

Genomitieto ja lääketieteellinen tutkimus

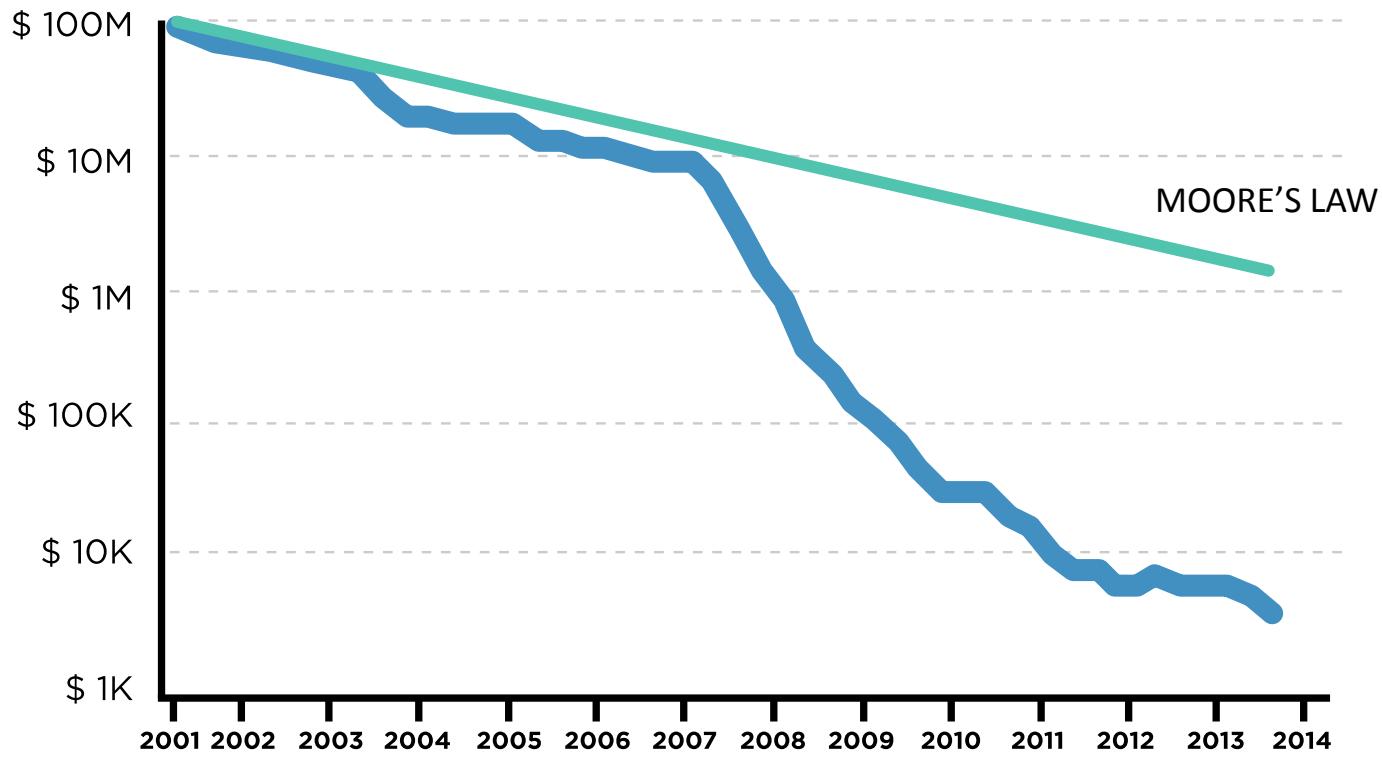
Majvik, lokakuun 30, 2015

Aarno Palotie M.D., Ph.D.



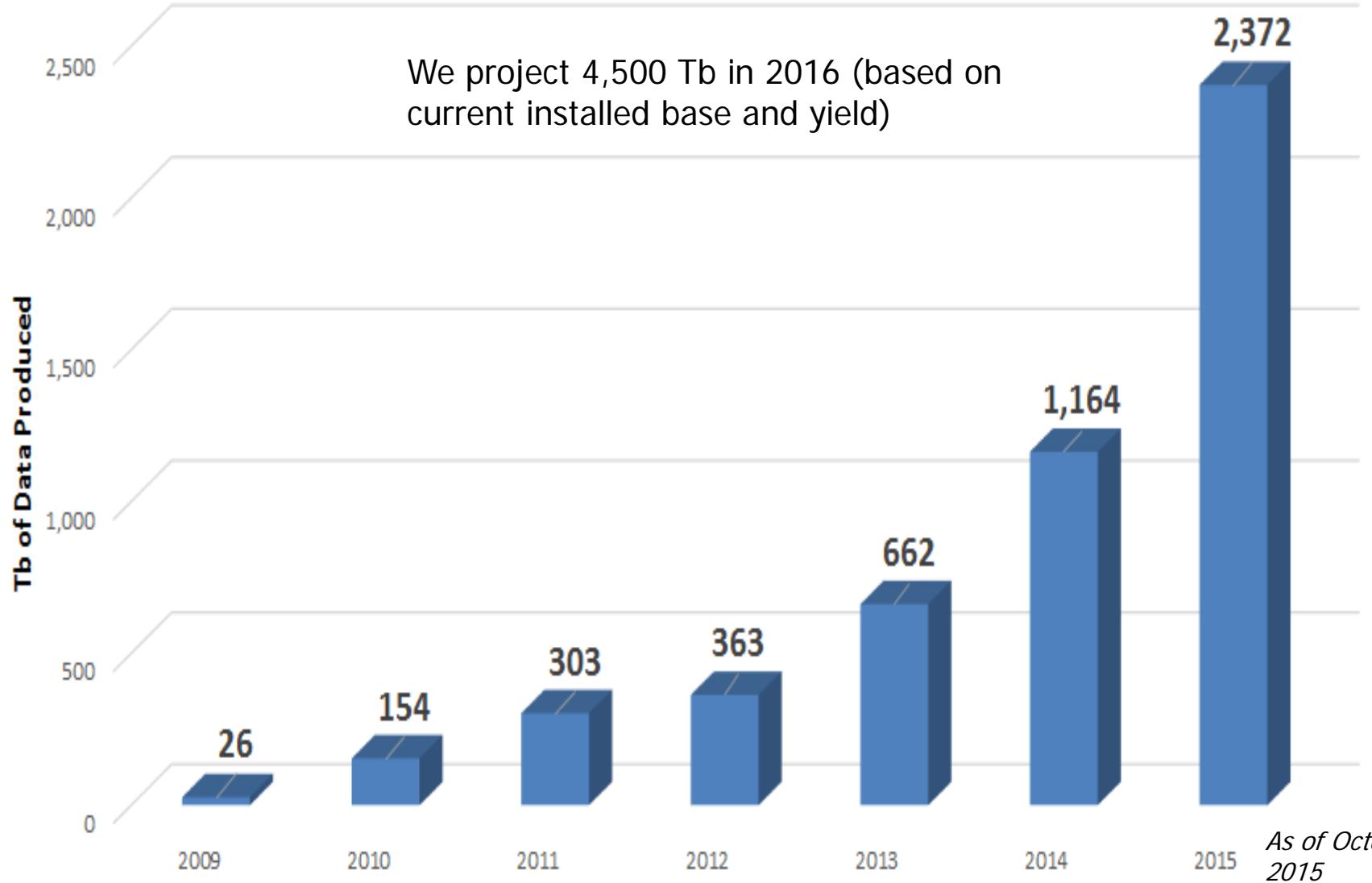


The technology drives the change



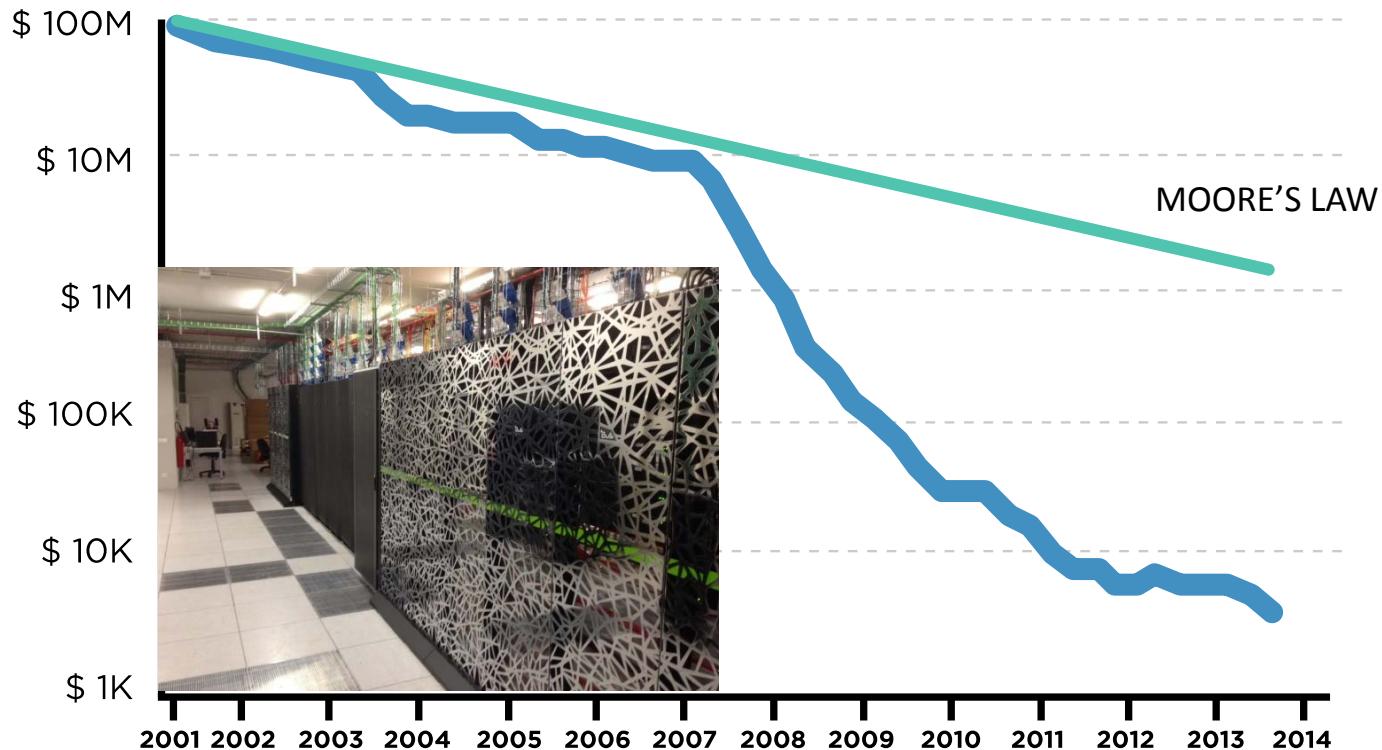


Tb Produced per Year





THE COST AND SPEED OF GENOME SEQUENCING IS NO LONGER THE PROBLEM



New York Bestseller

BIG DATA

"No other book offers such an accessible
and balanced tour of the many benefits
and downsides of our continuing
infatuation with data."

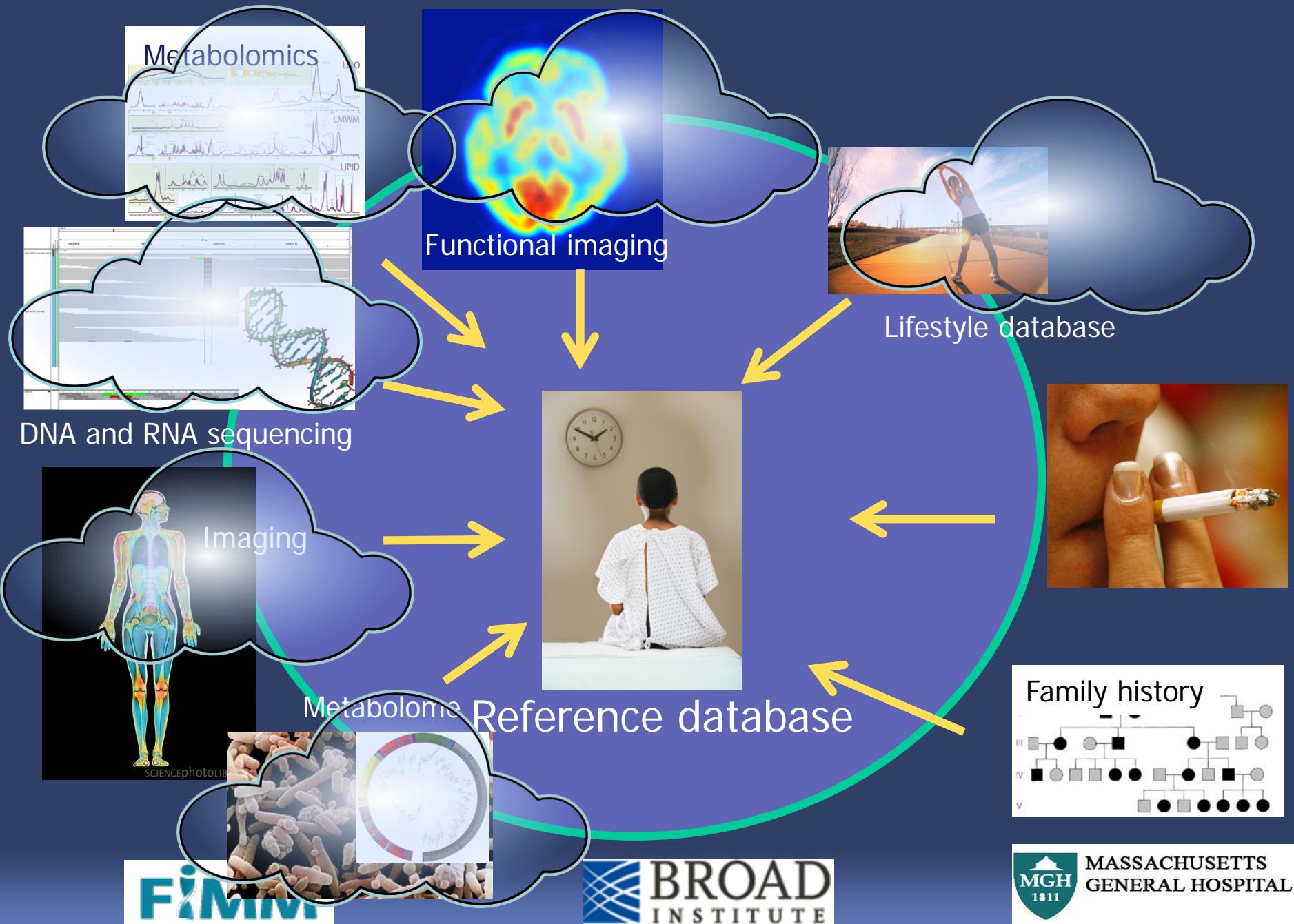
— WALL STREET JOURNAL

Viktor Mayer-Schönberger
and
Kenneth Cukier

FIMM



MASSACHUSETTS
GENERAL HOSPITAL





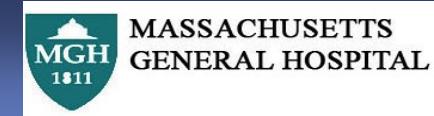
Tietojen käsittelyn muutos,
onko lääketiede samassa
muroksessa?

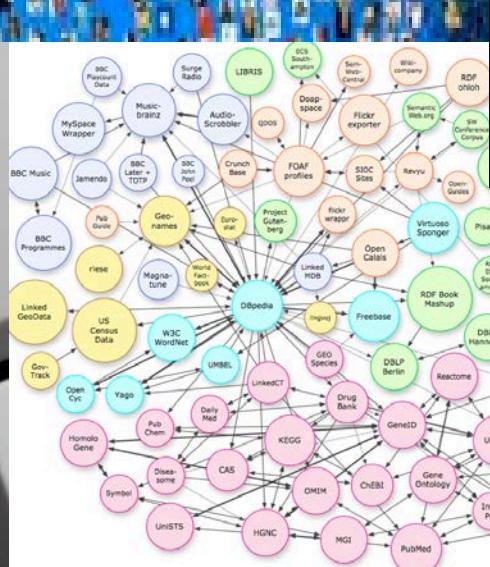
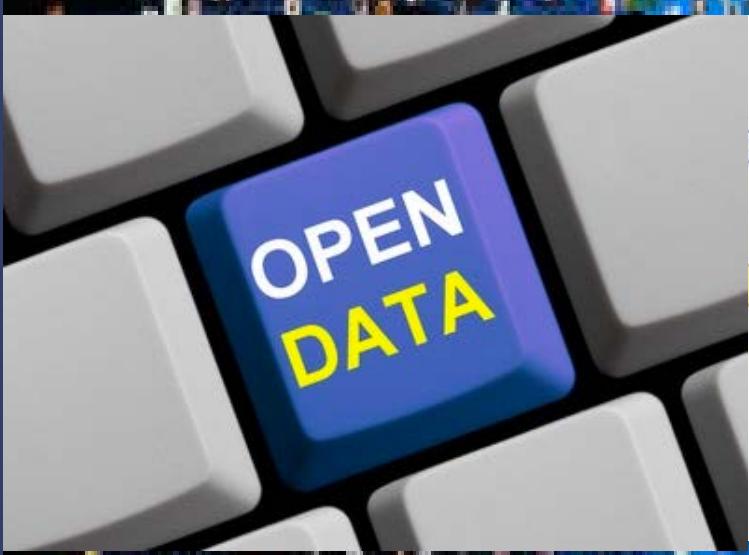
OAD
TUTE



MASSACHUSETTS
GENERAL HOSPITAL

Genome data and other trends

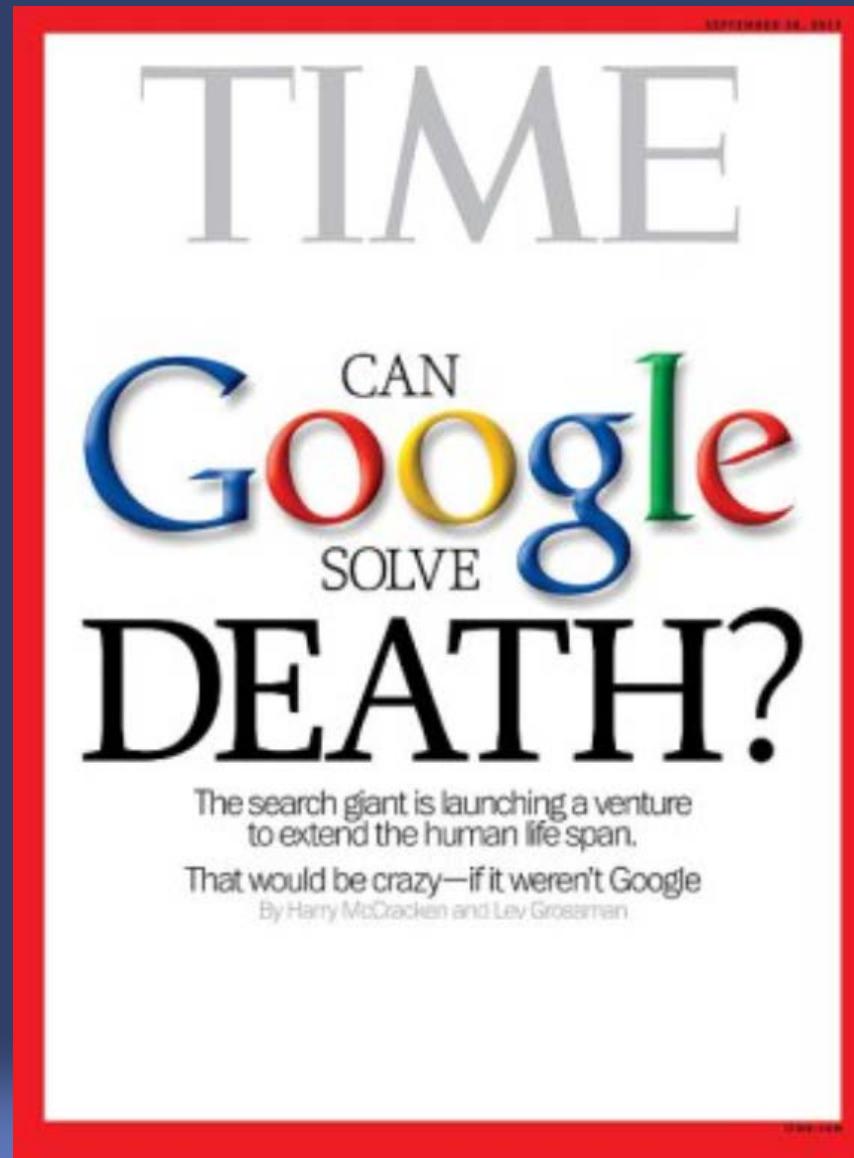




Global IT companies interested in health applications

Google

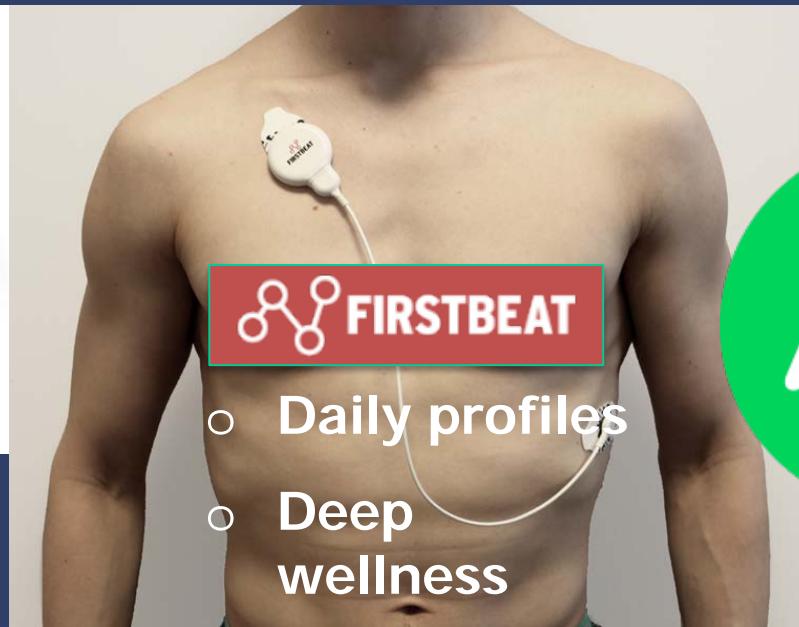
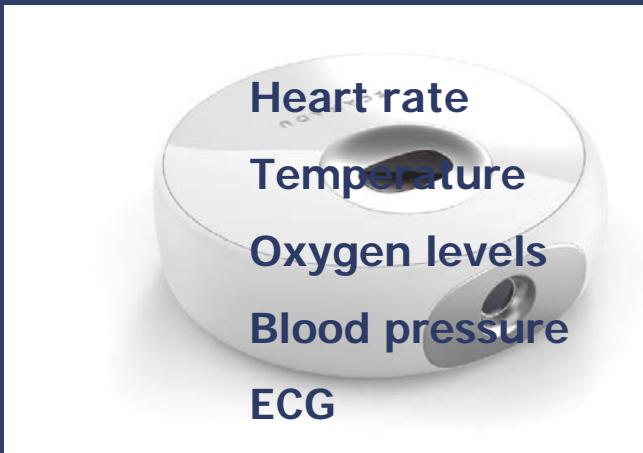
will spend up to \$1.5 billion to develop treatments for age-related diseases.



