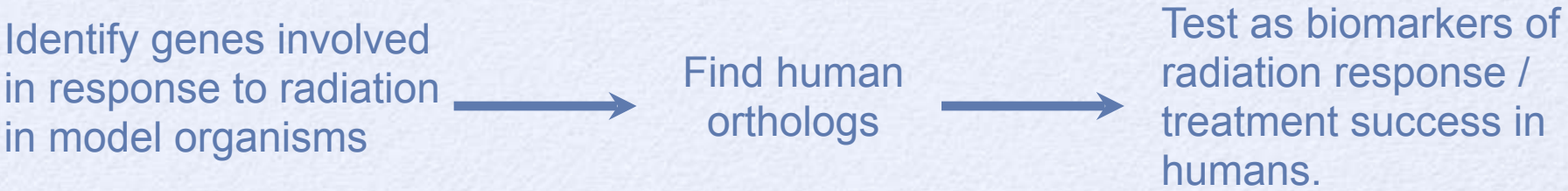
Работы по системной биологии – это...

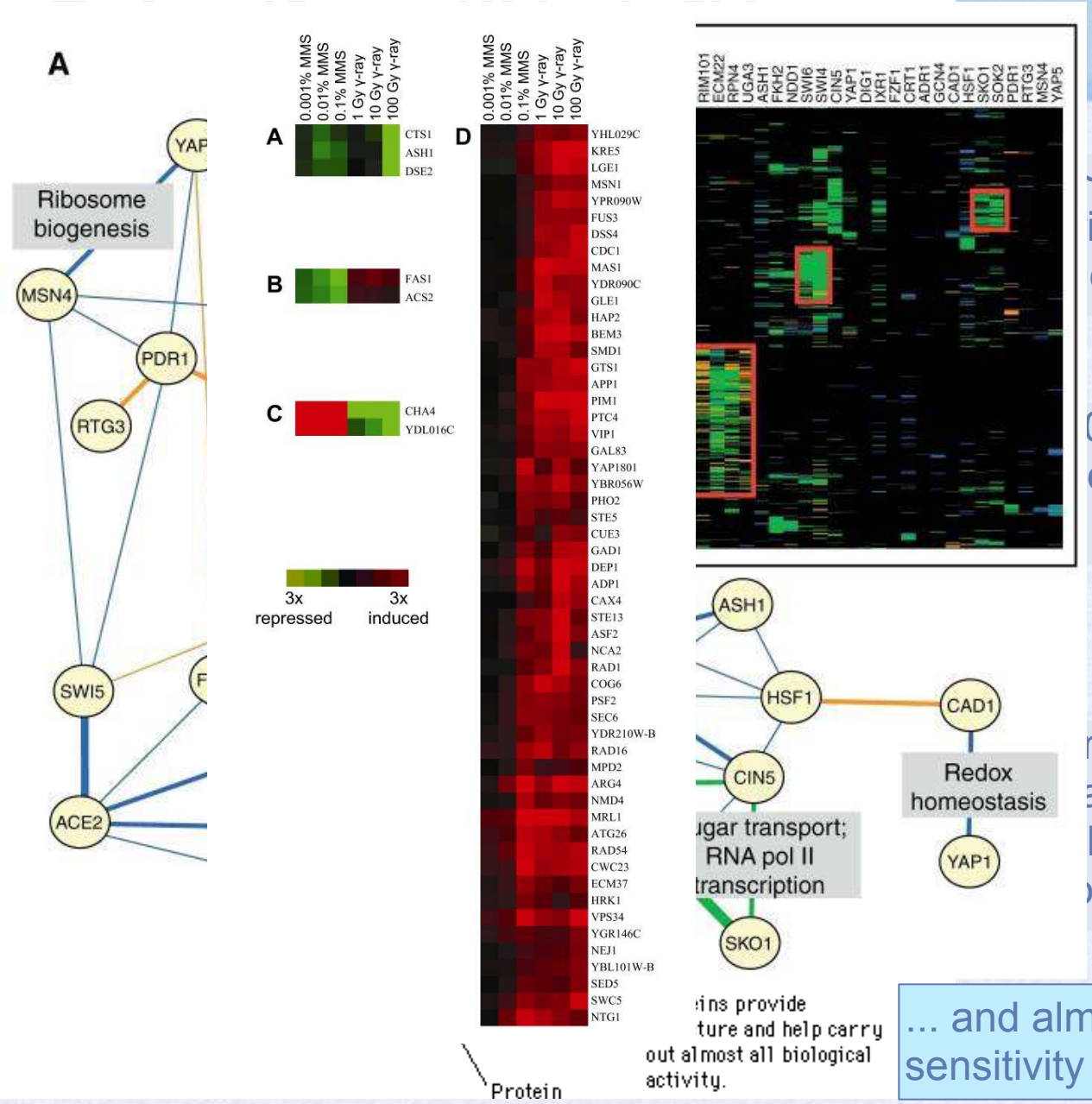
«А вдруг они не золотые? - спросил любимый сын лейтенанта Шмидта»

Проблемы с биологией...
С системной ли?



Mainly, data mining

Working with yeast data…



~5000 DDR-related
iption factors binding
entified on DNA

0 genes are responsive to
e

roteins responsive to
amage are identified,
hem are NOT
onally responsive

... and almost **NONE** change the sensitivity to radiation when mutated

Why Most Published Research Findings Are False?

PLoS MEDICINE

John P. A. Ioannidis

August 2005 | Volume 2
Issue 8 | e124

?

