Shared Challenges and Opportunities
in Aging and Disaster Management:
Potential for US-Cuba Scientific Collaboration

Promotion of Basic Science:

- *Why basic science when applied goals are clear?*
- *Potential for US-Cuba basic science collaboration?*

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1945: US framework for federal support of science

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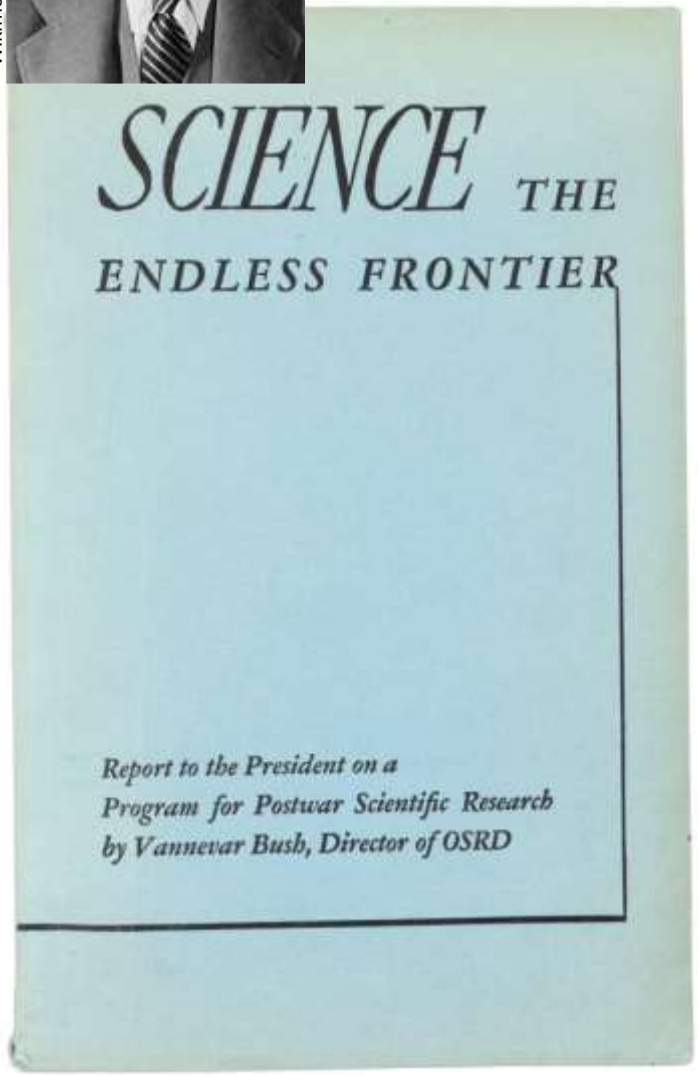


Vannevar Bush: *Science the Endless Frontier, a Program for Postwar Scientific Research* (1945)

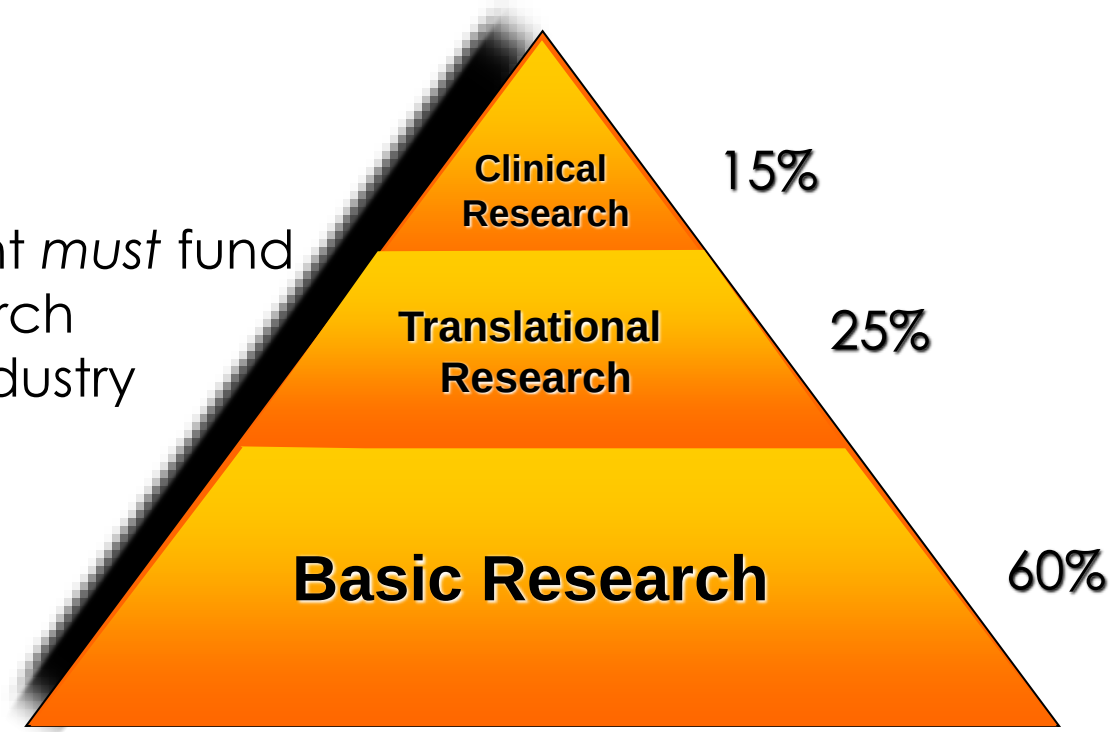
"New products and processes are not born full-grown. They are founded on new principles and new conceptions which in turn result from basic scientific research. Basic scientific research is scientific capital.

