NIH 101:
Peer Review and Priority Setting

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Coalition to Promote Research
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Biology is complicated

Gene OFF ⟷ Gene ON

Fertilized Egg → Adult

Fat buildup ⟷ Fat breakdown

Non-dividing cell ⟷ Dividing cell

Unconnected neuron → Connected neuron

Young organism → Old organism

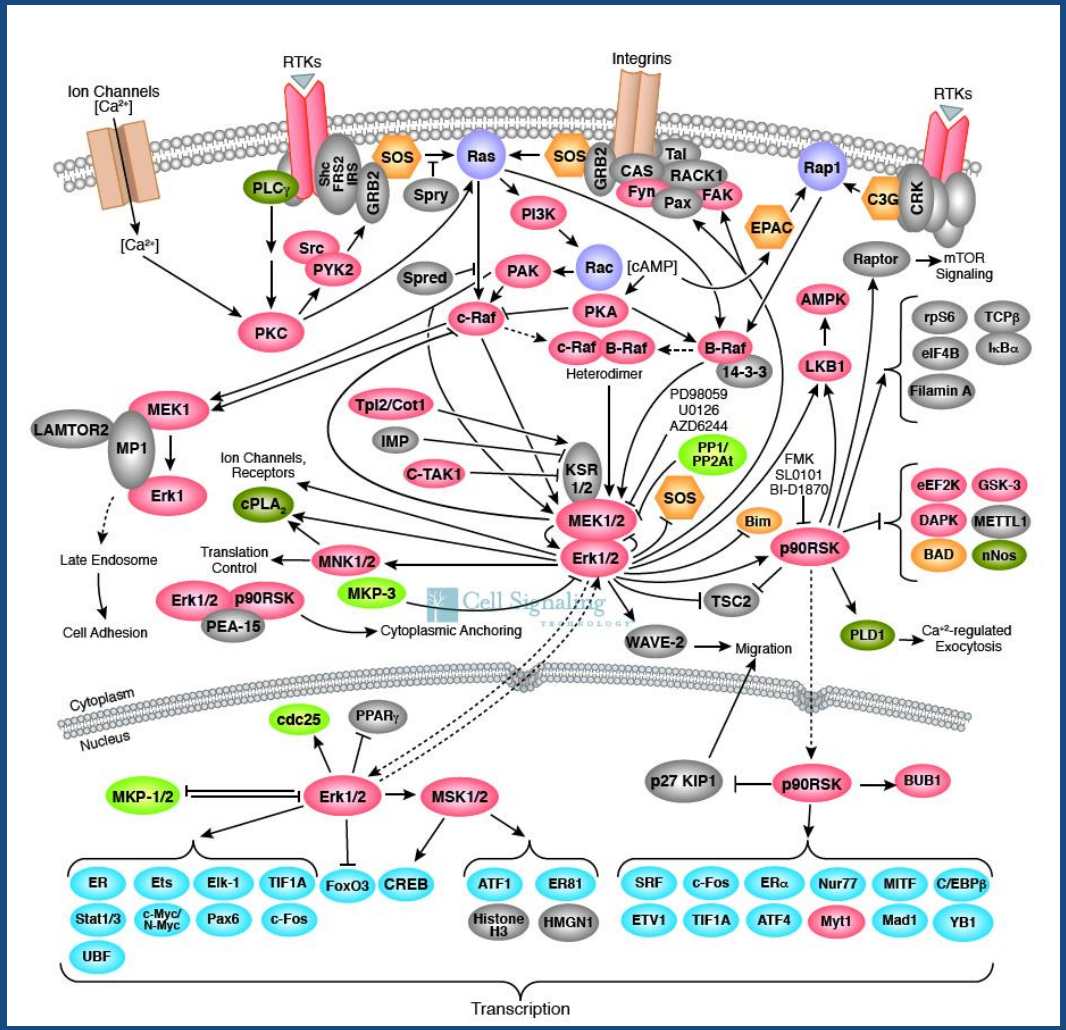
These processes are not controlled by simple switches, or even by long, multi-step, linear pathways.

Such "hard-wiring" would render us unable to sense and respond to changes in time and environment.