Publishers withdraw more than 120 gibberish papers

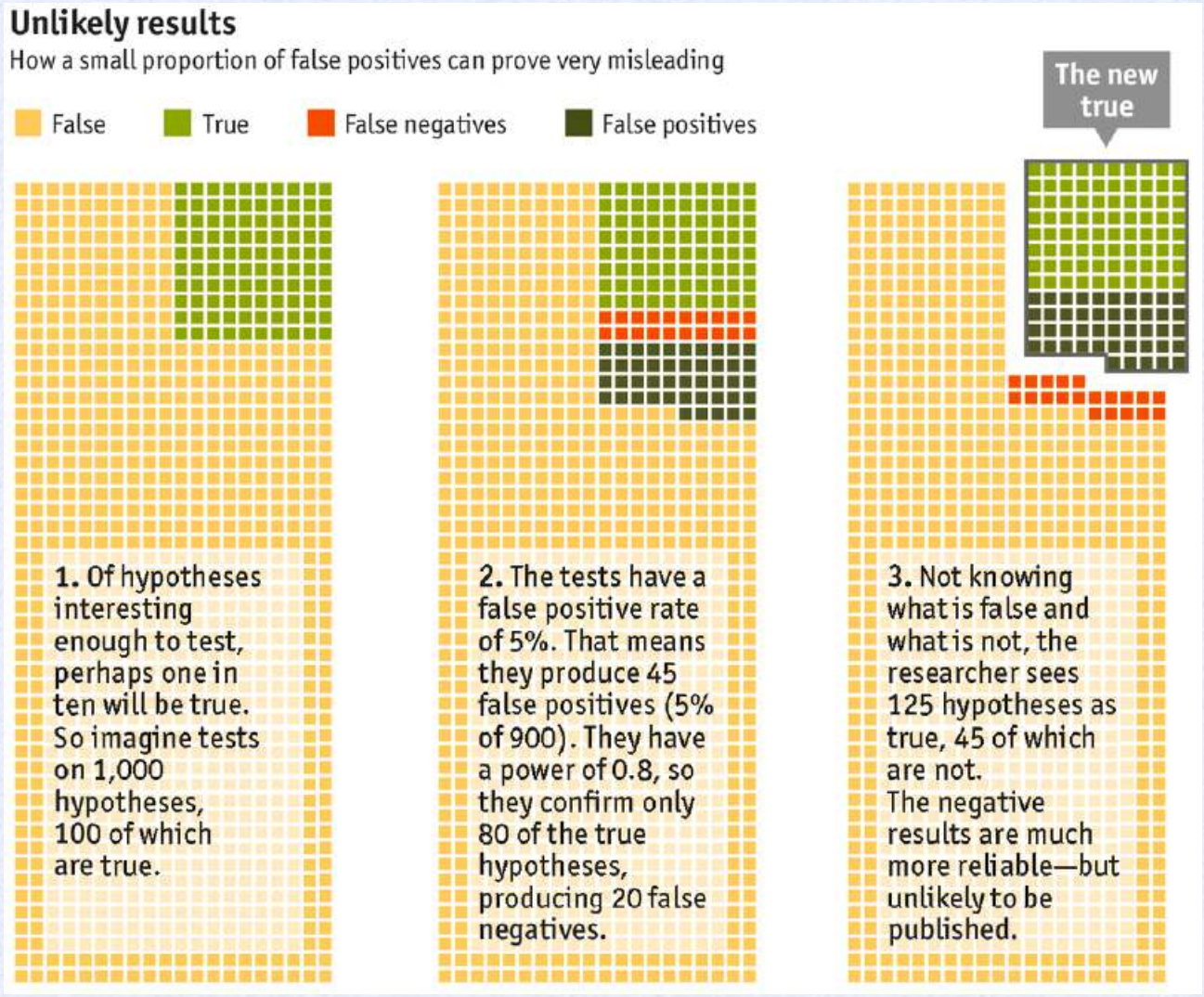
… after scientist reveals that they were computer-generated.

Richard Van Noorden

Scientific world getting duped by computerized fake research papers

CBS NEWS

Why Most Published Research Findings Are False?



PLoS MEDICINE

John P. A. Ioannidis

вероятность правильности найденного тем меньше...

... чем больше количество проверяемых взаимоотношений

... чем больше гибкости в постановке опытов, их анализе и интерпретации

... чем больше финансовая заинтересованность

... чем «горячее» поле исследований

Why Most Published Research Findings Are False?

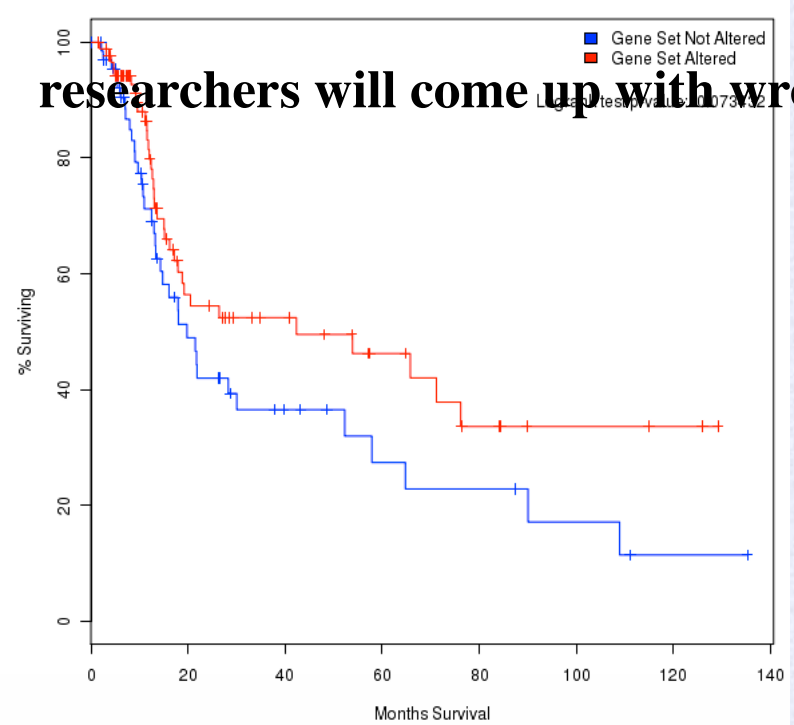
a detailed mathematical proof that, assuming

PLoS MEDICINE

John P. A. Ioannidis

modest levels of researcher bias
typically imperfect research techniques
the well-known tendency to focus on exciting rather than highly plausible theories

researchers will come up with wrong findings most of the time.



cutoff	p-value
2.1	**0.0273**

We really don't care what statistical method you used

Abstract

Formula display: MathJax

Background

Many groups, including our own, have proposed the use of DNA methylation profiles as biomarkers for various disease states. While much research has been done identifying DNA methylation signatures in cancer vs. normal etc., we still lack sufficient knowledge of t
methylation plays during normal cellular differentiation and tissue specific
thorough, genome level studies to determine the meaning of methylation
dinucleotides in terms of gene expression.

Results

In this study, we have used (insert statistical method here) to compile uni
signatures from normal human heart, lung, and kidney using the Illumina
methylation arraysand compared those to gene expression by RNA seque
unique signatures of global DNA methylation for human heart, kidney and
DNA methylation data can be used to correctly classify various tissues. It
methylation reflects tissue specificity and may play an important role in tissue dif
integrative analysis of methylation and RNA-Seq data showed that gene methylat
transcriptional levels were comprehensively correlated. The location of methylatic
terms of distance to transcription start site and CpG island showed no effects on t
gene expression by DNA methylation in normal tissues.

Conclusions

This study showed that an integrative analysis of methylation array and RNA-Seq
utilized to discover the global regulation of gene expression by DNA methylation and suggests that DNA methylation plays an important role in normal tissue differentiation via modulation of gene expression.