Sensors, >10,000 health apps

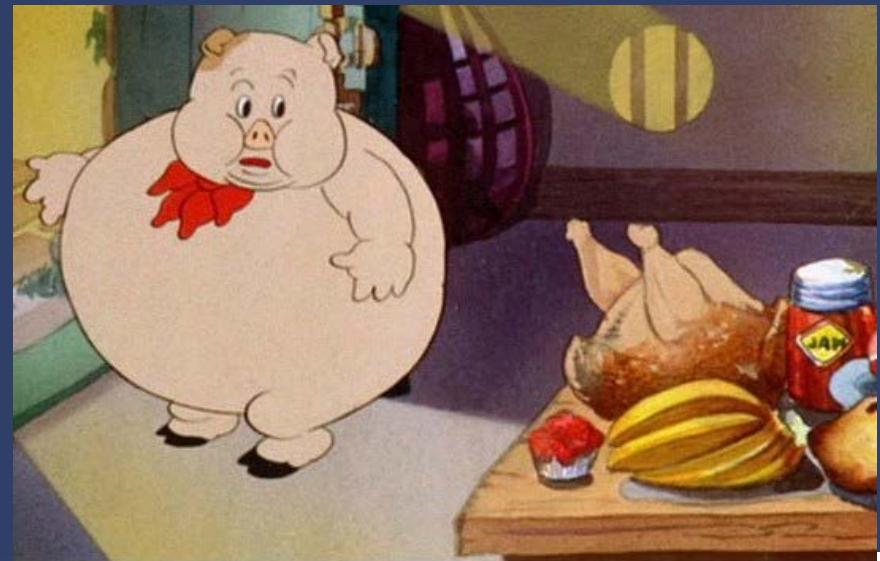
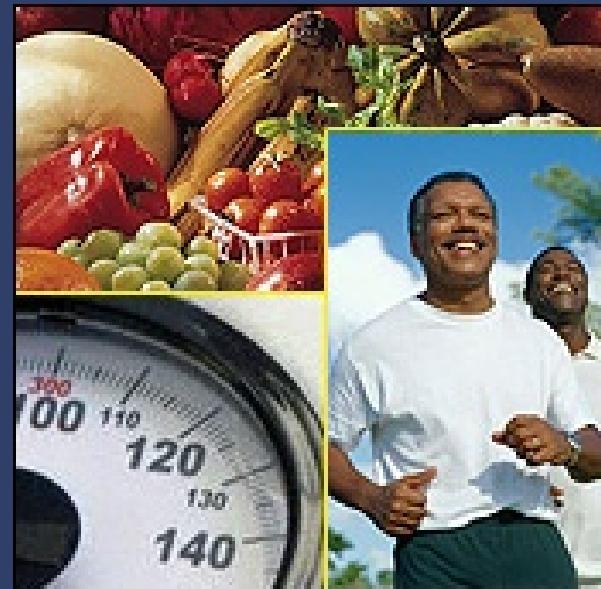


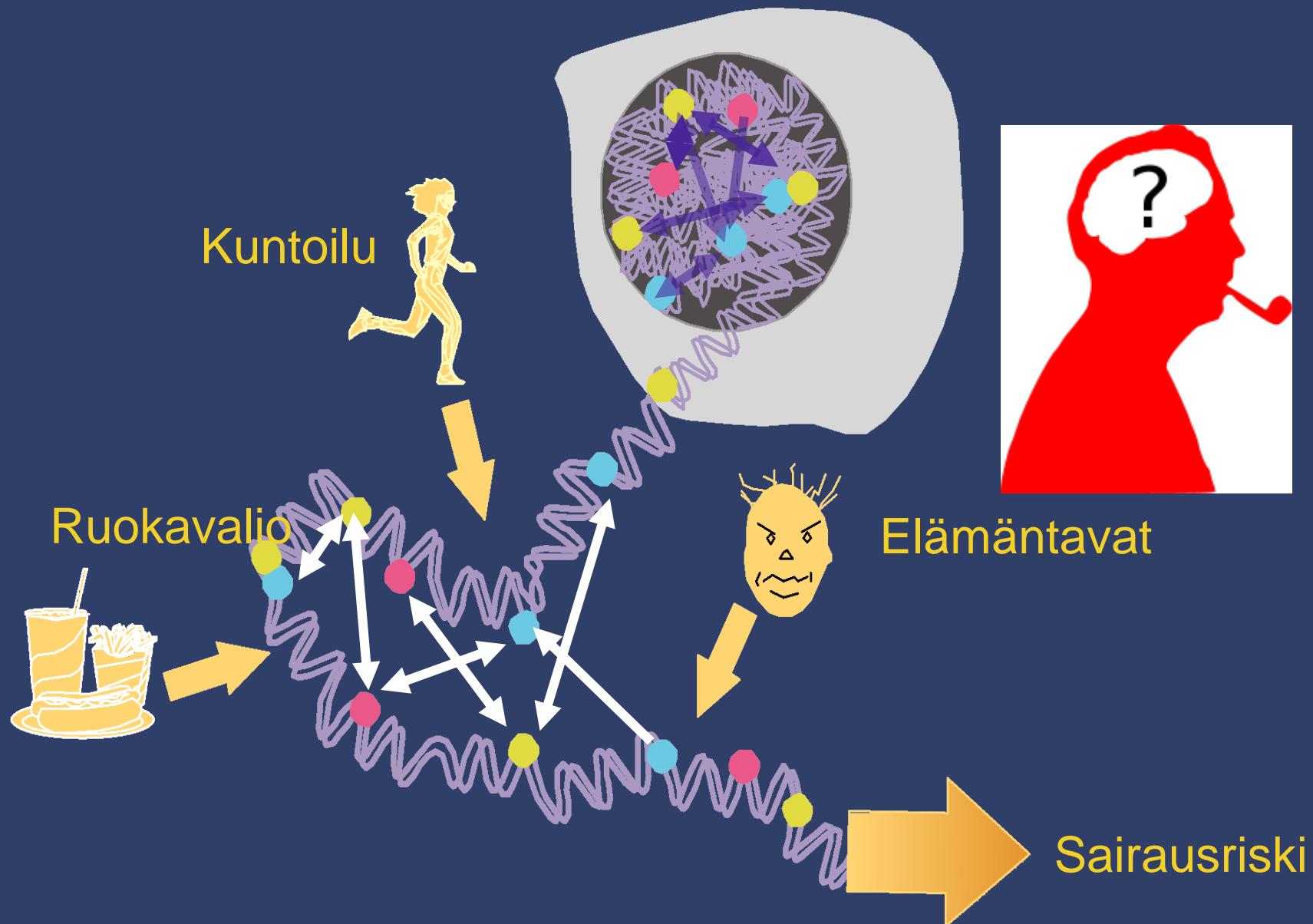
Quantified Self



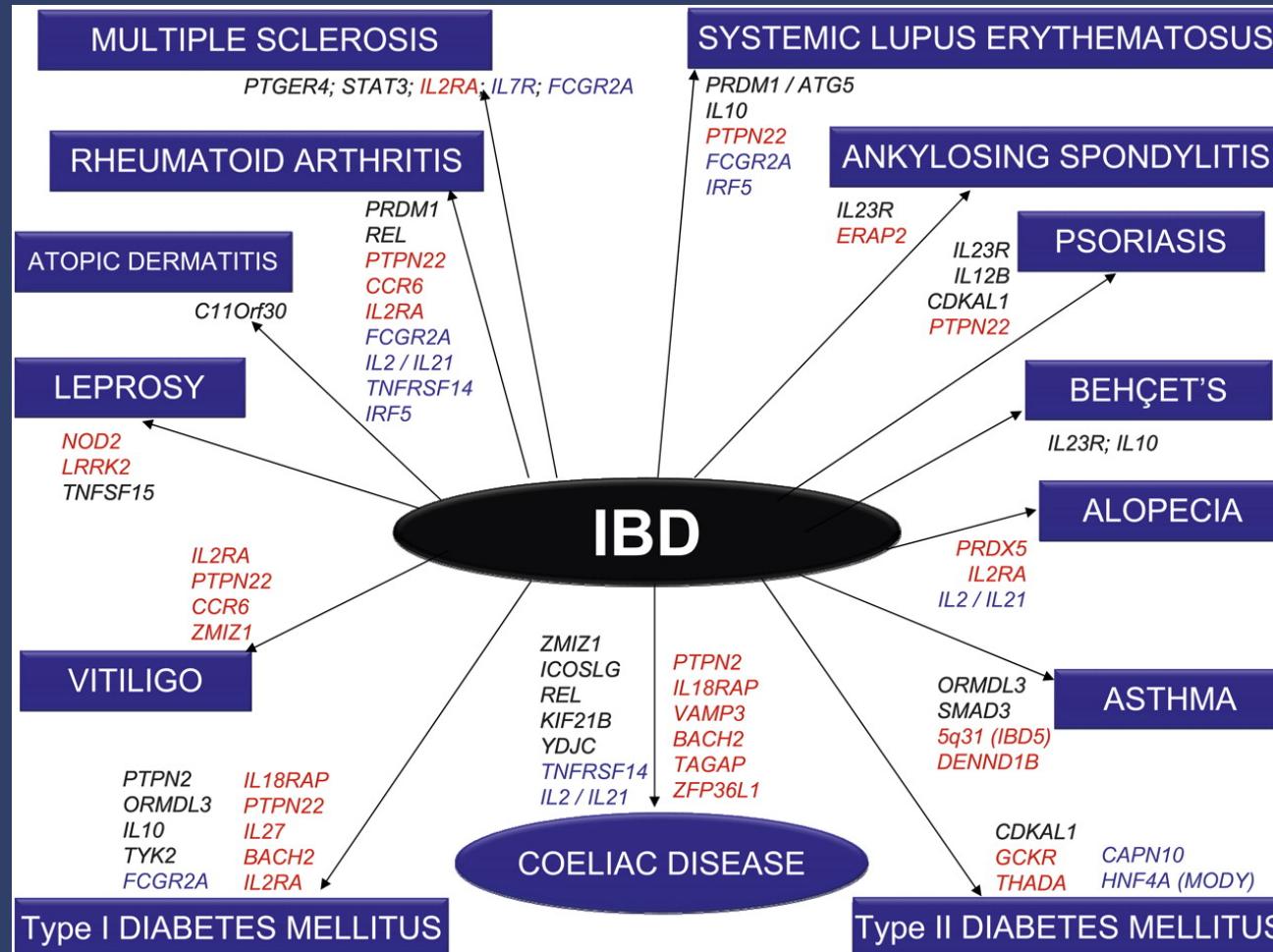


Geenit ja ympäristö





Shared genes behind immune mediated diseases



Change in
disease
classification

Individual
organ group
approach

Systems
approach

Technology driving and supporting

Effect on ICD classification?

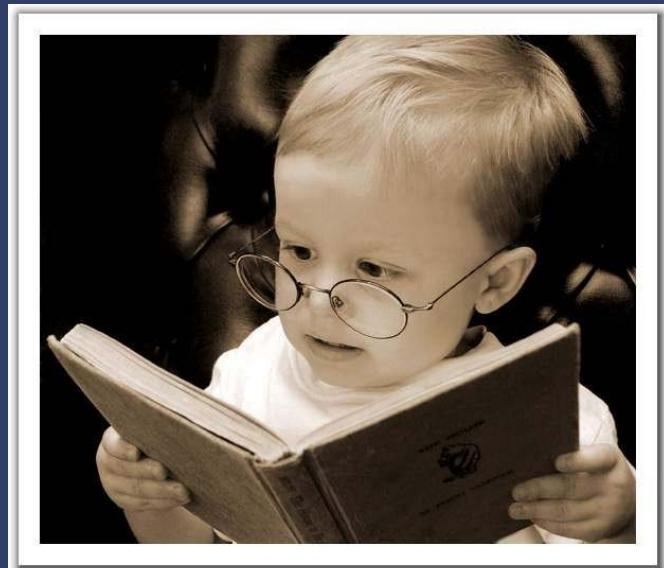
The opportunity

- An explosion of genomic information from individuals with known clinical characteristics and disease outcomes
 - Learning from these data, we should accelerate progress in:
 - Understanding the basis of inherited disease
 - Cancer outcomes and targeted therapy
 - Identifying targets for drug development
 - Infectious disease
- Clinical interpretation of individual genome sequences

David Altshuler, Global Alliance

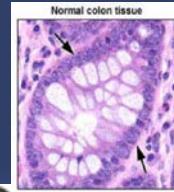
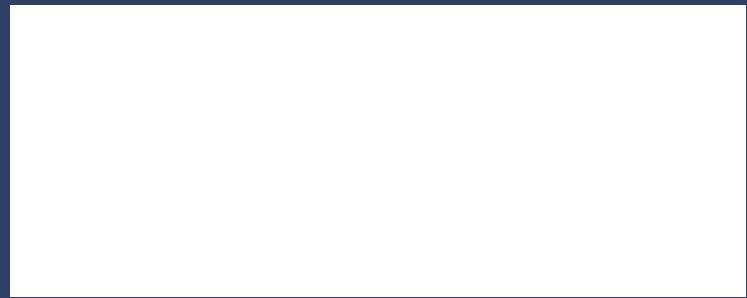


The challenge: we can write down genomes,
but we don't yet know how to read them



To learn, we must compare

VS

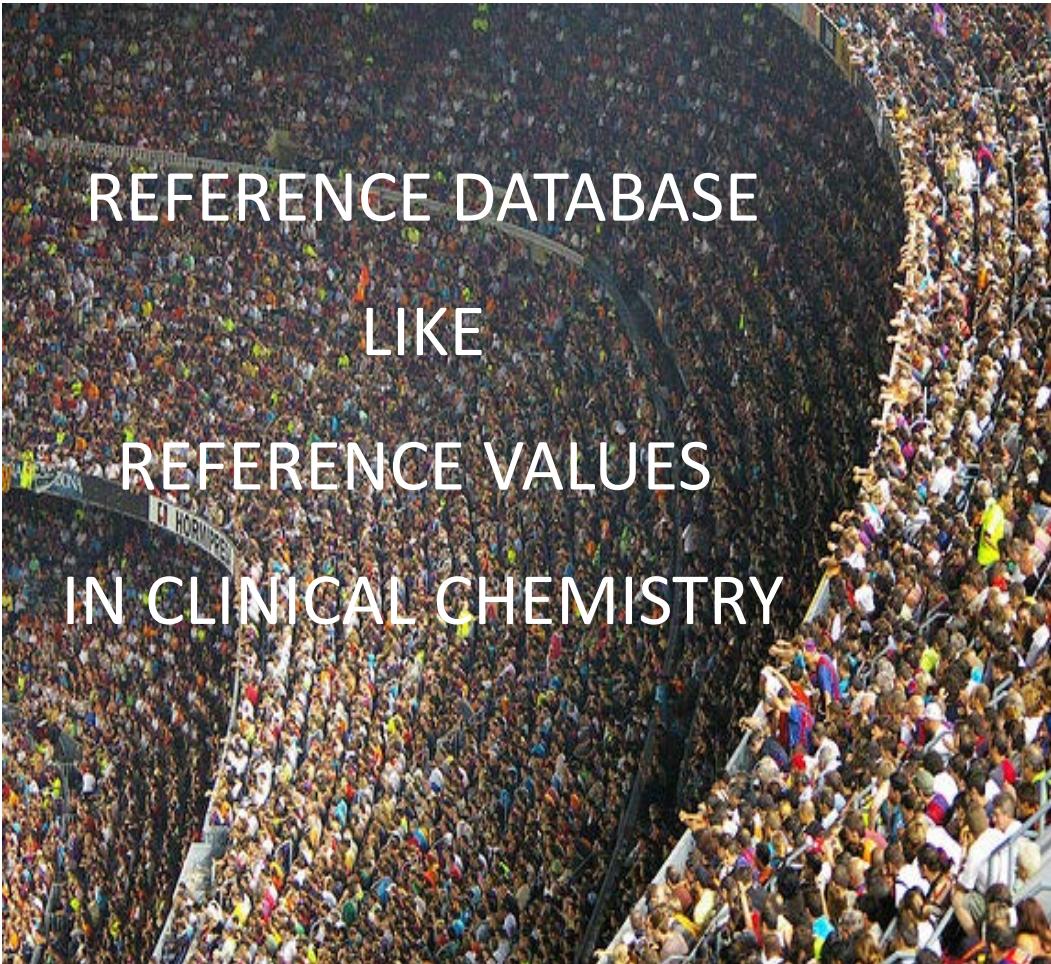
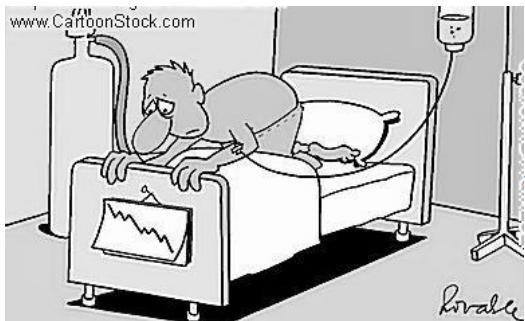