So, instead…

Networks of interacting genes control biological processes

"Sensors" allow adaptation to physiologic and environmental changes



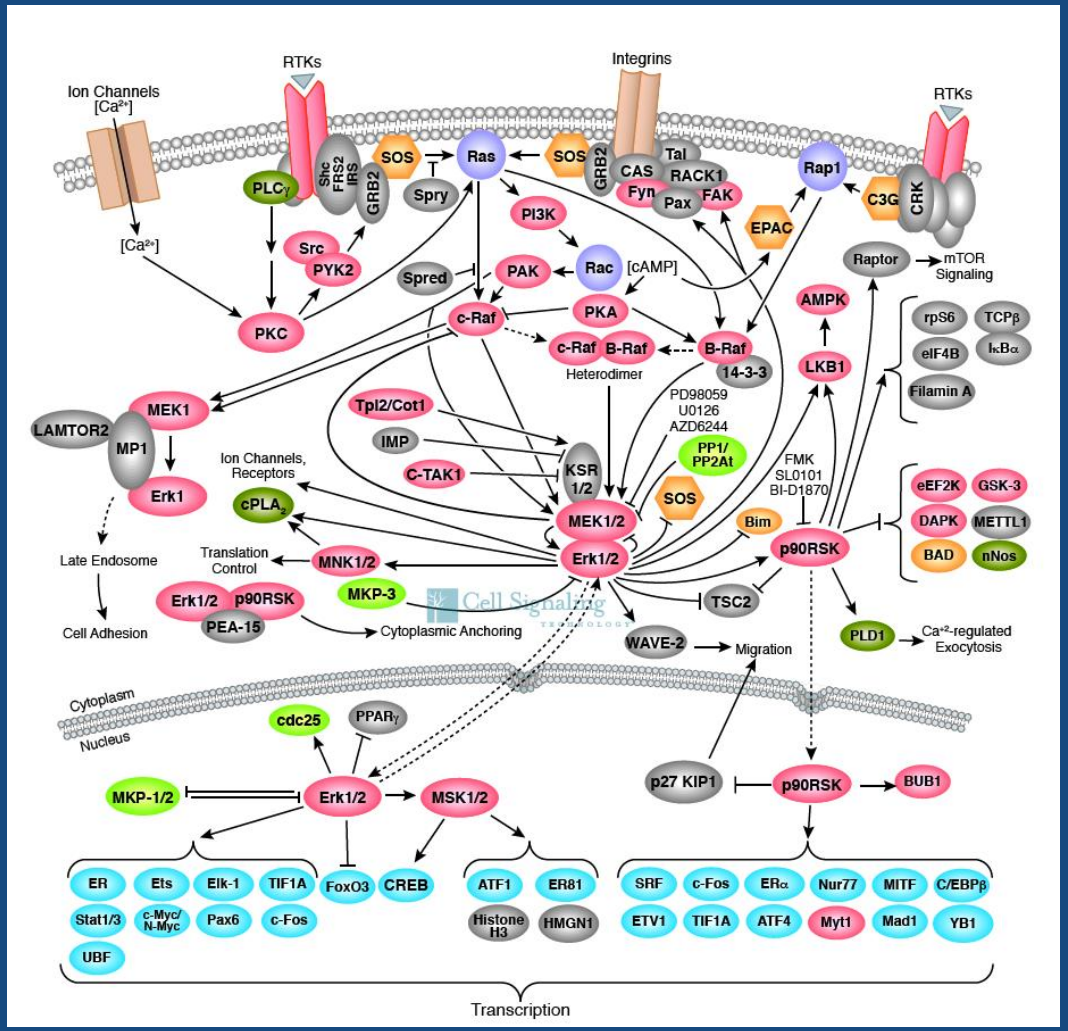
The result: Biology is complicated. Therefore, so is disease.

NIH Research: Understand *biology* to treat and cure *disease*

What is a disease gene?

If I have one, why does it only change the "risk", sometimes by tiny amounts, that I will get the disease?

Why does disease diagnosis so often seem almost like guesswork?



How could gathering more information about me, about other people, about mice, fruit flies and yeast, make my health better?

Complex organisms (like us) evolved from simpler ones

Complex organisms evolved by addition of new "layers" of sensors and regulators onto those in simpler organisms

Therefore, we can "unpack" complexity by basic (fundamental, discovery) research on both simple and complex organisms

It works. Look at the sources of big breakthroughs:

