The Nobel Prize in Chemistry 2012 was awarded jointly to Robert J. Lefkowitz and Brian K. Kobilka "for studies of G-protein-coupled receptors"

"Dr. Lefkowitz said that although the notion of cell receptors went back more than a century, ‘When we started our work in the area in the early ‘70s, there was still a lot of skepticism as to whether there really was such a thing.’ Over the years, he was able to extract receptor proteins and show they were specific molecules. Other researchers had discovered a class of proteins called ‘G-proteins’ inside the cell that, when activated, set off a Rube Goldberg cascade of molecular machinery. The receptor was the last missing piece. ‘If you have something like adrenaline, it sticks in there, turns the key, changes the shape of the receptor, and now the receptor, having changed shape, is able to tickle the G-protein.’ There was a ‘Eureka moment’ when he realized that this receptor was the same as the light receptor rhodopsin in the retina. We said, ‘well wait a moment maybe anything which couples to a G-protein looks like this.’ Within a year they were able to decode the genetic blueprints for several other similar receptors, and they were right.”  

The New York Times, 10 October 2012
The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".

“With our discovery of the structure of DNA, we knew that a new world had been opened and that an old world which seemed rather mystical was gone. At that time some biologists were not very sympathetic with us because we wanted to solve a biological truth by physical means. But fortunately some understood that by using the techniques of physics and chemistry a real contribution to biology could be made.

“Good science as a way of life is sometimes difficult. It often is hard to have confidence that you really know where the future lies. It is therefore important to remember that science does not stand by itself, but is the creation of very human people. We must continue to work in the humane spirit in which we were fortunate to grow up. If we do, we shall help insure that our science continues and that civilization will prevail.”

James Watson, December 10, 1962, Stockholm Sweden
The Central Dogma of Modern Molecular Biology

DNA → RNA → Protein

Transcription → Translation

Replication
Genes contain instructions for making proteins.

Proteins act alone or in complexes to perform many cellular functions.

From Genes to Proteins
The Human Genome Project (HGP)

**Purpose:** To sequence and map all of the genes (together known as genome) of species *Homo sapiens*.

**Time Frame:** The project was begun in October 1990 with first working draft announced in 2000.

**Completion:** Final draft was published in April 2003, mapping nucleotides in the Haploid Reference Genome giving us the ability for the first time to read nature’s complete blueprint for building a human.

**The Math:** The Human Genome contains 3 Billion Base Pairs but only 25,000 Identified Proteins from Genes. (3 Nucleotides/AA x 400 AAs/Protein x 25,000 Proteins = 30 Million Base Pairs or 1% total!?!)

**Questions:** James Watson, HGP head, resigned in 1992 2º plans to acquire patents on gene sequences.

A decade after its deciphering we know little about specific relationship between genotype & phenotype.

James Watson, 2nd person to publish his fully sequenced genome online said that he was doing this “to encourage the development of an era of personalized medicine in which information contained in our genomes can be used to identify and prevent disease and to create individualized medical therapies.”
Personal Genome Project

George Church, Ph.D., Professor of Genetics
Harvard University School of Medicine

Overview:

• 1. GENES = Genome Sequencing
• 2. ENVIRONMENT = Environmental Factor Identification
• 3. TRAITS = Phenotypic Identification
• 4. Research Project Input = Additional Trait Identification
• 5. Public Sharing on Internet = Correlating GET
Sequencing the Human Genome

Human Genome Project
1988 - 2001
13 years

James Watson
2007
2 months

The near future?
2013
3 minutes

Nature, 1 June 2007. doi:10.1038/news070528-10
1. Genome Sequencing:

- 1. HGP 1990-2003 Craig Venter $3 Billion/Genome x 13 years
- 2. HGP 2007 James Watson $100,000/Genome x 2 months
- 3. PGP-10 2008 George Church $20,000/Genome x 1 month
- 4. PGP-1K 2011 Clifford Andrew $5,000/Genome x 1 week
- 5. PGP-100K 2014 Duke Med School Class of ‘72 $1000@ x 3 days
Inside the Personal Genome Project
The project will turn information from 100,000 subjects into a huge database that can reveal the connections between our genes and our physical selves. Here's how. — Thomas Goetz

1. Entrance Exam
Volunteers take a quiz to show genetic literacy. One question: How many chromosomes do unfertilized human egg cells contain? a) 11, b) 22, c) 23, d) 46, or e) 92? (Answer: c.) Only those with a perfect score proceed, but retests are allowed.