Colleges, universities, and research institutes provide the environment most conducive to the creation of new scientific knowledge and are least under pressure for immediate, tangible results.

Government can increase the flow of new scientific knowledge through support of basic research, and the development of scientific talent."

NIH Research Portfolio

Government *must* fund basic research because industry *can't*.

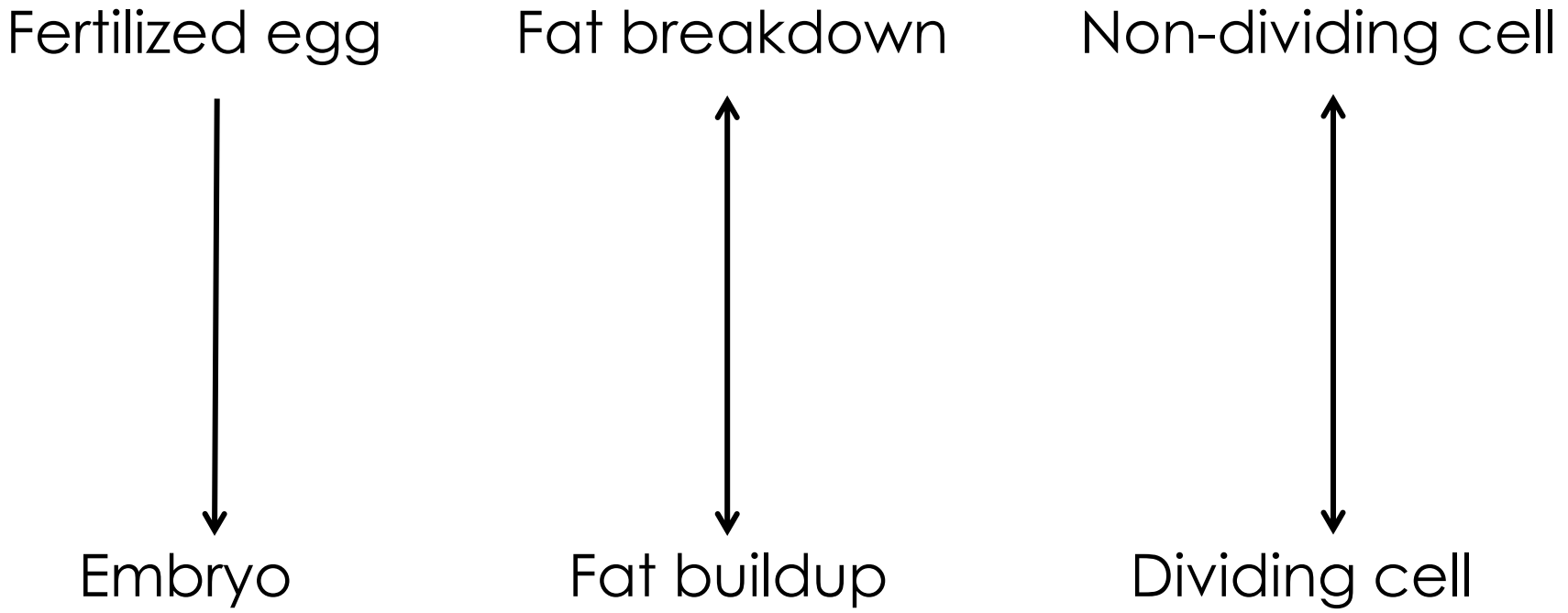


"Basic scientific research is scientific capital."

