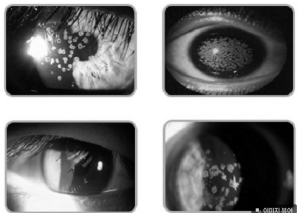


Genotype of CYP2D6 in 130 cases and 170 control cases

Application of Clinical Genomics

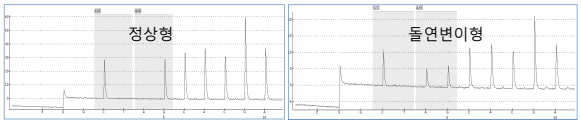


각막 이영양증/ 라식 수술



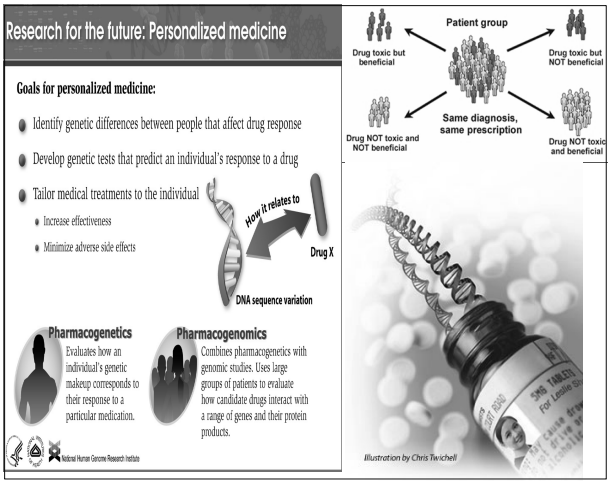
각막 이영양증은 인간염색체 5q에 위치하는 TGFBI 유전자의 돌연변이가 주 원인으로 알려져 있는 상염색체 우성 유전질환.

한국인은 1300명당 1명에서 발병.
아벨리노(Avellino) 각막이영양증은 라식수술을 시행한 경우 각막 혼탁이 증가되는 것으로 보고되고 있습니다. 따라서 아벨리노(Avellino) 각막이영양증 돌연변이를 갖는 경우, 라식수술은 금기



장기 이식 수술과 이식 거부 예측 프로그램 : 알로맵(AlloMap)

- Reduce the immune response leading to organ rejection



Erbitux (Cetuximab)

Developed by Merck, under license from Imclone

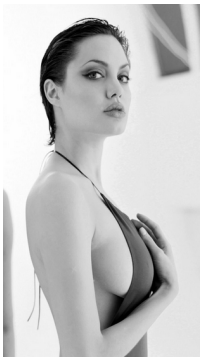
The First Targeted Drug For Colorectal Cancer

The Effectiveness Of Erbitux Is Determined By The Genetic Makeup Of A Colorectal Tumor.

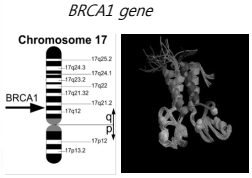
암 종	유전자 검사	관련 항암제
폐 암	EGFR 유전자 돌연변이검사 (2종) - 염기서열검사 - PNA 기반 실시간 중합효소연쇄반응 클램핑법	이레사정 타세바정
대장암	EGFR pharmDx kit 면역조직화학 염색검사 KRAS 유전자 돌연변이검사 (2종) - 염기서열검사 - PNA 기반 실시간 중합효소연쇄반응 클램핑법	얼비툭스주 벡티빅스주
만성골수성백혈병	BCR/ABL 유전자재배열검사 (정량) BCR/ABL 유전자 Imatinib 내성 돌연변이검사	글리벡정
급성골수성백혈병 GIST	C-Kit 유전자 돌연변이검사 - 염기서열검사	글리벡정 수탄정

And Vectibix. (Journal Of Clinical Oncology In 2008)

BRACA 1 유전자와 유방암



BRCA1 gene



24 exons, 1863 Amino Acids coding

일반 USA 여성의 평생 유방암 유병률 12.5%이나 BRCA1 돌연변이 인 경우 7배에 해당하는 80% 이상의 확률,전체 대상자의 10%에서 돌연변이

(한국인 경우 유방암 평생 유병율은 72%, 난소암은 24.6% 한국인 유전성 유방암 연구, 서울대 김성원교수)

Rising debates

The NEW ENGLAND JOURNAL of MEDICINE

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Perspective

23andMe and the FDA

George J. Annas, J.D., M.P.H., and Sherman Elias, M.D.
N Engl J Med 2014; 370:985-988 | March 13, 2014 | DOI: 10.1056/NEJMp1316367

Comments open through March 19, 2014

FDA marketing authorization for the device." On December 5, the company announced that it was complying with the FDA's demands and **discontinued running the commercial**, noting on its website, "At this time, we have suspended our health-related genetic tests to comply immediately with the [FDA] directive to discontinue new consumer access during our regulatory review process."

JAMA The Journal of the American Medical Association

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March 12, 2014, Vol 311, No. 10 >

< Previous Article | Full Content is available to subscribers | Next Article >

Original Investigation | March 12, 2014

Clinical Interpretation and Implications of Whole-Genome Sequencing

In this exploratory study of 12 volunteer adults, the use of WGS was associated with **incomplete coverage of inherited disease genes**, **low reproducibility of detection of genetic variation with the highest potential clinical effects**, and **uncertainty about clinically reportable findings**. In certain cases, WGS will identify clinically actionable genetic variants warranting early medical intervention. These issues should be considered when determining the role of WGS in clinical medicine.

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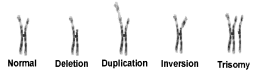
Causes of human genetic variation

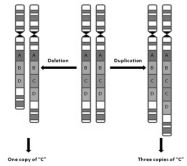
1. Chromosome aberrations

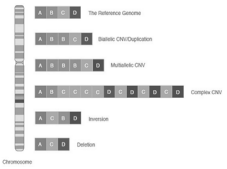


2. Tandem repeat polymorphisms

....ATTCCGATATATAT....
....ATTCCGATATATATATATAT....

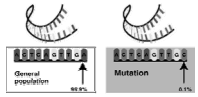
3. Insertion or deletion and copy number variation (CNV)



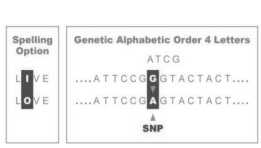


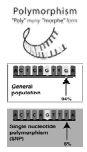
Causes of human genetic variation

4. Somatic mutations (*BRAF/KRAS..*)

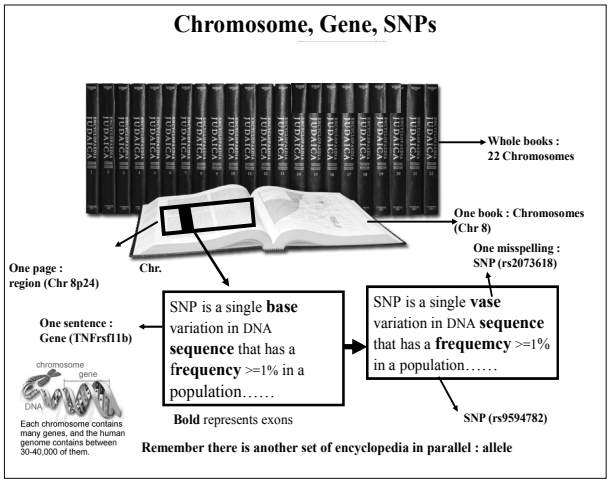


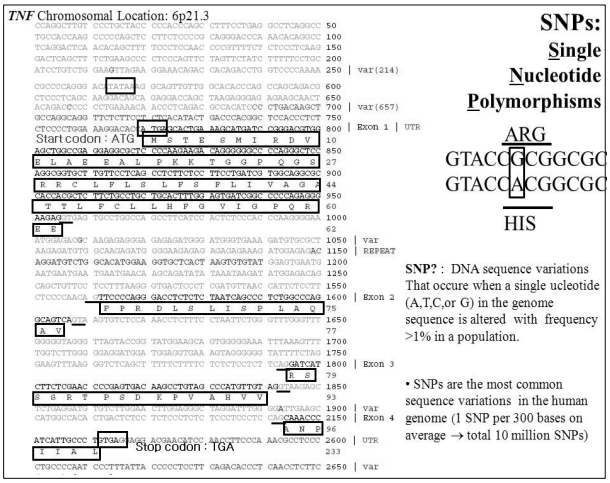
5. Single nucleotide polymorphisms (SNP),germline mutation

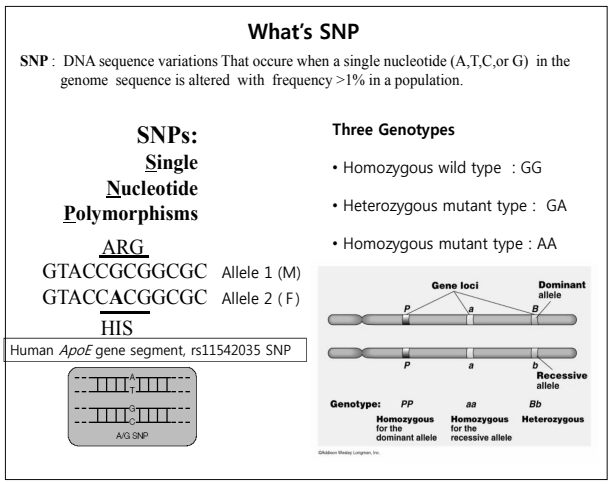


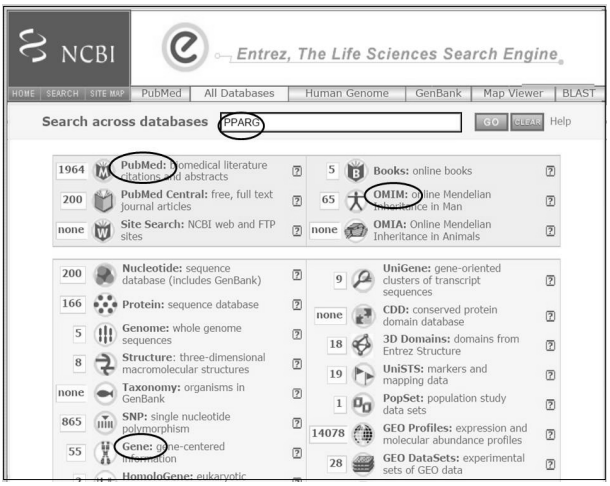


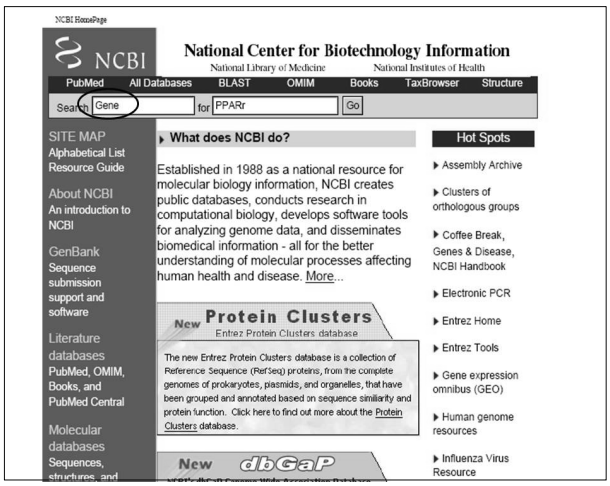
Informally, the term mutation is often used to refer to a harmful genome variation that is associated with a specific human disease, while the word polymorphism implies a variation that is neither harmful nor beneficial.


