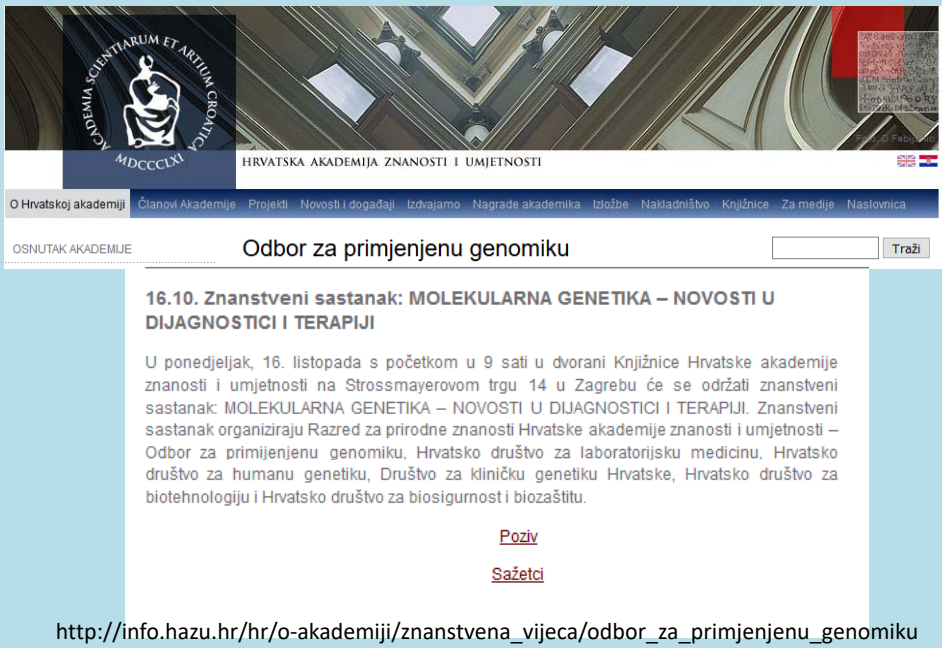


http://info.hazu.hr/hr/o-akademiji/znanstvena_vijeca/odbor_za_primjenjenu_genomiku

GENOMIKA I PRECIZNE MEDICINE

Stjepan Gamulin

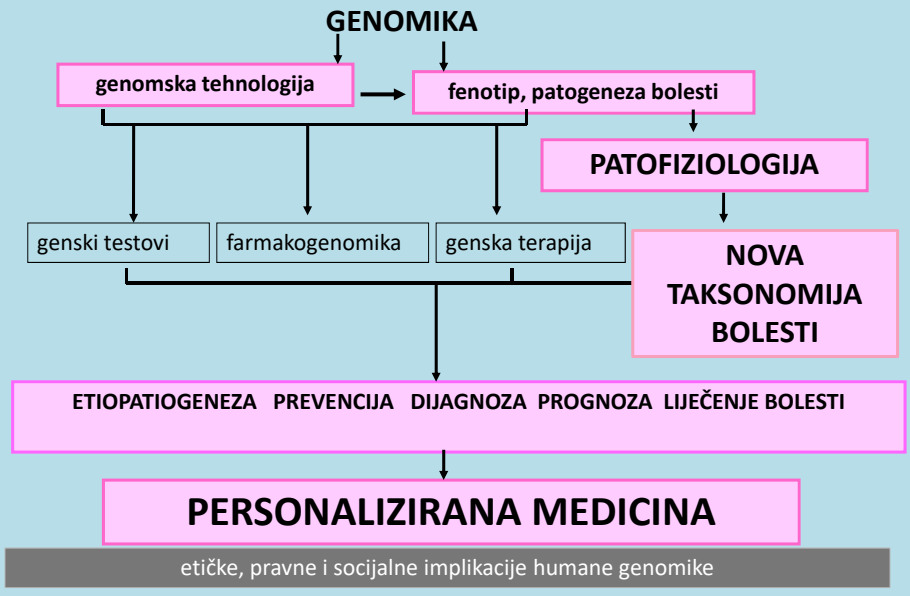
2001. objava humanog genoma

International Human genome Sequencing Consortium
15. veljače 2001

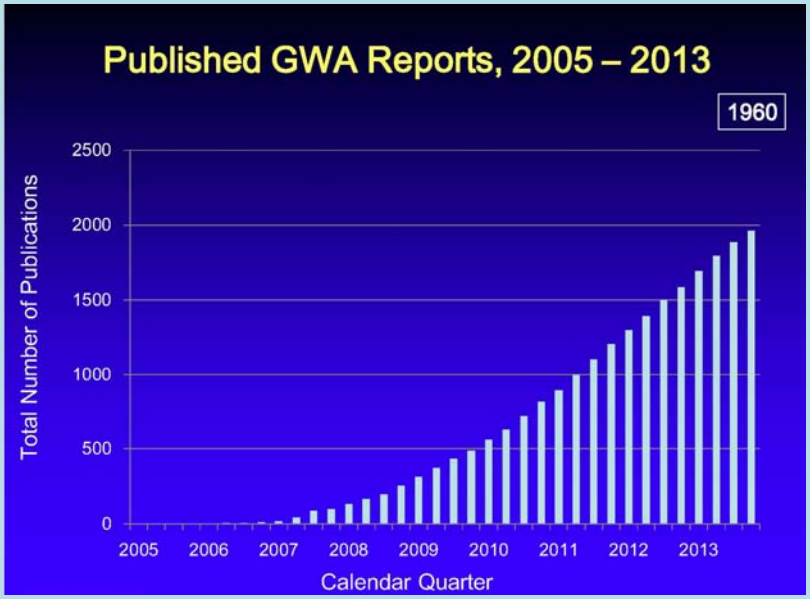
Celera (Craig Venter)
16. veljače 2001

2003. završetak projekta humanog genoma – sekvenca 99,7% eukromatičnog genoma .
- manjak: 300 praznina (~28Mb) i hetrokromatin (~200 Mb).