2. Data Collection
Volunteers sign an "open consent" form acknowledging that their information, though anonymized, will be accessible by others. They fill out their phenotype traits, listing everything from waist size to diet habits. Suitable respondents go on to the next step.

3. Sample Collection
Volunteers hit the medical center, where they are interviewed by an MD. Then a technician draws some blood, gathers a saliva sample, and takes a punch of skin. Don't worry: It hurts about as much as a bee sting.

4. Lab Work
The tissues are sent to a biobank, where DNA is extracted from the blood. One percent of it — the exome — is sequenced. Meanwhile, bacteria DNA is extracted from the saliva and sequenced to reveal the volunteer's microbiome.

5. Research
Now the fun part: Crunching the numbers. PGP scientists and other researchers start working with the data assembled from 100,000 individuals to investigate potential links between phenotypes and genotypes. The team will look for patterns and statistically significant anomalies.

6. Sharing
The volunteers get access to not only the raw data from their genome, but anything the research team glean from their information. Insights — a newly discovered cancer risk, for example — are posted in a volunteer's file, which they'll be free to share with other PGP participants.
Personal Genome Project

2. Data Collection for Environmental Factors:

- 1. Open Consent Form – Anonymous – But Accessible
- 2. Dietary, Nutrition, Weight
- 3. Habits (Alcohol, Drugs, Tobacco)
- 4. Exercise
- 5. Health, Illnesses, Medications
- 6. Mental Health, Stress
Physicians’ Health Study II

2. Environmental Factors & 3. Traits:

- 1. Harvard Medical School
- 2. 15,000 Male Physicians >50 yo
- 3. 15 years (1997-2012)
- 4. Vitamin E, C, Beta-Carotene, Multivitamin vs Placebo
- 5. Conclusion: Multivitamin Lowers Cancer Incidence by 12%
Multivitamins in the Prevention of Cancer in Men
The Physicians' Health Study II Randomized Controlled Trial

J. Michael Gaziano, MD, MPH; Howard D. Sesso, ScD, MPH; William G. Christen, ScD; Vadim Bubes, PhD; Joanne P. Smith, BA; Jean MacFadyen, BA; Miriam Schwartz, MD; JoAnn E. Manson, MD, DrPH; Robert J. Glynn, ScD; Julie E. Buring, ScD

Published online October 17, 2012

Context Multivitamin preparations are the most common dietary supplement, taken by at least one-third of all US adults. Observational studies have not provided evidence regarding associations of multivitamin use with total and site-specific cancer incidence or mortality.

Objective To determine whether long-term multivitamin supplementation decreases the risk of total and site-specific cancer events among men.

Design, Setting, and Participants A large-scale, randomized, double-blind, placebo-controlled trial (Physicians' Health Study II) of 14,641 male US physicians initially aged 50 years or older (mean [SD] age, 64.3 [9.2] years), including 1312 men with a history of cancer at randomization, enrolled in a common multivitamin study that began in 1997 with treatment and follow-up through June 1, 2011.

Intervention Daily multivitamin or placebo.

Main Outcome Measures Total cancer (excluding nonmelanoma skin cancer), with prostate, colorectal, and other site-specific cancers among the secondary end points.

Results During a median follow-up of 11.2 (10.7-13.3) years, there were 2669 men with confirmed cancer, including 1373 cases of prostate cancer and 210 cases of colorectal cancer. Compared with placebo, men taking a daily multivitamin had a statistically significant reduction in the incidence of total cancer (multivitamin and placebo groups, 17.0 and 18.3 events, respectively, per 1000 person-years. Daily multivitamin use was associated with a reduction in total cancer among 1312 men with a baseline history of cancer. This did not differ significantly from that among 13,329 men initially without cancer.

Conclusion In this large prevention trial of male physicians, daily multivitamin supplementation modestly but significantly reduced the risk of total cancer.
Personal Genome Project

3. Traits and Phenotypic Identification:

• 1. Medical Data – Google Health, Microsoft HealthVault
• 2. Laboratory Studies
• 3. Physical Characteristics – Weight, Waist Size, Exercise Tolerance
• 4. Mental Health Data
• 5. Questionnaires
WHAT DOES IT MEAN THAT I HAVE A GENE THAT GIVES ME ‘TYPICAL ODDS’ FOR HAVING RED HAIR?

I HAVE CHOSEN NOT TO LEARN WHETHER I HAVE A GENE THAT INCREASES THE RISK OF ALZHEIMER’S DISEASE.