Wo aber auf der Oberfläche der Zufall sein Spiel treibt, da wird er stets durch innre verborgne Gesetze beherrscht

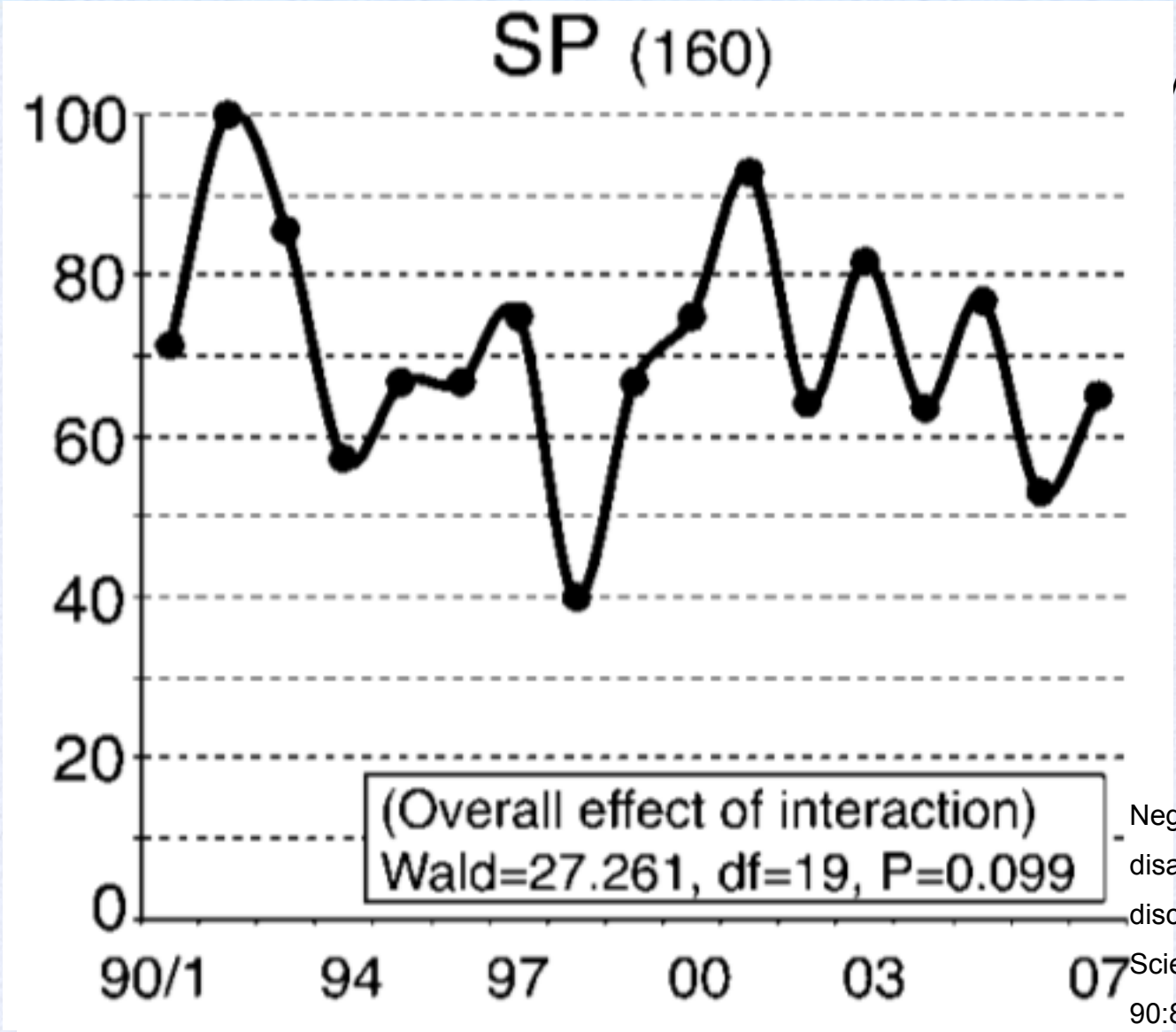
F. Engels. «Ludwig Feuerbach und der Ausgang der klassischen deutschen Philosophie».

https://nsaunders.wordpress.com/2012/07/23/we-really-dont-care-what-statistical-method-you-used/

***Update**: as pointed out in the comments, the amusing error in this article has been "corrected" (or at least, "edited away").*

An integrative analysis of DNA methylation and RNA-Seq data for human heart, kidney and liver
BMC Systems Biology 2011, 5(Suppl 3):S4

Percent of research papers with positive results



& Genetics

Negative results are disappearing from most disciplines and countries

Scientometrics (2012) 90:891–904

Open Journals are the answer!

- Online only
- Peer-reviewed
- Should be not afraid of publishing negative data
- Directory of Open Access Journals (DOAJ) lists >8000 journals

Who's Afraid of Peer Review?

- The goal was to create a credible but mundane scientific paper, one with such grave errors that a competent peer reviewer should easily identify it as flawed and unpublishable.

- Molecule X from lichen species Y inhibits the growth of cancer cell Z. (a database of molecules, lichens, and cancer cell lines and a computer program to generate hundreds of unique papers was used.

- The fictitious authors are affiliated with fictitious African institutions. Authors' names (such as Ocorrafoo M. L. Cobange) were generated by randomly permuting African first and last names harvested from online databases.

- For the affiliations, such as the Wassee Institute of Medicine, Swahili words and African names were randomly combined with generic institutional words and African capital cities.

- Paper was translated into French with Google Translate, and then translated the result back into English. After correcting the worst mistranslations, the result was a grammatically correct paper with the idiom of a non-native speaker.

Science 4 October 2013:
Vol. 342 no. 6154 pp. 60-65

Who's Afraid of Peer Review?