Normal





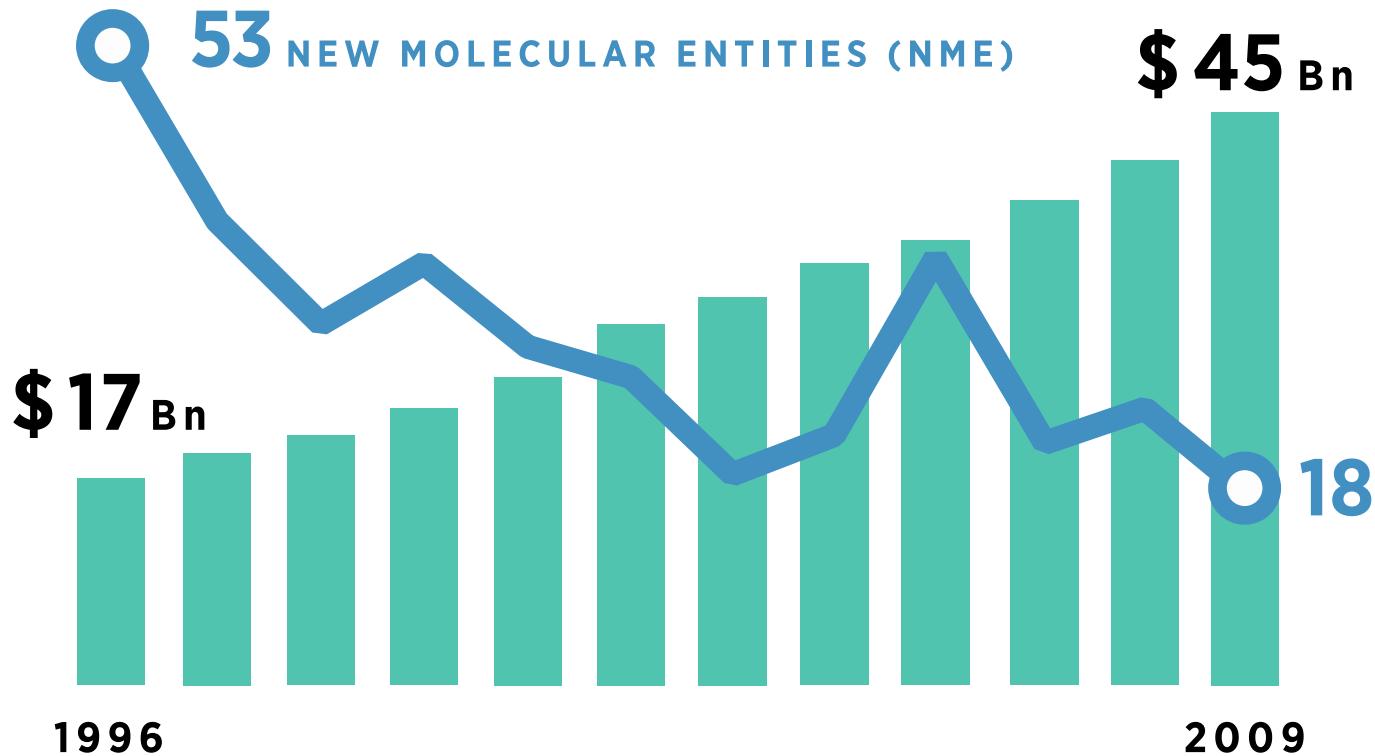
A A T G G T



EACH GENE VARIANT HAS A SMALL EFFECT



PHARMA R&D SPEND



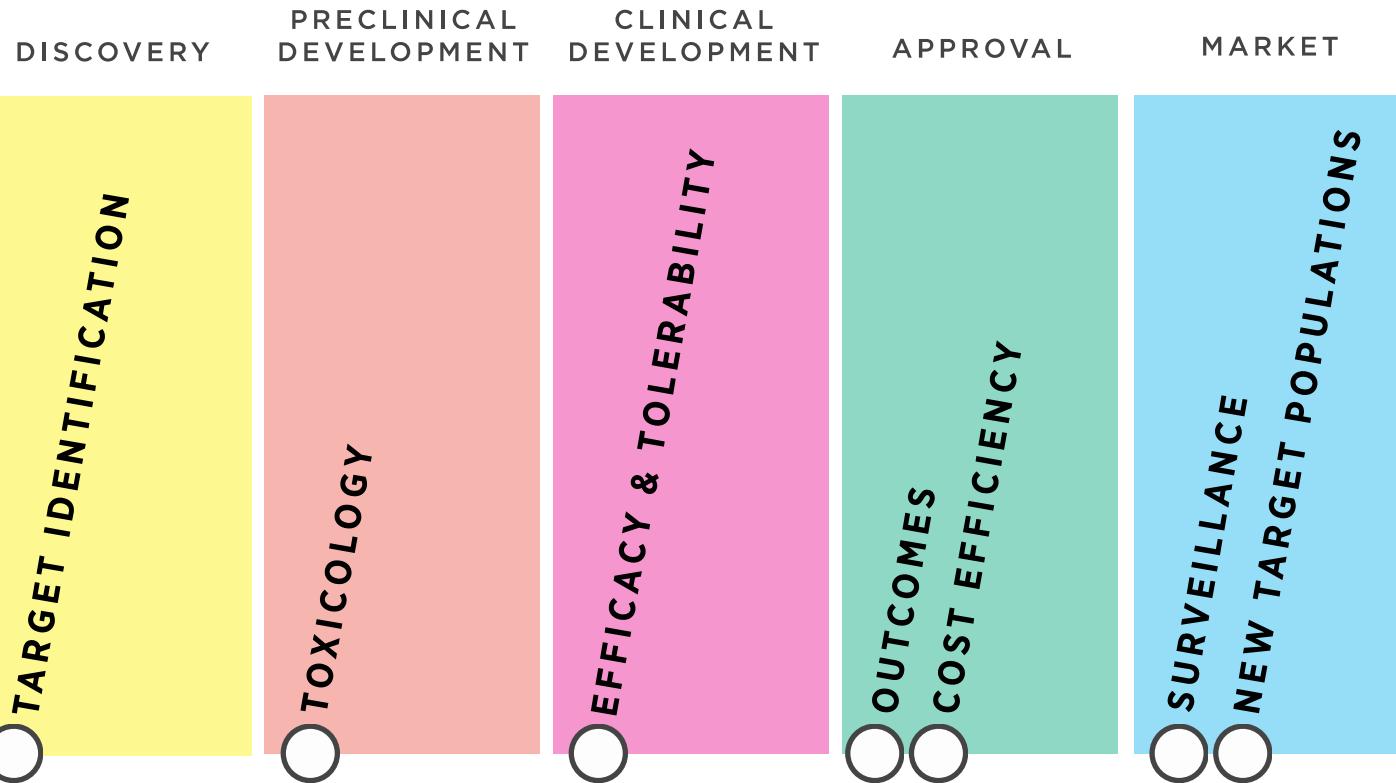


Finland

YOUR TESTBED FOR NEXT GENERATION REASEARCH & INNOVATION

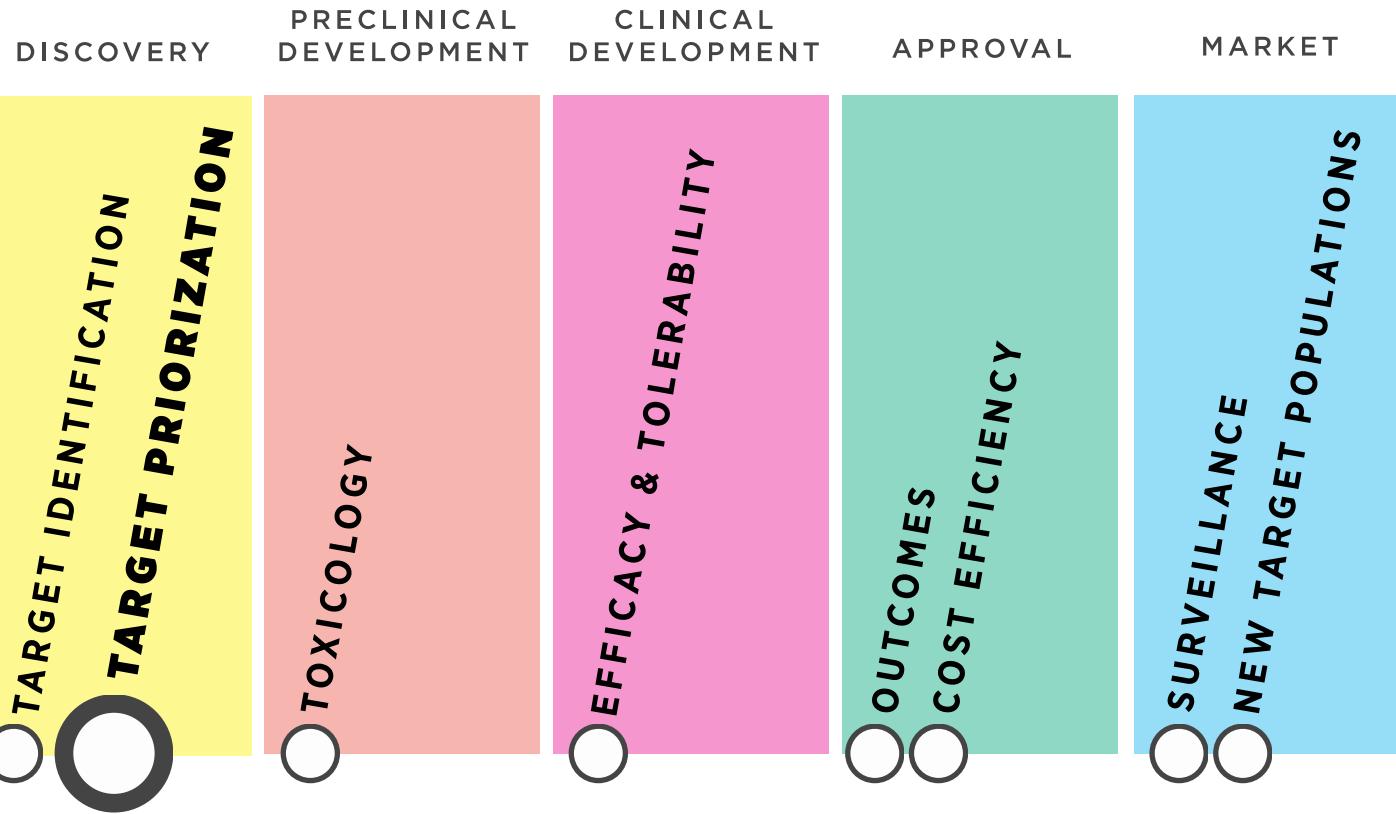


HIGH COSTS THROUGHOUT THE DRUG DEVELOPMENT PROCESS



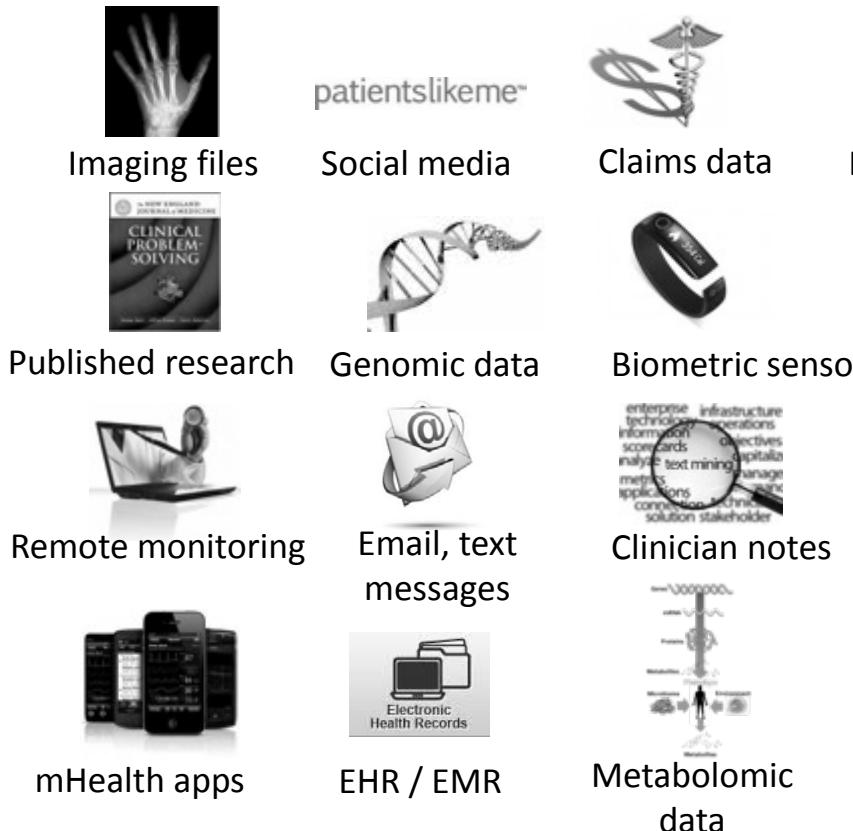


COULD GENOMICS HELP TO CONTROL THE RISING COSTS





LEVERAGING BIG DATA TO CONTROL HEALTHCARE COST INCREASE



COLLECTING,
COMBINING
AND ANALYZING



INFORMATION PAGES ON

FINNISH SAMPLE COLLECTIONS



ORGANIZATION

BIOBANK INFO

CONTACT

STUDY

LINKS

Organization

- »» [Organization](#)
- »» [Study](#)
- »» [GWAS](#)
- »» [Summary](#)

Published on Tuesday, 12 June 2012 20:28 | Written by Super User | | | Hits: 6833

Epidemiological and Clinical Finnish Sample Collections

In these pages we have collected information on epidemiological and clinical Finnish study collections with available DNA samples, though the list is not comprehensive. The pages include short description of the projects, contact information, as well as information on genome-wide SNP genotyping studies involving these study collections. The pages are meant to serve as a resource for investigators and promote collaboration between research groups and institutes.

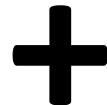
If you wish to add information on your own study collections, please contact us: Kaisa Silander or Markus Perola (firstname.lastnamename (at) thl.fi).

[Link to Studies Summary Table](#)



TOWARDS NEW INNOVATIONS

ACADEMIC RESEARCH



INDUSTRY



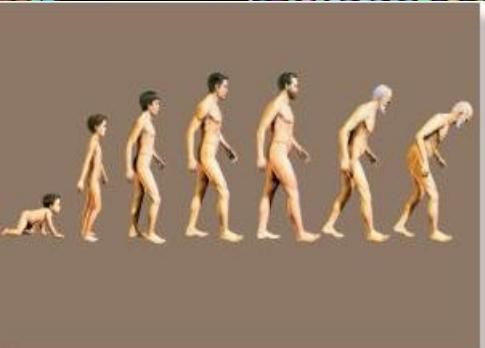
FIMM



UNIVERSITY OF HELSINKI

BROAD
INSTITUTE

From biobanks to personalized medicine

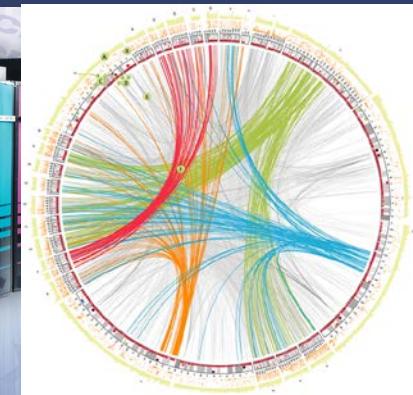


Biobanks

Gene information

Extensive health records

Data storage and integration



Implementation in Health Care





- 1
- 2
- 3
- 4
- 5

ACCESS TO DIGITAL HEALTH DATA

NATIONAL REGISTERS

NAME OF REGISTER	DATA INCLUDED IN REGISTER	KEEPER	ESTABLISHED IN COMPUTER FORMAT
Hospital Discharge Register (HILMO)	Homes and institutions for the mentally disabled, including information on treatment	THL	1967
Finnish Registry for Kidney Diseases	Diseases, type of treatment, and laboratory tests	ETK	1964
Cancer Register	Cancer patient information from hospitals, pathology, laboratory measurements etc.	THL	1953
Finnish Register of Visual Impairment	Patient's visual ability	THL	1983
National Infectious Diseases Register	Detailed information on cases in infectious diseases	THL	1989
Register of Congenital Malformations	Infants and foetuses	THL	1963
Drug Reimbursement Registers	Disease that is being treated and medication used	KELA	1967
Medical Birth Register	Information on all births in Finland, from gestation week 22+0 or birthweight 500g	THL	1987
Cause-of-Death Register	Intermediate case of death and contributing causes of death	STAT	1969
Register on Occupational Disease	Diagnosis of occupational disease	FIOH	1964
Drug Surveillance Register		FIMEA	1982
National Sickness Insurance	Social benefit information	KELA	1967
Register on Pensions	Work pension information, age of individual, type of pension	ETK	1962
Finnish Employment Register	Work in private sector, work as entrepreneur and work without pay	ETK	
Central Population Register	Relations (stillbirths are not registered)	VRK	1973
Register on Social Assistance		THL	1985
Child Welfare Register	Individual-level information on children taken into custody	THL	1991

THL = National Institute of Health and Welfare

ETK = The Finnish Kidney and Liver Association

KELA = Social Insurance Institution

STAT = Statistics Finland

FIOH = Finnish Institute of Occupational Health

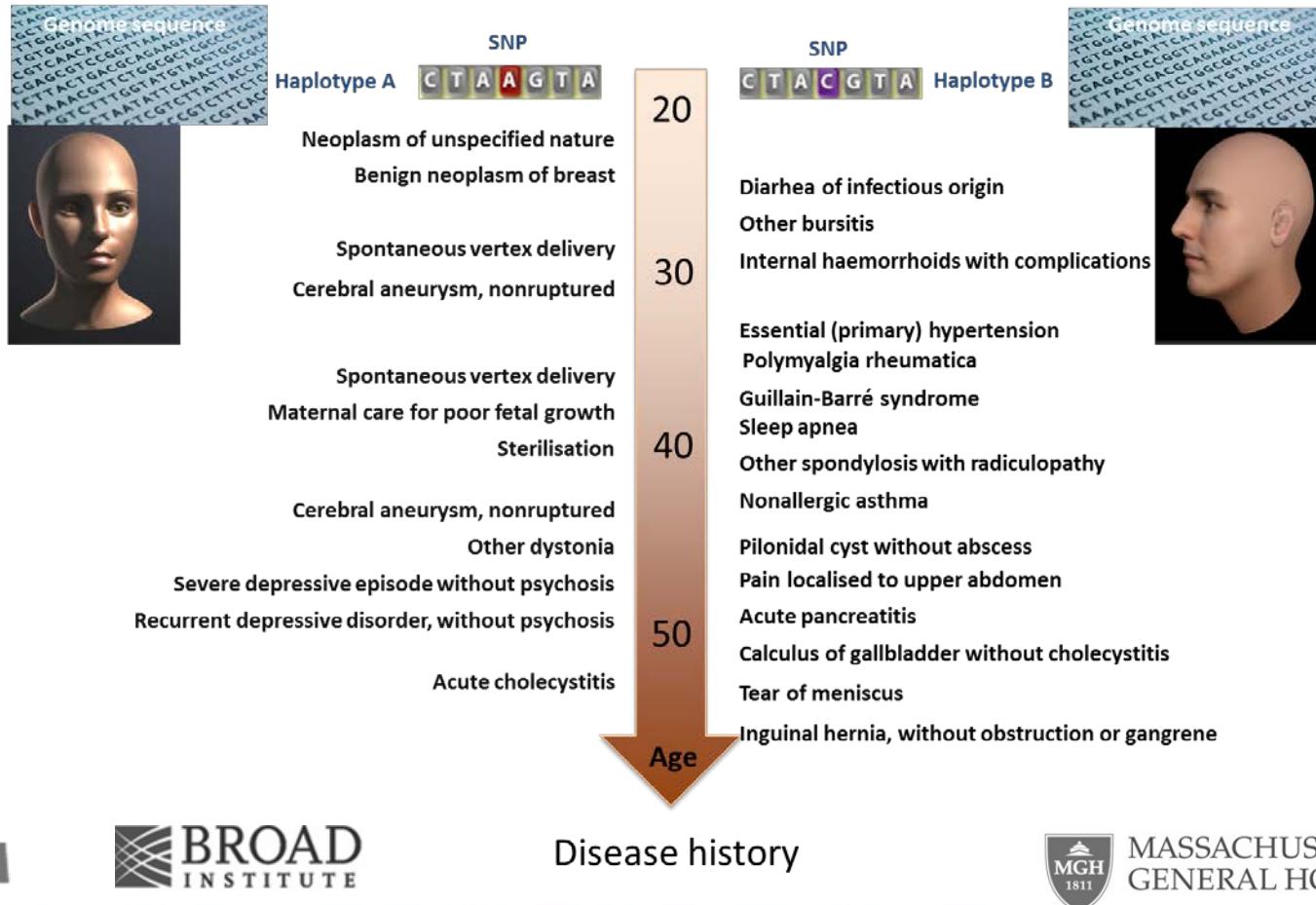
FIMEA = National Agency for Medicine

ETK = Finnish Centre for Pensions

VRK = Central Population Register



EXAMPLE OF HEALTH HISTORIES FROM TWO PERSONS FROM THE NATIONAL BIOBANKS WITH A 40 YEAR FOLLOW-UP



FIMM

**BROAD
INSTITUTE**

Finland



MASSACHUSETTS
GENERAL HOSPITAL

YOUR TESTBED FOR NEXT GENERATION RESEARCH & INNOVATION

National Biobanks Finland portal

130 000 individuals from population cohorts

70 000 individuals from disease collections

REGISTROMICS

Cardiovascular events

stroke, CHD

25 000 individuals



Life course events



Type 2 Diabetes

> 10 000 individuals

High Blood pressure



Cardiovascular risk factor data

100 000 individuals

Severe mental illness

- schizophrenia

- > 5000 individuals

Migraine

15 000 individuals

Old age dementia,

~ 5000 individuals

National Biobank

201 858 individuals

Cancer

> 10 000 cases

Prescription medication data

18 000 statin users

20 000 estrogen substitution th

Life style and socio-economic data

- education, economic state, smoking



100K Genome project



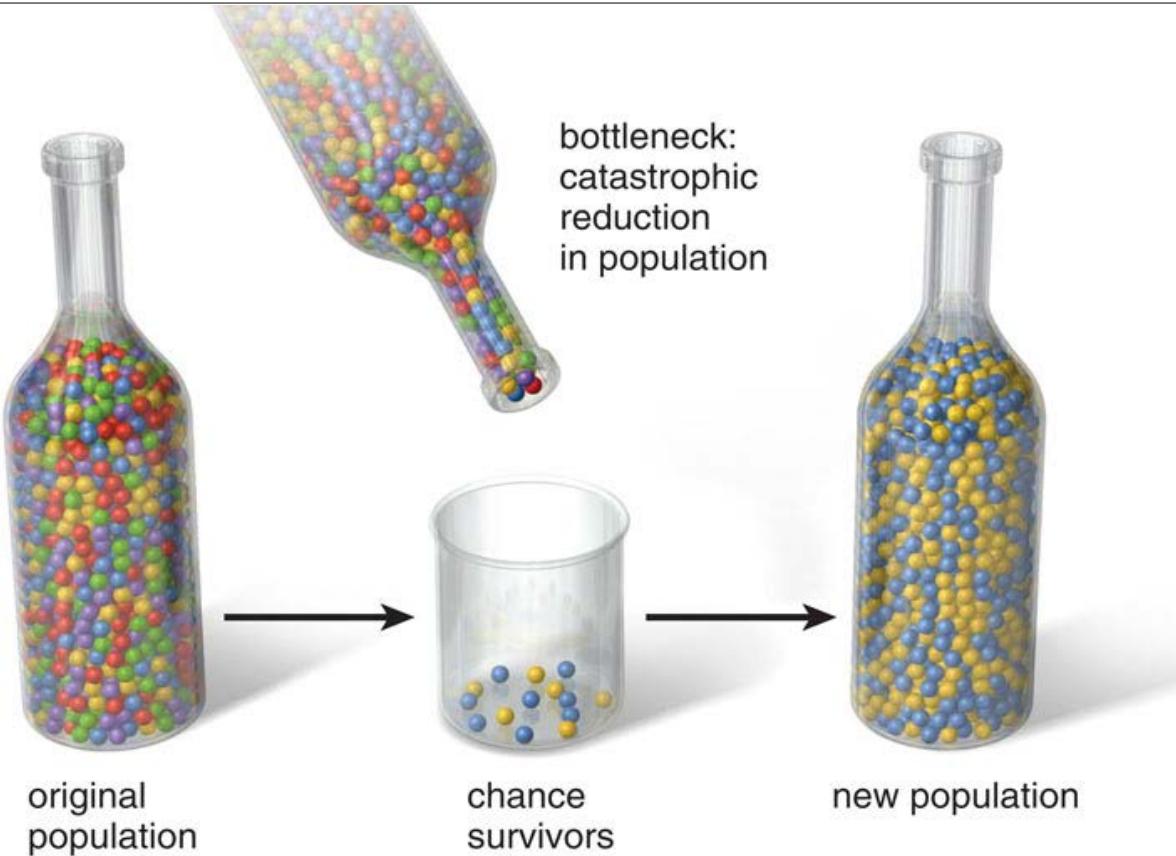
\$215 million Precision
Medicine Project