Chromosome, Gene, SNPs
Whole books : 22 Chromosomes
One book : Chromosomes (Chr 8)
One misspelling : SNP (rs2073618)
One page : region (Chr 8p24)
Chr.
One sentence : Gene (TNFrsf11b)
SNP is a single base variation in DNA sequence that has a frequency >=1% in a population……
SNP is a single vase variation in DNA sequence that has a frequemcy >=1% in a population……
chromosome
gene
DNA
Each chromosome contains many genes, and the human genome contains between 30-40,000 of them.
Bold represents exons
SNP (rs9594782)
Remember there is another set of encyclopedia in parallel : allele


TNF Chromosomal Location: 6p21.3
SNPs: Single Nucleotide Polymorphisms
ARG
GTACCGCGGCGC
GTACCACGGCGC
HIS
Start codon : ATG
Stop codon : TGA
SNP? : DNA sequence variations That occure when a single ucleotide (A,T,C,or G) in the genome sequence is altered with frequency >1% in a population.
• SNPs are the most common sequence variations in the human genome (1 SNP per 300 bases on average → total 10 million SNPs)


What's SNP
SNP : DNA sequence variations That occure when a single nucleotide (A,T,C,or G) in the genome sequence is altered with frequency >1% in a population.
SNPs: Single Nucleotide Polymorphisms
ARG
GTACCGCGGCGC Allele 1 (M)
GTACCACGGCGC Allele 2 (F)
HIS
Human ApoE gene segment, rs11542035 SNP
A/G SNP
Three Genotypes
• Homozygous wild type : GG
• Heterozygous mutant type : GA
• Homozygous mutant type : AA
Gene loci
Dominant allele
Recessive allele
Genotype: PP aa Bb
Homozygous for the dominant allele
Homozygous for the recessive allele
Heterozygous


NCBI
Entrez, The Life Sciences Search Engine
Search across databases PPARG
PubMed: Biomedical literature citations and abstracts
PubMed Central: free, full text journal articles
Site Search: NCBI web and FTP sites
Books: online books
OMIM: Online Mendelian Inheritance in Man
OMIA: Online Mendelian Inheritance in Animals
Nucleotide: sequence database (includes GenBank)
Protein: sequence database
Genome: whole genome sequences
Structure: three-dimensional macromolecular structures
Taxonomy: organisms in GenBank
SNP: single nucleotide polymorphism
Gene: gene-centered information
UniGene: gene-oriented clusters of transcript sequences
CDD: conserved protein domain database
3D Domains: domains from Entrez Structure
UniSTS: markers and mapping data
PopSet: population study data sets
GEO Profiles: expression and molecular abundance profiles
GEO DataSets: experimental sets of GEO data


NCBI HomePage
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SITE MAP
Alphabetical List Resource Guide
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Sequence submission support and software
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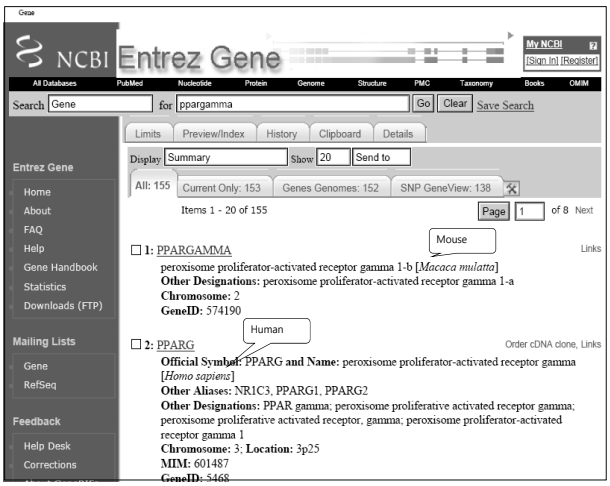
Molecular databases
Sequences, structures, and
What does NCBI do?
Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information - all for the better understanding of molecular processes affecting human health and disease. More...
New Protein Clusters
Entrez Protein Clusters database
The new Entrez Protein Clusters database is a collection of Reference Sequence (RefSeq) proteins, from the complete genomes of prokaryotes, plasmids, organelles, that have been grouped and annotated based on sequence similarity and protein function. Click here to find out more about the Protein Clusters database.
New dbGaP
Hot Spots
Assembly Archive
Clusters of orthologous groups
Coffee Break, Genes & Disease, NCBI Handbook
Electronic PCR
Entrez Home
Entrez Tools
Gene expression omnibus (GEO)
Human genome resources
Influenza Virus Resource


Gene
NCBI Entrez Gene
My NCBI [Sign In] [Register]
All Databases PubMed Nucleotide Protein Genome Structure PMC Taxonomy Books OMIM
Search Gene for ppargamma Go Clear Save Search
Limits Preview/Index History Clipboard Details
Display Summary Show 20 Send to
All: 155 Current Only: 153 Genes Genomes: 152 SNP GeneView: 138
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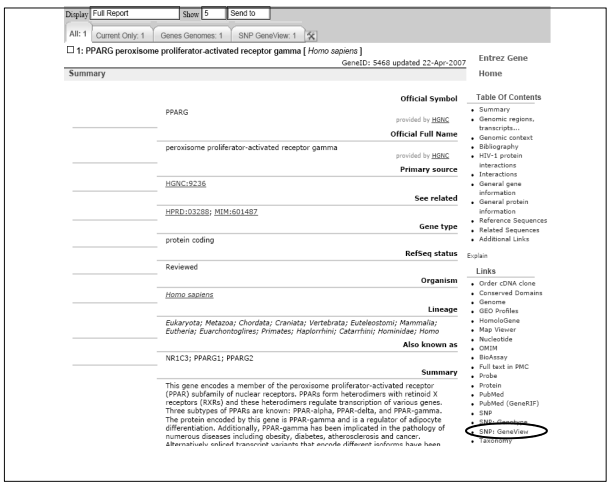
Entrez Gene
Home
About
FAQ
Help
Gene Handbook
Statistics
Downloads (FTP)
Mailing Lists
Gene
RefSeq
Feedback
Help Desk
Corrections
Mouse
1: PPARGAMMA
peroxisome proliferator-activated receptor gamma 1-b [Macaca mulatta]
Other Designations: peroxisome proliferator-activated receptor gamma 1-a
Chromosome: 2
GeneID: 574190
Human
2: PPARG
Official Symbol: PPARG and Name: peroxisome proliferator-activated receptor gamma [Homo sapiens]
Other Aliases: NR1C3, PPARG1, PPARG2
Other Designations: PPAR gamma; peroxisome proliferative activated receptor gamma; peroxisome proliferative activated receptor, gamma; peroxisome proliferator-activated receptor gamma 1
Chromosome: 3; Location: 3p25
MIM: 601487
GeneID: 5468