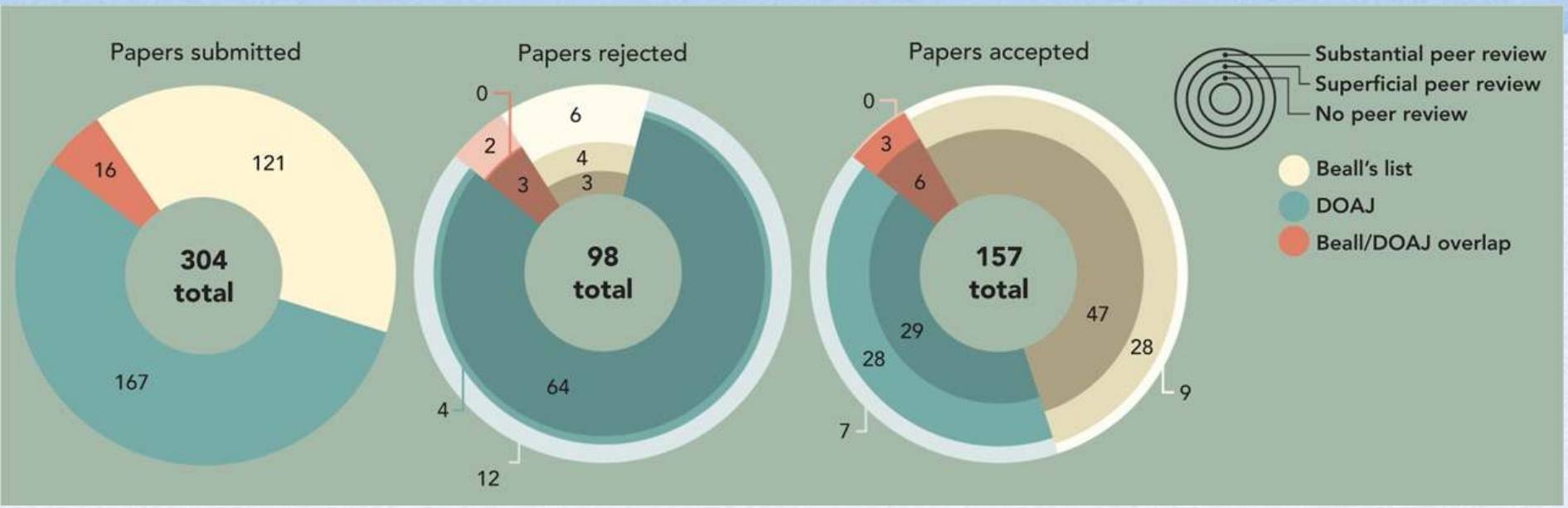
- The papers describe a simple test of whether cancer cells grow more slowly in a test tube when treated with increasing concentrations of a molecule. In a second experiment, the cells were also treated with increasing doses of radiation to simulate cancer radiotherapy. The data are the same across papers, and so are the conclusions: The molecule is a powerful inhibitor of cancer cell growth, and it increases the sensitivity of cancer cells to radiotherapy.

- There are numerous red flags in the papers, with the most obvious in the first data plot. The graph's caption claims that it shows a "dose-dependent" effect on cell growth—the paper's linchpin result—but the data clearly show the opposite. The molecule is tested across a staggering five orders of magnitude of concentrations, all the way down to picomolar levels. And yet, the effect on the cells is modest and identical at every concentration.

- One glance at the paper's Materials & Methods section reveals the obvious explanation for this outlandish result. The molecule was dissolved in a buffer containing an unusually large amount of ethanol. The control group of cells should have been treated with the same buffer, but they were not. Thus, the molecule's observed "effect" on cell growth is nothing more than the well-known cytotoxic effect of alcohol.

- The second experiment is more outrageous. The control cells were not exposed to any radiation at all. So the observed "interactive effect" is nothing more than the standard inhibition of cell growth by radiation. Indeed, it would be impossible to conclude anything from this experiment.

Who's Afraid of Peer Review?



- Only 36 of the 304 submissions generated review comments recognizing any of the paper's scientific problems. And 16 of those papers were accepted by the editors despite the damning reviews
- Black list (Beall's): 82% accepted the paper.
- "Good" list: 45% accepted the bogus paper.

•In 2012, Sage was named the Independent Publishers Guild Academic and Professional Publisher of the Year. The Sage's *Journal of International Medical Research*, without asking for any changes to the paper's scientific content, sent an acceptance letter and an invoice for $3100.

Cell

5-Year Impact Factor: 35

nature International weekly journal of science

5-Year Impact Factor: 42

Science AAAS

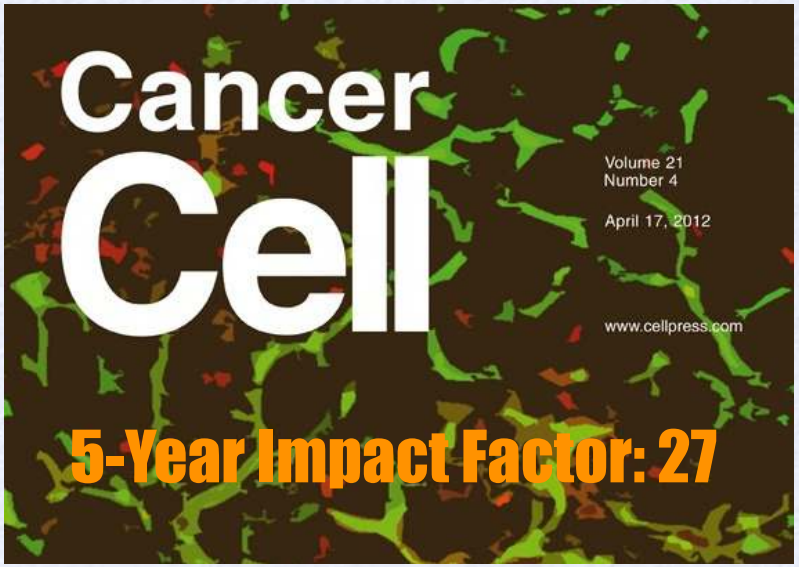
5-Year Impact Factor: 34

PNAS

5-Year Impact Factor: 11

Chemical Genomics Identifies Small-Molecule *MCL1* Repressors and BCL-xL as a Predictor of MCL1 Dependency

Guo Wei,[1,2,*] Adam A. Margolin,[1,5,*] Leila Haery,[1] Emily Brown,[1] Lisa Cucolo,[1] Bina Julian,[1] Shyemaa Shehata,[3] Andrew L. Kung,[2] Rameen Beroukhim,[1,3] and Todd R. Golub[1,2,4,#]



PubMed

Golub TR[Author]

Results: 1 to 20 of 200

Cancer Discov

J Clin Invest

Nat Genet.

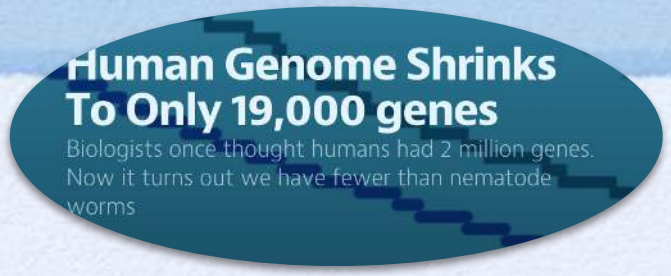
Nature

1) Cancer Program, The Broad Institute of MIT and Harvard, Cambridge

2) Department of Pediatric Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA 02115