Priority: Discover fundamental mechanisms of biological processes. Use *untargeted, curiosity-driven research* as foundation to understand, treat and cure disease.

Why? Because…

…biology is complicated, and for a good reason!



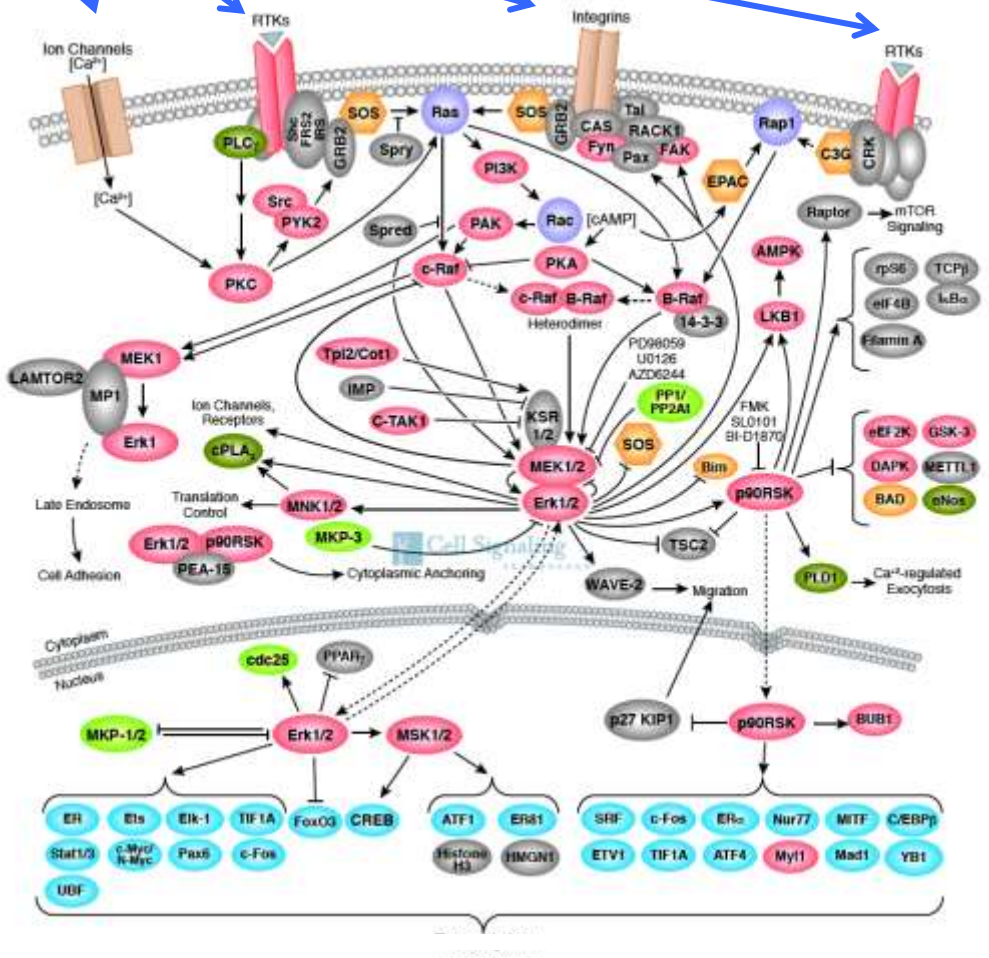
These processes are encoded in our DNA. But the processes themselves are not "hard wired"-- not simple switches, or even long, multi-step, linear pathways.

"Hard-wiring" would render us unable to sense and respond to differences in physiology, environment and experience.

So, instead…

Networks of interacting proteins alter expression of genes

Receptors receive physiological and environmental signals,
triggering signaling and regulatory pathways