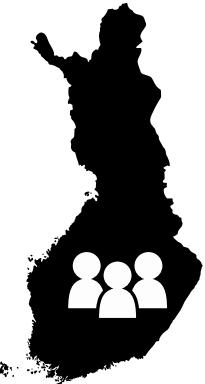
€360 million Personalized
Medicine Initiative



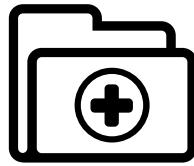
GENETIC ISOLATION



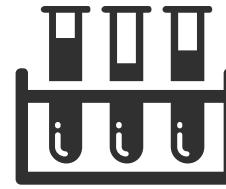
Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



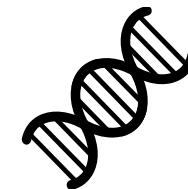
POPULATION
ISOLATE



HEALTH
REGISTERS



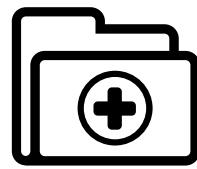
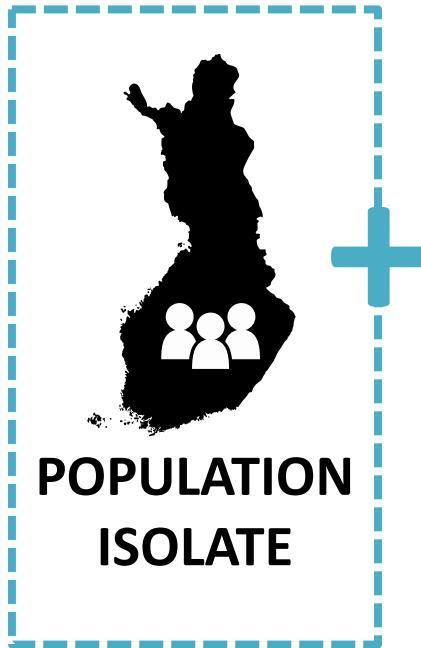
BIOBANKS



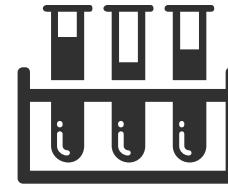
GENOME DATA



TARGET EVALUATION



HEALTH
REGISTERS



BIOBANKS



GENOME DATA



TARGET EVALUATION



EARLY SETTLEMENT

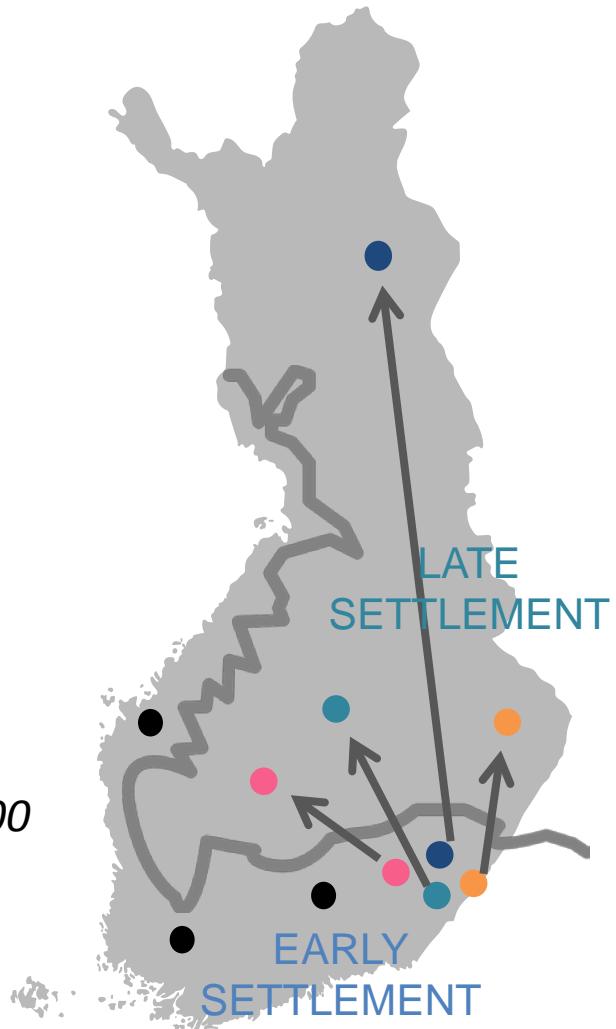
- 2000-10 000 years ago
- South and Coast

LATE SETTLEMENT

- 16th century
- multiple bottle necks

EXPANSION

- 18th century – *population 250 000*
- Today – ***population 5.4 million***

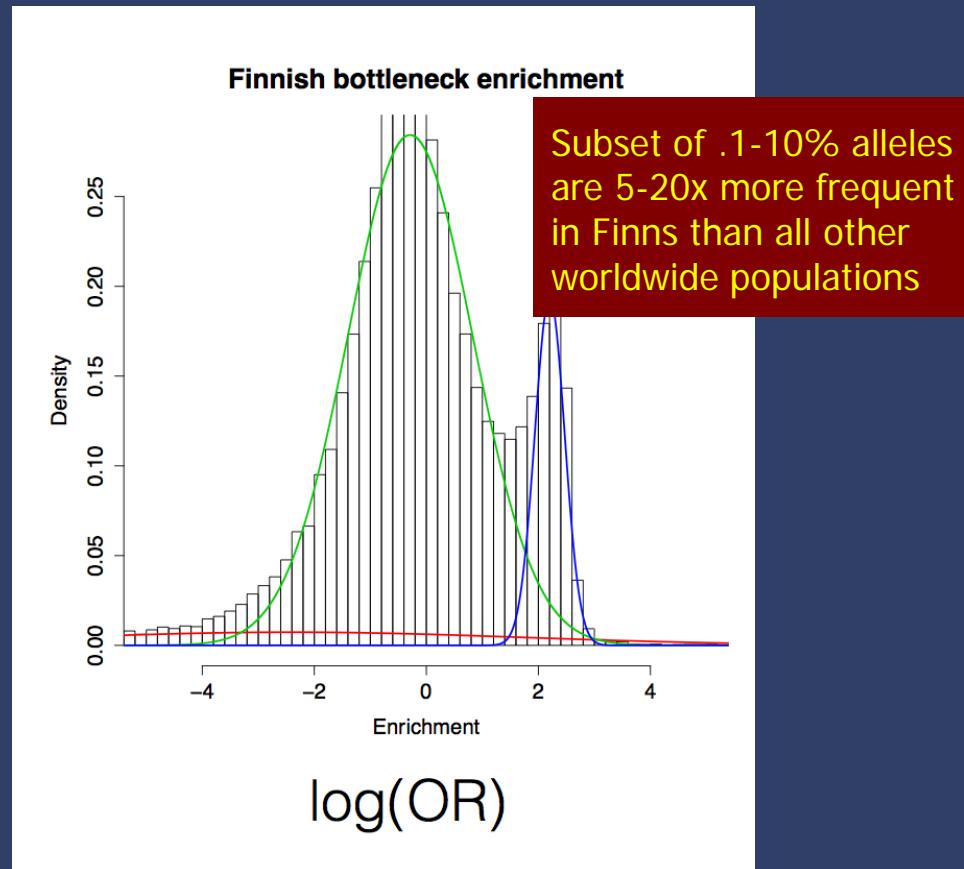


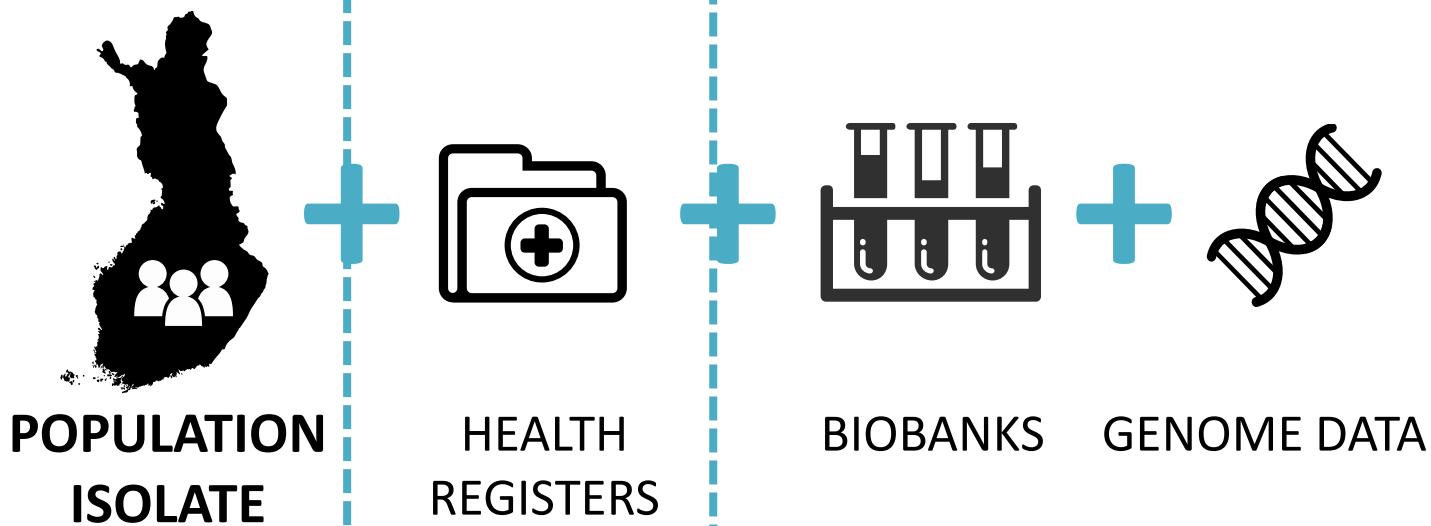


ICELAND

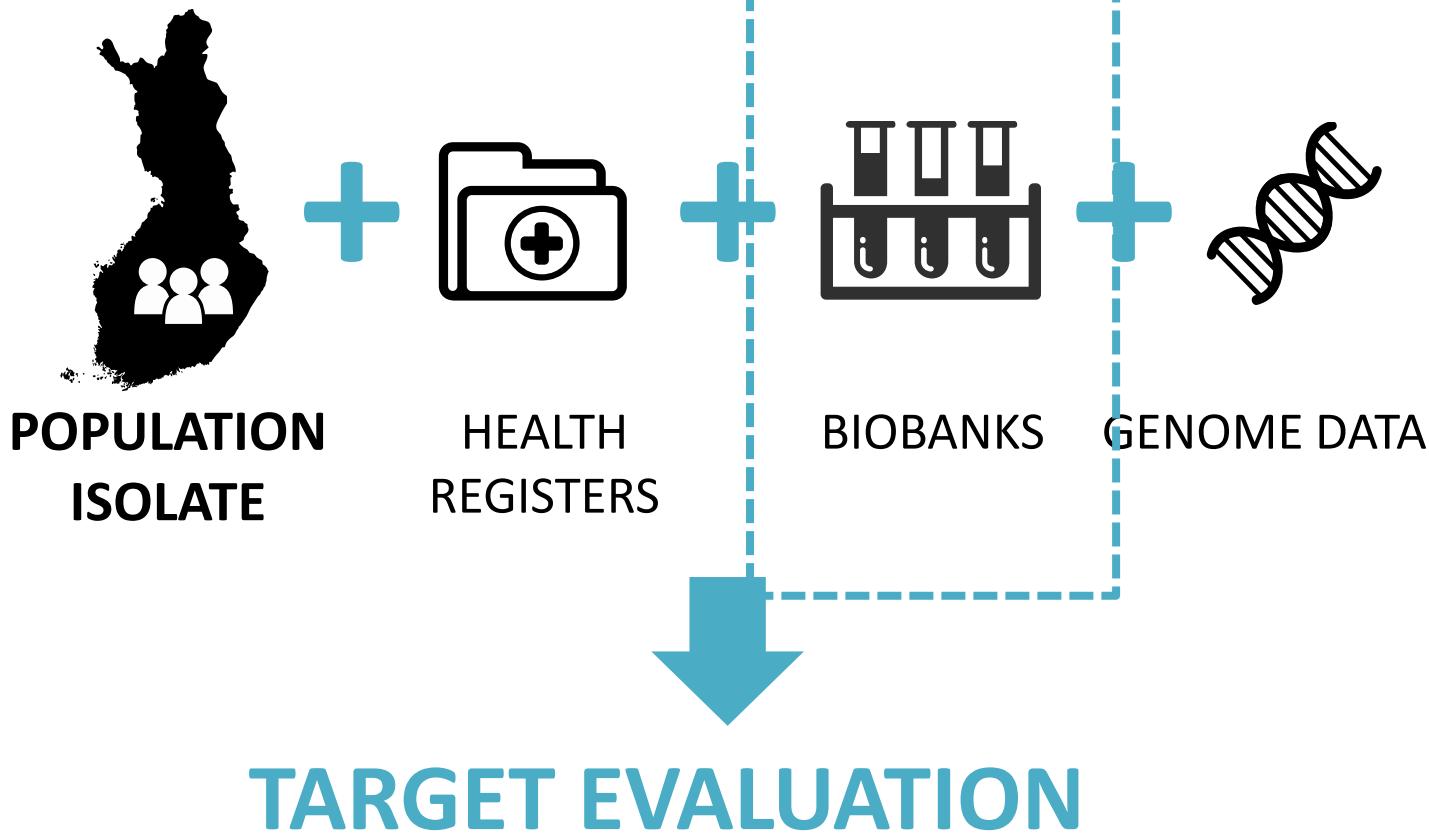
What are the unique opportunities in a bottlenecked population?

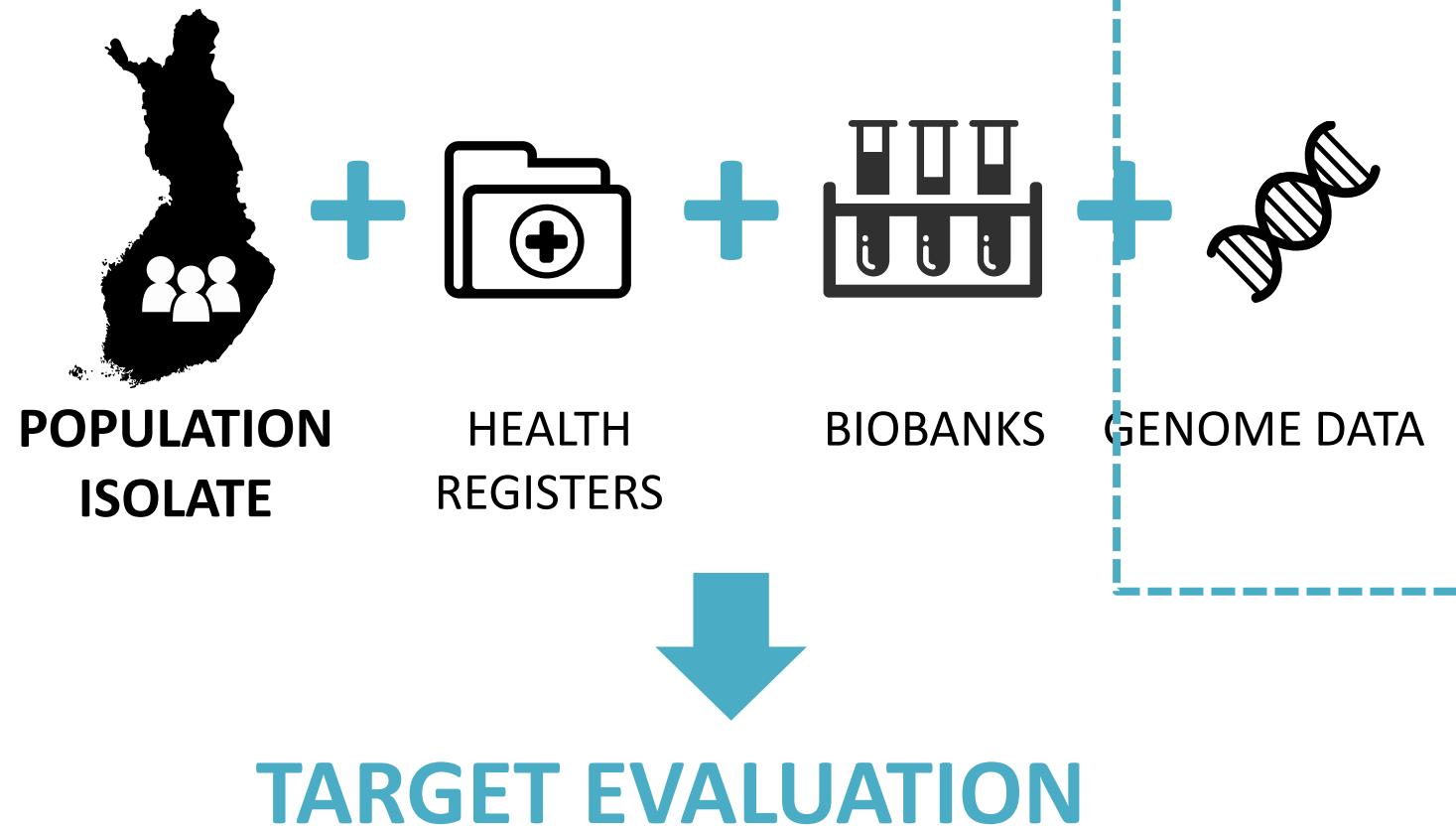
- Recessive lethal alleles can exist at or above 1%
- Alleles with OR of 2-5 can exist at low frequencies
- Both of these types of variation are incredibly unlikely to reach even .001 frequency in broader European sample





TARGET EVALUATION







SISU

Sequencing Initiative Suomi



YOUR TESTBED FOR NEXT GENERATION RESEARCH & INNOVATION





SISU-PROJECT

SEQUENCING INITIATIVE SUOMI (FINLAND)



THE 200K

Genome wide genotype data
73 000

Genome or exome sequences
>26 000

200 000 individuals
4% of the population

Population cohorts

Extensive health,
phenotype,
metabolomic data

Disease specific
collections

NATIONAL
BIOBANK

IMPUTATION

POPULATION SPECIFIC CHIP/GENOTYPING

REFERENCE DATABASE



Sequencing Initiative Suomi - Data resource for the research community

Data resource for the research community

The Sequencing Initiative Suomi (The SISU project) is an international collaboration between research groups aiming to build tools for genomic medicine.

-  **This SISU v3.0 (2015-08-28) release includes:**
- 
- 
- 

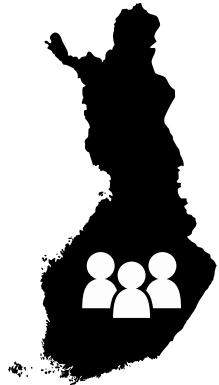
- 1 037 122 sites with 1 137 703 variants
- 6118 Finnish samples from 10 cohorts that were sequenced in Broad and Sanger Institutes
- Original sequencing was done using three different platforms (Agilent 1.1 refseq plus 3 boosters, Agilent sureselect 50mb, Illumina coding v1)
- Multiallelic sites and indels are now included
- Finnish enrichment and other information fields for custom filtering purposes now available

Search

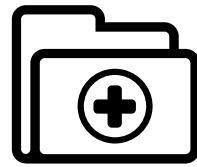
The SISU data resource currently covers exons only and data is restricted to autosomal SNPs and Indels. Genome build used in this release was GRCh37. Minor allele frequencies before QC and after QC provided.