Humana genomika i medicina



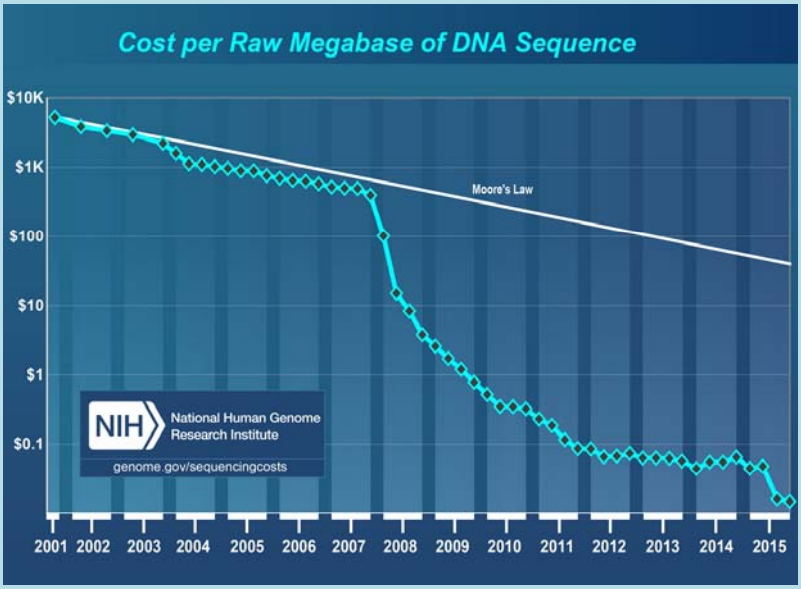
CIJELOGENOMSKE STUDIJE POVEZANOSTI



KATALOG CIJELOGENOMSKIH STUDIJA POVEZANOSTI (10-2017)

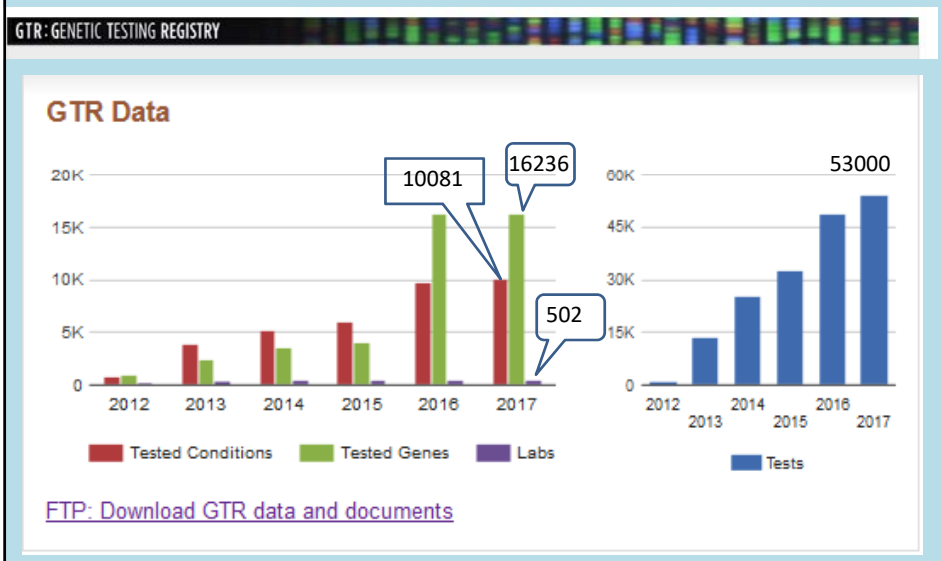
All SNP-trait associations with p-value ≤ 5.0×10^{-8}, published in the GWAS Catalog

http://www.ebi.ac.uk/gwas/diagram



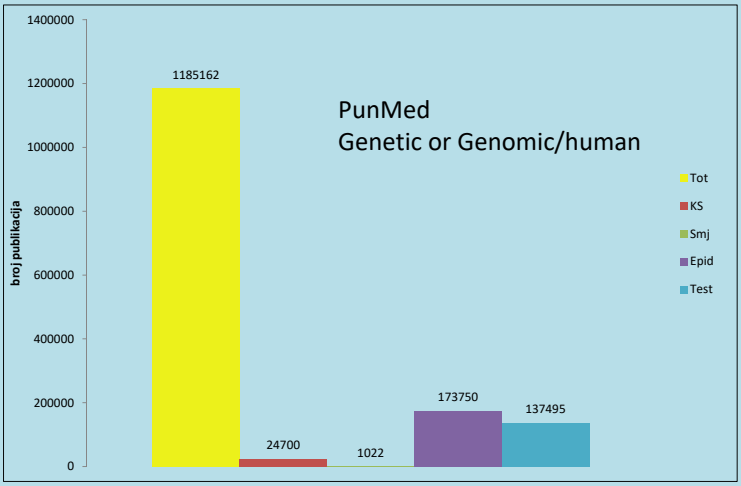
https://www.genome.gov/images/content/costpermb2015_4.jpg