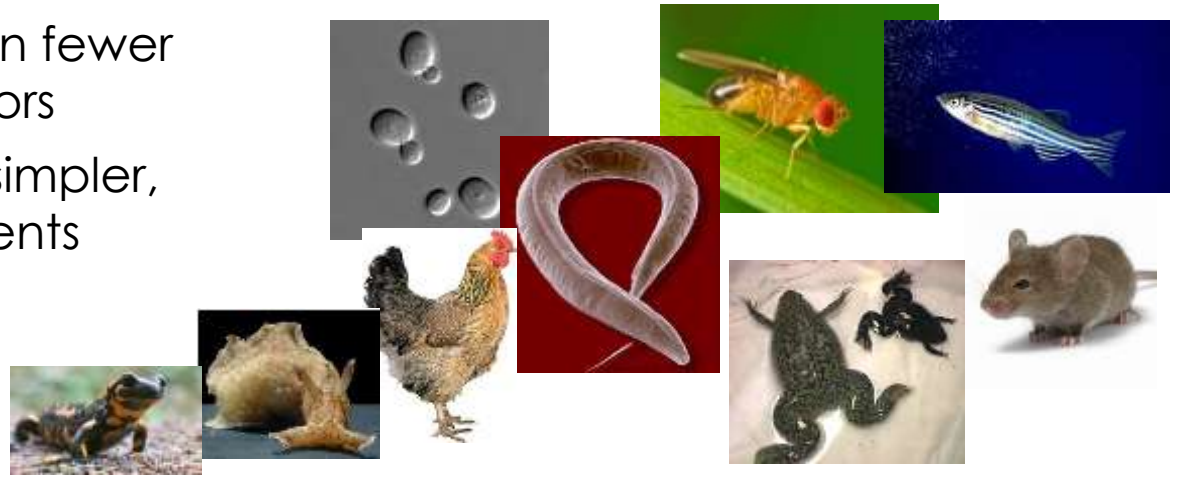
Genes for biological (or disease) process
(e.g., increased cell division, blood glucose, *etc.)*

- Biology is complicated; therefore, so is disease
- Mutations affecting receptors or protein networks affect risk or course of disease; all are "disease genes"
- *Basic research is essential to discover receptors, signaling genes, networks, interactions*

And a corollary…

Fundamental biological processes are often solved in simple organisms

- Simple organisms contain fewer layers of sensors/regulators
- Simple organisms allow simpler, more definitive experiments
- Complex organisms evolved from simple organisms



It works. Recall 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

And the new knowledge translates into applications…

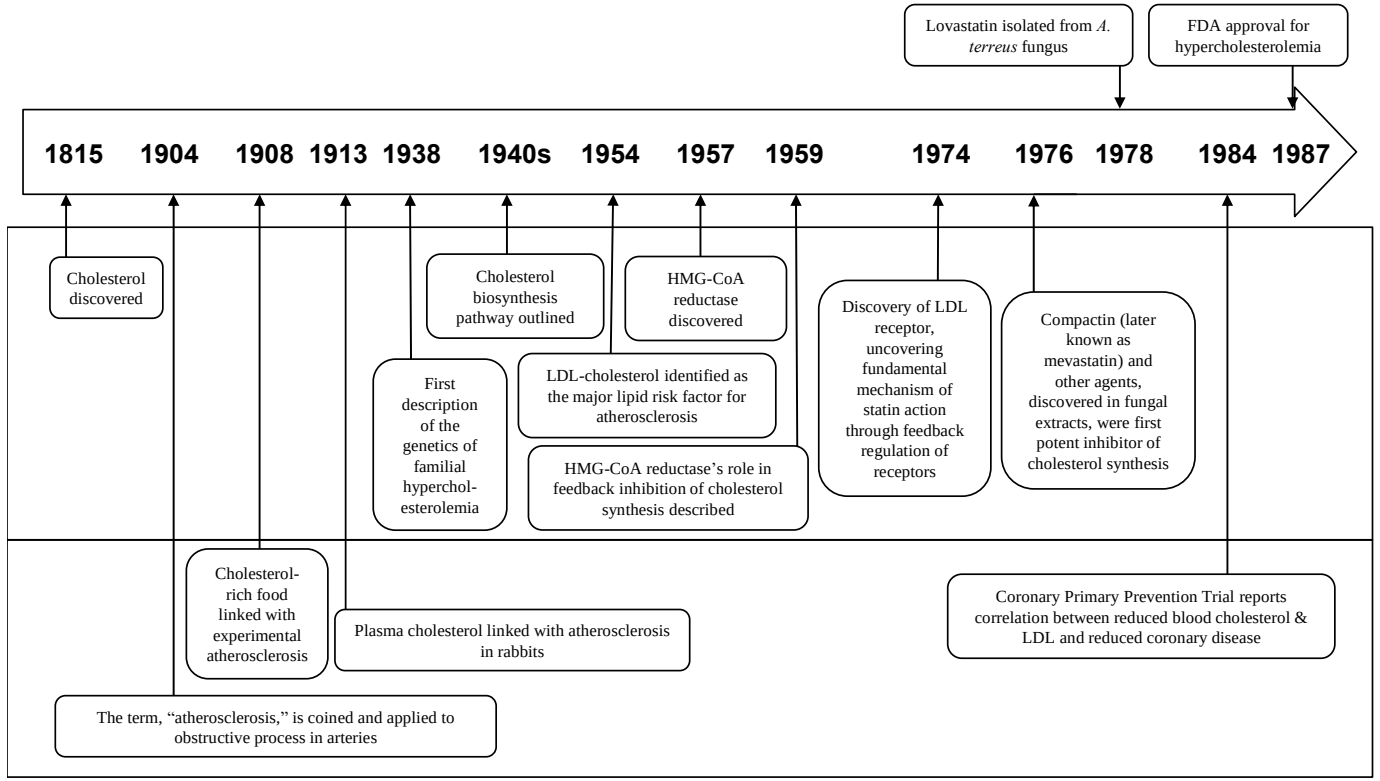
Basic research is the foundation for today's medicines