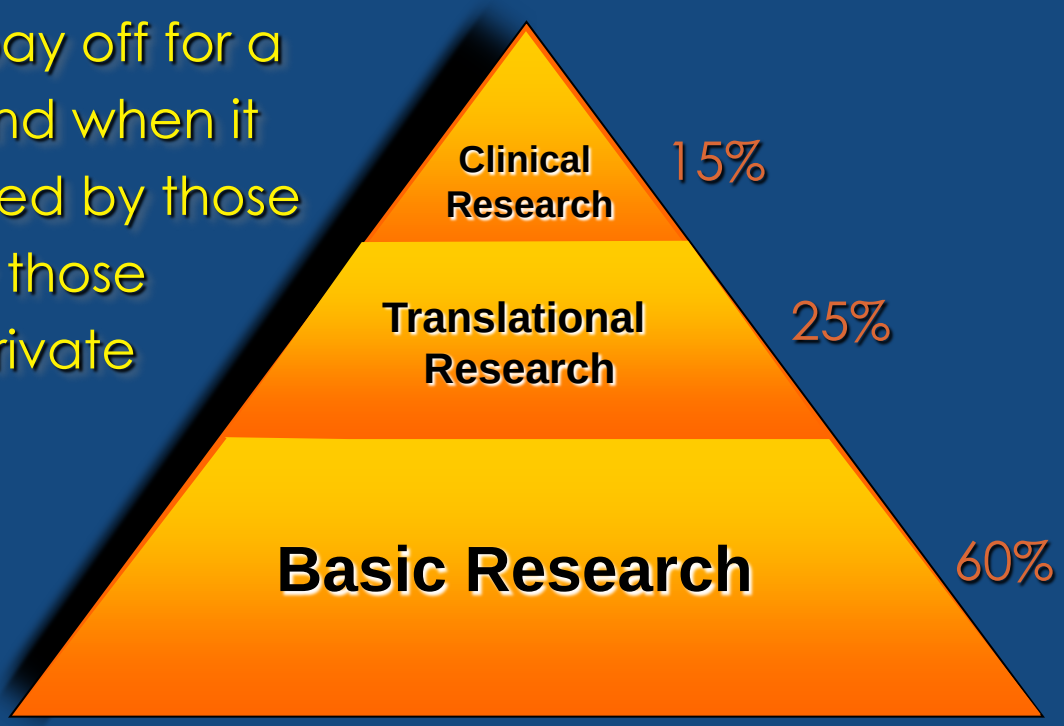
Breakthrough	Experimental organism
Gene regulation	*bacteria and their viruses*
Cell division	*baker's yeast, clawed toad*
Cancer genes	*chicken virus*
Development	*fruit fly, sea urchin, fish*
Aging and lifespan	*soil worm, pond scum*
Learning and memory	*sea snail*
Neuron-target connections	*chicken*

We still have a long way to go. How organize and prioritize?

The NIH research portfolio

An investigation… might not pay off for a year, or a decade, or at all. And when it does, the rewards are… enjoyed by those who bore its costs, but also by those who did not. That's why the private sector under-invests in basic science – and why the public sector *must* invest in this kind of research.

President Barack Obama
2009



Basic scientific research… provides scientific capital.