GENETIČKO TESTIRANJE



https://www.ncbi.nlm.nih.gov/gtr/

Medicinska primjena humane genomike 2000- danas

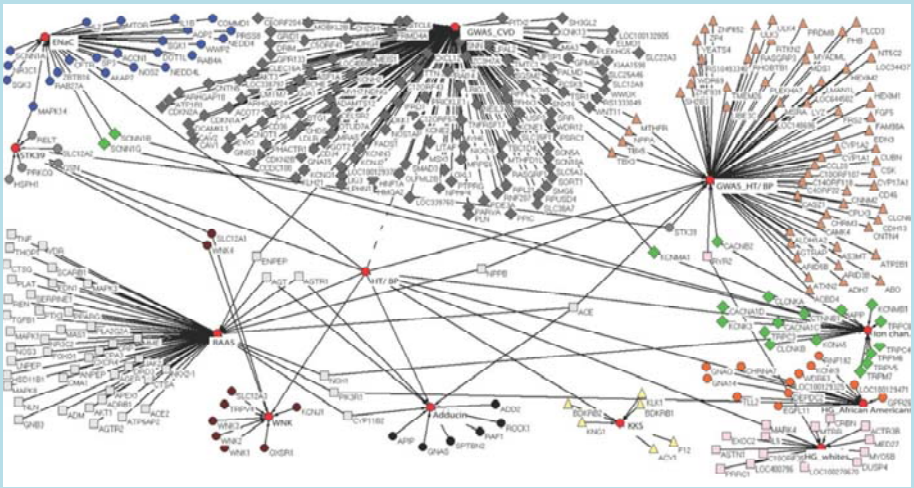


Poligenska nasljednost u običnim kompleksnim bolestima

Poligenske bolesti i osobine	
Bolest/osobina	Broj gena prema GWAS
Pretilost	1905
Šećerna bolest tipa 2	62
Koronarna arterijska bolest	45
Ulcerozni kolitis	134
Reumatoidni artritis	181
Shizofrenija	16
Alzheimerova bolest	203
Šećerna bolest tipa 1	14
Plazmatska koncentracija LDL kolesterola	58
Arterijska hipertenzija	29
Tjelesna visina	173
Tjelesma masa	17

GWAS – genome-wide association study, genomski široke studije povezanosti
Podatci su izabrani iz GWAS kataloga http://www.ebi.ac.uk/gwas/home (25.03.2017)

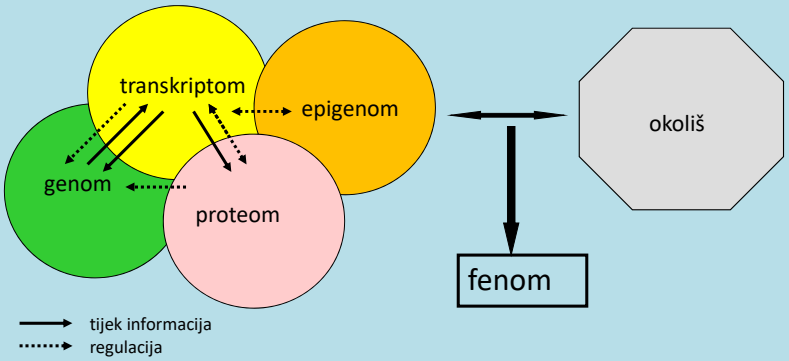
Genomski široke studije povezanosti – hipertenzija i zatajenje srca



Kraja A. T. et al. Curr Hypertens Rep (2011) 13:46–54

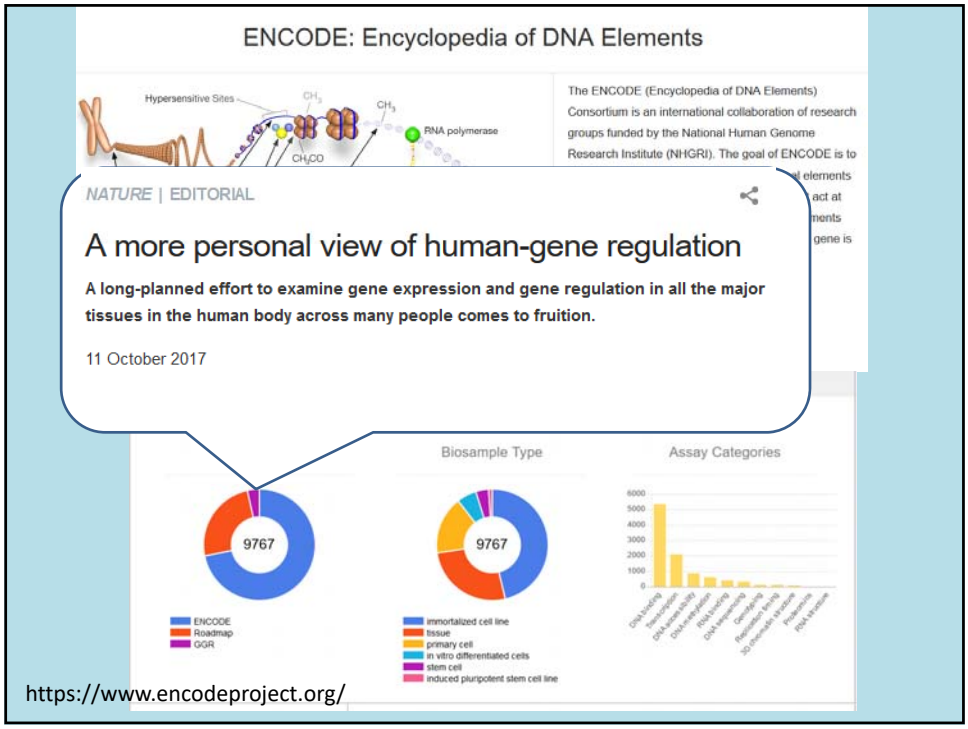
Centralna dogma molekularne biologije – kompleksnost genoma