4) Howard Hughes Medical Institute

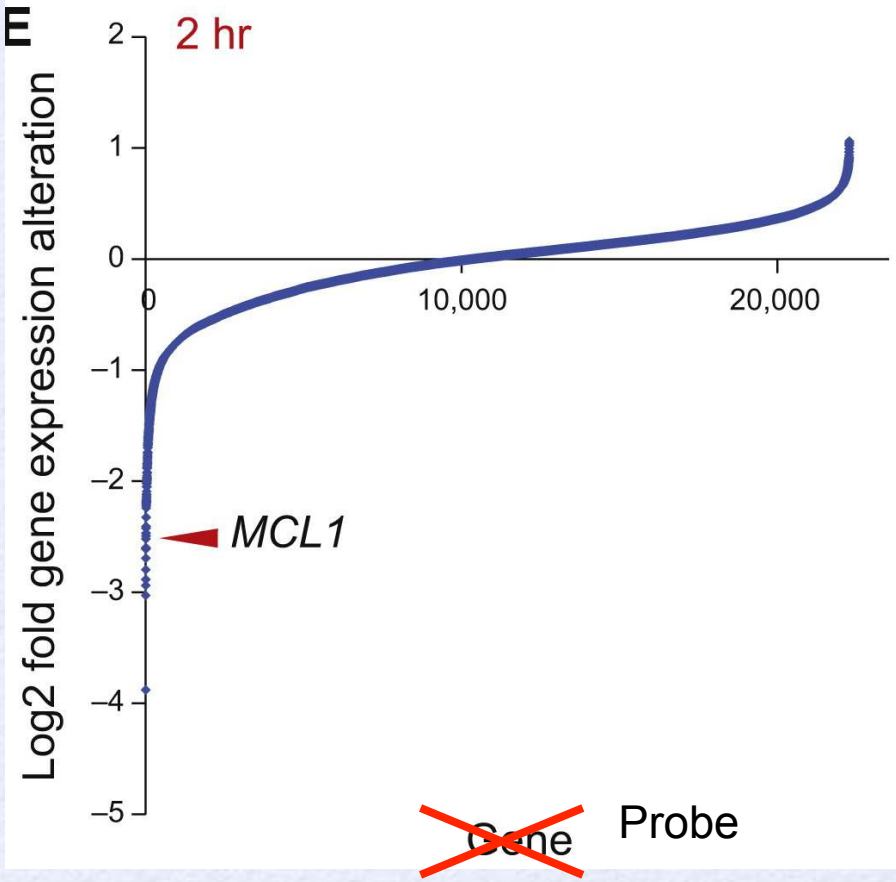
Figure 1



affymetrix
Biology for a better world

GeneChip Human Genome U133A 2.0 Array

representing **14,500** well-characterized human genes



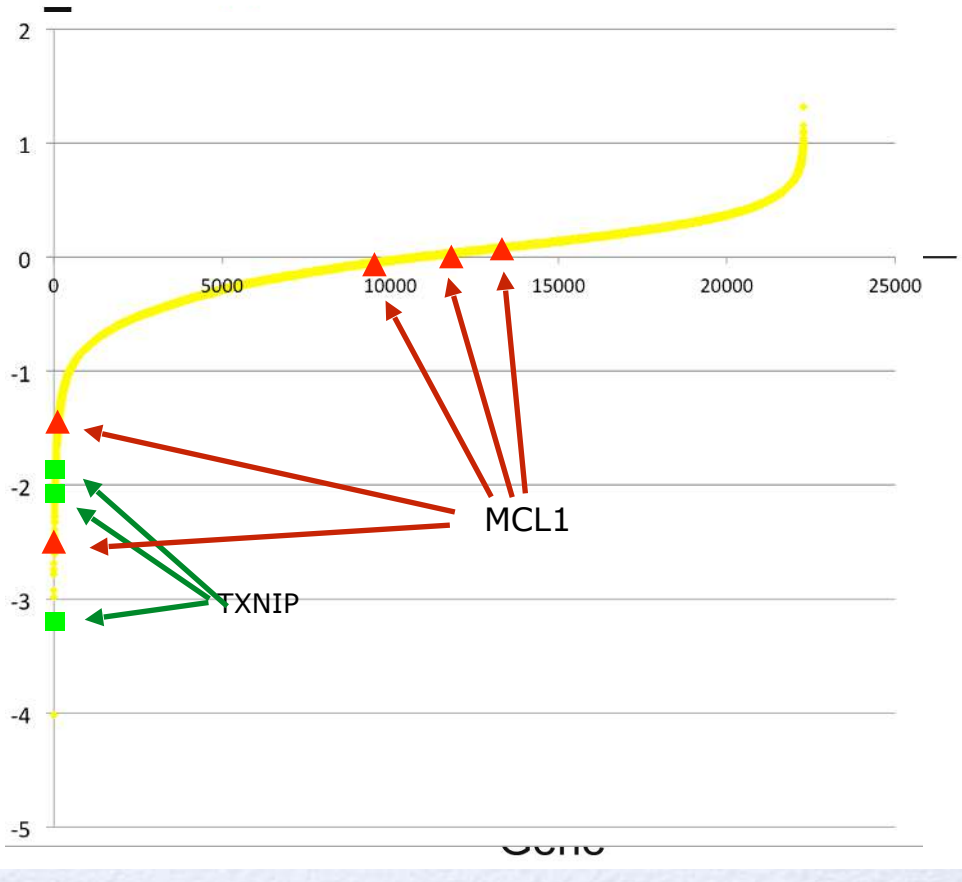
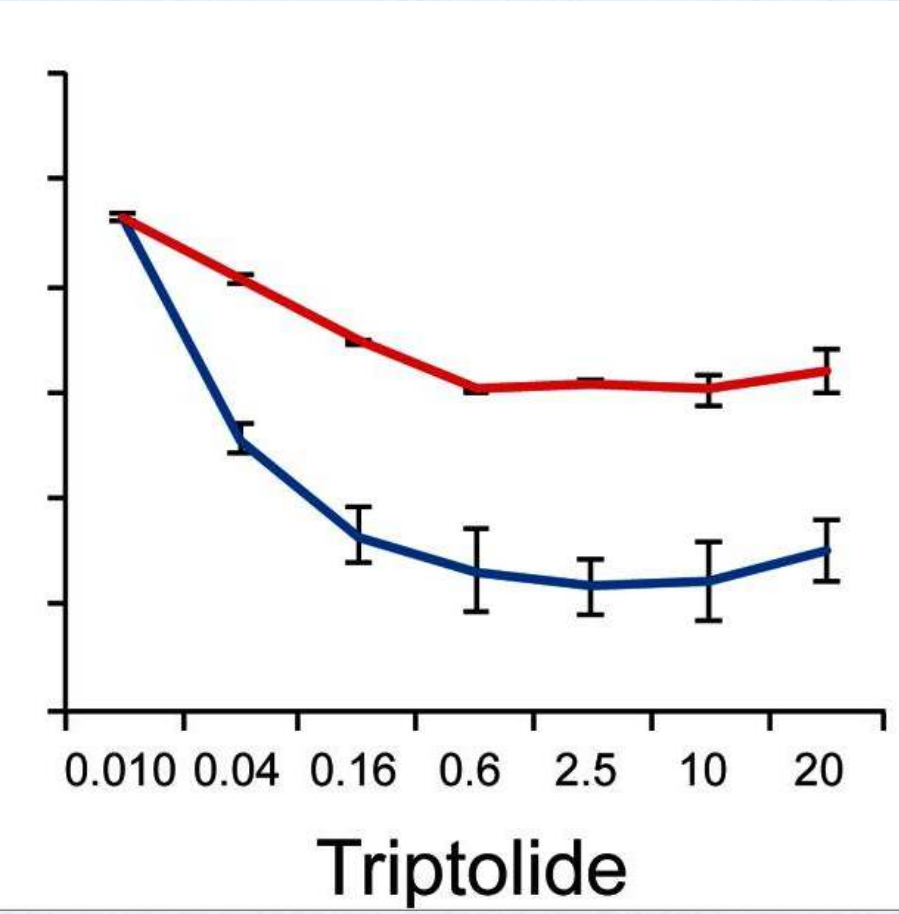
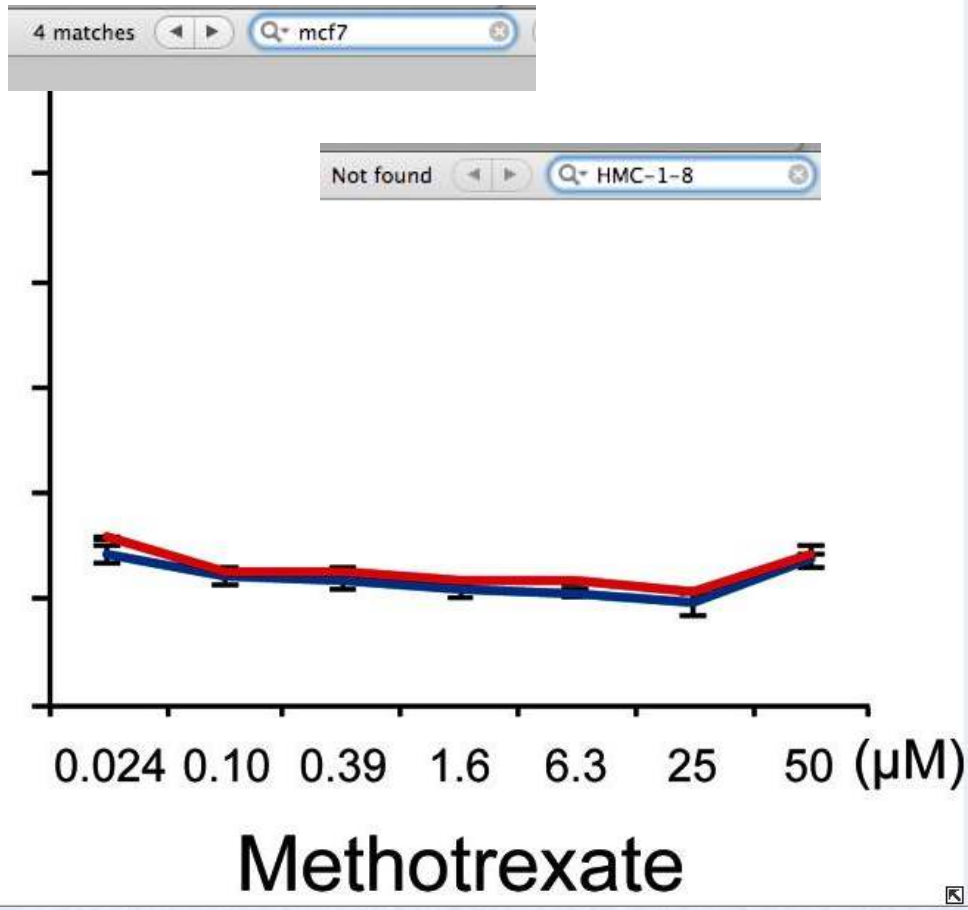