Display Full Report
Show 5
Send to
All: 1
Current Only: 1
Genes Genomes: 1
SNP GeneView: 1
1: PPARG peroxisome proliferator-activated receptor gamma [Homo sapiens]
GeneID: 5468 updated 22-Apr-2007
Summary
Official Symbol
PPARG
Official Full Name
peroxisome proliferator-activated receptor gamma
Primary source
HGNC:9236
See related
HPRD:03288; MIM:601487
Gene type
protein coding
RefSeq status
Reviewed
Organism
Homo sapiens
Lineage
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
Also known as
NR1C3; PPARG1; PPARG2
Summary
This gene encodes a member of the peroxisome proliferator-activated receptor (PPAR) subfamily of nuclear receptors. PPARs form heterodimers with retinoid X receptors (RXRs) and these heterodimers regulate transcription of various genes. Three subtypes of PPARs are known: PPAR-alpha, PPAR-delta, and PPAR-gamma. The protein encoded by this gene is PPAR-gamma and is a regulator of adipocyte differentiation. Additionally, PPAR-gamma has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis and cancer.
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OMIM
BioAssay
Full text in PMC
Probe
Protein
PubMed
PubMed (GeneRIF)
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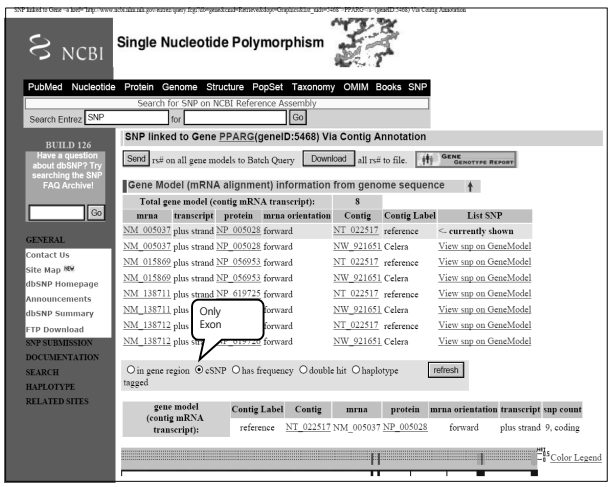
SNP: GeneView
Taxonomy
Entrez Gene Home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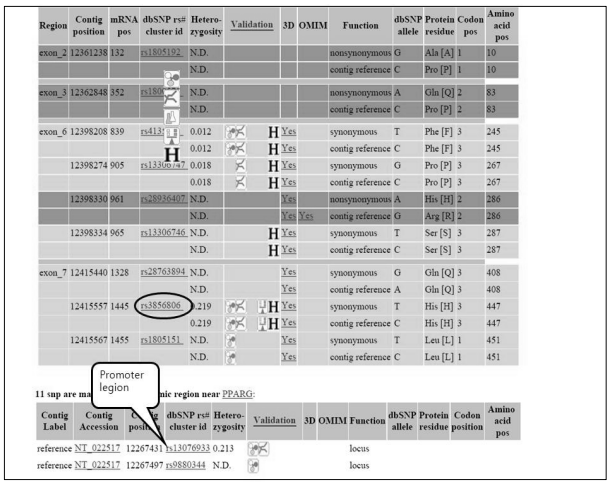
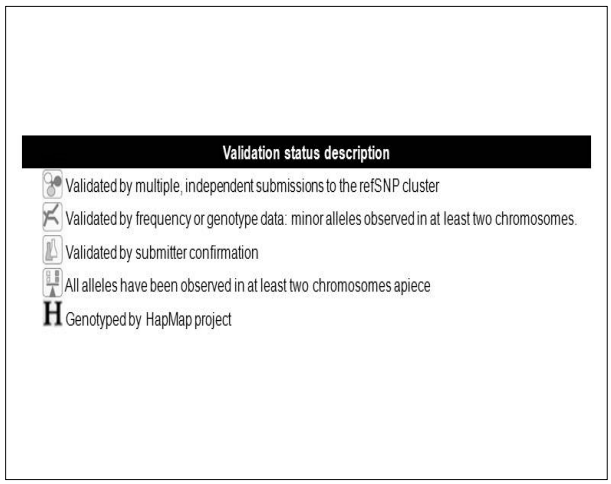
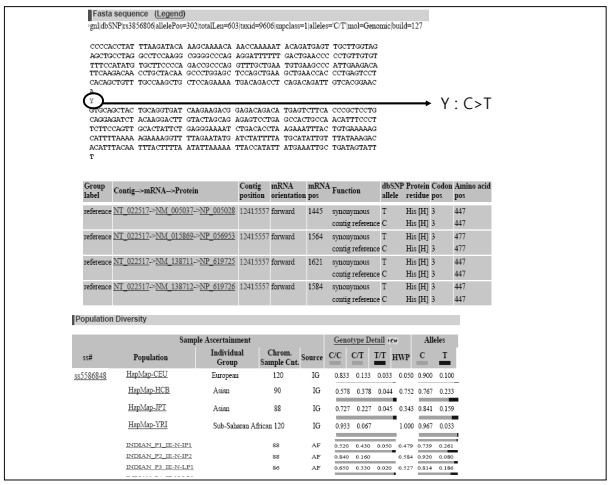
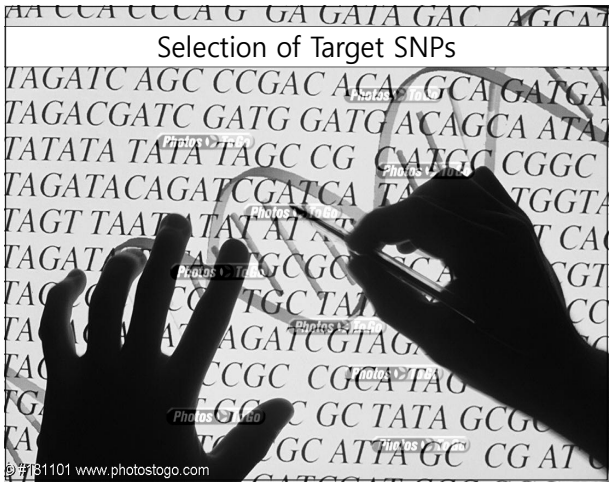
RELATED SITES
SNP linked to Gene PPARG(geneID:5468) Via Contig Annotation
Send rs# on all gene models to Batch Query
Download all rs# to file.
Gene Model (mRNA alignment) information from genome sequence
Total gene model (contig mRNA transcript): 8
mrna transcript protein mrna orientation Contig Contig Label List SNP
NM_005037 plus strand NP_005028 forward NT_022517 reference <- currently shown
NM_005037 plus strand NP_005028 forward NW_921651 Celera View snp on GeneModel
NM_015869 plus strand NP_056953 forward NT_022517 reference View snp on GeneModel
NM_015869 plus strand NP_056953 forward NW_921651 Celera View snp on GeneModel
NM_138711 plus strand NP_619725 forward NT_022517 reference View snp on GeneModel
NM_138711 plus forward NW_921651 Celera View snp on GeneModel
NM_138712 plus forward NT_022517 reference View snp on GeneModel
NM_138712 plus forward NW_921651 Celera View snp on GeneModel
Only Exon
in gene region cSNP has frequency double hit haplotype tagged
refresh
gene model (contig mRNA transcript):
Contig Label Contig mrna protein mrna orientation transcript snp count
reference NT_022517 NM_005037 NP_005028 forward plus strand 9, coding
Color Legend


Region Contig position mRNA pos dbSNP rs# cluster id Hetero-zygosity Validation 3D OMIM Function dbSNP allele Protein residue Codon pos Amino acid pos
exon_2 12361238 132 rs1805192 N.D. nonsynonymous G Ala [A] 1 10
N.D. contig reference C Pro [P] 1 10
exon_3 12362848 352 N.D. nonsynonymous A Gln [Q] 2 83
N.D. contig reference C Pro [P] 2 83
exon_6 12398208 839 rs4135 0.012 Yes synonymous T Phe [F] 3 245
0.012 Yes contig reference C Phe [F] 3 245
12398274 905 rs13306147 0.018 Yes synonymous G Pro [P] 3 267
0.018 Yes contig reference C Pro [P] 3 267
12398330 961 rs28936407 N.D. Yes nonsynonymous A His [H] 2 286
N.D. Yes Yes contig reference G Arg [R] 2 286
12398334 965 rs13306746 N.D. Yes synonymous T Ser [S] 3 287
N.D. Yes contig reference C Ser [S] 3 287
exon_7 12415440 1328 rs28763894 N.D. Yes synonymous G Gln [Q] 3 408
N.D. Yes contig reference A Gln [Q] 3 408
12415557 1445 rs3856806 0.219 Yes synonymous T His [H] 3 447
0.219 Yes contig reference C His [H] 3 447
12415567 1455 rs1805151 N.D. Yes synonymous T Leu [L] 1 451
N.D. Yes contig reference C Leu [L] 1 451
Promoter legion
11 snp are ma ic region near PPARG:
Contig Label Contig Accession Contig position dbSNP rs# cluster id Hetero-zygosity Validation 3D OMIM Function dbSNP allele Protein residue Codon position Amino acid pos
reference NT_022517 12267431 rs13076933 0.213 locus
reference NT_022517 12267497 rs9880344 N.D. locus


Validation status description
Validated by multiple, independent submissions to the refSNP cluster
Validated by frequency or genotype data: minor alleles observed in at least two chromosomes.
Validated by submitter confirmation
All alleles have been observed in at least two chromosomes apiece
Genotyped by HapMap project


Fasta sequence (Legend)
gnl|dbSNP|rs3856806|alleleFreq=302|totalLen=603|mxid=9606|mpclass=1|alleles=C/T|mol=Genomic|build=127
Y : C>T
Group label Contig-->mRNA-->Protein Contig position mRNA orientation mRNA pos Function dbSNP allele Protein residue Codon pos Amino acid
reference NT_022517->NM_005037->NP_005028 12415557 forward 1445 synonymous T His [H] 3 447
contig reference C His [H] 3 447
reference NT_022517->NM_015869->NP_056953 12415557 forward 1564 synonymous T His [H] 3 477
contig reference C His [H] 3 477
reference NT_022517->NM_138711->NP_619725 12415557 forward 1621 synonymous T His [H] 3 447
contig reference C His [H] 3 447
reference NT_022517->NM_138712->NP_619726 12415557 forward 1584 synonymous T His [H] 3 447
contig reference C His [H] 3 447
Population Diversity
Sample Ascertainment
ss# Population Individual Group Chrom. Sample Cnt. Source
Genotype Detail
C/C C/T T/T HWP
Alleles
C T
ss5586848 HapMap-CEU European 120 IG 0.833 0.133 0.033 0.050 0.900 0.100
HapMap-HCB Asian 90 IG 0.578 0.378 0.044 0.752 0.767 0.233
HapMap-JPT Asian 88 IG 0.727 0.227 0.045 0.343 0.841 0.159
HapMap-YRI Sub-Saharan African 120 IG 0.933 0.067 1.000 0.947 0.053
INDIAN_P1_IE-N-IP1 88 AF 0.520 0.430 0.050 0.479 0.739 0.261
INDIAN_P2_IE-N-IP2 88 AF 0.840 0.160 0.584 0.920 0.080
INDIAN_P3_IE-N-LP1 86 AF 0.650 0.330 0.020 0.527 0.814 0.186


Selection of Target SNPs
© #181101 www.photostogo.com

Selection of SNPs in Candidate Genes

Give high priority

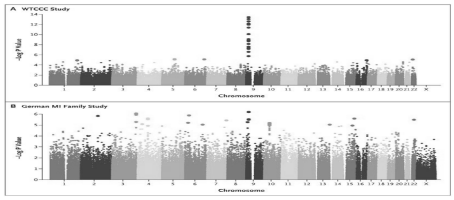
1) SNPs that are part of the HapMap project
2) SNPs mentioned in the literature as associating with a phenotype of interest
3) SNPs with good minor allele frequencies (MAF) (>5%)
4) **SNPs altering an amino acid – a change in protein sequence dictates a change in protein structure, which alters function (non-synonymous SNPs)**
5) **SNPs affecting mRNA splicing – splice site SNPs**
6) Others – ABI, Perlegen, comparative genomics, transcription factor binding site, etc
7) Tag SNP – LD block : Haplotype
8) GWAS data

Genome wide association (GWA) study

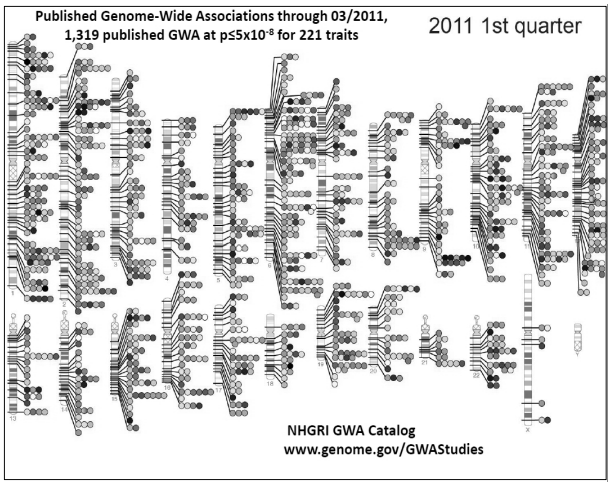
• The first major GWAS was published in Nature in February 2007 by Robert Sladek *et al.* in a study searching for type II diabetes variants

• Numerous genome-wide association studies for the diseases coronary heart disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, Crohn's disease, bipolar disorder, and hypertension has studied.