I CONSUME BEER, BROCCOLI AND BRUSSELS SPROUTS, EVEN THOUGH I HAVE THE GENE FOR TASTING THEIR BITTERNESS.
4. Research into Additional Phenotypic Traits:

- 1. Researchers at Annual GET Conference in April
- 2. Facial Appearance and Emotional Characteristics
- 3. Microbiome Kit for (Endogenous Bacteria) in Skin and Gut
- 4. Digital Pedometer to Monitor Daily Exercise
- 5. Sweat Gland Density and Distribution
- 6. Telomere Study
5. Open Sharing of Genes and Traits on Web:

- 1. Raw Data from Genome
- 2. Personal Traits and Phenotypic Characteristics
- 3. Research Studies Identifying More Genotypic Phenotypic Variations
- 4. Data Anonymous but Accessible to Researchers and Participants
- 5. Additional Research Studies from Analysis of 100K Data
- 6. Goal to Investigate and Identify Genotype - Phenotype Links
**Background**

Public genomes...

The Personal Genome Project (PGP) was founded in 2005 at Harvard Medical School by George Church as an “open source” research project dedicated to collecting and publicly releasing genomes and other personal health data. The PGP contrasts with the standard methods for human subjects research in its dedication to maximizing the sharing of data and resources. Traditionally, biomedical research projects assured privacy for their subjects—a promise that drastically limited the ability to share resulting data with others. The PGP has taken a new approach towards research: recruitment of participants willing to make their personal health data publicly available, risking re-identification to build an invaluable public resource.

...environments and traits

Genomes contain rich information, but it is the interaction of genomes with environments that produces traits. Understanding these interactions requires more than genomes alone. Because the PGP does not guarantee privacy and anonymity, it can collect diverse personal data for an individual and publicly connect them. Over 1,000 health records have been imported by participants, demonstrating their commitment to public knowledge. The PGP is exploring using a variety of measurements and samples to capture additional information about each participant. The combined data—capturing aspects of genomes, environments, and traits—forms a critically needed resource to publicly understand and improve personalized medicine.

**Goals**

Enabling Discovery

The PGP is working together with other groups to pilot technologies for analysis, measurement, and interpretation. Resulting data will be integrated to create public, analytically comprehensive personal profiles. Research groups will be able to use these data to discover unexpected links between genomes, environment, and traits, and to validate methods developed privately.

**Participation**

Open consent

The PGP uses an innovative method for consent in human subjects research: “open consent”. In this research, participants agree to the following:

- Data and samples can be shared publicly
- No guarantees are made regarding privacy, anonymity, and confidentiality
- Participation has various risks associated with potential loss of privacy
- Once shared, data and samples may be used used by others in unanticipated ways, without the participant's permission
- Participation is not expected to directly benefit the participant
- Withdrawal is possible at any time, but it may be impossible to remove data from the public domain after it has been shared.

Who can participate?

Anyone may participate provided they:

- Wish to publicly share samples & data and agree to terms of open consent (above)
- Are at least 21 years of age
- Are a US citizen or permanent resident
- Demonstrate understanding of risks involved

Understanding is demonstrated by taking our enrollment exam. This must be done by the participant themselves—not by caretakers or relatives. The exam tests understanding of the potential risks, PGP protocols, and basic genetics.

Participation is an ongoing relationship: participants are expected to communicate with the PGP and may be recontacted with news of specimen collection events and follow-up studies.
PGP around the world

While the Personal Genome Project began at Harvard Medical School, PersonalGenomes.org is working together with researchers around the world to establish additional PGP projects.

We’re thrilled to announce the approval of "PGP Canada" at the University of Toronto, and we look forward to more projects starting in coming years.

Find PGP on the web

PGP website:
http://www.personalgenomes.org

PGP blog:
http://blog.personalgenomes.org

Participant profiles:
http://www.personalgenomes.org/community

Our consent forms:
http://www.personalgenomes.org/consent

Sign up to be a participant:
http://www.personalgenomes.org/signup

PGP Network:
http://www.personalgenomes.org/network
Duke University Med School Class of '72
Tour of the Eno River
Sunday October 21, 2012 12:30PM

with Eno River Assn Milo Pyne & Executive Director Robin Jacobs

We will meet in Washington Duke Inn lobby and carpool/caravan 10 minutes to the newest section of the Eno River State Park for either 1.5 hour (3 mile) or 3 hour (6 mile) hike along this scenic river.

“The Eno River Association has been working on land and water quality conservation in the Eno River Basin for more than 45 years. It was instrumental in the creation of the Eno River State Park in the early 1970s and continues to actively work to expand protected areas. The Association’s efforts have resulted in the protection of more than 6,700 acres in the watershed.”