Vannevar Bush
1945

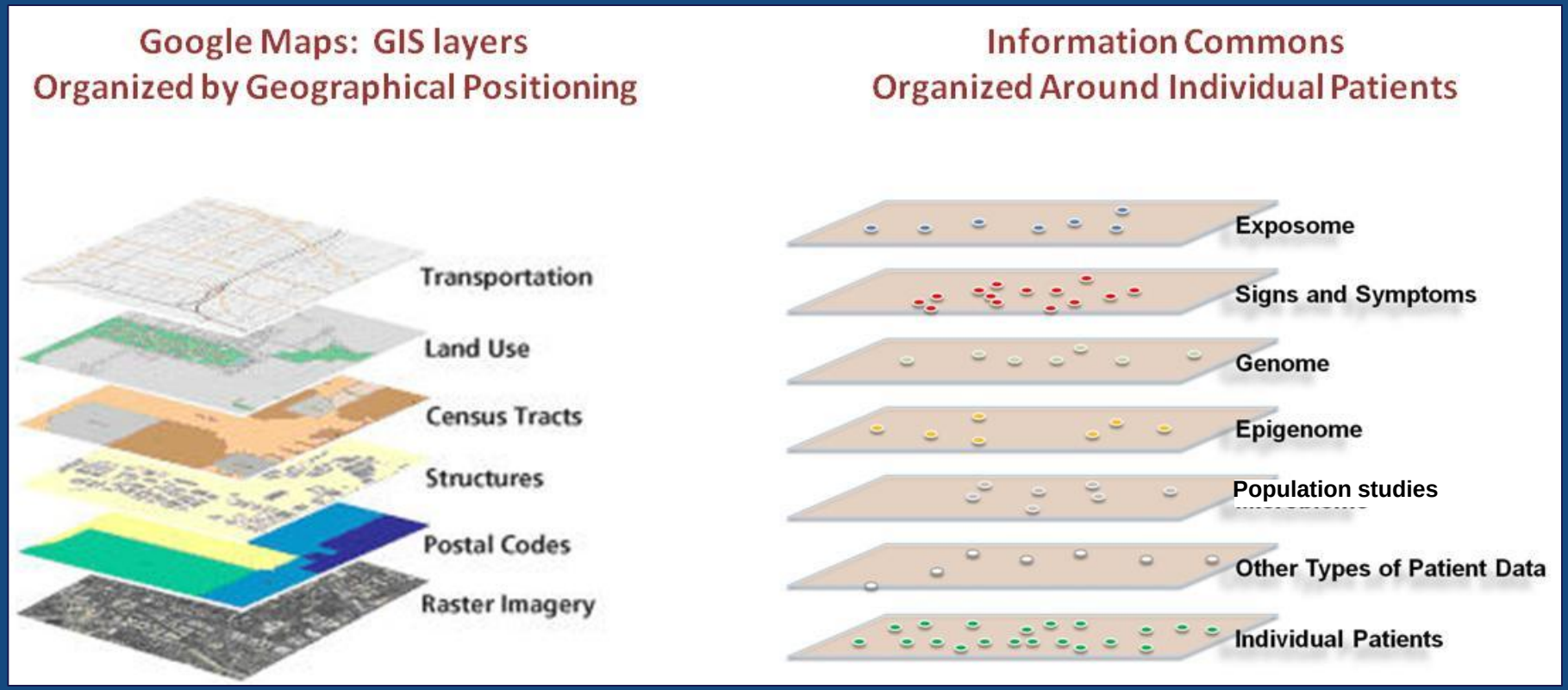
Prioritization: Collect lots of data about lots of processes in lots of organisms. And use to understand and treat disease.

“And that’s why we’re here today. Because something called precision medicine … gives us one of the greatest opportunities for new medical breakthroughs that we have ever seen.”

President Barack Obama

January 30, 2015

Precision Medicine: Google maps for biology and disease



Precision medicine:

Build massive data network to aggregate and analyze information from patient cohorts, healthy populations, experimental organisms; determine disease mechanisms and networks; precise health advice, diagnosis, treatment for each individual

The challenges and outcomes of NIH research

- Prioritization

  [1] Study all biological processes where they can best be understood; [2] aggregate, integrate, analyze vast collections of biological data, creating a knowledge network; [3] use to inform diagnosis and treatment decisions for each individual, to empower further research, and to advance clinical care and inform patients and citizens.

- Compelling outcomes of precision medicine

  -- a research ecosystem that makes full use of discoveries in basic, clinical and social/behavioral sciences;
  -- health and health care tailored precisely to each individual; -
  - greater worker productivity, with a higher quality of life;
  -- reduced health care costs due to improved prevention, early precise diagnosis, better control of chronic disease, and avoidance of unnecessary tests and ineffective therapies.

But how can this be organized? How decide what to do and who will do it?

National Institutes of Health

A federation of **27 separate Institutes and Centers**; one of the agencies of the **Public Health Service**, which in turn is part of the **US Department of Health and Human Services**.

Nineteen Institutes fund biomedical research grants:

National Cancer Institute
National Eye Institute
National Heart, Lung, and Blood Institute
National Human Genome Research Institute
National Institute on Aging
National Institute on Alcohol Abuse and Alcoholism
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Biomedical Imaging and Bioengineering
National Institute of Child Health and Human Development
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute on Drug Abuse
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
National Institute of Nursing Research

Also:

- Center for Scientific Review (CSR)

Center for Information Technology
National Center for Complementary and Alternative Medicine
National Center for Research Resources
National Library of Medicine

NIH R01 Grants: Investigator-Initiated

Two levels of evaluation for every grant application:

1. *Study Section (peer review by expert scientists)*

   —> Knowledge

   Assess scientific merit

2. *Institute Council (scientists and nonscientists)*

   —> Money

   Assess relevance to institute, program portfolio

The Center for Scientific Review (CSR)

CSR oversees referral for the **>80,000 NIH Grant Applications** submitted per year, and reviews 70% of them in ~250 **Study Sections**, which are clustered under 24 **Integrated Review Groups (IRGs).**