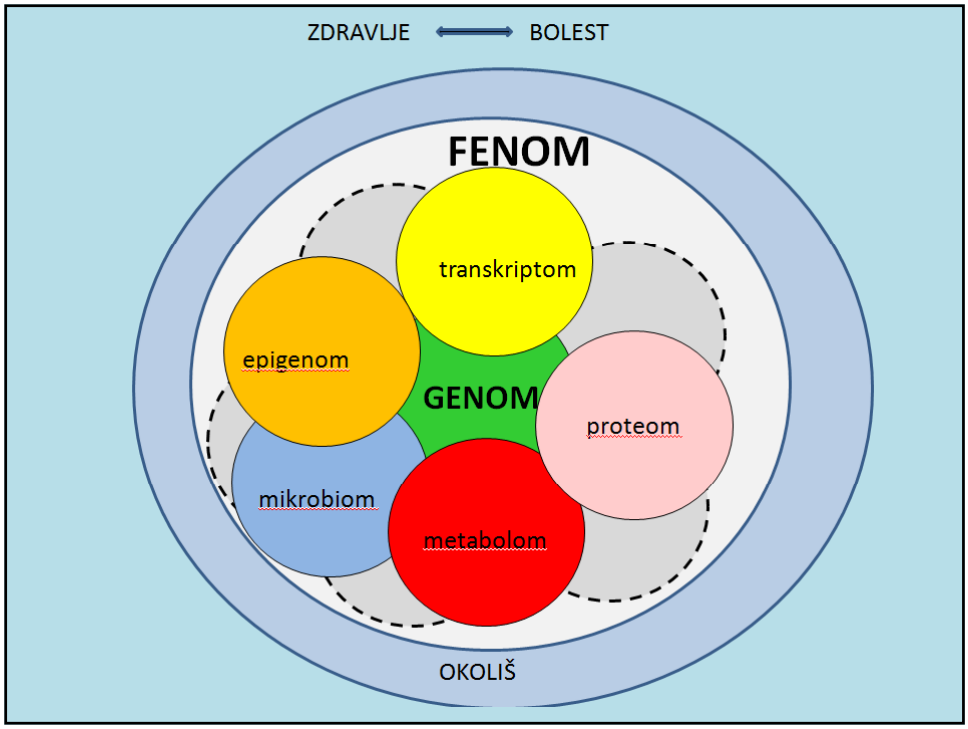
DNA ⇄ RNA → BJELANČEVINE

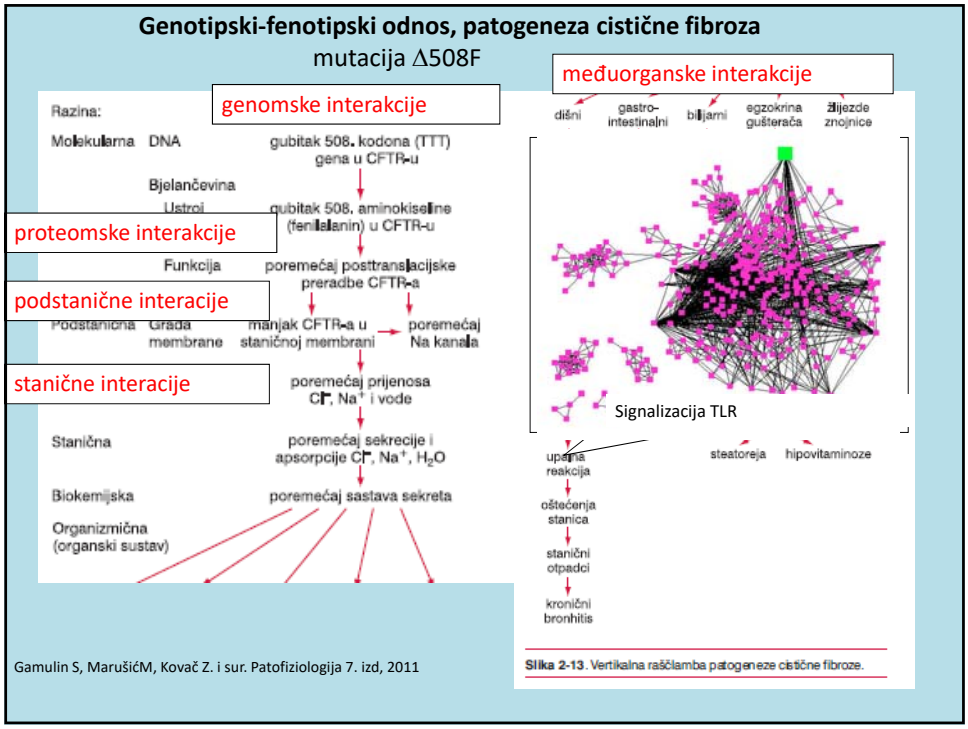


PROJEKT HUMANOG GENOMA
STRUKTURNA GENOMIKA

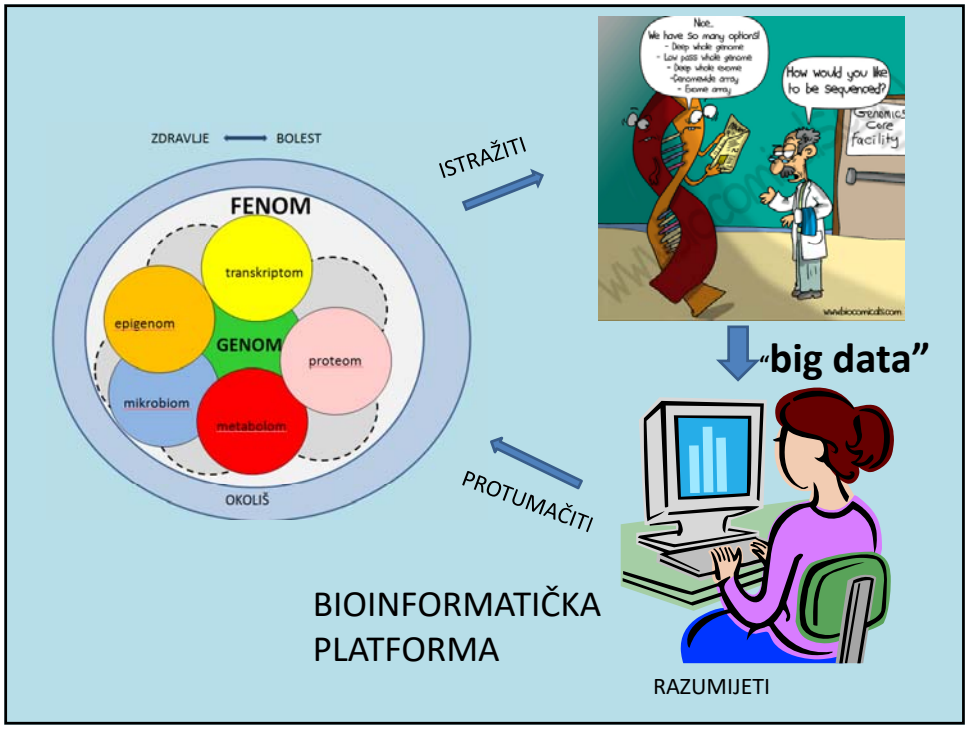
ENCODE PROJEKT 2007.
FUNKCIONALNA GENOMIKA


ENCODE: Encyclopedia of DNA Elements
Hypersensitive Sites
RNA polymerase
The ENCODE (Encyclopedia of DNA Elements) Consortium is an international collaboration of research groups funded by the National Human Genome Research Institute (NHGRI). The goal of ENCODE is to
NATURE | EDITORIAL
A more personal view of human-gene regulation
A long-planned effort to examine gene expression and gene regulation in all the major tissues in the human body across many people comes to fruition.
11 October 2017
Biosample Type
Assay Categories
9767
9767
ENCODE
Roadmap
GGR
immortalized cell line
tissue
primary cell
in vitro differentiated cells
stem cell
induced pluripotent stem cell line
https://www.encodeproject.org/