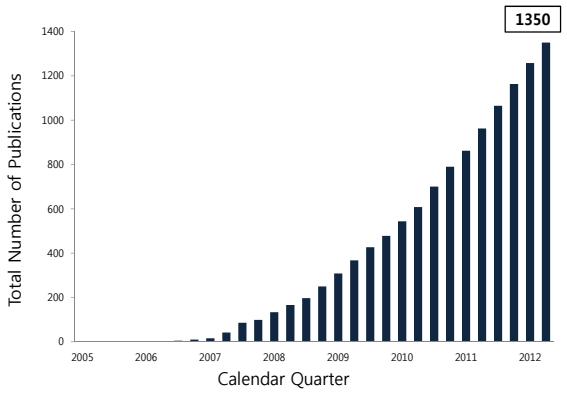
• One of the challenges for a successful GWAS in the future will be to apply the findings in a way that accelerates drug and diagnostics development



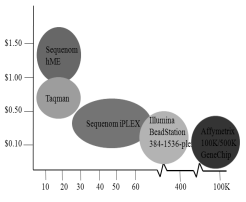
A WTCC study in coronary artery disease (Samani ,NEJM 2007)

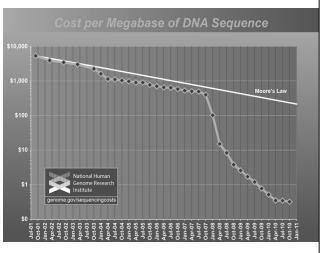


Published GWAS Reports, 2005 – 6/2012

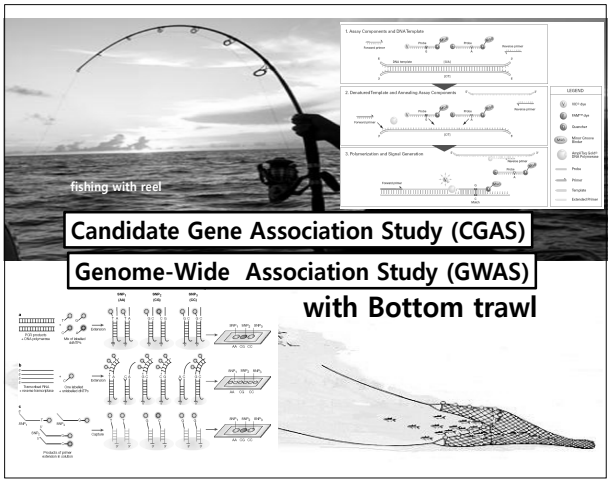


Comparison of Methods





	RFLP	TaqMan	Sequenom	Illumina
Reaction steps	2	1	3	2-3
Multiplex	no	yes	yes	yes
Bioinformatics	no	yes	yes	yes
DNA cost	25ng	5ng	1ng	<1ng
Cost per SNP	$1.50	60c	<50c	<10c
Overhead	Very low	modest	high	~$200,00



Whole genome sequencing history

연도	주체	기술	소요시간	비용
2000	Human Genome Project	Sanger sequencing	10년	30억 달러
2000	Celera Genomics	Sanger sequencing	4년	3억 달러
2007	Craig Venter Institute	Sanger sequencing	4년	7,000만 달러
2007	Baylor College of Medicine	Roche 454 (제임스왓슨)	수개월	100만달러
2007	Beijing Genome Institute	Illumina Solexa	수개월	50만 달러
2009	Stanford University	Helicos Heliscope	수개월	48,000달러
2009	서울 의대 유전체의학연구소	Illumina, Solexa Macrogen	수개월	30,000달러
2010	Complete Genomics	Complete Genomics	수개월	4,400달러
2011	Life Technology(ABI)	SOLID5500, NGS(2세대)	48시간	3,000달러
2012~2013	The Ion PGM™	Next-NGS (3세대)	8시간	2,000달러
2013 ~	Oxford Nanopore(TBD)	Nanopore,(4세대)	15분	1,000달러

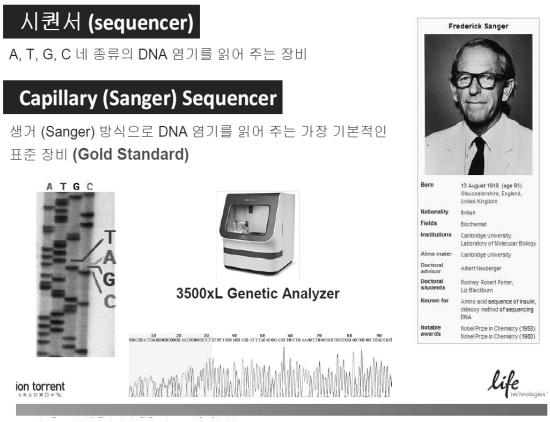
1,000달러 게놈 시장의 시작!!

시퀀서 (sequencer)

A, T, G, C 네 종류의 DNA 염기를 읽어 주는 장비

Capillary (Sanger) Sequencer

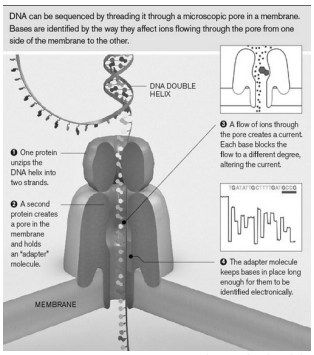
생거 (Sanger) 방식으로 DNA 염기를 읽어 주는 가장 기본적인 표준 장비 **(Gold Standard)**



NGS(Next Generation Sequencing)

	ABI 3730XL	Roche (GS FLX+)	Roche (GS Junior)	Illumina (MiSeq)	Illumina (HiSeq) High Output	Illumina (HiSeq) Rapid Run	Ion-torrent PGM(318)	Ion-torrent Proton	PacBio RS C2
Chemistry	Sanger Sequencing	Pyrosequencing	Pyrosequencing	sequencing by synthesis(SBS)	sequencing by synthesis(SBS)		semiconductor	semiconductor	Single molecule real time sequencing
Amplification	x	Emulsion PCR	Emulsion PCR	Bridge PCR	Bridge PCR		Emulsion PCR	Emulsion PCR	x
Sequencing Speed	20kb/h	30 Mb/h	3.5 Mb/h	200 - 210 Mb/h	2.2 Gb/h	4.4 Gb/h	130- 270Mb/h	-	50 Mb/h
output/run	1.9~84Kb	700Mb	35Mb	7.8 ~ 8.5 Gb	600G	120G	1-2 G	10 G	100Mb
Time/run	20min~3h	23h	10h	39 h	11 days	27 h	7.3 h	2-4 h	2h
Read length	400-900bp	700bp	400bp	2*250bp	2*100bp	2*150bp	400bp	200bp	2900bp
# of reads/run	-	1M	0.1M	30 - 34 million	6 million	1.2 million	-	60-80 million	-
Cost per run (total)	-	$7,000	-	$128K	$654K	-	-	-	$695K
Cost per Gb	$2,457,600	$10,240	-	$502	$41	-	$1,000	-	$2,000
Accuracy	99.9%	99.9%	99.9%	98%	98%	98%	98%	98%	87%(CLR), 99%(CCS)
Advantage	Long individual reads, useful for many applications	Long read size, Fast		potential for high sequence yield, depending upon sequencer model and desired application			less expensive equipment, Fast		Longest read length, Fast Detects 4mC, 5mC, 6mA
Disadvantage	More expensive and	Runs are expensive Homopolymer errors		Equipment can be very expensive			Homopolymer errors		Low yield at high accuarcy Equipment can be very expensive

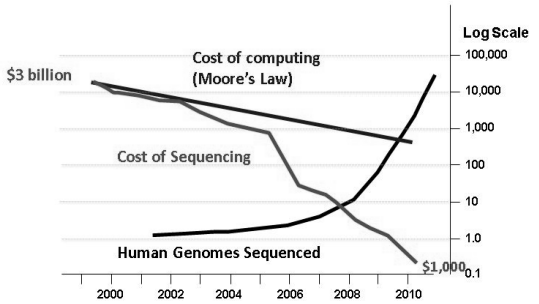
Oxford Nanopore in 2013



나노 : 10억분의 1 미터

Adapted from The Economist

The Sequencing Explosion

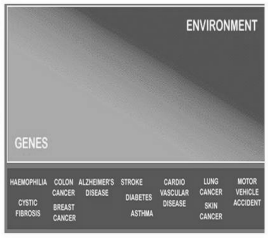


Today's Topic

1. **Personalized Medicine 이란 무엇인가?**
2. **Genomics 의 기본 개념과 발전 상황**
3. **유전과 환경의 상호작용에 대한 이해**
4. **유전체학의 임상 적용 : 질병예측 및 건강증진**

Gene-Environment interaction for cardiovascular disease prevention

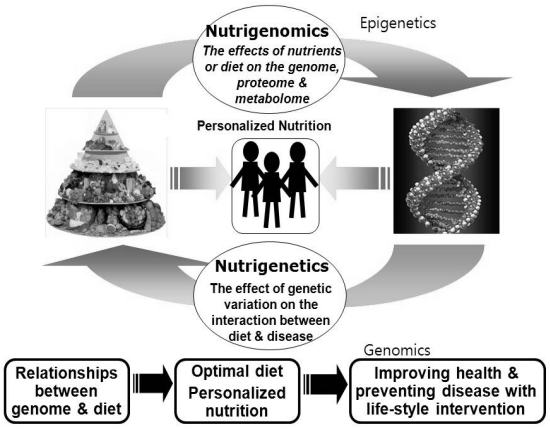
Gene vs Diet



NATURE VS NURTURE?
WE HAVE THEM BOTH.

Nature vs Nurture

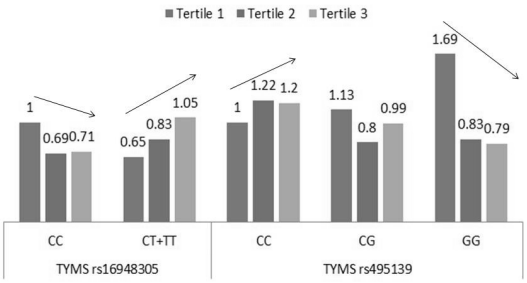
The figures colored black represent the proportion of each group expected to go on to develop the disease.



Colon Cancer Study

case-control study in Pennsylvania (686 cases,740 controls)

folate intake - Genotype interation

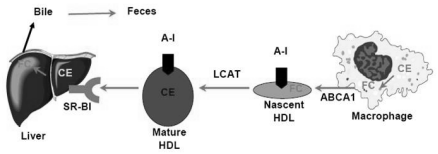


Tertile cutpoints: 555/1095 mg/d.

GENES, CHROMOSOMES & CANCER 2013

Gene-Environment interaction for cardiovascular disease prevention

HDL Metabolism and Reverse Cholesterol Transport



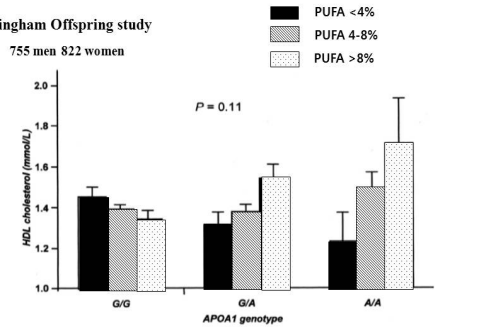
- Apo A-1 is a key component of HDL reverse transport.
- APOA1 75G>A in long arm chain of chromosome 11
- A Meta-analysis shows that rare A allele is associated increased apoA-1

Gene-Environment interaction for cardiovascular disease prevention

Mean (SE) HDL-cholesterol concentrations by *APOA1* genotype and polyunsaturated fatty acid (PUFA) intake

Framingham Offspring study

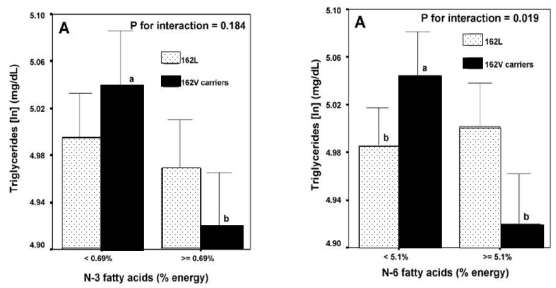
755 men 822 women



José M Ordovas. Am. J. Clinical Nutrition, Feb 2006; 83: 443S - 446S.

