Quality and performance improvement in life sciences research

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TO ACCELERATE DISCOVERIES

Major quality defects and their frequencies in research

Defect	Evidence	Reference
High rate of non-reproducible preclinical research results in studies (75%-89%)	Bayer scientists were able to reproduce only 21% of 67 target-validation projects; Amgen scientists found only 11% reproducible in among 53 studies	Prinz, 2011 Begley, 2012
Frequent design and conduct deficiencies of preclinical research (22% - 82%)	In study design category, missing power calculation 82.3%); In cell line category, mixed contamination 22.4% In analysis category, the use of chi-square test when expected cells < 5 frequency 15.7% In reporting category, failure to state number of tails 65%	Mansour, 2019
Between 40 to 74% of clinical trials provide uninformative results that are not meaningful for patient care, research or policy-making	The avoidable waste due to inadequate clinical trial methods was estimated at 42% The proportion of clinical trials meeting four conditions for informativeness was only 26.4%	Yordanov, 2015; Hutchinson, 2022
More than half of clinical trials become unfinished or non-reported.	Among completed trials, almost a third not published in the peer-reviewed literature after 4 years. More than half of clinical trials yielding negative results remain unpublished	Ioannidis, 2014, Rees, 2019

Reproducibility Deficiencies in Life Sciences Research I.

Group	Deficiency	Frequency
Study design	Sample/power calculation error	82%
Study design	Eligibility criteria not mentioned or inappropriate	50%
Study design	Randomization error	29%
Cell lines	Mixed contamination of cell lines	20%
Cell lines	Cell line cross contamination	17%
Cell lines	Misidentified cell lines	14%
Cell lines	Mycoplasma cell line contamination	8%
Cell lines	Cell line bacterial contamination	1%
Statistical analysis	Chi-square used when expected cells frequency < 5	14%
Statistical analysis	Parametric test for nonparametric data	13%
Statistical analysis	Related data independent test & vice versa	12%
Statistical analysis	Mean (SD) used for non-normal or ordinal data	7%

Mansour, N. M., Balas, E. A., Yang, F. M., & Vernon, M. M. (2020). Prevalence and Prevention of Reproducibility Deficiencies in Life Sciences Research: Large-Scale Meta-Analyses. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research, 26, e922016-1.

Preclinical to clinical transfer failure: Off-target toxicity

97% of drug-indication pairs that are tested in clinical trials in oncology never advance to receive U.S. Food and Drug Administration approval.

In a study of 10 cancer drugs targeting 6 proteins, the proteins ostensibly targeted by the drugs were nonessential for cancer cell proliferation. Moreover, the effect of each drug was unchanged by the loss of its putative target, (i.e., they kill cells via off-target effects).

Lin, A., Giuliano, C. J., Palladino, A., John, K. M., Abramowicz, C., Yuan, M. L., ... & Sheltzer, J. M. (2019). Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. Science translational medicine, 11(509), eaaw8412.

My 1st Paradox of Modern Life Sciences:

Huge benefits of research come from mostly wasted effort!

Science has never been so beneficial, appreciated, and exciting as it is today. It gave us the COVID vaccine within one year, made many cancers curable, and hugely increased our overall life expectancy, among others.

At the same time, vast amounts of scientific publications are non-reproducible uninformative and generally useless.

Corollary: societal benefits could probably double by just 10% better scientific productivity and quality research.

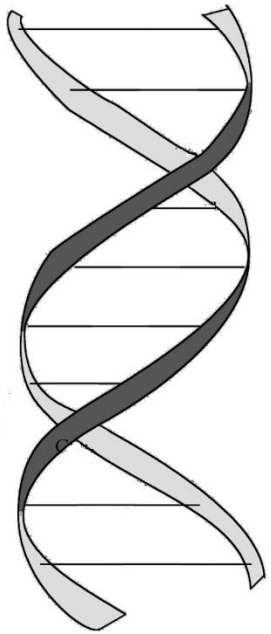
Biomedical research innovation

Science

Replicable

Generalizable

Peer-reviewed



Invention

Useful

Novel

Non-obvious

Nobel Prize for discoveries of machinery regulating vesicle traffic

Thomas C. Südhof, M.D.

"In my personal case the work that we performed that I think led to this prize was actually work that initiated 25 years ago and there were a lot of important observations, but in the end the promise of these observations only materialized or became more concrete very recently because continuing experiments in our lab backed them up, expanded them, explained them and gave them substance. I actually don't think that there was any single eureka moment in my career, **there were many small eureka moments, but not just one discovery,** it's in fact the whole question I am working on and I think that **our work has contributed to understanding a process** that involves or necessitates, more than understanding one little thing or one big thing, but understanding really how it works."