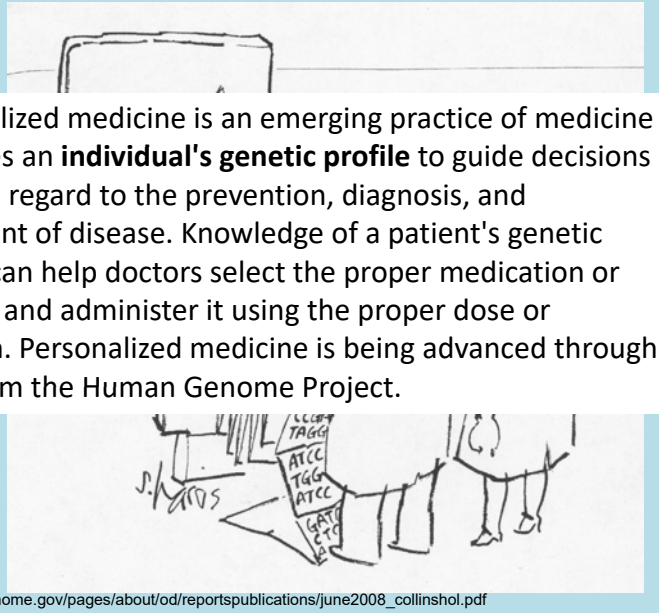

ZDRAVLJE
BOLEST
FENOM
transkriptom
epigenom
GENOM
proteom
mikrobiom
metabolom
OKOLIŠ



Gamulin S, MarušićM, Kovač Z. i sur. Patofiziologija 7. izd, 2011

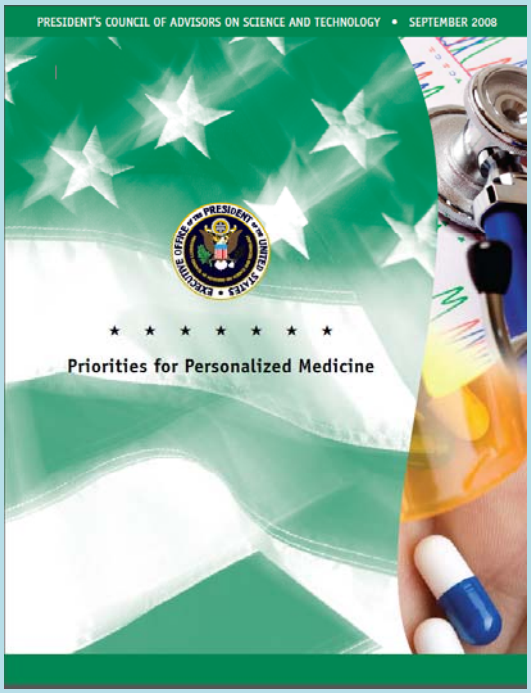


Vizija personalizirane medicine
F.S. Collins, 2007. House of Lords UK



Personalized medicine is an emerging practice of medicine that uses an **individual's genetic profile** to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen. Personalized medicine is being advanced through data from the Human Genome Project.

https://www.genome.gov/pages/about/od/reportspublications/june2008_collinshol.pdf



https://www.whitehouse.gov/files/documents/ostp/PCAST/pcast_report_v2.pdf

Congress (/congress) / Bills (/congress/bills) / H.R. 6498 (110th) (/congress/bills/110/hr6498) / Text

Text of the Genomics and Personalized Medicine Act of 2008

The text of the bill below is as of **Jul 15, 2008** (Introduced). Download PDF

https://www.govtrack.us/congress/bills/110/hr6498/text/ih

Congress (/congress) / Bills (/congress/bills) / H.R. 5440 (111th) (/congress/bills/111/hr5440) / Text

Text of the Genomics and Personalized Medicine Act of 2010

The text of the bill below is as of **May 27, 2010** (Introduced). Download PDF

https://www.govtrack.us/congress/bills/111/hr5440/text/ih

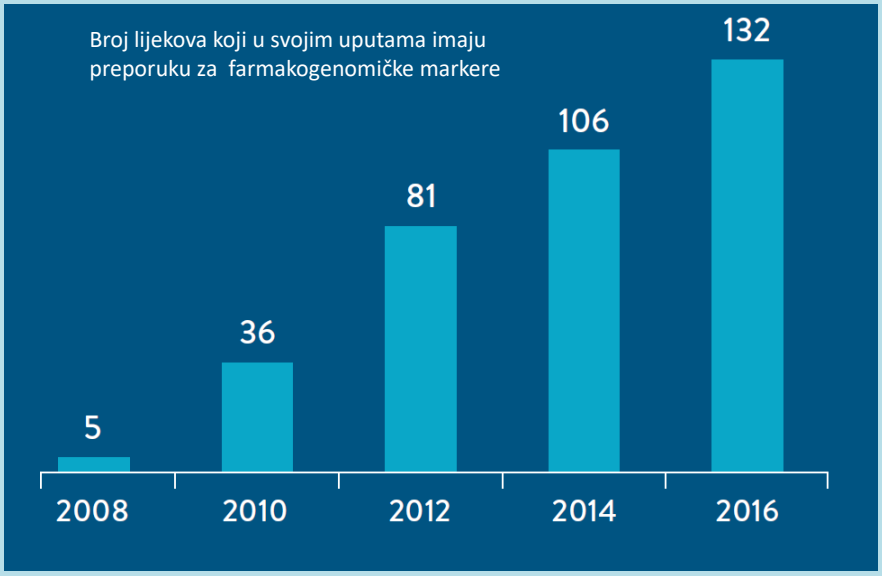
PMC PERSONALIZED MEDICINE COALITION

What Is Personalized Medicine?