Figure 2





F. Ectopic expression of physiological levels of FLAG-MCL1 rescued HMC-1-8 cells from TR compounds, but not methotrexate, as measured by …cell viability at 24 hours (F). Error bars indicate standard deviation of duplicate measurements.

His model predicted,

- *in different fields of medical research, rates of wrongness roughly corresponding to the observed rates at which findings were later convincingly refuted:*

80 % of non-randomized studies

25 % of gold-standard randomized trials

10 % of the platinum-standard large

- **are wrong**

Quality of our science?

49 of the most highly regarded research findings in medicine over in the 13 years
- journals were most widely cited
- articles themselves were the most widely cited articles in these journals

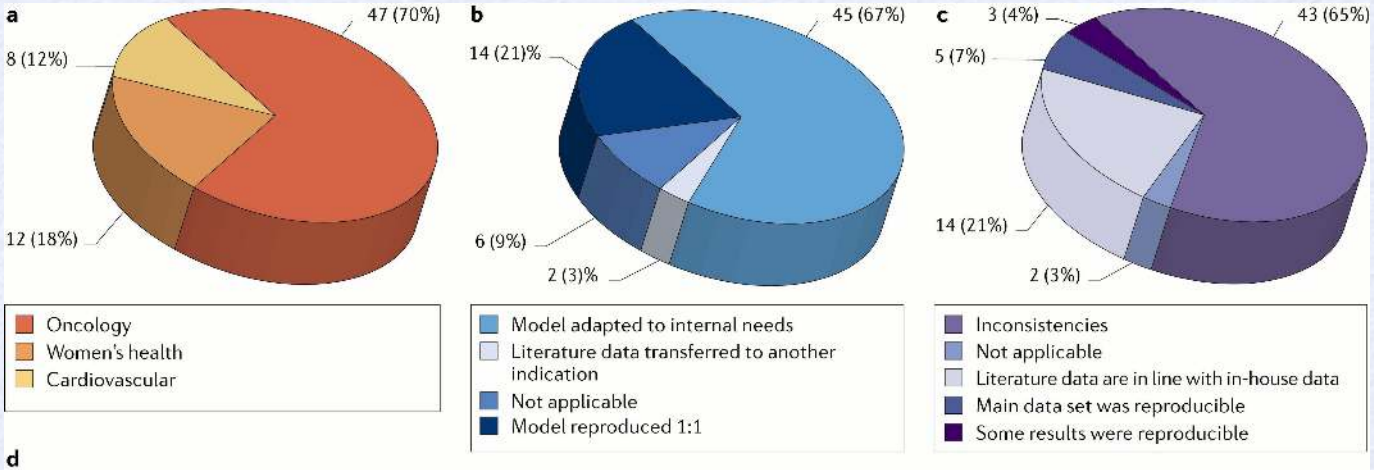
John P. A. Ioannidis

- 45 claimed to have found effective interventions.
- 34 had been retested
- 14 of these, or 41 percent, had been convincingly shown to be wrong or significantly exaggerated.
- If between a third and a half of the most acclaimed research in medicine was proving untrustworthy, the scope and impact of the problem are undeniable.