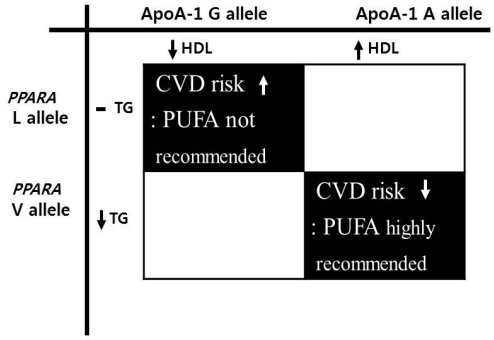
Gene-Environment interaction for cardiovascular disease prevention

Polyunsaturated Fatty Acids Interact with the *PPARA*-L162V Polymorphism to Affect Plasma Triglyceride Concentrations in the Framingham Heart Study.



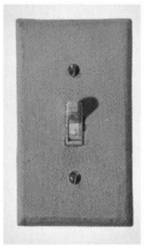
E. Shyong Tai etcJ. Nutr., Mar 2005; 135: 397 - 403.

Gene-Environment interaction for cardiovascular disease prevention

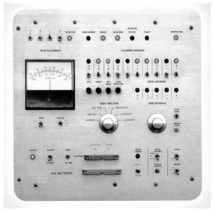


Gene-Gene Interaction

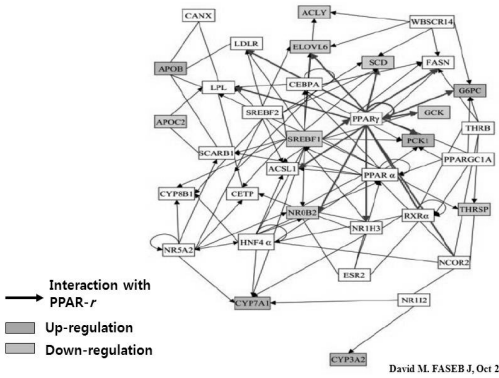
Monogenic disease



Polygenic or Multifactorial Disease

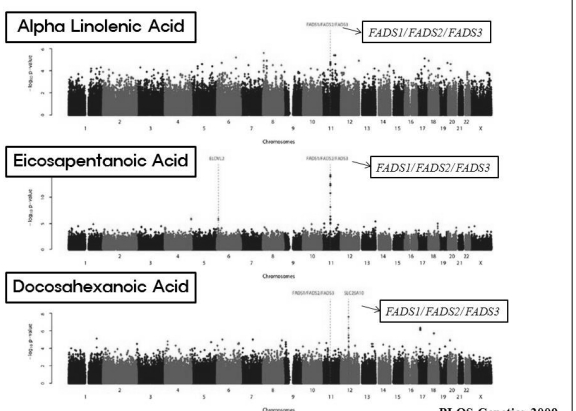


Biological network triggered after the PUFA intake



David M. FASEB J, Oct 2005; 19: 1602 - 1616.

GxE Wide Association of PUFA

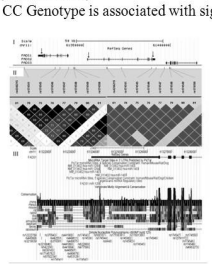


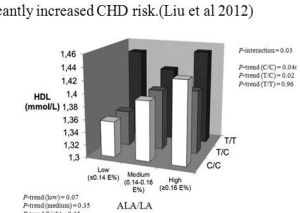
PLOS Genetics 2009

FADS1(Fatty acid desaturases 1)

Two rate-limiting enzymes in PUFA biosynthesis, Δ5- and Δ6-desaturases, are encoded by the *FADS1* and *FADS2* genes, respectively.

- CC Genotype of rs174547 in *FADS1* gene is associated with elevated TG, LDL , Blood Glucose and decreased HDL.(Nakayama et al 2010)
- CC Genotype is associated with lower level of omega-3 and omega-6 (Mathias 2010)
- CC Genotype is associated with significantly increased CHD risk.(Liu et al 2012)





Hellstrand, 2012

PATHWAY GENOMICS®

PATHWAY*FIT*®

DIET, NUTRITION & EXERCISE

PERSONAL GENETIC REPORT

FADS1 and Omega 3,6

NAME/ID: KYONG-CHOL KIM
SEX: MALE
ACC #: D3515283
DATE: MAY 28, 2013

DIET
PAGE 12
PATHWAY GENOMICS

DIET
OMEGA-6 AND OMEGA-3 LEVELS

Polyunsaturated fats (PUFAs) in our diet are composed of omega-3 and omega-6 fatty acids, both of which are recommended by the American Heart Association (AHA) for good heart health. Long-chain PUFAs are provided by our diet, but can also be synthesized in our bodies starting from the precursor essential fatty acids, linoleic acid (LA, omega-6) and alpha-linolenic acid (ALA, omega-3). Both omega-3 and omega-6 fats are processed in the body by the same enzyme complex[10]. The major dietary sources of omega-3 fatty acids include foods, such as flaxseed and walnuts, as well as fish oils and fish such as salmon. Processed foods often contain high levels of omega-6, while healthy sources of omega-6 include evening primrose and borage oils, as well as olives, nuts and poultry. Historically, the ratio of omega-6 to omega-3 fats in the diet was maintained close to a healthy 1:1, while in the current Western diet it is estimated to be about 15:1[11].

In recent genome-wide association studies that included over 10,000 people, it was found that those with the C/C or C/T genotypes at a variant in the FADS1 gene, which codes for one of the enzymes involved in processing omega-3 and omega-6 fats, had "Decreased" blood levels of arachidonic acid (AA), a long-chain omega-6 fat, as well as eicosapentaenoic acid (EPA), a long-chain omega-3 fat. On the other hand, those with a T/T genotype had "Typical" levels of these two omega-fats[12,13]. Since both AA and EPA are precursors of biologically important metabolites, those with a "Decreased" outcome should increase their dietary intake of both omega-3 and omega-6 fatty acids. However, considering the current skewed ratio of omega-6:omega-3 fats, it is recommended that people monitor the intake of omega-6 fats from processed foods, while increasing their intake of omega-3 fats.

YOUR RESULT

DECREASED

People with your genotype were found to have decreased blood levels of an important omega-6 fat and an important omega-3 fat.

YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
FADS1-rs174547	C/C	★★★★

FADS1-rs174547 C/C

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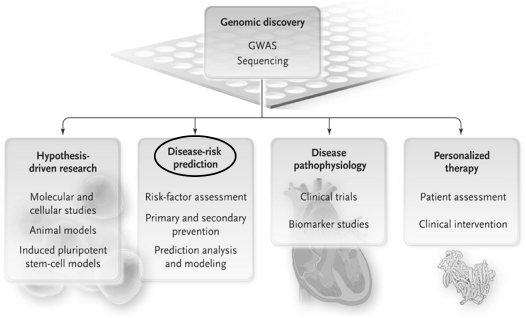
Investigative Pathways Leading from Gene Discovery to Clinical Application



O'Donnell CJ, Nabel EG. N Engl J Med 2011

세계 유전체 시장의 현황 : 분야별 유전체 분석 시장 전망

(단위: 백만달러)

분류	2007	2008	2009	2014	CAGR% 2009-2014
Tools	541	611.1	691.8	1,315.10	13.7
Services	254.2	293	338.8	713.5	16.1
응용분야					
Drug development	508.9	569.6	639	1298.3	15.2
- Clinical trials	178.1	193.7	210.9	460.9	16.9
- Whole geneome testing	127.2	142.4	159.7	331.1	15.7
- Toxicology prediction	112	125.3	147	285.6	14.2
- Identifiation of drug resistance	91.6	108.2	121.4	220.7	12.7
Drug discovery	286.3	334.5	391.6	730.3	13.3
- Genotyping and DNA fragment analysis	100.2	110.4	133.1	270.2	15.2
- Genetic variation and interaction	85.9	97	113.6	219.1	14
- Cellular functions	57.3	73.6	82.2	138.8	11
- Others	42.9	53.5	62.7	102.2	10.3
전체	795.2	904.1	1,030.60	2,028.60	14.5

출처: Business Insights, 'DNA sequencing in Drug Discovery'(2009)

※ 임상실험, 전장유전체 검사, 독성예측, 약제내성판별
※ 유전적 다형성 및 유전형 분석, 세포 기능분석

- 연평균 성장률 14.5%로 증가(2009-2014)
- 2014년 20억 달러 이상 예상 (분석툴 시장 / 서비스 시장)

1) 유전체 분석툴 시장
- 개인 맞춤의학 및 신약개발 등의 응용분야 기반 기술
- 시장규모 13억 달러 이상 전망(2014)

2) 유전체 분석 서비스 시장
- 연평균 성장률이 분석툴 시장보다 더욱 높음
- 유전체 분석이 대중화되고 점차 소비가 증가하고 있어 산업규모가 더욱 커질 것으로 전망

세계 유전체 시장의 현황 : 국가별 유전체 분석 시장 전망

(단위: 백만달러)

국가	2007	2008	2009	2014	CAGR% 2009-2014
북미	361.4	411.9	470.7	935.1	14.7
Tools	245.8	278.2	316	605.7	13.9
Service	115.6	133.7	154.7	329.4	16.3
유럽	265.6	300	339.9	645.1	13.7
Tools	179.7	201.8	227	416.4	12.9
Service	85.8	98.2	112.9	228.7	15.2
아시아	115.4	133.6	155	334.4	16.6
Tools	79.7	91.7	105.6	220.2	15.8
Service	35.7	41.9	49.4	114.2	18.2
기타	52.9	58.6	65	114	11.9
Tools	35.8	39.4	43.2	72.8	11
Service	17.1	19.2	21.8	41.2	13.6
total	795.2	904.1	1,030.60	2,028.60	14.5

출처: Business Insights, 'DNA sequencing in Drug Discovery'(2009)

- 미국과 캐나다를 포함하는 북아메리카 시장이 가장 큰 규모 2014년 935백만 달러의 시장 형성 전망

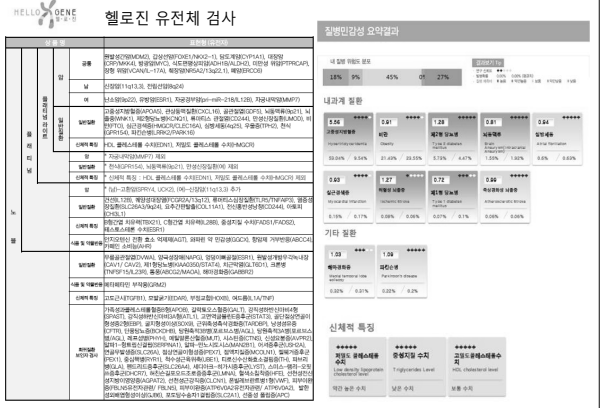
- 아시아의 유전체 분석 시장은 2014년 334백만 달러 규모 예상 평균성장률이 가장 높은 16.6%로, 빠르게 발달하고 있음을 알 수 있음