Personalized medicine, which **is also called precision** or individualized medicine, is an evolving field in which physicians use **diagnostic tests** to determine to determine which medical treatments will work best for each patient. ……..By combining the data from diagnostic tests with an individual's medical history, circumstances and values, health care providers can develop targeted treatment and prevention plans. This has benefits for both patients and the health system.

10.10.2017
http://www.personalizedmedicinecoalition.org/Education/The_Basics

PRIMJENA FARMAKOGENOMIKE



PMC- The personalized medicine report 2017
http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pd

PERSONALIZIRANA MEDICINA U PRIMJENI -PRIMJERI

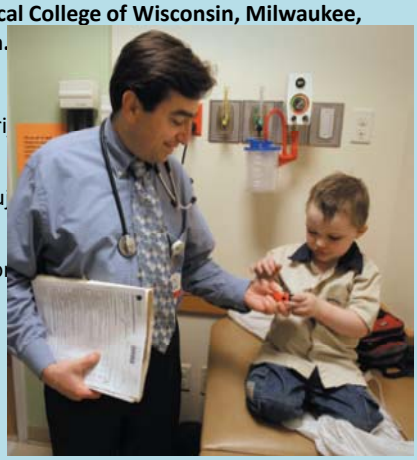
▪**Cistična fibroza - oko 2000 mutacija**
terapija prema mutacijama CFRT gena oko 30 kliničkih pokusa u tijeku
2 lijeka odobrena - LUMACAFTOR+IVACAFTOR - del 508F, IVACAFTOR . G551D mutacija

▪**Primjena warfarina** – genotipizacija CYP2C9 i VKORC1

▪**Rak dojke**
Estrogenski i progesteronski receptori u izboru liječenje 1972 god-
HER2 – primjena trastuzumaba 2000-god
BRCA1, BRCA2 mutacije – prevencija raka dojke
▪**Metastatski rak pluća ne-malih stanica**
BRAF V600E mutacija za primjenu dabrafeniba i trametiniba
▪**Melanom**
BRAF V600E mutacija za primjenu vemurafeniba
▪**Metastatski kolorektalni rak**
RAS Panel (Illumina, Inc.), test sekvencioniranjem nove generacije - mutacije ras-gena
kontraindikacija za primjenu panitumumaba, antagonista EGFR

PERSONALIZIRANA
ILI
STRATIFICIRANA MEDICINA ?
PRECIZNA MEDICINA
2011

Worthey EA et al, Making a definitive diagnosis:
Successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease,
Genet Med 2011;13:255–262.
The Medical College of Wisconsin, Milwaukee, Wisconsin.



Dječak 7 godina star, s 15 mjeseci upalna bolest cri
zahvata, hranjen nazogastričnom sondom.

Mutacija X-povezanog inhibitora apoptoze, uzroku
limfohitiocitozu

Transplatacija alogenih hematopoetskih progenito
pupčane vrpce

Nakon 40 dana dijete prvi put normalno jede bez intestinalnih smatnja

The National Academies of SCIENCES ENGINEERING MEDICINE

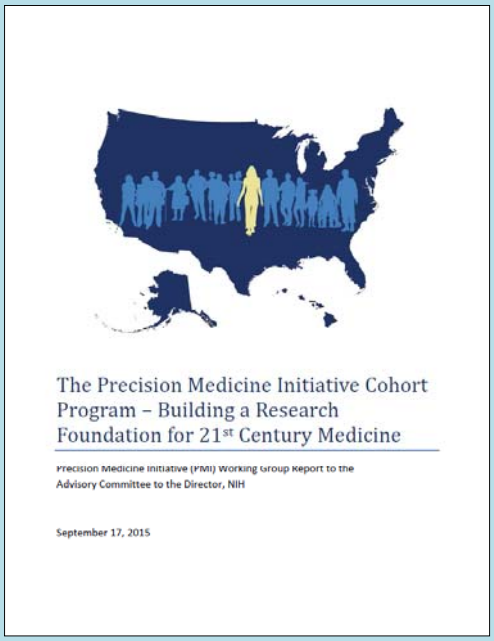
Toward Precision Medicine:
Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease
(2011)

https://www.nap.edu/catalog/13284/toward-precision-medicine-building-a-knowledge-network-for-biomedical-research

https://www.whitehouse.gov
s-precision-medicine-initiati
The White House
Office of the Press Secretary
For Immediate Release
January 30, 2015

NIH Director Francis Collins, wearing a double helix necktie, joined President Barack Obama during a 2015 event to unveil the Precision Medicine Initiative.

FACT SHEET: President Obama's Precision Medicine Initiative



http://acd.od.nih.gov/reports/DRAFT-PMI-WG-Report-9-11-2015-508.pdf

PRECIZNA MEDICINA - DEFINICIJA

We define precision medicine as an approach to disease treatment and prevention that seeks to maximize effectiveness **by taking into account individual variability in genes, environment, and lifestyle.** Precision medicine endeavors to redefine our understanding of disease onset and progression, treatment response, and health outcomes through the more precise measurement of potential contributors – for example, molecular measurements as captured through DNA sequencing technologies or environmental exposures or other information captured through increasingly ubiquitous mobile devices. **A precise delineation of the molecular, environmental, behavioral, and other factors that contribute to health and disease will lead to more accurate diagnoses, more rational disease prevention strategies, better treatment selection, and the development of novel therapies.**

http://acd.od.nih.gov/reports/DRAFT-PMI-WG-Report-9-11-2015-508.pdf

NIH National Institutes of Health
All of Us Research Program

About the *All of Us* Research Program

The All of Us Research Program seeks to extend precision medicine to all diseases by building a national research cohort of one million or more U.S. participants. Many factors have converged to make now the right time to begin a program of this scale and scope.

https://allofus.nih.gov/about/about-all-us-research-program

Program Components

Through a set of funding awards, NIH has established the essential components of the *All of Us* Research Program to build a research cohort of one million or more U.S. volunteers to advance precision medicine. Click the images below to learn more about each of these components.