[Information about quality control process](#)

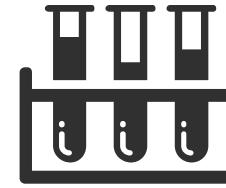
→ [Enter search](#)



**POPULATION
ISOLATE**



**HEALTH
REGISTERS**



BIOBANKS



GENOME DATA



TARGET EVALUATION



HUMAN GENE KNOCK OUTS

NEED FOR HUMAN MODELS





HUMAN GENE KNOCK OUTS

NEED FOR HUMAN MODELS



MERCK



YOUR TESTBED FOR NEXT GENERATION REASEARCH & INNOVATION



HUMAN GENE KNOCK OUTS

NEED FOR HUMAN MODELS

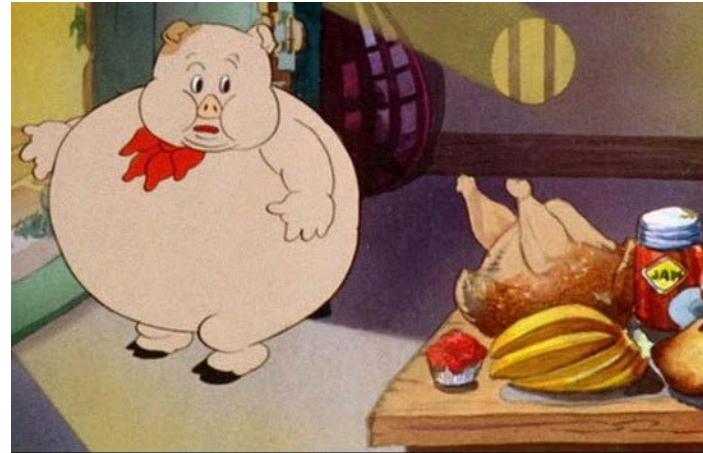
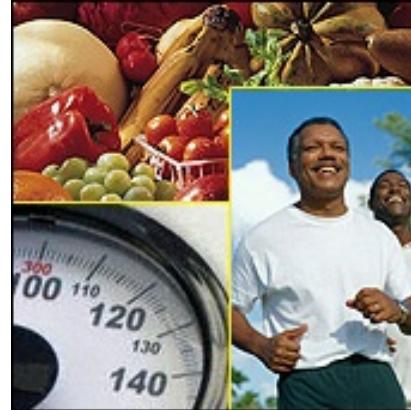


MERCK

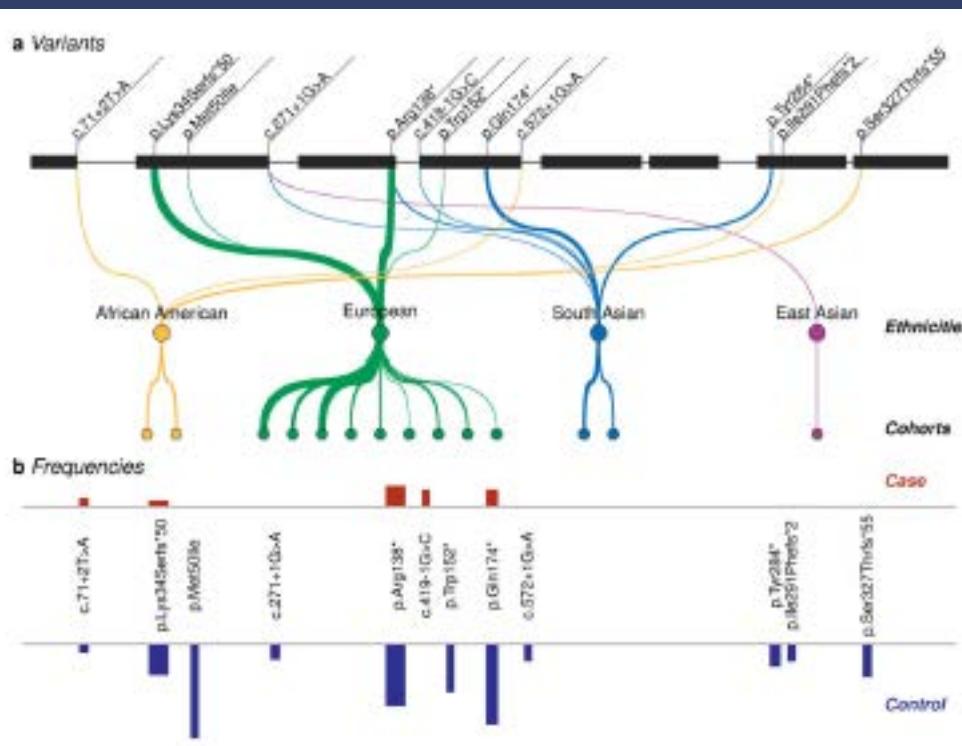




PROTECTIVE GENE VARIANTS



Loss-of-function mutations in *SLC30A8* protect against type 2 diabetes



Truncating mutations in *SLC30A8* seen 3x more often in healthy controls than diabetics

STRONG protection against diabetes !!!

Elaine Lim



Peter Wurtz



OPEN ACCESS Freely available online

PLOS GENETICS

Distribution and Medical Impact of Loss-of-Function Variants in the Finnish Founder Population

Elaine T. Lim^{1,2,3,4}, Peter Würtz^{5,6,7}, Aki S. Havulinna⁶, Priit Palta^{5,8}, Taru Tukiainen^{1,2,3}, Karola Rehnström⁸, Tönu Esko^{2,3,9,10}, Reedik Mägi⁹, Michael Inouye¹¹, Tuuli Lappalainen^{12,13}, Yingleong Chan^{2,4,10}, Rany M. Salem^{2,10}, Monkol Lek^{1,2,3}, Jason Flannick^{2,3}, Xueling Sim¹⁴, Alisa Manning², Claes Ladenvall^{5,15}, Suzannah Bumpstead⁸, Eija Hämäläinen^{5,8}, Kristiina Aalto¹⁶, Mikael Maksimow¹⁶, Marko Salmi¹⁷, Stefan Blankenberg^{18,19}, Diego Ardiissino²⁰, Svari Shah²¹, Benjamin Horne²², Ruth McPherson²³, Gerald K. Hovingh²⁴, Muredach P. Reilly²⁵, Hugh Watkins²⁶, Anuj Goel²⁶, Martin Farrall²⁶, Domenico Girelli²⁷, Alex P. Reiner²⁸, Nathan O. Stitzel²⁹, Sekar Kathiresan³⁰, Stacey Gabriel², Jeffrey C. Barrett⁸, Terho Lehtimäki³¹, Markku Laakso³², Leif Groop^{5,15}, Jaakko Kaprio^{5,33,34}, Markus Perola⁵, Mark I. McCarthy^{35,36,37}, Michael Boehnke¹⁴, David M. Altshuler^{2,3}, Cecilia M. Lindgren^{1,2,38}, Joel N. Hirschhorn^{2,10}, Andres Metspalu⁹, Nelson B. Freimer³⁹, Tanja Zeller^{18,19}, Sirpa Jalkanen¹⁷, Seppo Koskinen⁴⁰, Olli Raitakari^{41,42}, Richard Durbin⁸, Daniel G. MacArthur^{1,2,3}, Veikko Salomaa⁶, Samuli Ripatti^{5,6,8,33,43}, Mark J. Daly^{1,2,39*}, Aarno Palotie^{1,2,5,44*} for the Sequencing Initiative Suomi (SISu) Project

There are proportionally more LoF variants in Finns

Effects of Bottleneck

1. Extremely rare variation is depleted:

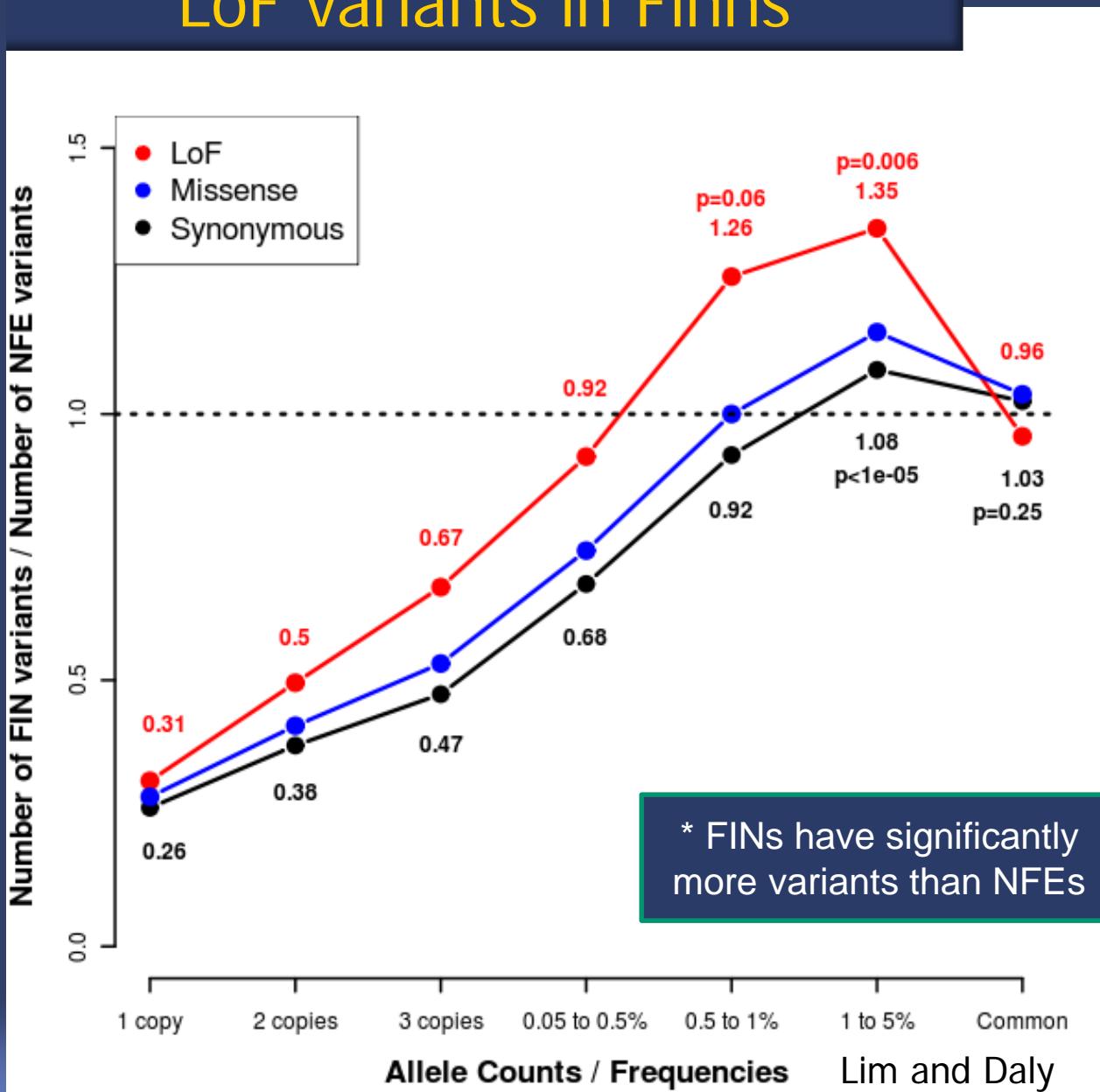
Most rare variants do not make it through

2. Increase in low frequency damaging variants:

Surviving rare variants get a big frequency boost to (0.5-5%) in FINs.

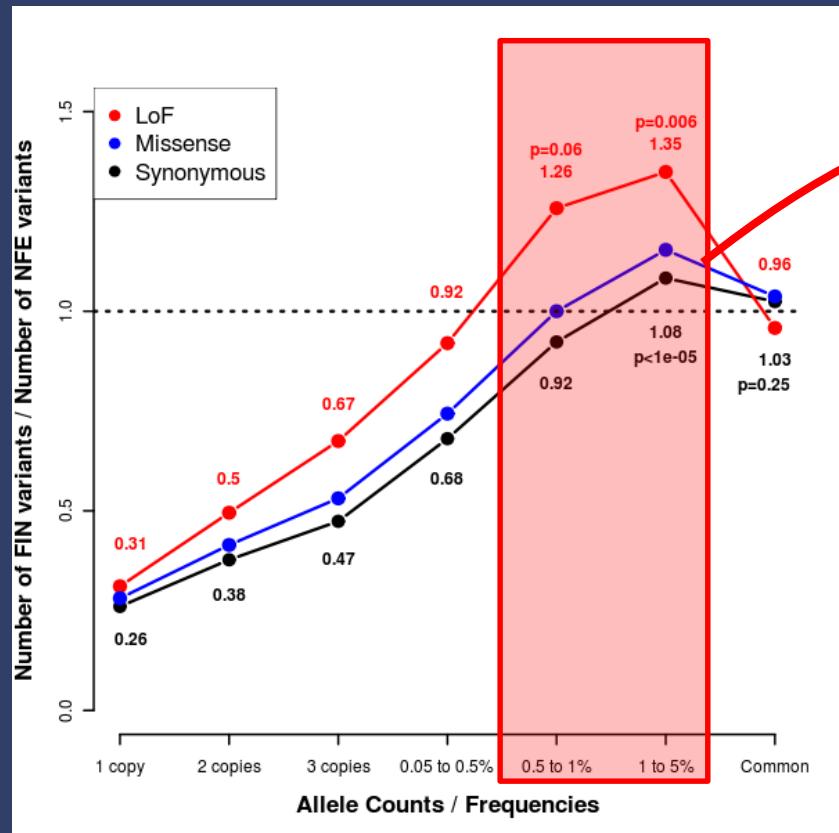
3. Boosted variants are more damaging:

And bottleneck is recent enough that selection has not eliminated them



MASSACHUSETTS
GENERAL HOSPITAL

Targeted LoF genotyping pilot in 35,000 Finns



LoF SNVs and indels



83 LoF variants

35,000 population cohort

w/ 73 medically relevant
quantitative traits

Lim et al, PLoS Genetics, 2014



MASSACHUSETTS
GENERAL HOSPITAL

Pilot study in 35,000 Finns

Traits studied include:

LDL

HDL

TG

BMI

SBP

DBP

CRP

HGF

FGF

VEGF

GALECTIN3

VitB12

G_CSF

IL4, IL6, IL10

D_DIMER

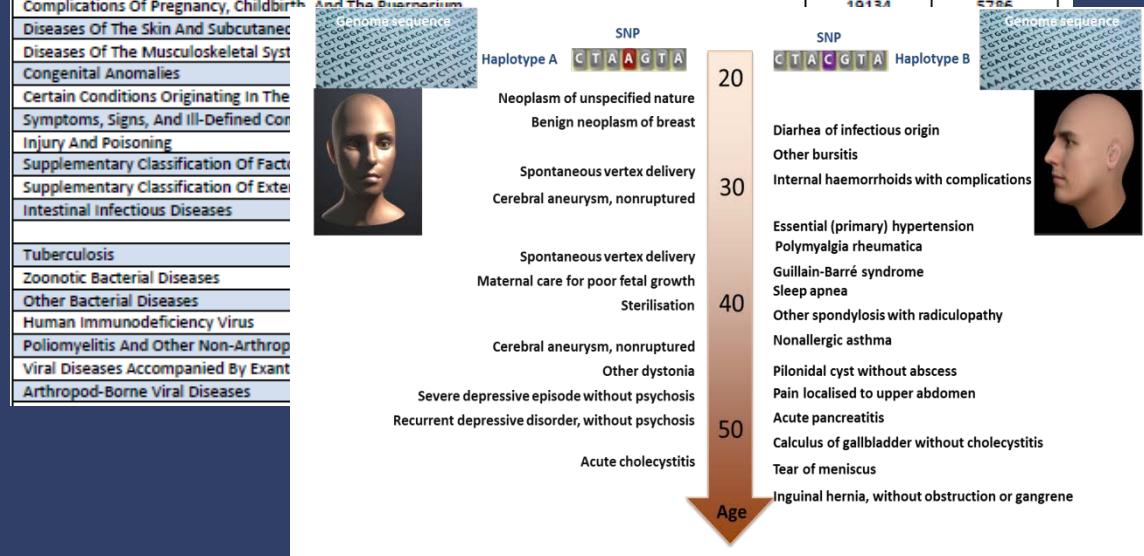
With reach through into complete medical records:

ICD-9 & ICD-10 diagnosis count (1986-2010); FINRISK 1992-2007; n= 29,286

ICD-10 converted to ICD-9

Peter Würtz, March 11, 2013

Diagnosis	Total hospitalizations	Person hospitalizations
ICD-9 chapters		
Infectious And Parasitic Diseases	5293	3039
Neoplasms	17207	5295
Endocrine, Nutritional And Metabolic Diseases, And Immunity Disorders	7318	2805
Diseases Of The Blood And Blood-Forming Organs	1055	590
Mental Disorders	10653	2520
Diseases Of The Nervous System And Sense Organs	14279	5973
Diseases Of The Circulatory System	38019	8410
Diseases Of The Respiratory System	13547	5633
Diseases Of The Digestive System	13782	7270
Diseases Of The Genitourinary System	13363	6789
Complications Of Pregnancy, Childbirth And The Puerperium	10124	5786
Diseases Of The Skin And Subcutaneous Tissue		
Diseases Of The Musculoskeletal System And Connective Tissue		
Congenital Anomalies		
Certain Conditions Originating In The Perinatal Period		
Symptoms, Signs, And Ill-Defined Conditions		
Injury And Poisoning		
Supplementary Classification Of External Causes		
Supplementary Classification Of External Factors		
Intestinal Infectious Diseases		
Tuberculosis		
Zoonotic Bacterial Diseases		
Other Bacterial Diseases		
Human Immunodeficiency Virus		
Poliomyelitis And Other Non-Arthropod-Borne Viral Diseases		
Viral Diseases Accompanied By Exanthema		
Arthropod-Borne Viral Diseases		



Two LPA LoF variants

LoF variant	Frequency in Finns	Frequency in non Finns
LPA1(4974)	2.8%	0.47%
LPA2(4289)	4.8%	3.6%



227 Finns LoF homozygotes

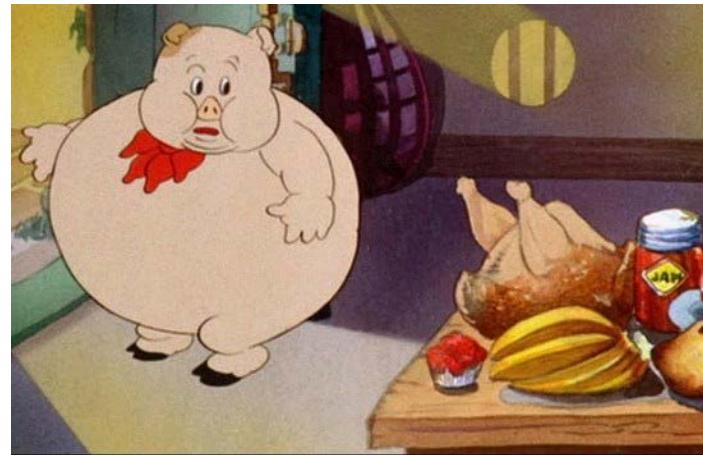
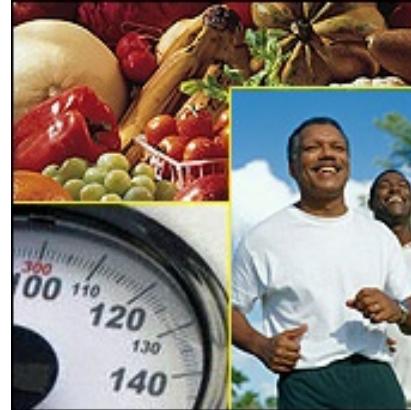
Two LPA LoF variants

LoF variant	Frequency in Finns	Frequency in non Finns
LPA1(4974)	2.8%	0.47%
LPA2(4289)	4.8%	3.6%