2010-2016: FDA approved 210 new drugs; >90% emerged from NIH-supported untargeted, curiosity-driven knowledge discovery (Cleary et al. PNAS 2018)

24 of the 28 most transformative drugs on the market emerged from untargeted knowledge discovery (Spector et al. Science Trans Med 2018)

Median time from first curiosity-driven basic discovery to FDA approval: 32 years

Example: *Lovastatin*



Spector et al. Science Trans Med 2018

But, can curiosity-driven research be done by international collaboratives?

International collaborative basic research: an example

QBI Coronavirus Research Group (QCRG)

Launched March 2020 by Nevan Krogan, UCSF;
Initially 10 UCSF labs, grew to 113 labs, 44 institutions, 12 countries, >1000 researchers; partner with 15 companies

Shared basic research goals: SARS CoV2 biology, COVID pathology, identification of molecules that contact or interact with viral proteins

Collaborating teams bring different resources and expertise, approach shared goals with different conceptual or technological strategies; rapid basic progress, "handoff" to partners for application development.

- >50 papers published
- Provided reagents and resources with >400 labs world-wide
- Identified 332 cellular proteins that interact with SARS CoV2 proteins
- Gained fundamental understanding of transmissibility; identified targets
- 26 drugs in clinical trials, one in Phase 3

Promotion of basic science?

Basic knowledge discovery remains essential

- Must maintain robust commitment to basic research
  - Today's *applied goals* are clear only because of yesterday's *discovered knowledge*
  - In all fields, *e.g.,* biology, still vastly more *unknown* than *known*
  - New knowledge enables innovation, development, products

- A formula for US-Cuba basic research collaboration:
  - Identify shared interest by US and Cuban scientists in a particular matter (*e.g.,* virus-host interactions, aging, disaster management) to be addressed
  - "Work backward" to identify related foundational unresolved questions/problems that stir curiosity of basic scientists
  - Assemble teams from US and Cuba that bring different resources, disciplinary expertise or technologies to the collaborative

Promotion of, defense of, basic knowledge discovery

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ding pain, ugliness, and
world has always been a
sed sort of place—yet
and scientists have ig-
that would, if attended
m. From a practical
tellectual and spiritual
life is, on the surface, a useless form of activity, in which men indulge because they procure for themselves greater satisfactions than are otherwise obtainable. In this paper I shall concern myself with the question of the extent to which the pursuit of these useless satisfactions proves unexpectedly the source from which un-

their pupils and students are destined to pass their lives. Now I sometimes wonder whether that current has not become too strong and whether there would be sufficient opportunity for a full life if the world were emptied of some of the useless things that give it spiritual significance; in other words, whether our conception of what is useful may not have become too narrow to be adequate to the roaming and capricious possibilities of the human spirit.

We may look at this question from two points of view: the scientific and the humanistic or spiritual. Let us take the

- essay in Harpers, 1939

Curiosity, which may or may not eventuate in something useful, is probably the outstanding characteristic of modern thinking. It must be absolutely unhampered.

I [am] pleading for the abolition of the word 'use', and for the freeing of the human spirit.

- Flexner 1939

Flexner describes a great paradox of scientific research: the search for answers to deep questions, motivated solely by curiosity and without concern for applications, often leads not only to the greatest scientific discoveries but also to the most revolutionary technological breakthroughs. In short, no quantum mechanics, no computer chips.

- Princeton University Press 2017