Biobank

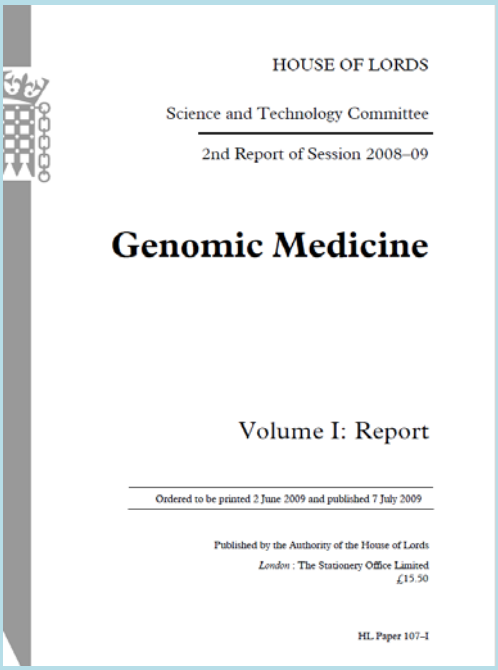
Communications and Engagement

Data & Research Center

Health Care Provider Organizations

Participant Center

Participant Technology Systems Center



HOUSE OF LORDS

Science and Technology Committee

2nd Report of Session 2008–09

Genomic Medicine

Volume I: Report

Ordered to be printed 2 June 2009 and published 7 July 2009

Published by the Authority of the House of Lords

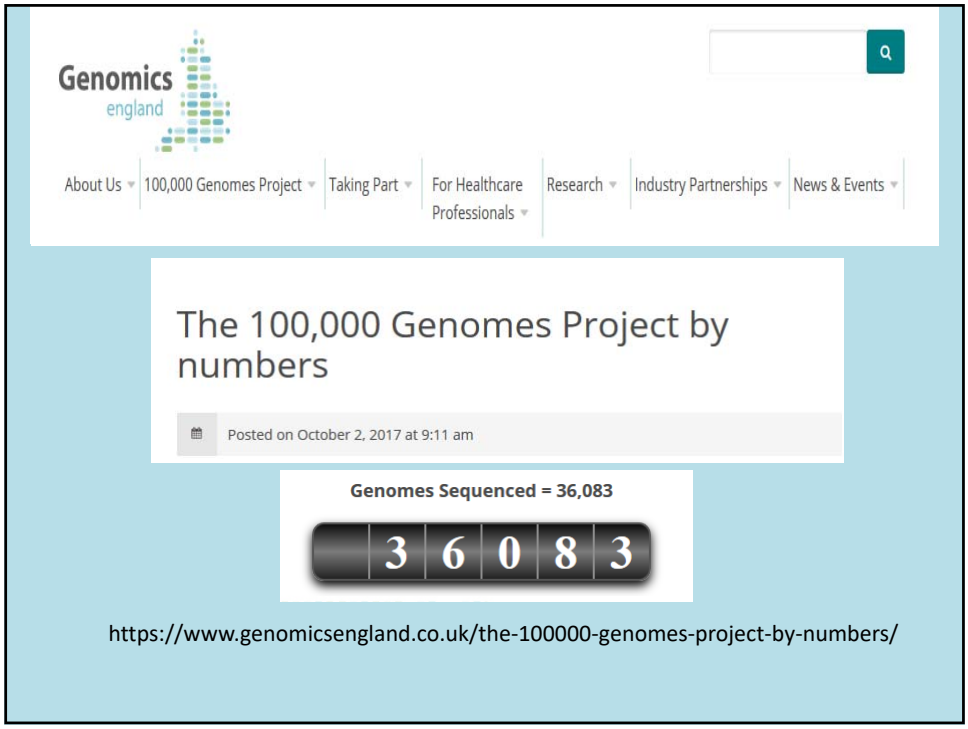
London : The Stationery Office Limited

£15.50

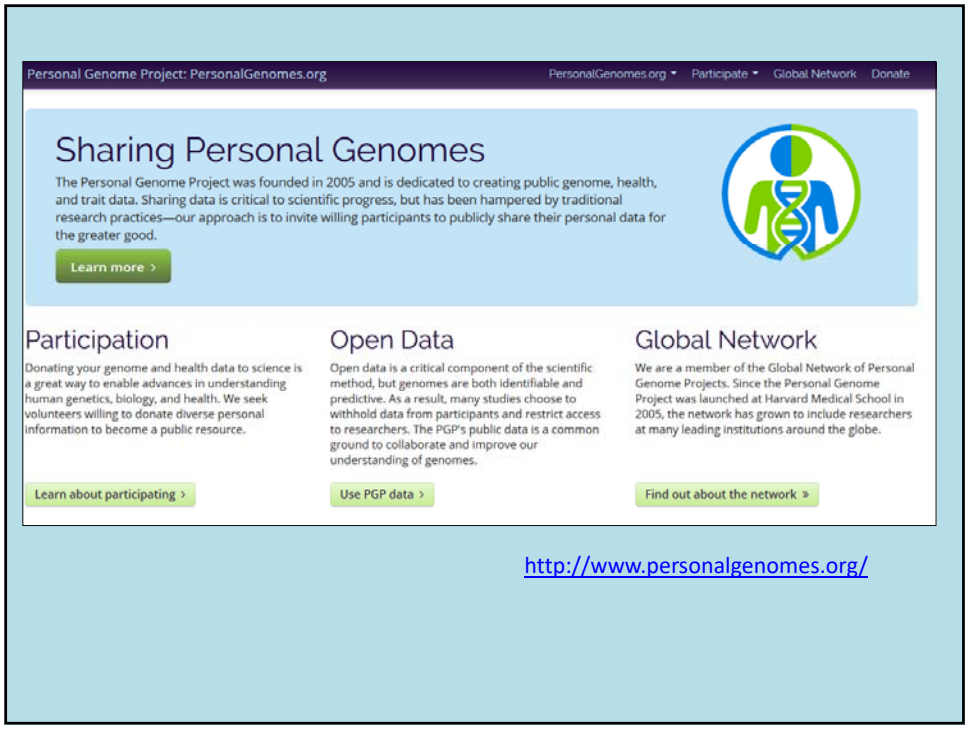
HL Paper 107–I

http://www.publications.parliament.uk/pa/ld200809/ldselect/ldsctech/107/107i.pdf

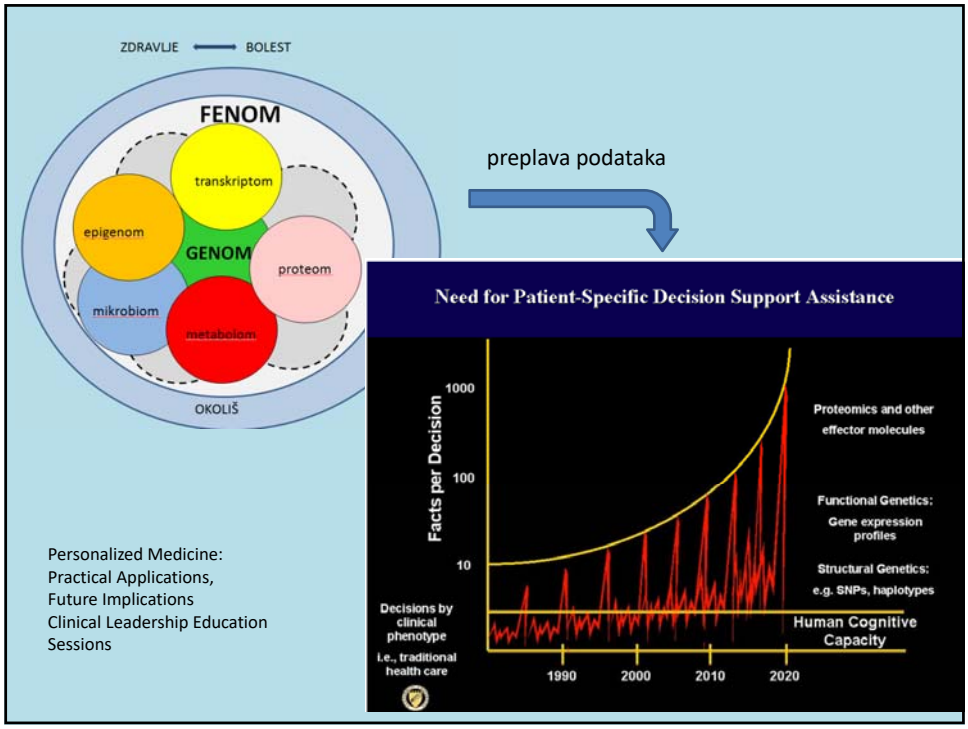
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_132369



https://www.genomicsengland.co.uk/the-100000-genomes-project-by-numbers/



http://www.personalgenomes.org/

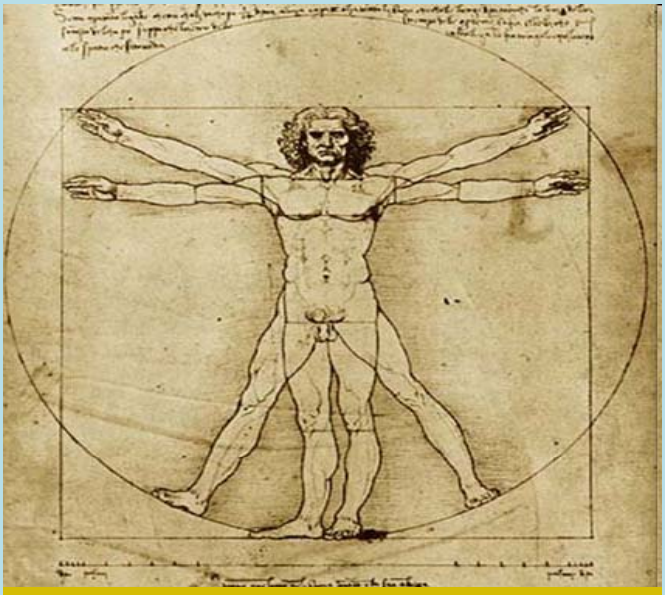

ZDRAVLJE
BOLEST
FENOM
transkriptom
epigenom
GENOM
proteom
mikrobiom
metabolom
OKOLIŠ
preplava podataka
Need for Patient-Specific Decision Support Assistance
Facts per Decision
1000
100
10
Proteomics and other effector molecules
Functional Genetics: Gene expression profiles
Structural Genetics: e.g. SNPs, haplotypes
Human Cognitive Capacity
Decisions by clinical phenotype i.e., traditional health care
1990
2000
2010
2020
Personalized Medicine:
Practical Applications,
Future Implications
Clinical Leadership Education
Sessions


The NEW ENGLAND JOURNAL of MEDICINE
Lost in Thought — The Lim and the Future of Medicine
Ziad Obermeyer, M.D., and Thomas H. Lee, M.D.
RAZVOJ BIOINFORMATIČKIH SUSTAVA MEDICINSKOG ODLUČIVANJA

Svaki je organizam pa i ljudsko biće derivat preezistentnih jedinaka, biološki je kvant u bioreuzi života.
....Svako je ljudsko biće integralna biološka, psihička i socijalna ličnost sa sebi svojstvenoj reaktivnosti…

Pavao Sokolić (1907-1977)

(bilješke s predavanja)



Hvala na pozornosti

Personalizirana medicina – holistički pristup osobi s primjerenim uvažavanjem genoma