AARR	AIDS and Related Research
BBBP	Behavioral and Biobehavioral Processes
BCS	Biochemical Sciences
BDA	Biology of Development and Aging
BPC	Biophysical and Chemical Sciences
BST	Bioengineering Sciences and Technologies
BDCN	Brain Disorders and Clinical Neuroscience
CVS	Cardiovascular Sciences
CDF	Cell Development and Function
DIG	Digestive Sciences
EMNR	Endocrinology, Metabolism, Nutrition and Reproductive Sciences
GGG	Genes, Genomes and Genetics
HEME	Hematology
IMM	Immunology
IDM	Infectious Diseases and Microbiology
IFCN	Integrative, Functional, and Cognitive Neuroscience
MDCN	Molecular, Cellular, and Developmental Neuroscience
MOSS	Musculoskeletal, Oral and Skin Sciences
ONC	Oncological Sciences
RES	Respiratory Sciences
RPHB	Risk, Prevention and Health Behavior
RUS	Renal and Urological Sciences
HOP	Health of the Population
SBIB	Surgical Sciences, Biomedical Imaging, and Bioengineering

What is NIH Peer Review? How does it work?

- Evaluation by biomedical scientists of the scientific merit of the research or proposed research of others; 83% of the $30B NIH budget allocated this way.

- Process is managed by the NIH Center for Scientific Review (CSR), which is independent of the NIH Institutes.

- Reviews are executed by Study Sections, committees of experts in a defined area, made up of working scientists who volunteer to serve.

CORE REVIEW CRITERIA FOR NIH GRANT APPLICATIONS

Each review must address and individually score (1 – 9) each:

Impact

- address an important problem?
- will scientific knowledge be advanced?
- effect on concepts or methods in this field?

Approach

- experimental design and methods appropriate to aims?
- acknowledge problem areas and consider alternative tactics?

Innovation

- employ novel concepts, approaches or methods?
- challenge existing paradigms or develop new methodologies?

Investigator

- appropriately trained to carry out work?
- appropriate work for experience of P.I. and collaborators?

Environment

- contribute to the probability of success?
- evidence of institutional support?

Scoring of NIH grant applications by study sections

Score	Descriptor	Strengths/Weaknesses
1	Exceptional	Exceptionally strong with essentially no weaknesses
2	Outstanding	Extremely strong with negligible weaknesses
3	Excellent	Very strong with only some minor weaknesses
4	Very Good	Strong but with numerous minor weaknesses
5	Good	Strong but with at least one moderate weakness
6	Satisfactory	Some strengths but also some moderate weaknesses
7	Fair	Some strengths but with at least one major weakness
8	Marginal	A few strengths and a few major weaknesses
9	Poor	Very few strengths and numerous major weaknesses

Reviewers assign integer scores to each of five criteria
Overall Impact/Priority Score computed as average of all committee member scores x 10: 10 - 90 (81 gradations)

Complexities of peer review and limits of knowledge

NIH peer review:

- acknowledges and manages intrinsic conflicts of interest
- operates on a massive scale across a broad scope
- incorporates complex metrics for *merit* and *success*
- imperfect; continues to evolve and improve

- Different types and styles of research merit support
  - >> Basic, translational, clinical, social/behavioral
  - >> Incremental, transformative

Is NIH peer review the best system? Alternatives?

NIH R01 grants are "bottom up": investigator initiated proposals evaluated by fellow working scientists

Alternatives:

- Central planning of research topics and projects
- Hierarchical (seniority, title) control of process
- ~Equal sharing of resources across community

By any measure, NIH peer review is not the *best* 'good way' to allocate resources for biomedical research—it's the *only* good way.

By any measure, NIH peer review is best…

Scientific publications, conceptual and technical advances, Nobel Prizes, effectiveness and efficiency (the "Starbuck's Test")

Ongoing commitment to excellence and enhancement offers continued promise for extraordinary scientific discovery and development.

BUT…

-Budget has been stagnant since 2003

-Only 1 in 7 meritorious grant applications is funded

-enormous opportunities and advances lost

What's the Starbuck's Test

… for effectiveness and efficiency of NIH research?

Over past 40 years, cardiovascular disease mortality has declined 60%
This means 1 million fewer deaths per year

What was the NIH investment, per American citizen per year, in $5 Starbucks beverages, that saved a million lives per year?

1

Would you give up one Starbucks per year to save a million lives?

Just think of what could be done if we gave up two!

NIH: The crown jewel of federal spending

Quality
Efficiency
Impact

Thanks to the volunteer efforts of your extramural scientists to identify the best research proposals and flag them for support

You can increase funding going to NIH research-- to institutions and scientists in your district