PROTECTIVE GENE VARIANTS

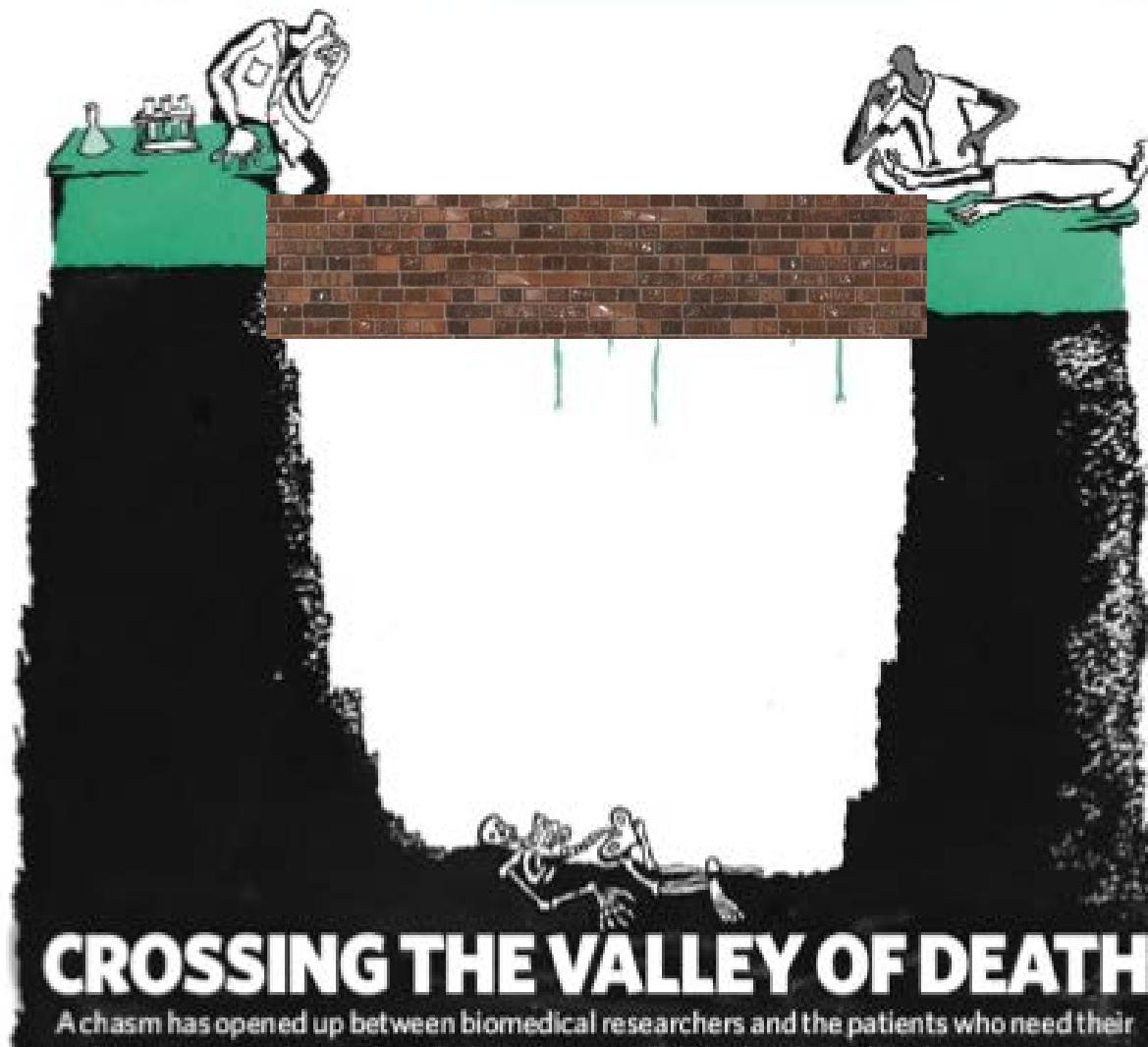


Scientist

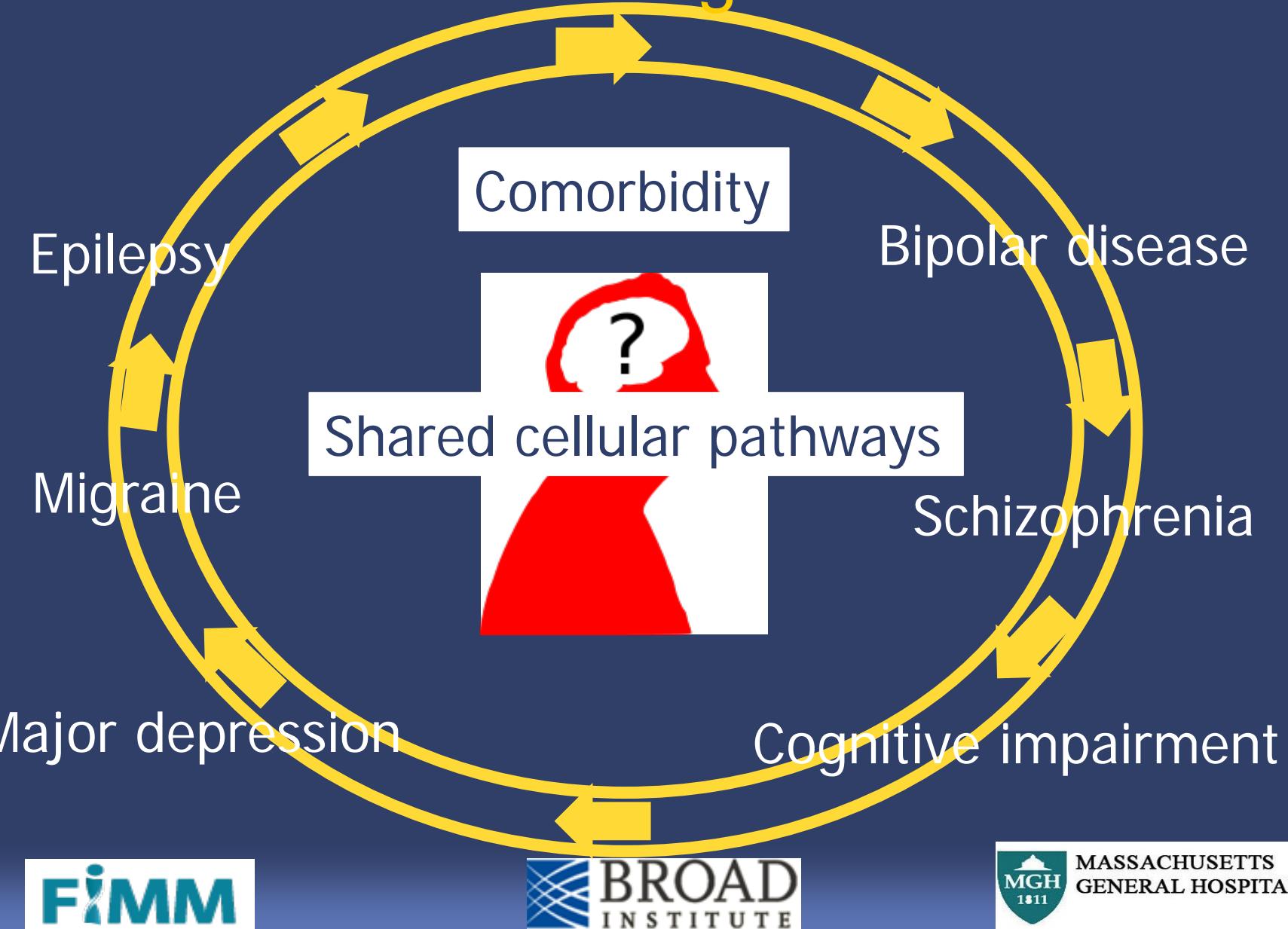
Discovery

Physician/
patient

Diagnostics/
therapeutics



Traditional classifications need re-thinking





FIMM

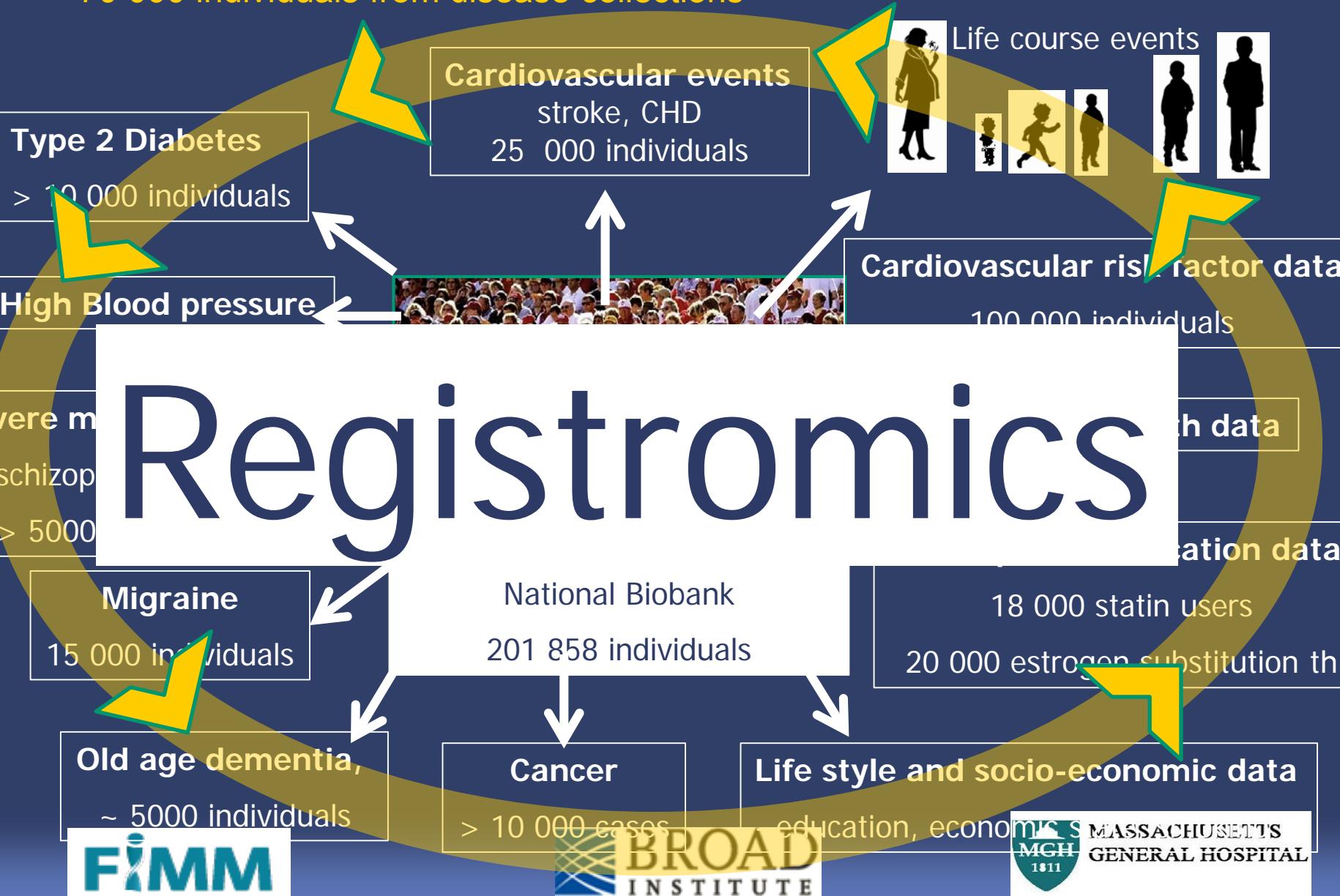
 **BROAD**
INSTITUTE

 MASSACHUSETTS
GENERAL HOSPITAL

National Biobanks Finland portal

130 000 individuals from population cohorts

70 000 individuals from disease collections



Nordic population opportunities more generally

National biobank and registry
solutions in Finland and Denmark



The National Patient Register

The Psychiatric Central Register

The Register of Causes of Death

The Medical Birth Register

Social factors including income, wealth, education, household crowding, marital status, type of job

The Danish Civil Registration System

Unique person identifier used across all records from birth to death or emigration

All data available for cases, controls/general population and relatives/spouses

Redeemed prescriptions

First degree relatives, Current and past spouses, residences in Denmark, immigration and emigration

Life events and stressors as unemployment, criminal records, custodial care etc. etc.

Total dynamic population of Denmark
App 8 million. Can all be followed up in registers

Danish population born since 1955
Can be linked to first degree relatives,
Allowing construction of individual and familial medical
and social history over decades, etc.

Danish Neonatal Screening Biobank

All individuals born in Denmark since 1981. 2 million persons.
Can be linked to first degree relatives, and in many cases also
grandparents, uncles and aunts and cousins.

The neonatal blood spots allow GWAS, sequencing, epigenetics,
gene expression, metabolomics, IgG measurement, etc.

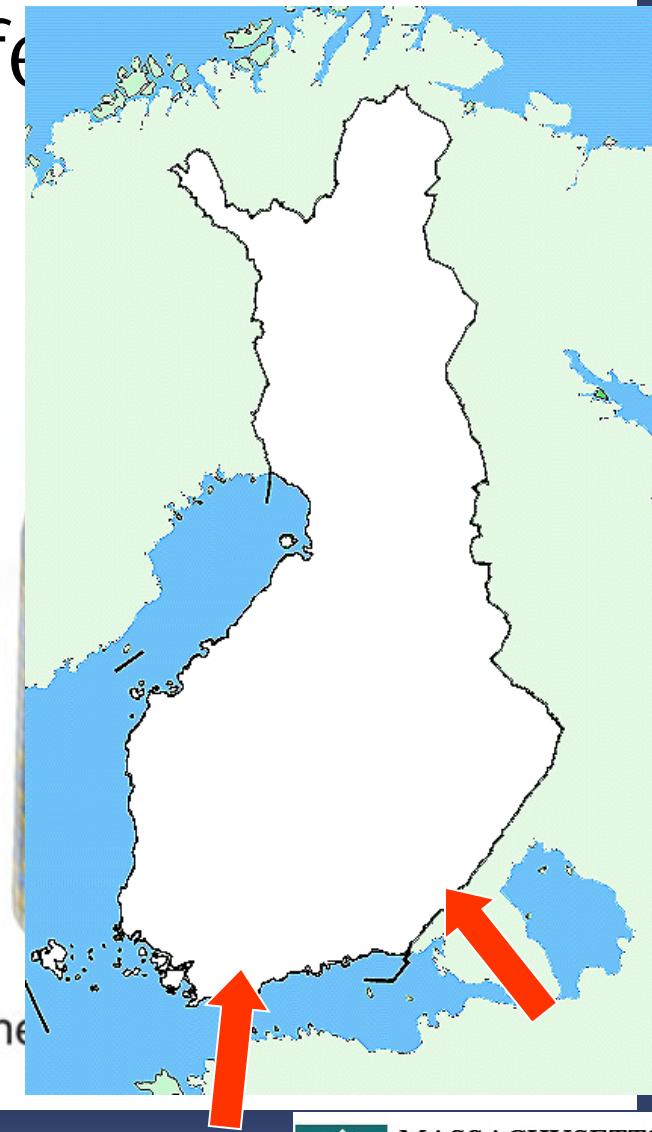
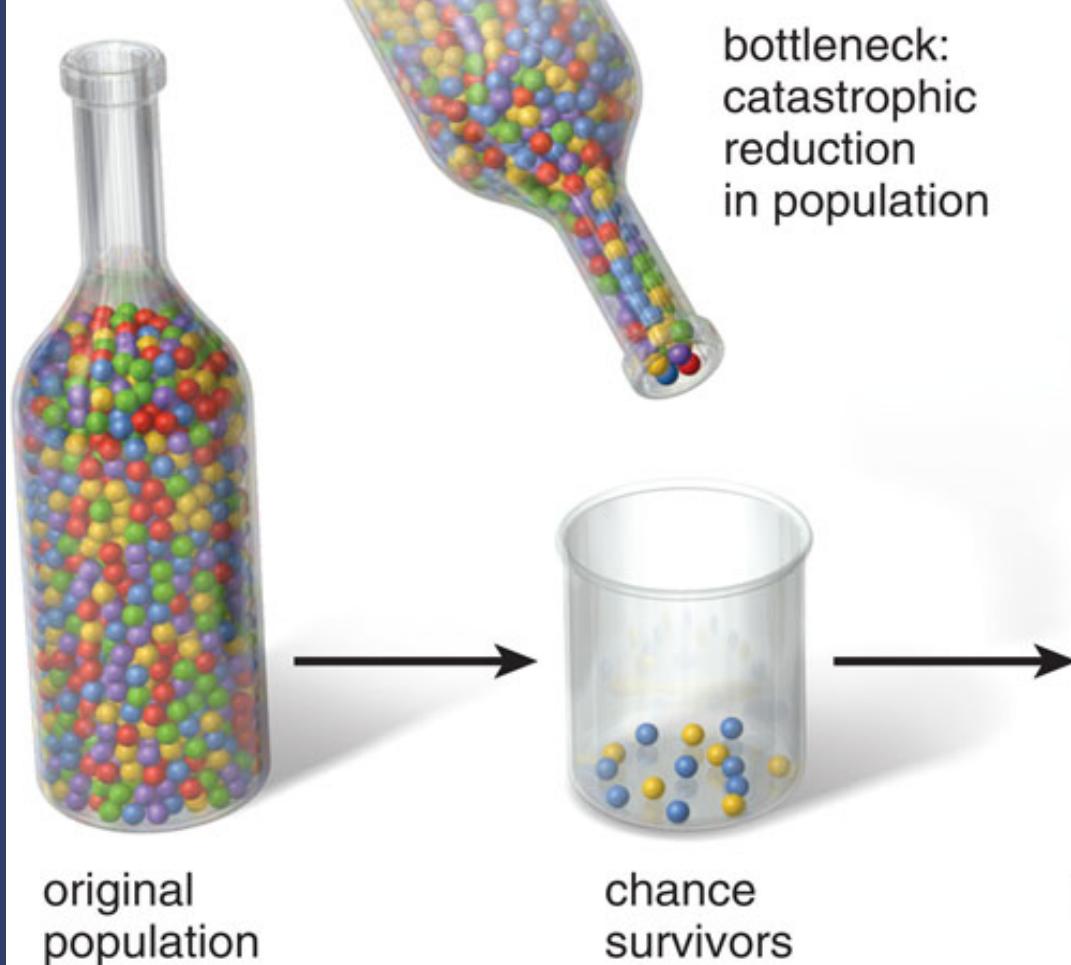
>15,000 diagnosed cases of autism

Different strengths

- Finland
 - Targeted case collection can be costly
 - Recontacting permitted
 - Broad set of registry data available for analysis
 - Targeted phenotyping possible
- Denmark
 - Targeted case collection straightforward
 - No recontacting
 - Broad set of registry data available for analysis
 - Only existing registry and clinical phenotyping

Population isolate

Bottleneck effect

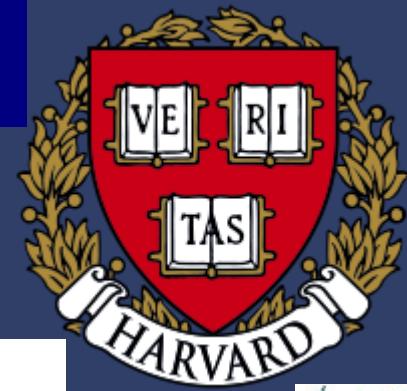




UNIVERSITY OF
OXFORD



LUND UNIVERSITY
Faculty of Medicine



ACHUSETTS
GENERAL HOSPITAL

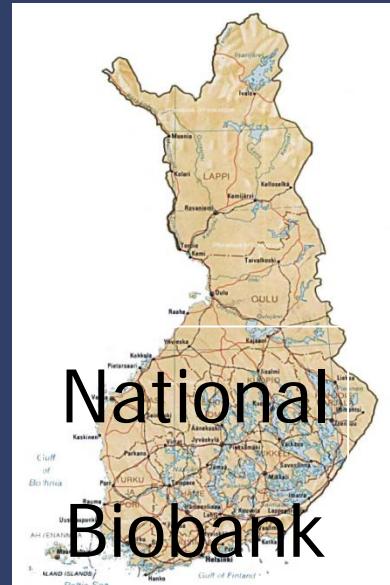
SISU-project

Sequencing Initiative Suomi (Finland)

The 200K

Genome wide genotype data
73 000

Genome exome sequences
>26 000



200 000 individuals
4% of the population

Population cohorts

Extensive health,
phenotype,
metabolomic data

Disease specific
collections

Imputation

Population specific
chip/genotyping

Washington
University in St.Louis



Reference database





Sequencing Initiative Suomi - Data resource for the research community

Data resource for the research community

The Sequencing Initiative Suomi (The SISU project) is an international collaboration between research groups aiming to build tools for genomic medicine.

-  **This SISU v3.0 (2015-08-28) release includes:**
- 
- 
- 

This SISU v3.0 (2015-08-28) release includes:

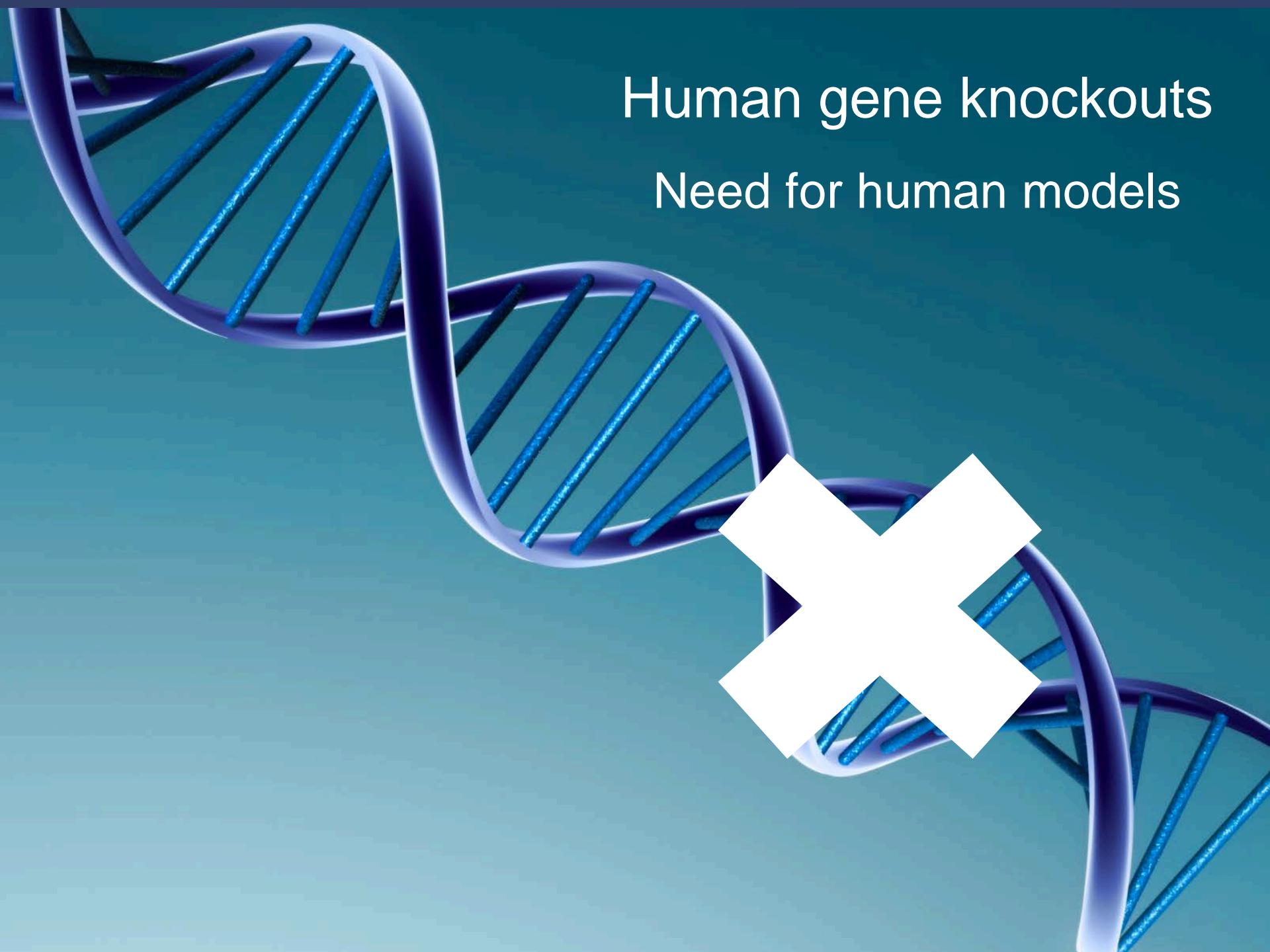
- 1 037 122 sites with 1 137 703 variants
- 6118 Finnish samples from 10 cohorts that were sequenced in Broad and Sanger Institutes
- Original sequencing was done using three different platforms (Agilent 1.1 refseq plus 3 boosters, Agilent sureselect 50mb, Illumina coding v1)
- Multiallelic sites and indels are now included
- Finnish enrichment and other information fields for custom filtering purposes now available

Search

The SISU data resource currently covers exons only and data is restricted to autosomal SNPs and Indels.
Genome build used in this release was GRCh37. Minor allele frequencies before QC and after QC provided.