Believe it or not: how much can we rely on published data on potential drug targets?

Nature Reviews Drug Discovery 10, 712 (September 2011)

Reanalyzed 67 projects, most of them (47) from the field of oncology. This analysis revealed that **only in ~20–25%** of the projects were the relevant published data completely in line with our in-house findings…



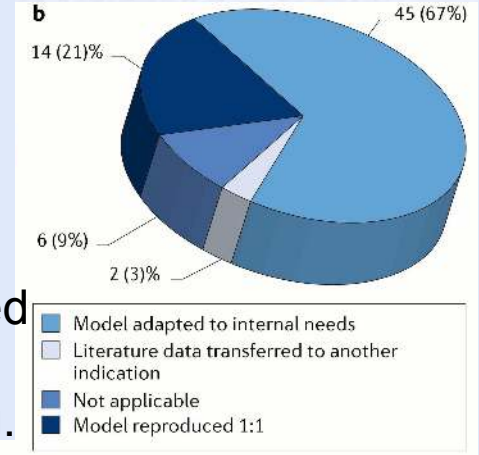
d

	Model reproduced 1:1	Model adapted to internal needs (cell line, assays)	Literature data transferred to another indication	Not applicable
In-house data in line with published results	1 (7%)	12 (86%)	0	1 (7%)
Inconsistencies that led to project termination	11 (26%)	26 (60%)	2 (5%)	4 (9%)

Nature Reviews | Drug Discovery

Believe it or not: how much can we rely on published data on potential drug targets?

• We wondered whether heterogeneous experimental conditions could be an explanation for the frequent inconsistencies. Interestingly, a transfer of the models — for example, by changes in the cell lines or assay formats — was not crucial for the discrepancies that were detected. Rather, either the results were reproducible and showed transferability in other models, or even a 1:1 reproduction of published experimental procedures revealed inconsistencies between published and in-house data (Fig. 1d).

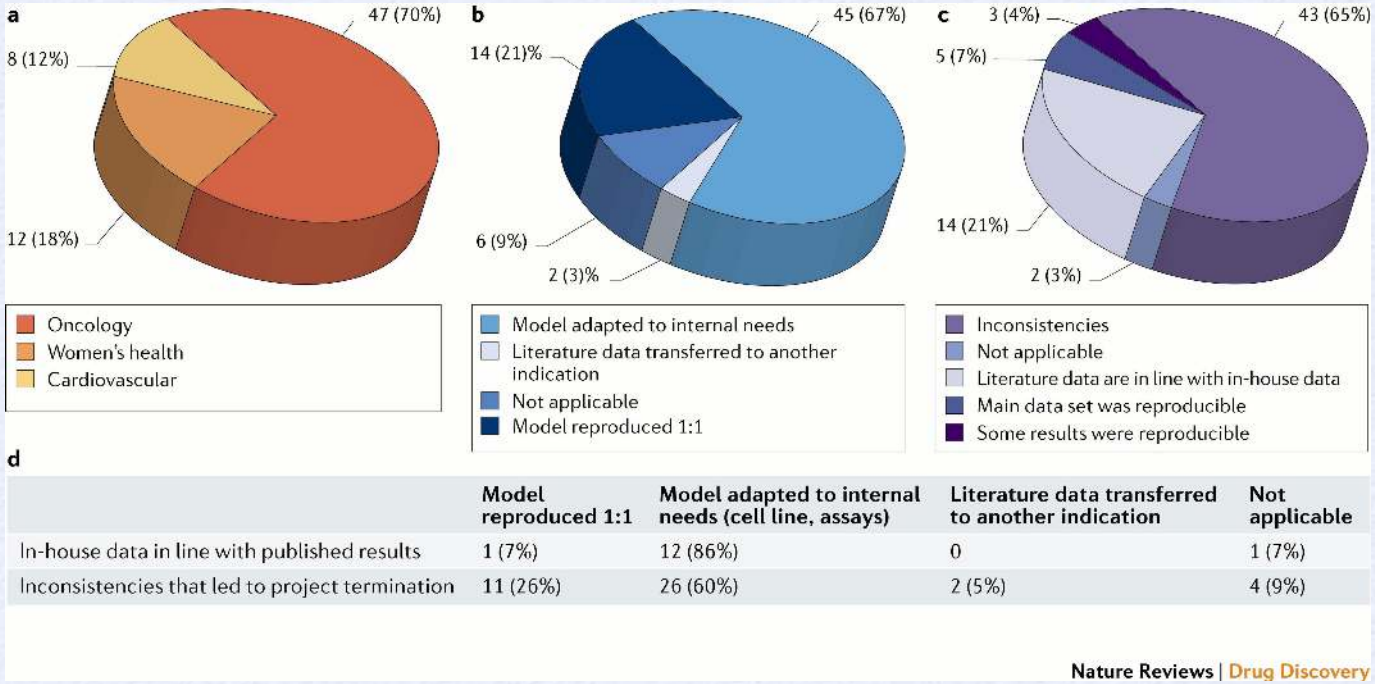


•Our analysis revealed that the reproducibility of published data did not significantly correlate with journal impact factors, the number of publications on the respective target or the number of independent groups that authored the publications.

d

	Model reproduced 1:1	Model adapted to internal needs (cell line, assays)	Literature data transferred to another indication	Not applicable
In-house data in line with published results	1 (7%)	12 (86%)	0	1 (7%)
Inconsistencies that led to project termination	11 (26%)	26 (60%)	2 (5%)	4 (9%)

Believe it or not: how much can we rely on published data on potential drug targets?



d

	Model reproduced 1:1	Model adapted to internal needs (cell line, assays)	Literature data transferred to another indication	Not applicable
In-house data in line with published results	1 (7%)	12 (86%)	0	1 (7%)
Inconsistencies that led to project termination	11 (26%)	26 (60%)	2 (5%)	4 (9%)

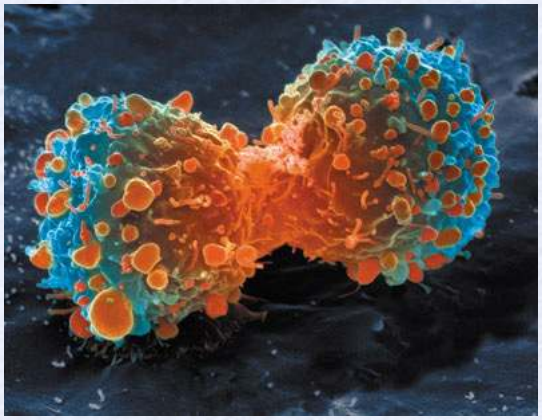
Nature Reviews | Drug Discovery

Our analysis revealed that the reproducibility of published data did not significantly correlate with journal impact factors, the number of publications on the respective target or the number of independent groups that authored the publications.

Believe it or not: how much can we rely on published data on potential drug targets?