세계 유전체 시장의 현황 : 북미 주요 업체의 특징 비교

	23andMe	Navigenics	Pathway Genomics
설립 현황	• 2006년 설립(Mountain View, CA) • 2007년 DTC 런칭	• 2007년 설립(Foster City, CA) • 2008년 DTC 런칭 • Life Technologies가 인수 -> 현재 DTC 중단	• 2008년 설립(San Diego, CA) • 2008년 DTC 런칭 -> 현재 DTC 중단
성격	• Entertainment 성격의 서비스 • 유방암, 천식 등 중병과 간단한 질병 검사 • 오른손/왼손 잡이, 쓴 맛 인식 정도, 유당 분해 능력 등 검사 -> 개인의 유전적 특징 파악 목적	• 건강 및 치료목적의 서비스 • 위암, 대장암, 폐암, 유방암, 뇌졸중, 뇌동맥류, 심장마비 등 29가지 질병에 대한 예측과 맞춤관리 정보를 제공	• 건강 및 치료목적의 서비스 • 열성질환, 약물반응효과, 복합성 질환 뿐만 아니라 23andMe와 같이 개인 조상 추적
전략	• 가장 저렴한 DTC 서비스 -> 현재까지 가장 많은 고객 유치 -> 100만 고객 유치 목표	• Corporate 중심의 마케팅 -> 기업의 사원 복지정책의 일환	• Blue shield 보험사와 계약 • 다이어트, 올림픽 운동 선수 건강 가이드라인에 이용 • 해외 시장 적극적으로 개척

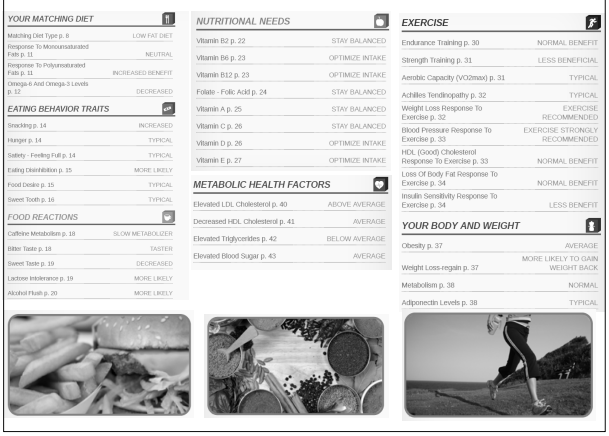
차움의 특화 검진 : 맞춤 유전체 검사

헬로진 유전체 검사



차움의 특화 검진 : 맞춤 유전체 검사

Overall summary of Pathway Fit Program and recommendation

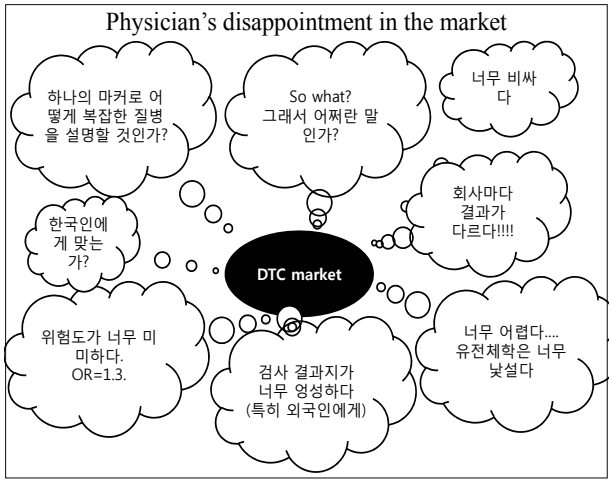


Prediction for disease relative risks for five individuals

Disease	Female A	Female B	Female C	Male D	Male E
Breast cancer	↑↑	↑↑	↓↓		
Coeliac disease	↓↓	↓↓	↓↓	↓↓	↓↓
Colon cancer	==	==	=↓	↑↑	=↓
Crohn's disease	↓↑	↓↑	↓↓	↓↓	↓=
Heart attack	↓↓	=↓	=↓	=↓	↑↑
Lupus	↑↓	↓↓	↓↓	↑=	↑=
Macular degeneration	↓↓	↓↓	↑=	↓↓	↓↓
Multiple sclerosis	↑↑		↓↓	↓↓	↓↓
Prostate cancer				↑↑	↓↑
Psoriasis	↓↑		↑↓	↑↑	↓↓
Restless legs syndrome	=↓	↑↑	↓=	↓↑	↑↑
Rheumatoid arthritis	↑↑	↑↑	↓↓	↓↓	↑↑
Type 2 diabetes	↓↓	=↓	↓↓	↑↓	=↓

↑ increased risk (RR > 1.05), ↓ decreased risk (relative risk (RR) < 0.95), = average risk (0.95 ≤ RR ≤ 1.05). First prediction is from 23andMe; second prediction is from Navigenics.
Different predictions are highlighted in beige.

Physician's disappointment in the market



체크1
: 다중 마커 (multiple marker)를 사용하는지

헬로진 암	
Phenotype	Gene
담도계암	*CYP1A1*
방광암	*MYC*
자궁내막암	*MMP7*
유방암	*ESR1*
원발성 간암	*MDM2*
대장암	*CRP*
췌장암	*NR5A2*
미만성 위암	*PTPRCAP*
난소암	*9p22*
장형위암	*IL-17A*
갑상선암	*FOXE1*
폐암	*ERCC6*
고환암	*UCK2*
자궁경부암	*IL12B*
전립선암	*8q24*
식도편평상피암	*ALDH2*

헬로진 일반질환	
Phenotype	Gene
심근경색증	*APOA5*
심방세동	*4q25*
관상동맥질환	*HMGCR*
뇌동맥류	*9p21*
뇌졸중	*WNK1*
골관절염	*FTO*
류마티스관절염	*GDF5*
만성신장질환	*UMOD*
파킨스병	*PARK16*
천식	*GPR154*
우울증	*TPH2*
비만	*FTO*
제 2 형당뇨병	*KCNQ1*
고중성지방혈증	*APOA5*
고밀도콜레스테롤수치	*EDN1*
저밀도콜레스테롤수치	*HMGCR*

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대장암	*CRP*
췌장암	*NR5A2*
미만성 위암	*PTPRCAP*
난소암	*9p22*
장형위암	*IL-17A*
갑상선암	*FOXE1*
폐암	*ERCC6*
고환암	*UCK2*
자궁경부암	*IL12B*
전립선암	*8q24*
식도편평상피암	*ALDH2*

헬로진 일반질환	
Phenotype	Gene
심근경색증	*APOA5*
심방세동	*4q25*
관상동맥질환	*HMGCR*
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뇌졸중	*WNK1*
골관절염	*FTO*
류마티스관절염	*GDF5*
만성신장질환	*UMOD*
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천식	*GPR154*
우울증	*TPH2*
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고밀도콜레스테롤수치	*EDN1*
저밀도콜레스테롤수치	*HMGCR*

질병민감성 상세결과

위암 (Gastric cancer)

전체 위암 환자의 5~10%를 차지하는 유전성 위암은 형태학적으로 미만성 위암과 장형 위암으로 분류됩니다. 미만성 위암은 암세포가 서로 떨어져 있으며 위벽에 넓게 퍼져나가면서 생기고, 심해지면 위벽이 딱딱한 가죽처럼 굳어집니다. 특히 젊은 여성에게 많이 생기는데 복막으로 전이가 흔하며 위암 중에서 예후가 가장 나쁩니다. 장형 위암은 암세포가 이웃 세포와 결합하고 있는 위암을 말하며 주로 위에 서식하는 헬리코박터 파일로리균에 감염되어 발병합니다. 남성과 고령자에게 발병할 확률이 높으며, 주로 궤양을 형성하여 위의 전정부와 소만부에 발생합니다.

유전형 분석 결과

유전자	유전형	대립인자	위험인자
IL17A	A G	A/G	A
VCAN	G G	G/T	G
PTPRCAP	A C	A/C	A

FADS1 and HDL Cholesterol

METABOLIC HEALTH FACTORS
DECREASED HDL CHOLESTEROL

High-density lipoprotein (HDL) cholesterol is known as good cholesterol, because high levels of HDL cholesterol seem to protect against heart attack, while low levels of HDL cholesterol (less than 40 mg/dL) increase the risk of heart disease[84]. While multiple mechanisms are known to account for this, the major one is thought to be the role of HDL in transporting excess cholesterol away from the arteries and back to the liver, where it is passed from the body[85]. Your HDL cholesterol can be measured with a simple blood test. In men, typical HDL cholesterol levels range from 40 to 50 mg/dl. In women, female hormones cause typical HDL cholesterol levels to range from 50 to 60 mg/dl; however, after menopause there is a tendency for decreased HDL cholesterol levels. Foods containing trans fats can lower HDL cholesterol levels, which is unhealthy. Cholesterol levels should be monitored by your physician.

A genetic result of "High" or "Above Average" does not mean you have decreased HDL cholesterol levels, but tells you that you may have a high propensity for decreased HDL cholesterol levels. On the other hand, a result of "Low" or "Below Average," tells you that you have a lower than av... HDL cholesterol levels. Our genetic testing is bas... over 19,000 individuals. A result of "High" means that you share a similar genetic profile with individuals from the Framingham Heart Study who had decreased HDL cholesterol levels measuring, on average, below 46 mg/dl with approximately 37% of individuals measuring below 40 mg/dl[8]. On the other hand, a result of "Above Average" means that you share a similar genetic profile with individuals measuring, on average, below 50 mg/dl HDL cholesterol with approximately 30% of individuals measuring below 40 mg/dl HDL cholesterol[8].

YOUR PROBABILITY

AVERAGE
Based on your genetic profile you have an average likelihood for decreased HDL cholesterol levels.

YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
ABCA1-rs1883025	G/A	★★★★
ANGPTL4-rs2967605	A/A	★★★★
CETP-rs247616	C/T	★★★★
FADS1-rs174547	C/C	★★★★
GALNT2-rs4846914	A/G	★★★★
HNF4A-rs1800961	C/C	★★★★
KCTD10-rs2338104	G/G	★★★★
LCAT-rs2271293	G/G	★★★★
LIPC-rs10468017	C/T	★★★★
LIPG-rs4939883	C/C	★★★★
LPL-rs12678919	A/A	★★★★

FADS1-rs174547 C/C

Elevated LDL cholesterol

METABOLIC HEALTH FACTORS
ELEVATED LDL CHOLESTEROL

Low-density lipoprotein (LDL) is the type of cholesterol that can become dangerous if you have too much of it. Like gunk clogging up your kitchen drain, LDL cholesterol can form plaque and build up in the walls of your arteries. This can make your arteries narrower and less flexible, putting you at risk for conditions like a heart attack or stroke. Optimally, LDL levels should be less than 100 mg/dl. Near-optimal levels range from 100 to 129 mg/dl and borderline high from 130 to 159 mg/dl. A score greater than 160 mg/dl is high and greater than 190 mg/dl is very high. Your physician can measure your cholesterol levels.

A genetic result of "High" or "Above Average" does not mean you have elevated LDL cholesterol levels, but tells you that you may have a genetic propensity for elevated LDL cholesterol levels. On the other hand, a result of "Low" or "Below Average," tells you that you have a lower than average genetic likelihood for elevated LDL cholesterol levels. However, you could still develop problems with your LDL levels as a result of your diet and other factors. This report is based on genetic variants studied in over 19,000 individuals. A genetic result of "High" means that you share a similar genetic profile with individuals from the Framingham Heart Study who had elevated LDL cholesterol levels measuring, on average, above 139 mg/dl with approximately 25% of individuals measuring above 160 mg/dl[8]. A genetic result of "Above Average" means that you share a similar genetic profile with individuals measuring, on average, above 130 mg/dl LDL with approximately 17% of individuals measuring above 160 mg/dl LDL cholesterol[8]. A genetic result of "Average" means that you share a similar genetic profile with individuals measuring, on average, near-optimal LDL cholesterol levels. Diet plays an important part in LDL levels. Processed foods and foods high in trans fat contribute to elevated LDL levels.

YOUR PROBABILITY

ABOVE AVERAGE
You share a similar genetic profile with individuals who exhibit borderline-high LDL cholesterol levels. Therefore, you have a higher than average likelihood for elevated LDL (bad) cholesterol levels.

YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
ABCG8-rs6544713	C/C	★★★★
APOB-rs515135	G/G	★★★★
CELSR2-rs12740374	G/G	★★★★
HMGCR-rs3846663	C/T	★★★★
HNF1A-rs2650000	C/C	★★★★
INTERGENIC-rs1501908	G/G	★★★★
LDLR-rs6511720	G/G	★★★★
MAFB-rs6102059	C/T	★★★★
NCAN-rs10401969	C/T	★★★★
PCSK9-rs11206510	T/T	★★★★

Calculating my genome risk for CHD

MYOCARDIAL INFARCTION

GENE/LOCUS	MARKER	GENOTYPE	ODD RATIO
LTA	rs1041981	A/C	1.2
MIAT	rs2331291	C/C	1.5
PSMA6	rs1048990	C/C	1.6

1.2X1.5X1.6= 2.88?

	LTA		MITA		PSMA6		LTA+MITA		LTA+MITA+PSMA6	
	present	abscent	present	abscent	present	abscent	present	abscent	present	abscent
MI	12	10	15	10	16	10	10	12	6	15
healthy	100	100	100	100	100	100	40	160	20	180
Odd ratio	1.2		1.5		1.6		**3.3**		**3.60**	

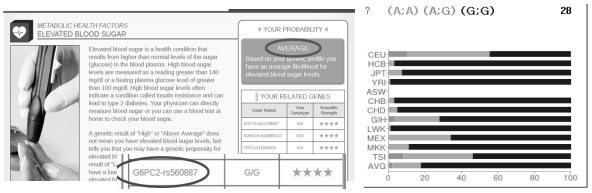
	Genetic high risk		Genetic high risk + smoking		Gene + smoking + obesity		smoking + obesity+inactivity	
	present	abscent	present	abscent	present	abscent	present	abscent
MI	6	15	5	16	5	16	5	16
healthy	20	180	15	185	14	186	12	188
Odd ratio	**3.60**		**3.85**		**4.15**		**4.90**	

Tell to patients their personalized risk for CHD according to genome*environmental data

체크 2

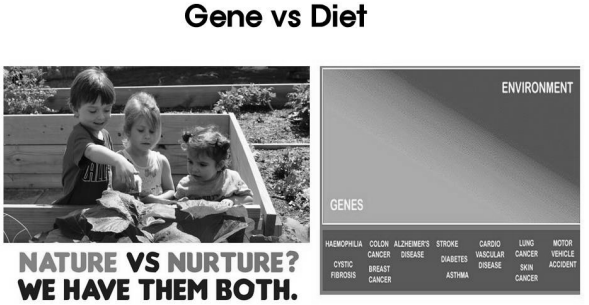
: 한국인의 관심 질병에 대해 검사하는가.

서양인의의 데이터로 만들어진 연구 논문에서 인용한 유전체별 질병의 위험도를 한국인에게 적용할 수 있는가?

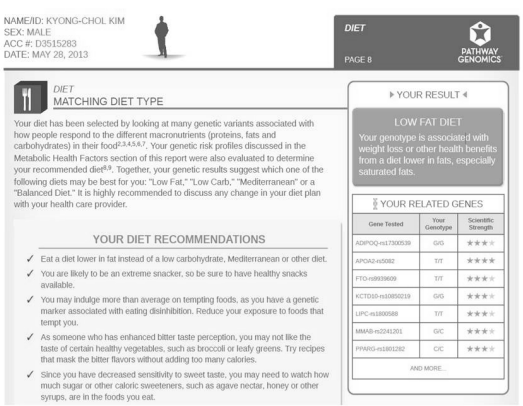


체크 3

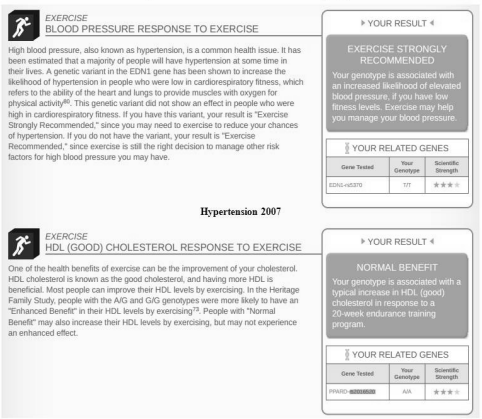
: 질병을 피할 수 있는 길을 제시하는가 (영양-유전체 상호작용)

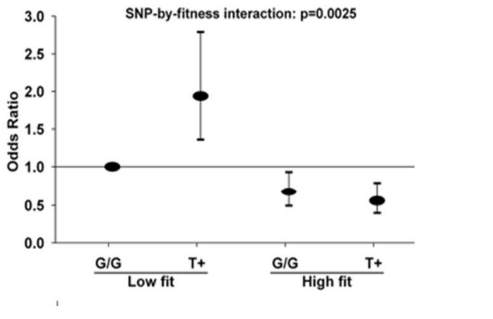


Matching diet based on my genome



Matching exercise based on my genome

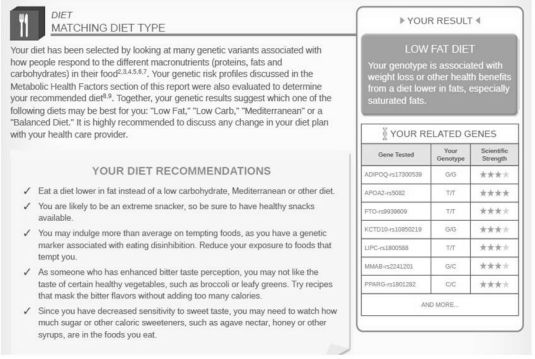




Hypertension 2007

체크 4

: 모든 검사에는 evidence와 한계를 명시하는가?



★★★★	Results derived from a large study of approximately 2,000 or more people, with at least one additional study showing the same results (replication study).
★★★☆	Results derived from a moderately-sized study of at least 400 people, with or without a replication study.
★★☆☆	Small study of less than 400 people in some cases, with other small replicated studies. Results in this category are preliminary, but pass our criteria for statistical significance.
★☆☆☆	Results in this category should be considered extremely preliminary.

체크 5

: 약물 유전체 검사 : 현재 사용하는 약물 중심으로 검사하는가

Personalized Medicine by the Numbers

13 prominent examples of personalized medicine drugs, treatments and diagnostics products available in 2006[1]
72 prominent examples of personalized medicine drugs, treatments and diagnostics products available in 2011[2]

$300,000,000 cost of sequencing a human genome in 2001[2]
$5,000 cost of sequencing a human genome in 2011[2]

4% U.S. hospitals with fully operational electronic health records in 2008[3]
22% U.S. hospitals with fully operational electronic health records in 2009[4]
50% U.S. population that had medical information recorded in electronic health records in some form in 2010[5]

차움 임상유전체 센터 (Chaum Clinical Genome Center)

차움·차병원과 함께하는 건강관리 맞춤형 유전체 건강검진

[중앙일보] 입력 2014.07.29 00:52

식탐 유전자 변이가 관찰됩니다, 식습관 조절로 비만 예방하세요

차움 안티에이징 임상유전체센터 김경철 교수가 맞춤형 유전체 건강검진 결과를 설명하고 있다.

Hello Gene 헬•로•진

PATHWAY GENOMICS

GENECARE

Bench to Bedside for Better Life

차움의 특화 검진 : 종합 보고서

성명	환자번호	성별	나이	국적	검진연도	종합검진	안티에이징	유전체검진
		Female	37	Kazakstan	2014.06.03	O	O	O

제 1군 : 종합 검사 주요 소견	주요 권고안
1. Gastro Endoscopy: Submucosal hemorrhagic gastritis	증상이 있을 경우 위장약 복용
2. Colonoscopy : colon polyp (0.3cm)	제거되었으며 3년 이후 추적 관찰
3. Thyroid sono : 0.2cm benign cyst	benign 소견으로 2년 이후 추적 관찰
4. increased APP : 10.8	간암수치로 약간 증가되었으나 간초음파 정상
5. 0.6cm round echogenic nodule in upper pole of right kidney	benign 소견으로 보이나 6개월 후 추적 관찰

제 2군 : 안티에이징 검사			
주요 기능 이상	관련증상 및 검사 의의	관련검사	결과 해석
만성피로	피로감,스트레스	부신기능검사	스트레스가 많을, 부신 기능 보충
		미토콘드리아 기능 저하	미토콘드리아 기능 저하
		유기산검사,포할검사	
자율신경계 검사	자율신경계 이상증상	HRV 검사, 포할검사	교감신경계 주세: 불안,초조함 등의 증상, 소화장애
세포노화, 산화스트레스	세포의 노화를 반영함	comet assay,DROM-BAP	산화스트레스와 항산화능력도 함께 측정
혈관 순환	모세혈관의 순환	Capillary scan	정상
음식 알러지 검사	주요 음식 알러지 검사	Food allergy test	바나나와 대부분 음식 알러지 없는 상태임
장내세균검사	가스장 변비, 설사 등	유기산검사	장내 세균이 증가되어 있습니다.
간독making 검사	주물,두근함	유기산 검사	간기능이 떨어져있어 의욕이 필요합니다.
항신경검사	우울불안,초조	신경전달물질대사프할	Norepinephrine 증가로 불안불안 가능성
주요영양지표검사	주요 미네랄의 과잉,부족	유기산검사,포할검사	마그네슘과 칼륨의 상대적 부족
종합 권고안			전반적으로 스트레스가 많고 고갈신경이 우세하여 불면불안 등이 있을 수 있습니다. 증상이 있는 경우 TS,Magnesium,신경안정제(amiolytic)가 도움이 될 수 있습니다. 피곤의 원인으로는 미토콘드리아 기능 의 저하가 주 원인으로 coQ10,arginine이 도움이 될 수 있습니다. 간해독이 필요한 경우 Glutathione이 도움됩니다. 장내세균 치료 위해 유산균(probiotics)이 필요합니다.