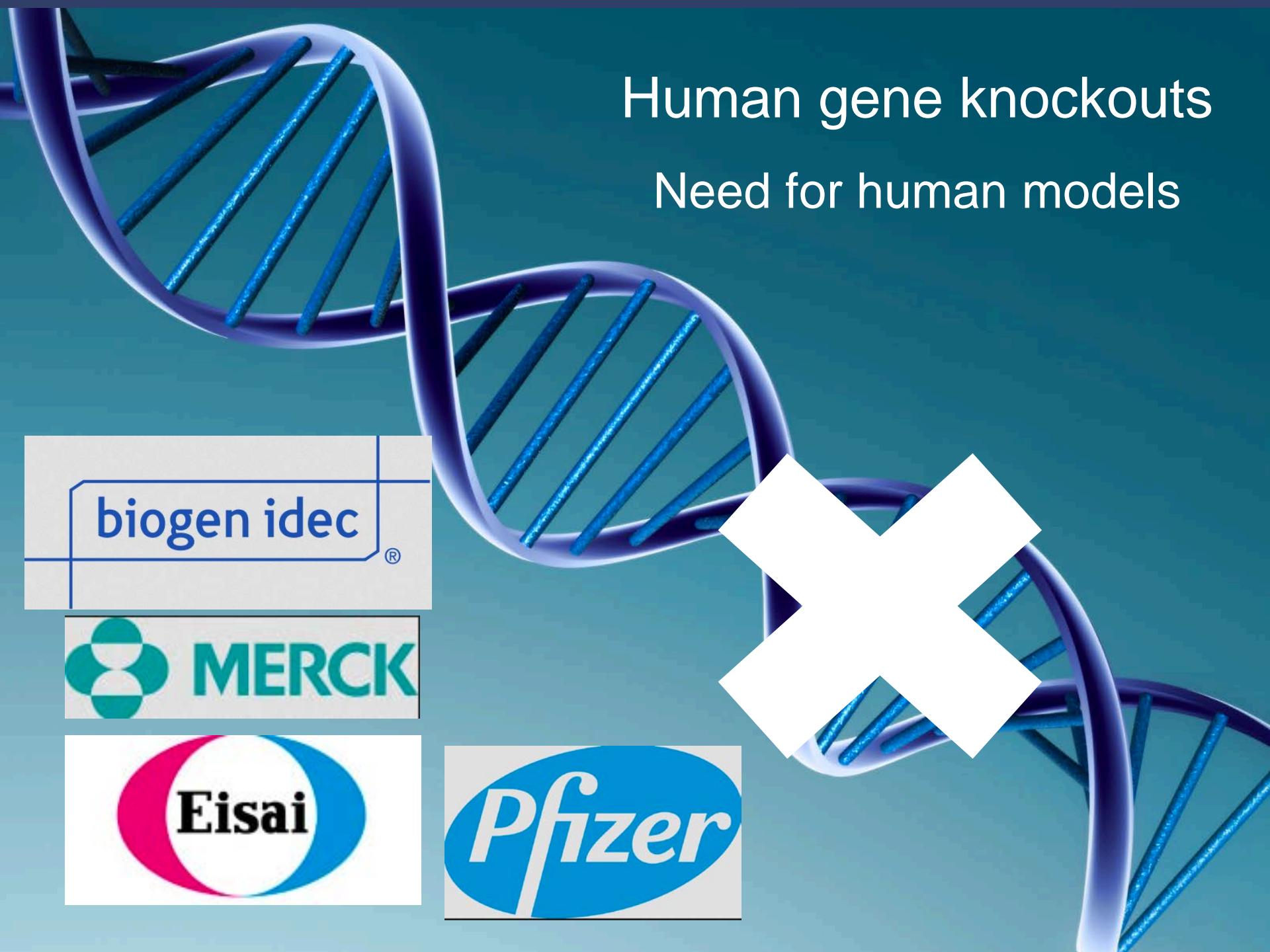
[Information about quality control process](#)

→ [Enter search](#)

A blue and white DNA double helix structure is positioned on the left side of the slide, oriented diagonally from top-left to bottom-right. It is set against a solid teal background.

Human gene knockouts

Need for human models



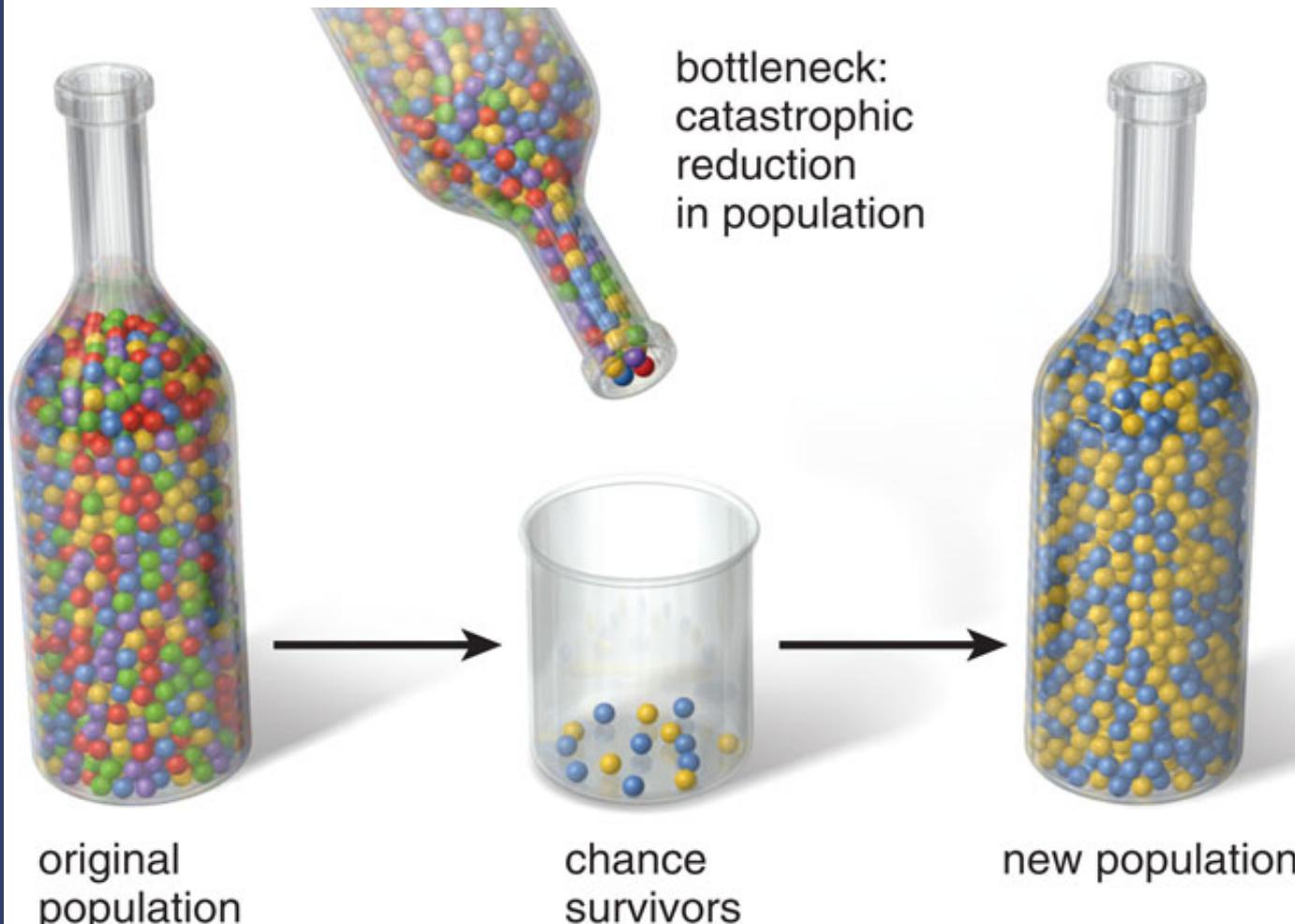
Human gene knockouts

Need for human models



Population isolates

Bottle neck effect and genetic drift



Nordic countries

- Similar health care systems
- Similar traditions in epidemiological studies
- Similar health registers
- Similar regulations
- Biobanks
- Positive attitude for research



Nordic countries

- Similar borders between public service sectors
- Similar protectionism within each governmental institution
- Similar worries
- “It cannot/should not be done” attitude, hardwired in Finns.....



What is quickly needed

- Developing pan-Nordic principals for data sharing
- Resolving unnecessary regulatory hurdles
- Changing the attitude of registry agencies
- Getting the IRB process updated

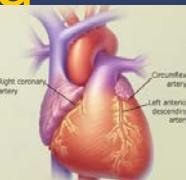


The train moves persistently



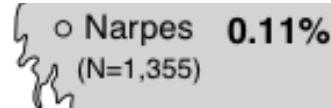
- Do we want to miss the train?
- Would we like to capitalize on your past investments in biobanks and eHealth?

Clustering of the Finnish mutation in a Botnia village around the town of Jakobstad



Loss-of-function mutations in *SLC30A8* protect against type 2 diabetes

Jason Flannick¹⁻³, Gudmar Thorleifsson⁴, Nicola L Beer^{1,5}, Suzanne B R Jacobs¹, Niels Grarup⁶, Noël P Burtt¹, Anubha Mahajan⁷, Christian Fuchsberger⁸, Gil Atzmon^{9,10}, Rafn Benediktsson¹¹, John Blangero¹², Don W Bowden¹³⁻¹⁶, Ivan Brandislund^{17,18}, Julia Brosnan¹⁹, Frank Burslem²⁰, John Chambers²¹⁻²³, Yoon Shin Cho²⁴, Cramer Christensen²⁵, Desirée A Douglas²⁶, Ravindranath Duggirala¹², Zachary Dymek¹, Yossi Farjoun¹, Timothy Fennell¹, Pierre Fontanillas¹, Tom Forsén^{27,28}, Stacey Gabriel¹, Benjamin Glaser^{29,30}, Daniel F Gudbjartsson⁴, Craig Hanis³¹, Torben Hansen^{6,32}, Astradur B Hreidarsson¹¹, Kristian Hveem³³, Erik Ingelsson^{7,34}, Bo Isomaa^{35,36}, Stefan Johansson³⁷⁻³⁹, Torben Jørgensen⁴⁰⁻⁴², Marit Eika Jørgensen⁴³, Sekar Kathiresan^{1,44-46}, Augustine Kong⁴, Jaspal Kooner^{22,23,47}, Jasmina Kravic⁴⁸, Markku Laakso⁴⁹, Jong-Young Lee⁵⁰, Lars Lind⁵¹, Cecilia M Lindgren^{1,7}, Allan Linneberg^{40,41,52}, Gisli Masson⁴, Thomas Meitinger⁵³, Karen L Mohlke⁵⁴, Anders Molven^{37,55,56}, Andrew P Morris^{7,57}, Shobha Potluri⁵⁸, Rainer Rauramaa^{59,60}, Rasmus Ribel-Madsen⁶, Ann-Marie Richard¹⁹, Tim Rolph¹⁹, Veikko Salomaa⁶¹, Ayellet V Segre^{1,2}, Hanna Skärstrand²⁶, Valgerdur Steinthorsdottir⁴, Heather M Stringham⁸, Patrick Sulem⁴, E Shyong Tai⁶²⁻⁶⁴, Yik Ying Teo^{62,65-68}, Tanya Teslovich⁸, Unnur Thorsteinsdottir^{4,69}, Jeff K Trimmer¹⁹, Tiinamaija Tuomi^{27,35}, Jaakko Tuomilehto⁷⁰⁻⁷², Fariba Vaziri-Sani²⁶, Benjamin F Voight^{1,73,74}, James G Wilson⁷⁵, Michael Boehnke⁸, Mark I McCarthy^{5,7,76}, Pål R Njølstad^{1,37,77}, Oluf Pedersen⁶, Go-T2D Consortium⁷⁸, T2D-GENES Consortium⁷⁸, Leif Groop^{48,79}, David R Cox⁵⁸, Kari Stefansson^{4,69} & David Altshuler^{1-3,44,45,80,81}



FIMM

**BROAD
INSTITUTE**

MASSACHUSETTS
GENERAL HOSPITAL
Flannick J et al, Nat Genet 46,357,2014

Pilot study in 35,000 Finns

Traits studied include:

LDL

HDL

TG

BMI

SBP

DBP

CRP

HGF

FGF

VEGF

GALECTIN3

VitB12

G_CSF

IL4, IL6, IL10

D_DIMER

With reachthrough into complete medical records:

ICD-9 & ICD-10 diagnosis count (1986-2010); FINRISK 1992-2007; n= 29,286

ICD-10 converted to ICD-9

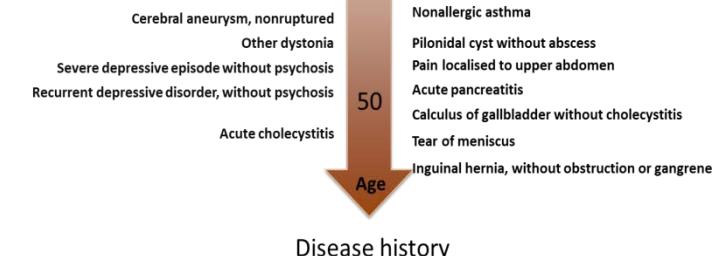
Peter Würtz, March 11, 2013

Diagnosis	Total hospitalizations	Person hospitalizations
ICD-9 chapters		
Infectious And Parasitic Diseases	5293	3039
17207	5295	
7318	2805	
1055	590	
10653	2520	
14279	5973	
38019	8410	
13547	5633	
13782	7270	
13363	6789	
10124	5786	

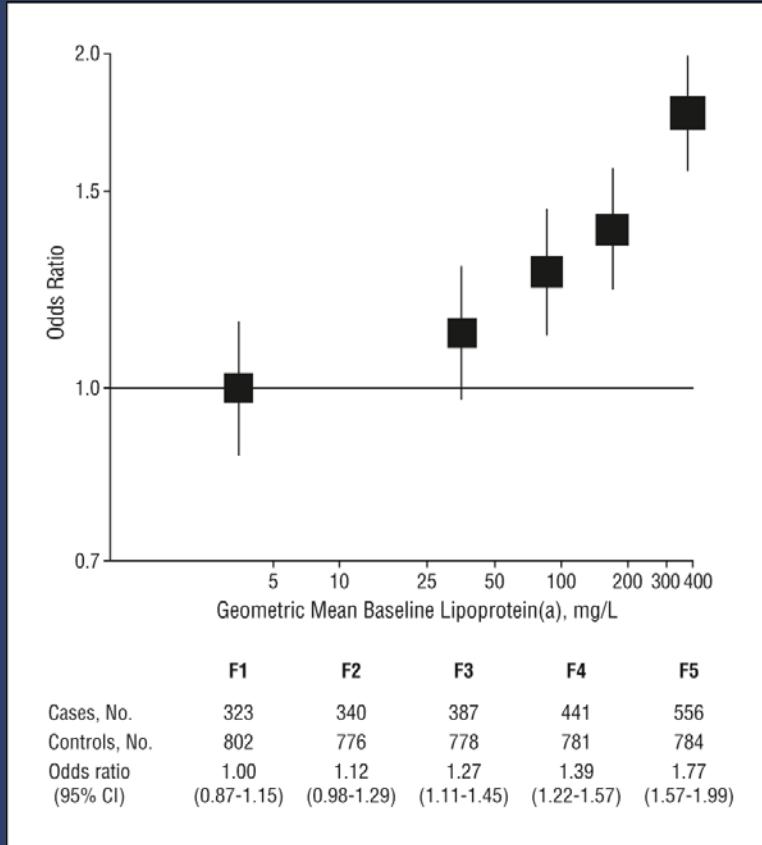
Novel associations to:

- * Reduced Lp(A) levels – and through this cardioprotection and, oddly, increased diabetes risk
 - Galectin3 levels
 - Triglyceride levels
- Systolic blood pressure and several immune markers
 - D_DIMER levels

Human Immunodeficiency Virus
Poliomyelitis And Other Non-Arthropod-Borne Viral Diseases
Viral Diseases Accompanied By Exanthem
Arthropod-Borne Viral Diseases

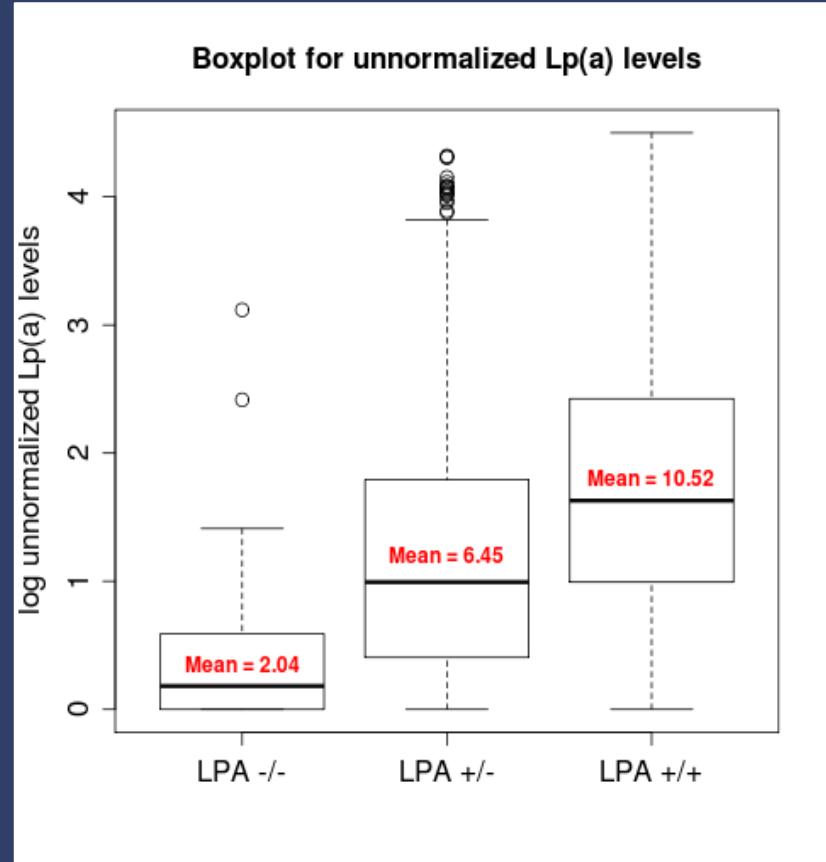


Data on cardioprotective LoF in LPA



Elevated Lp(a) levels known to associate with elevated CHD risk

(Bennel JAMA In Med 2008)



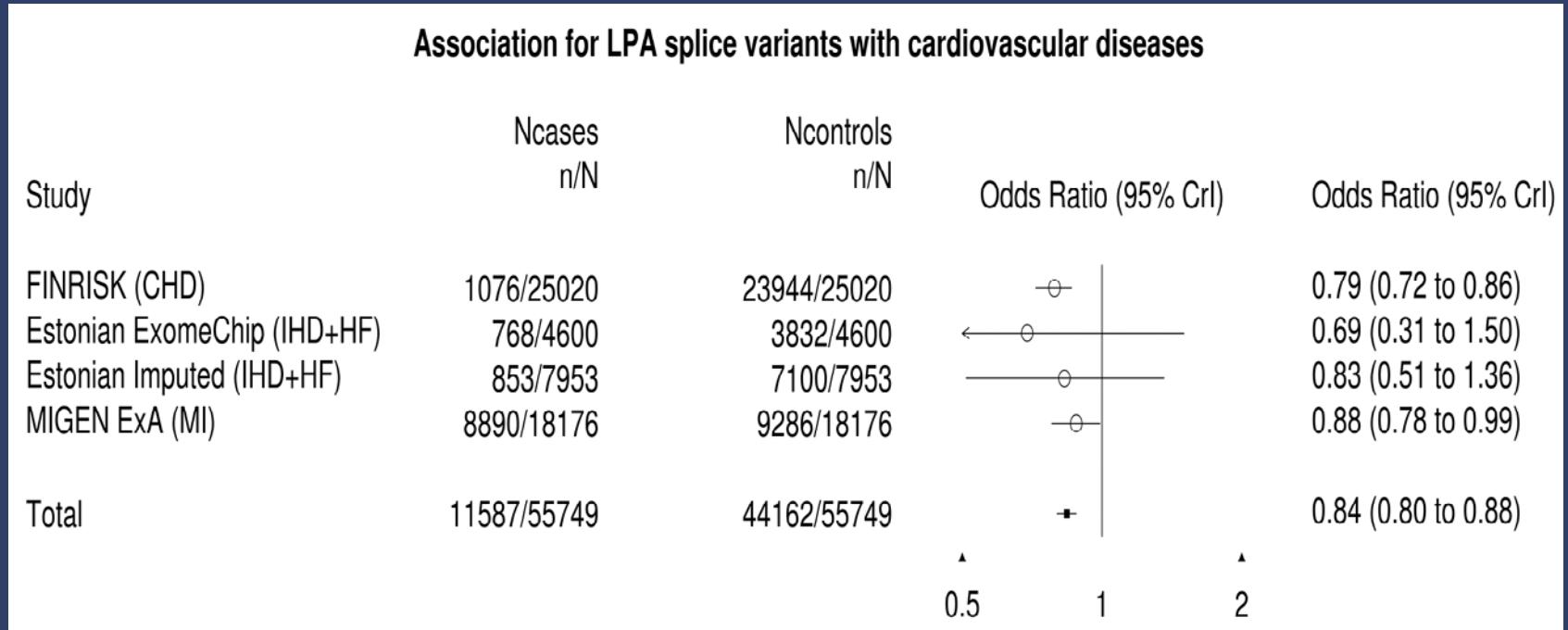
Newly identified protective LoF, 5.5x enriched in Finland (MAF=2.8%)

- 1) Lower Lp(a) levels ($p=3*10^{-58}$)
- 2) Lower CHD risk ($p=0.01$)

Lim et al PLoS



Similar effect in several study samples (heterozygote)