Transcript from an interview with Thomas C. Südhof. NobelPrize.org. Nobel Prize Outreach AB 2024. Sat. 2 Nov 2024.
https://www.nobelprize.org/prizes/medicine/2013/sudhof/160393-thomas-c-sudhof-interview-transcript/

Dr. Katalin Karikó, Prof. Ugur Sahin and Prof. Özlem Türeci Honored with the Friends of the National Library of Medicine's 2024 Distinguished Medical Science Award

My 2nd Paradox of Modern Life Sciences:

Effective research is hugely diverse but generally the same!

Every research projects is different regarding specialty, questions, sample, methods, proteomics, knock-out mouse, clinical trial, cell imaging, qualitative research, data science, and more.

Neither hyper-founded PIs (>$100M in NIH grants) nor hyper-prolific researchers (>72 publications per year), nor the geniuses (MacArthur Fellows) have ever received the Nobel prize for a great discovery.

Corollary: better understanding of common driving factors could make research much more effective.

Public Science

Public science recognizes that numerous, generally influential research factors, skills, and cultures drive research projects, teams, laboratories across highly diverse disciplines of life sciences.

Examples: obtaining funding for research; developing publishable results; maintaining well-functioning team culture; research quality control; producing results for use and benefit of society; filtering out imported research errors; and effectiveness in using research budget. Common science studies are often called 'research on research‘ or ‘science of science’

Public science aims to address the community factors of research by reducing waste, elevating productivity, and maximize societal benefits of research, including increasing impact on subsequent research, public health improvement, and economic progress.

Best practices of innovative laboratories

By drawing on lessons from 400 Nobel Prize winners, other award-winning scientists, serial innovators, and leading research universities, 12 transformative competencies of successful biomedical researchers are described, analyzed, and illustrated with many inspiring case studies.

Balas, E. A. (2018). Innovative Research in Life Sciences: Pathways to Scientific Impact, Public Health Improvement, and Economic Progress. Wiley.

The Next Game:

Impact of Research

Scientific impact

1. Publications
2. Citations
3. Collaborations and training
4. New research methods
5. Improved productivity

Public health improvement

1. Understanding of a disease, disorder or condition
2. New tests and treatments
3. Improved wellness and life expectancy
4. More effective health policy or legislation
5. Change in clinical practice
6. Enhancement of community health

Economic progress

New startup companies

New products and services

More efficient production

Breakthrough technologies

The Next Game:

Great scientist make a direct impact…

1. Robert Koch
   - microbiologist, discoverer of the causative agents of tuberculosis, cholera, and anthrax, Koch postulates, Nobel Laureate
   - He eradicated malaria in the Adriatic island of Brioni

2. Louis Pasteur
   - developments of vaccines for rabies and anthrax, germ theory of disease
   - Visited vineries and developed the pasteurization

Partnership of democracy and scientific progress

1) Widespread deficiencies of research quality and non-reproducible results
2) Tectonic shift in the production of life sciences
3) Scientific evidence is out of sight while misinformation puts lives at risk
4) Simply spending more on research will not be enough in the global competition

Balas, E. A., De Leo, G., & Shaw, K. B. (2024). Strategic policy options to improve quality and productivity of biomedical research. Politics and the Life Sciences, 1-12.

Headwinds of science: harms and risks of health misinformation

Defect	Evidence	Reference
High frequency of misinformation	Health misinformation was most prevalent related to smoking products and drugs such as opioids and marijuana (87%), vaccines (43%), diets or eating disorder (36%), non-communicable diseases and pandemics (40%), and medical treatments (30%).	Suarez-Lledo, 2021
High frequency of misinformation	800 vaccine-related Pinterest posts and found that 74% were anti-vaccine in sentiment	Guidry, 2015
Rapid spread of misinformation	Misinformation about Zika was three times more likely to be shared than verified stories on social media, with half of the top 10 news stories regarding Zika were misinformation.	Sommarive, 2018
Misinformation by peers is most difficult to correct	A meta-analysis of social media interventions designed to correct health-related misinformation. Interventions were more effective when misinformation was distributed by news organizations (vs. peers) and when debunked by experts (vs. non-experts).	Walter, 2021

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Strategic policy options to improve quality and productivity of biomedical research

1) Funding projects with higher expectations of reproducibility
2) Public-private partnerships for contemporaneous quality support in laboratories;
3) Making research institutions accountable for quality control;
4) Supporting new quality filtering standards for scientific journals and repositories, and
5) Establishing a new network of centers for scientific health communications.

Balas, E. A., De Leo, G., & Shaw, K. B. (2024). Strategic policy options to improve quality and productivity of biomedical research. Politics and the Life Sciences, 1-12.

Meaningful research is a marathon run, not short distance sprinting

<- from my 20th Marathon in 2024

Thank you!