제 3군 : 주요 유전체 검사		주요 권고안
질병 예측 유전자 검사	유방암/혈당뇨,고혈압, 류마티스 관절염 등의 질병 위험도가 상대적으로 높음 (별지 참조)	유방암 검진은 매년 받도록 하시고 혈압은 주기적으로 체크 요합,당뇨 및 관절염 증상에 대한 주기적 체크
주요 약물 유전자 검사	베타차단제(혈압약)에 잘 들음, MTX 항암제에 부작용 가능성 높음,	상기 약제를 사용할 경우 의사와의 상담이 필요함
선천성 유전자 이상	모든 선천적 희귀 유전병에 대한 carrier는 없음	특별한 위험 요인 없음
Pathway Fit : personalized Nutrition & Exercise	오메가3,6 레벨이 낮음, 식탈 유전자는 많은 편	지중해식 식이 추천, 오메가 3,6 더 많이 섭취
	카페인 대사가 느림. 우유내당불내성이 있음,	커피를 마시면 잠을 못잠, 우유를 마시면 설사함
	비타민 B2,b12,엽산,E 대사가 나쁨	비타민 B2, B12, 엽산, E 등의 섭취량을 늘릴 것
	운동을 통하여 혈압,체중 감량,당뇨예방 효과 좋음	지구력 운동 적극 권장됨

제 4군 : 대사증후군 유전체-위험요인 상호작용				주요 권고안
검사날짜	참고치	검사결과	Genetic risk	현재 비만 상태이며 혈압약을 드시는 상태입니다.
중성지방(TG)	150이하	229	평균 이하	식탐에 대한 유전자는 많으나, 비만 유전자는 적은 편
HDL 콜레스테롤	50이상	46	평균 이상	입니다. 즉 유전에 의한 비만이라기 보다는 생활습관과
LDL 콜레스테롤	130이하	108	평균 이상	관련이 있으므로 다이어트 및 운동을 열심히 하세요.
공복시혈당	100이하	77	평균	특별히 LOI 콜레스테롤의 유전적 위험이 높으므로 저지
혈압	120/80이하	130/90	평균 이상	방 식이를 통한 관리 요합니다.
비만(BMI)	25이하	41.3	평균	

유전체 및 환경 상호작용 을 통한 건강증진 예시

대항목	소항목	한00	안00	최00	오00
기본데이터	성별	2	1	2	2
	나이	28	31	53	28
신체측정	키	160	180	163	167
	몸무게	53	120	66.8	67
	BMI	20.7	**37.0**	**25.1**	24.0
	체지방% 전체	28.7	**42.3**	**37.3**	**43.2**
	체지방% 상체	33.6	52.9	48.5	47.5
	체지방% 하체	38.6	45.3	41.8	49.8
	상체/하체비	0.87	**1.17**	**1.17**	0.95
	내장지방/전체지방	28%	**44%**	**44%**	27%
	Lean	35.9	66.52	40.1	38.32
	골밀도 척추	0.939	1.069	0.973	1.171
	골밀도 골반	1.031	1.343	1.054	1.229
	신체 건강지수	1	5	3	3

유전체 및 환경 상호작용 을 통한 건강증진 예시

대항목	소항목	한00	안00	최00	오00
기본데이터	성별	2	1	2	2
	나이	28	31	53	28
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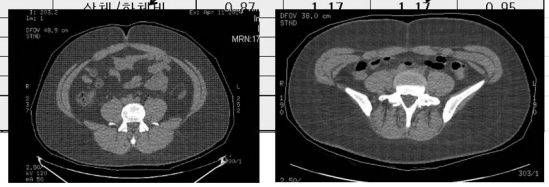
	체지방% 전체	28.7	**42.3**	**37.3**	**43.2**
	체지방% 상체	33.6	52.9	48.5	47.5
	체지방% 하체	38.6	45.3	41.8	49.8
	상체/하체대	0.87	1.17	1.17	0.95



유전체 및 환경 상호작용 을 통한 건강증진 예시

대항목	소항목	한00	안00	최00	오00
	스트레스지수	3	1	3	**5**
	식욕지수	2	**5**	4	4
영양조사	총kcal	2100/2011	**2400/2604**	1800/1557	2100/**2613**
	탄수화물(%)	65/45	65/50	65/63	65/43
	단백질(%)	15/17	15/17	15/15	15/15
	지방(%)	20/**38**	20/**32**	20/**24**	20/**43**
	식이섬유(g)	25/**22**	29/28	22/20	25/25
	식생활습관 건강지수	2	4	2	4
운동조사	운동빈도(회/1주)	1.5	0	4	1
	운동강도(분)	45	0	160	40
	운동타입	유산소운동	0	유산소운동	유산소운동
	운동습관 건강지수	2	5	1	4

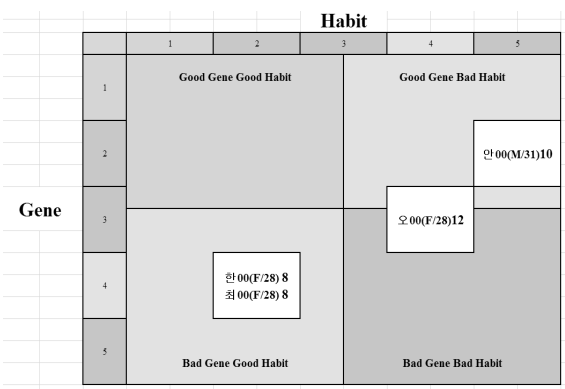
유전체 및 환경 상호작용 을 통한 건강증진 예시

대항목	소항목	한00	안00	최00	오00
대사검사	수축기혈압	95	**135**	**142**	124
	이완기혈압	65	**85**	**85**	79
	혈당	78	88	92	75
	SGOT	19	27	27	24
	SGPT	16	**55**	26	33
	총콜레스테롤	180	168	113	148
	중성지방	72	**165**	72	43
	HDL	67	42	56	54
	LDL	99	93	43	85
	f fatty acid	**667**	331	490	**745**
	CRP	0.03	**0.22**	**0.1**	0.02
	insulin	4.4	**11**	1.1	**7.4**
	Hb	14.2	16.2	12.6	14.6
	대사 건강지수	2	4	2	2

유전체 및 환경 상호작용 을 통한 건강증진 예시

대항목	소항목	한00	안00	최00	오00
	운동습관 건강지수	2	5	1	4
유전자검사	간식(LEPR)	2	1	1	1
	대사(LEPR)	1.5	1.5	1.5	1.5
	공복감(NMB)	1	1	1	1
	포만감(FTO)	1	1	1	1
	충동식탐(TAS2R38)	**1**	**1**	**2**	**2**
	설탕중독(SLC2A2)	1	1	1	1
	비만(FTO,MC4R)	1.25	1	1.25	**1.75**
	LDL 콜레스테롤	**1.8**	1.5	**1.7**	**1.7**
	고혈당 위험	1.5	1.5	**1.6**	1.5
	오메가3,6 감소	1	1	1.5	1.5
	유전자 건강지수	4	2	4	3

유전체 및 환경 상호작용 을 통한 건강증진 예시



한국인 비만 유전자의 특징

	Snacking	Hunger	Satiety	Fatty Deficiency	Food desire	Sweet tooth	Bitter taste		Obesity		Metabolism	Strength training	Aerobic capacity	Anti-oxidant & aging
	LEPR	NMB	FTO	TAS2R38	ANKK1/DRD2	SLC2A2	TAS2R38	TAS2R38	FTO	MC4R	ADIPOQ	INSIG2	PPARGC1A	FTO
	Rs2025804	Rs1051168	Rs9939609	Rs1726866	Rs1800497	Rs5400	Rs713598	Rs1726866	Rs9939609	Rs17782313	Rs17366568	rs7566605	rs8192678	rs1121980
risk allele	G	T	A	T	T	T	G	C	A	C	G	C	A	T
KOREAN														
AA(risk)	**79%**	2.8%	**1.4%**	**19.4%**	**19.4%**	**0%**	16.7%	36.1%	**1.4%**	5.6%	88.9%	13.9%	20.8%	**1.4%**
AB	**21%**	16.7%	**22.2%**	**44.4%**	**43.1%**	**0%**	47.2%	47.2%	**22.2%**	38.9%	9.7%	56.9%	44.4%	**27.8%**
BB	**0%**	80.6%	**73.6%**	**31.9%**	**37.5%**	**100%**	36.1%	16.7%	**73.6%**	55.6%	1.4%	29.2%	34.7%	**70.8%**
European														
AA(risk)	**15.9%**	8.1%	**17.7%**	**33.6%**	**5.3%**	**4.5%**	18.6%	19.5%	**17.7%**	3.5%	77.0%	7.1%	15.0%	**21.2%**
AB	**44.2%**	35.1%	**56.6%**	**46.9%**	**28.3%**	**19.8%**	49.2%	46.9%	**56.6%**	46.0%	22.1%	38.9%	39.8%	**54.0%**
BB	**39.8%**	56.8%	**25.7%**	**19.5%**	**66.4%**	**75.7%**	32.2%	33.6%	**25.7%**	50.4%	0.9%	54.0%	45.1%	**24.8%**

한국인 비만 유전자의 특성

1. 고도비만과 관련된 FTO 유전자의 비율은 서양인에 비해 적은 편이다 (17.7% vs 1.4%)
2. 중추 신경계의 식욕과 관련된 비만 유전자 MC4R 유전자는 비슷하다 (5.5% vs 3.5%)
3. 한국인은 간식섭취와 관련된 유전자 (LEPR) 변이가 더 많고, 서양인은 특식 (섭식무절제) 유전자 (TAS2R38) 변이가 더 많다
4. 서양사람에겐 단맛중독 유전자 (SLC2A2)변이가 있지만, 한국인에겐 거의 없다. 상대적으로 한국인은 쓴맛 예민자가 더 많다.
5. 한국인에게 가장 추천하는 다이어트 방식은 저탄수화물 식이 (58%)이다.

한국인의 추천 다이어트