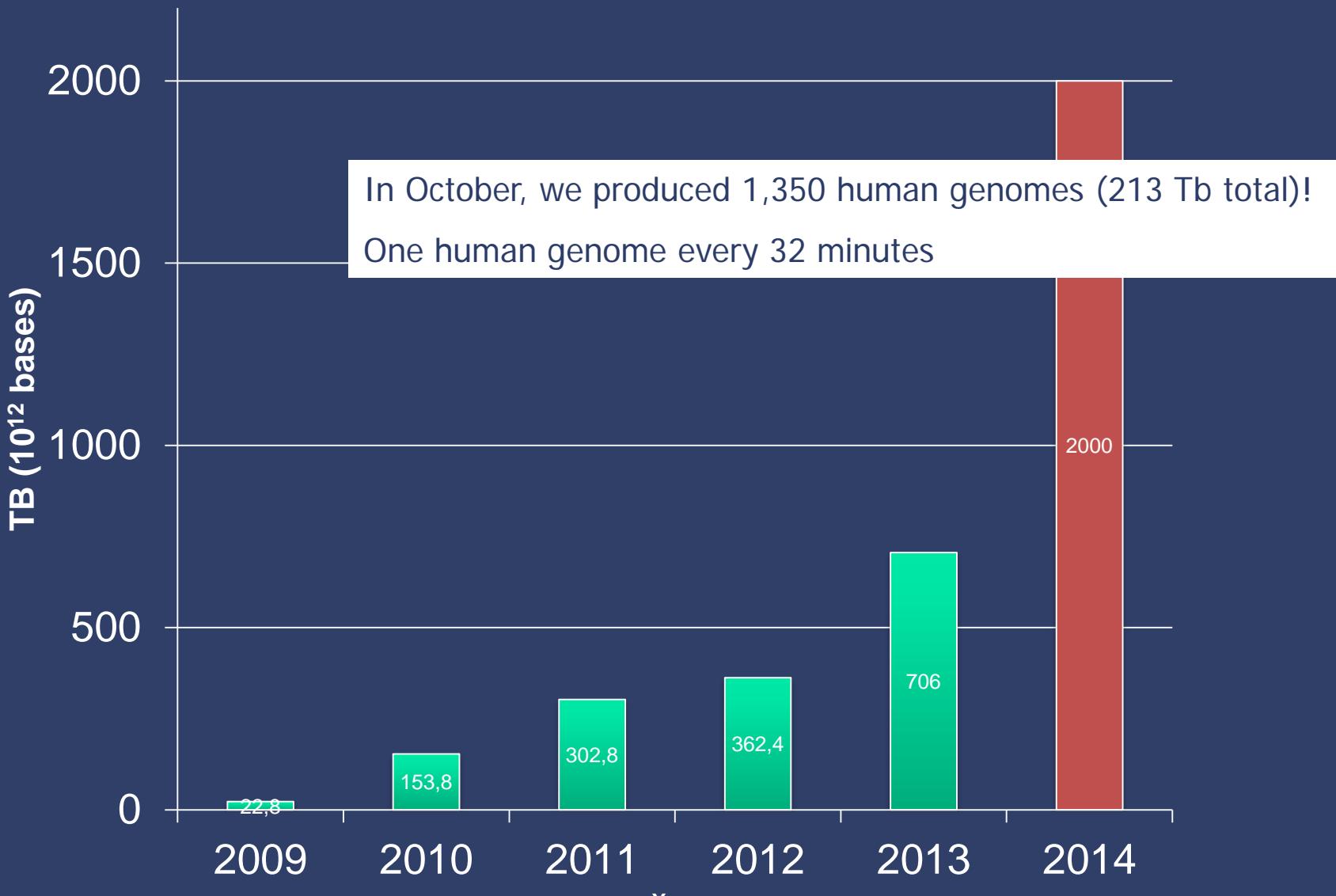
Change in
disease
classification

Individual
organ group
approach

Systems
approach

Technology driving and supporting

Dramatic increase in scale



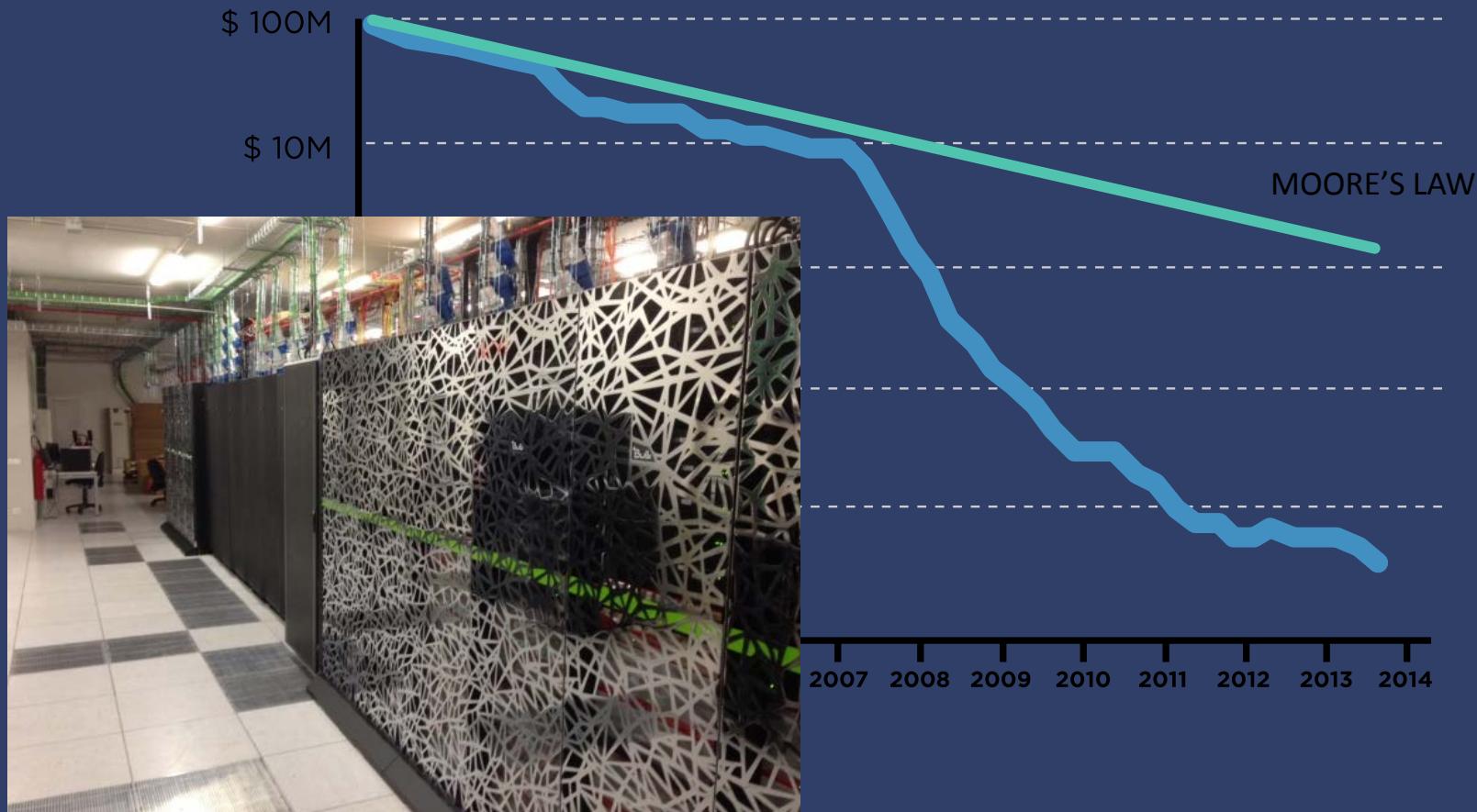
The change is inevitable

- Special opportunities for the Nordic countries
- An opportunity for better stratified medicine
- An opportunity for improved cost efficiency and better use of resources
- An opportunity for new innovations and commercialization





THE COST AND SPEED OF GENOME SEQUENCING IS NO LONGER THE PROBLEM



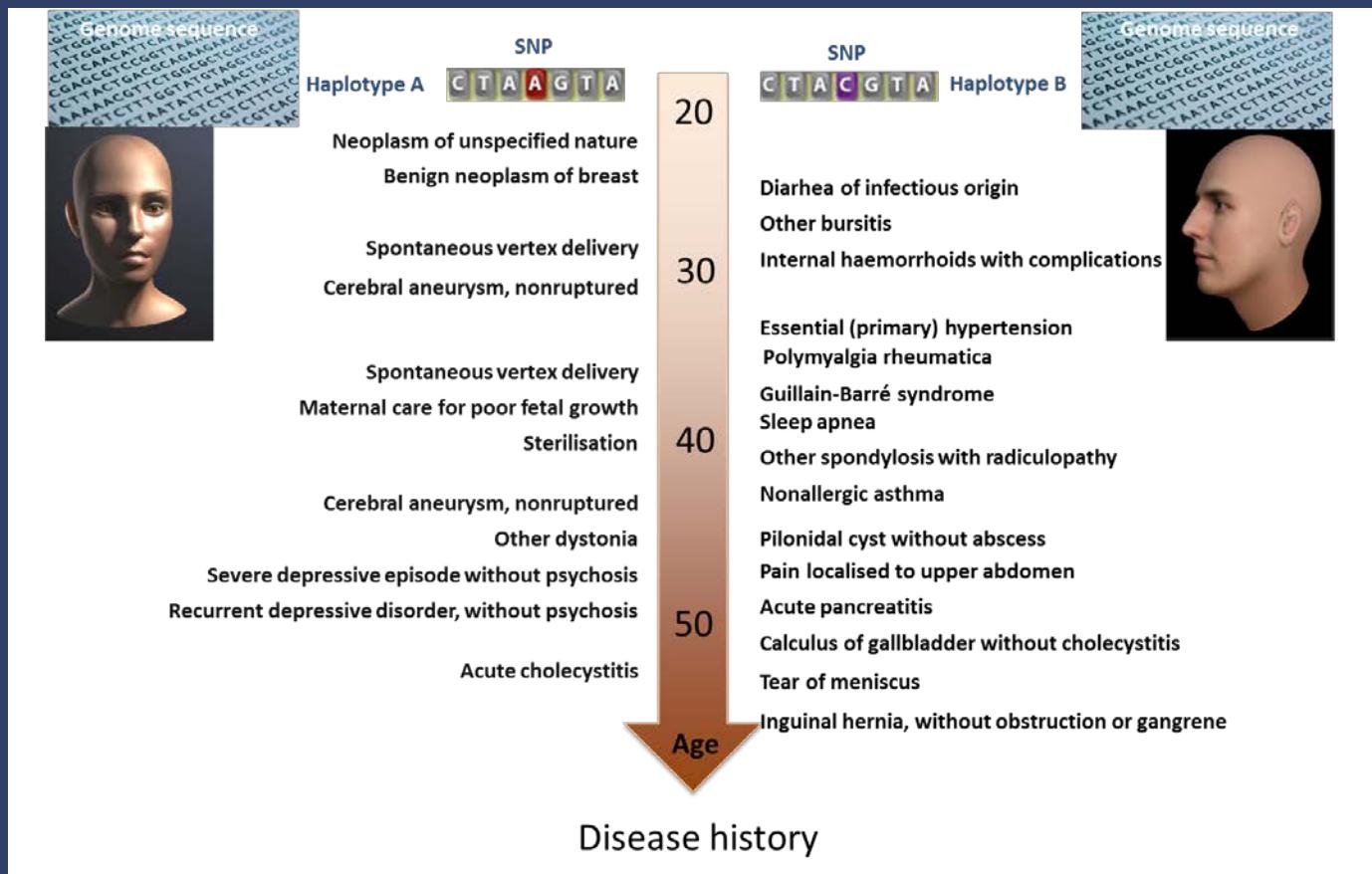
ICD-9 & ICD-10 diagnosis count (1986-2010); FINRISK 1992-2007; n= 29,286

ICD-10 converted to ICD-9

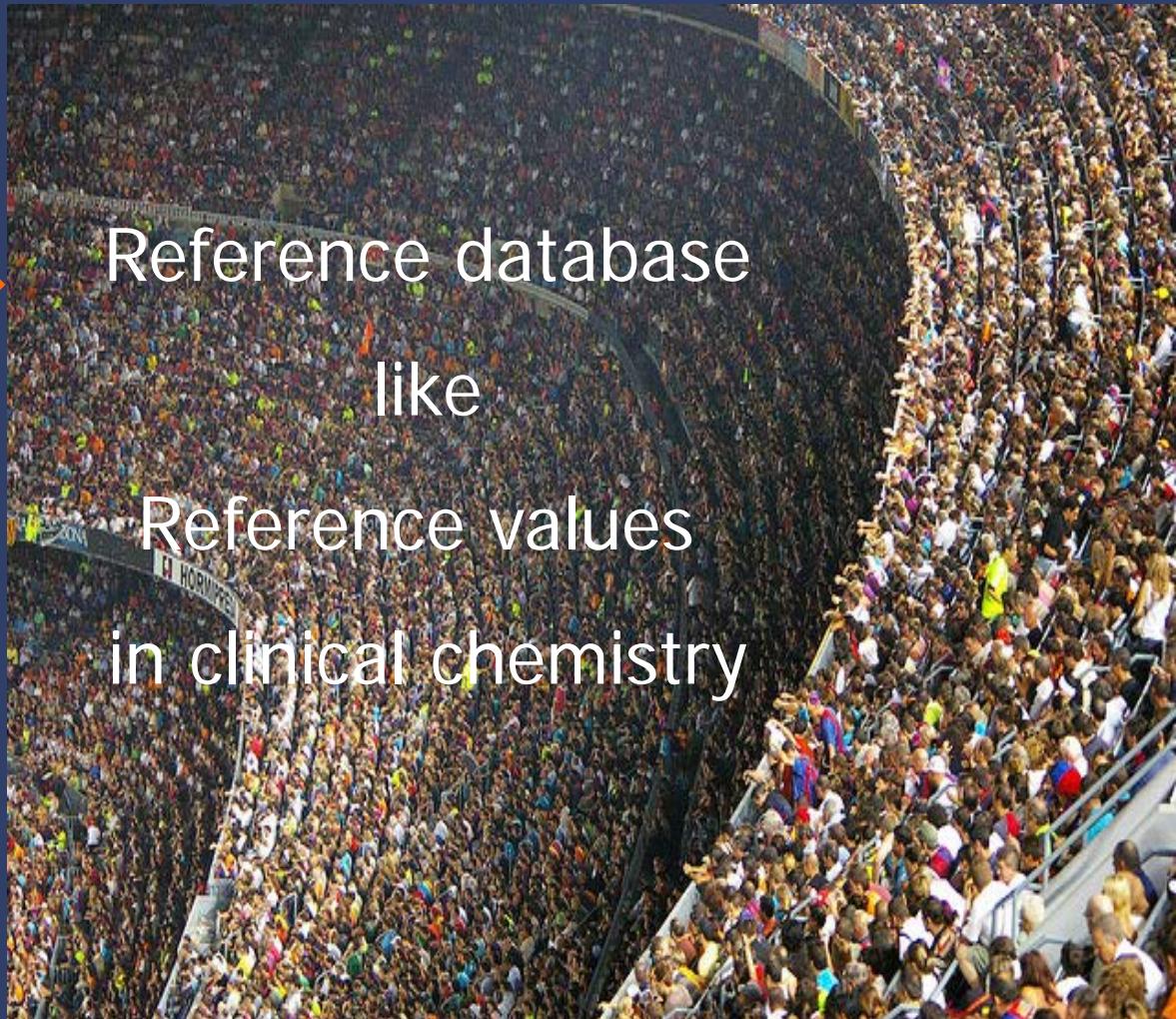
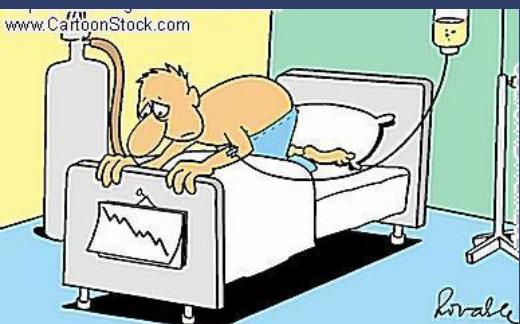
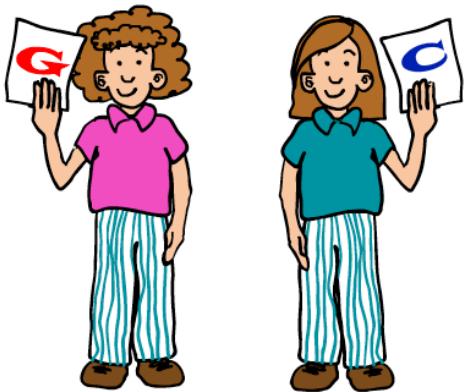
Peter Würtz, March 11, 2013

Diagnosis	Total hospitalizations	Person hospitalizations
ICD-9 chapters		
Infectious And Parasitic Diseases	5293	3039
Neoplasms	17207	5295
Endocrine, Nutritional And Metabolic Diseases, And Immunity Disorders	7318	2805
Diseases Of The Blood And Blood-Forming Organs	1055	590
Mental Disorders	10653	2520
Diseases Of The Nervous System And Sense Organs	14279	5973
Diseases Of The Circulatory System	38019	8410
Diseases Of The Respiratory System	13547	5633
Diseases Of The Digestive System	13782	7270
Diseases Of The Genitourinary System	13363	6789
Complications Of Pregnancy, Childbirth, And The Puerperium	19134	5786
Diseases Of The Skin And Subcutaneous Tissue	2275	1264
Diseases Of The Musculoskeletal System And Connective Tissue	24108	8881
Congenital Anomalies	745	432
Certain Conditions Originating In The Perinatal Period	23	19
Symptoms, Signs, And Ill-Defined Conditions	13498	6911
Injury And Poisoning	14726	7009
Supplementary Classification Of Factors Influencing Health Status And Contact With Health Services	2002	1749
Supplementary Classification Of External Causes Of Injury And Poisoning	0	0
Intestinal Infectious Diseases	1288	977
ICD-9 blocks		
Tuberculosis	147	78
Zoonotic Bacterial Diseases	22	19
Other Bacterial Diseases	1856	1096
Human Immunodeficiency Virus	2	1
Poliomyelitis And Other Non-Arthropod-Borne Viral Diseases Of Central Nervous System	51	44
Viral Diseases Accompanied By Exanthem	204	158
Arthropod-Borne Viral Diseases	29	24

Example of health histories from two persons from the national biobanks with a 40 year follow-up



A A T G G T



Reference database
like
Reference values
in clinical chemistry

Each gene variant has a small effect

FIMM

30th
BROAD
INSTITUTE

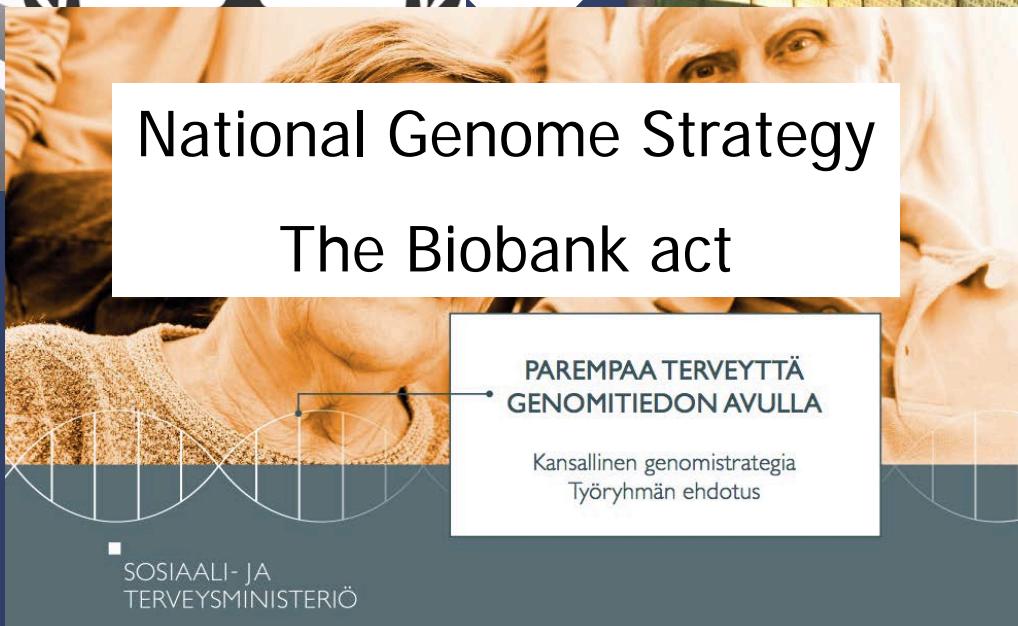


MASSACHUSETTS
GENERAL HOSPITAL



National Genome Strategy

The Biobank act





Collaborate. Innovate. Accelerate.

Working together to share knowledge, create networks and accelerate advances in genomics and health.

[Learn More](#)

"Internet of genomics and health"

Distributing and sharing data globally

Common data formats

Connecting parties globally

150 members worldwide

[What Is the Global Alliance?](#)[What Is the Global Alliance doing?](#)[Who Is Involved?](#)

An alternative view for research ethics, moving from the shadow of World War II to the next step

- In particular, it highlights, and is guided by, Article 27 of the 1948 *Universal Declaration of Human Rights*. Article 27 guarantees the rights of every individual in the world “*to share in scientific advancement and its benefits*” (including to freely engage in responsible scientific inquiry), and at the same time “*to the protection of the moral and material interests resulting from any scientific...production of which [a person] is the author*”.



Biobanks

Finnish Genome Strategy
Ministry of Health and Sitra



Genomes
SISu
Sequencing Initiative Suomi



Implementation in
health care

FIMM

 **BROAD**
INSTITUTE



Research



FIMM

 **BROAD**
INSTITUTE