- Over the past decade, before pursuing a particular line of research, scientists in the haematology and oncology department at the biotechnology firm Amgen in Thousand Oaks, California, tried to confirm published findings related to that work. **Fifty-three** papers were deemed 'landmark' studies Nevertheless, scientific findings were ***confirmed in only 6 (11%)*** cases. Even knowing the limitations of preclinical research, this was a shocking result.

- The Amgen scientists approached the papers' original authors to discuss findings and sometimes borrowed materials to repeat the experiments. In some cases, those authors required them to sign an agreement that they would not disclose their findings about specific papers. Begley and Ellis were therefore not free to identify the irreproducible papers



Believe it or not: how much can we rely on published data on potential drug targets?

From Drug development: Raise standards for preclinical cancer research
C. Glenn Begley & Lee M. Ellis
Nature 483, 531–533 (29 March 2012)

Table 1: Reproducibility of research findings

Journal impact factor	Number of articles	Mean number of citations of non-reproduced articles*	Mean number of citations of reproduced articles
*			
>20	*21*	*248 (range 3–800)*	*231 (range 82–519)*
5–19	*32*	*169 (range 6–1,909)*	*13 (range 3–24)*

Results from ten-year retrospective analysis of experiments performed prospectively. The term 'non-reproduced' was assigned on the basis of findings not being sufficiently robust to drive a drug-development programme.
Source of citations: Google Scholar, May 2011.

Price of Irreproducibility

Price of Irreproducibility

Jun 10, 2015

The inability to reproduce research findings is a long-standing issue in the sciences, and a new paper appearing in *PLOS Biology* estimates that some [redacted] is spent each year on preclinical research that's not reproducible.

A trio of researchers from the Global Biological Standards Institute and Boston University School of Management calculated that more than half of preclinical research isn't reproducible. They came up with this number by analyzing the four basic causes of irreproducibility: study design, biological reagents and reference materials, lab protocols, and data analysis and reporting. Based on past published error rates in those categories, errors in each of these categories lead all together to a between 18 percent and 88.5 percent irreproducibility rate, according to the researchers' probability bounds approach. The midpoint of that range is about 53 percent.

Note that the researchers caution that not all of that is money wasted. Some of these studies aren't reproducible because the methods were poorly described, not because the results aren't valid.

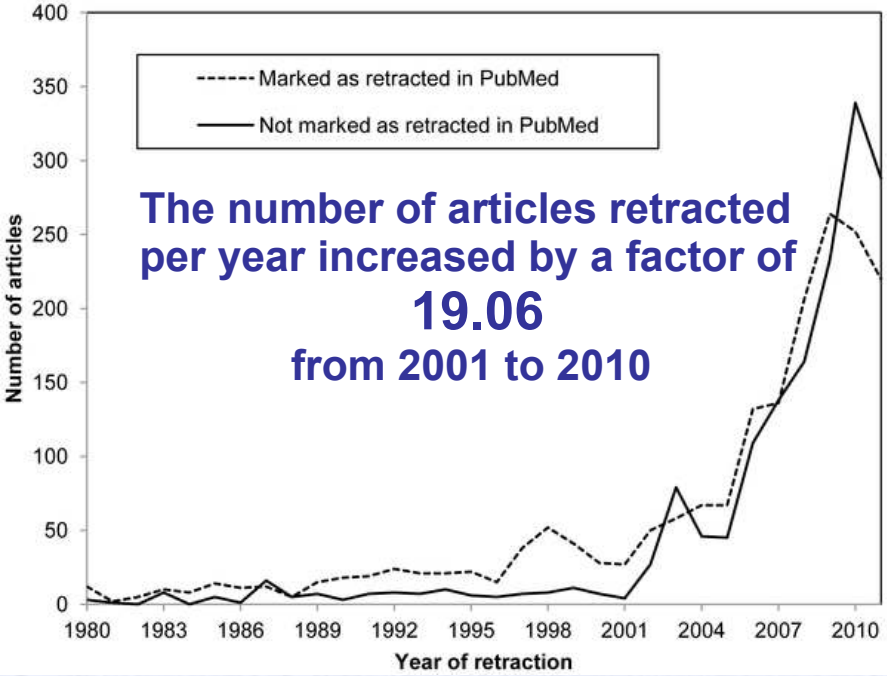
So, the paper is retracted, and then?..

Retraction Watch

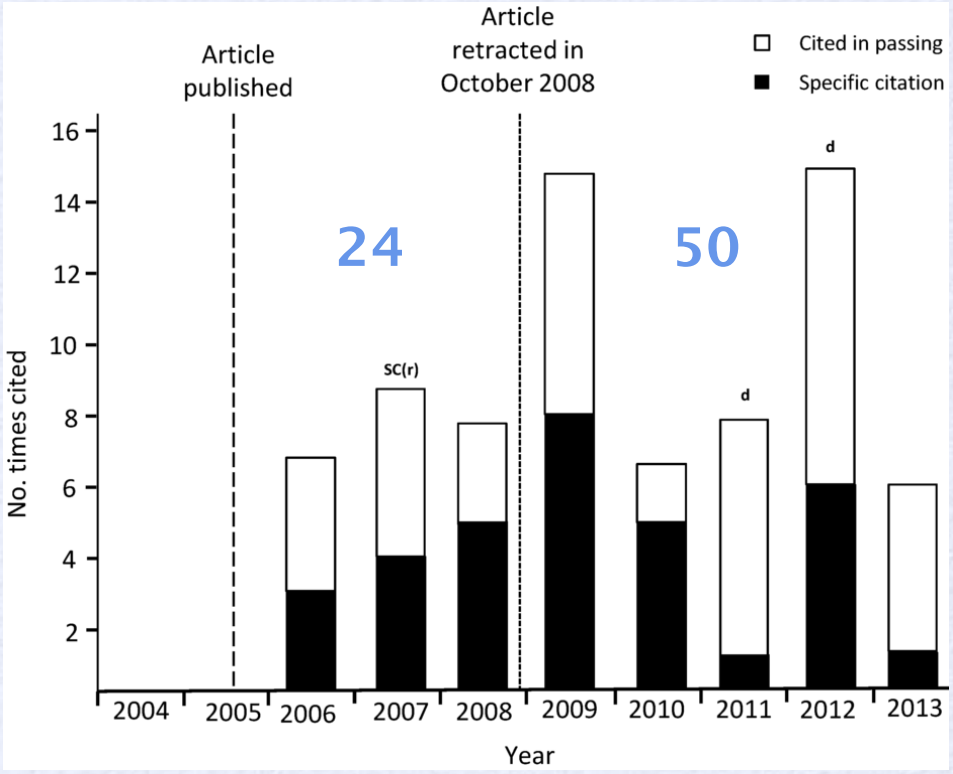
Tracking retractions as a window into the scientific process

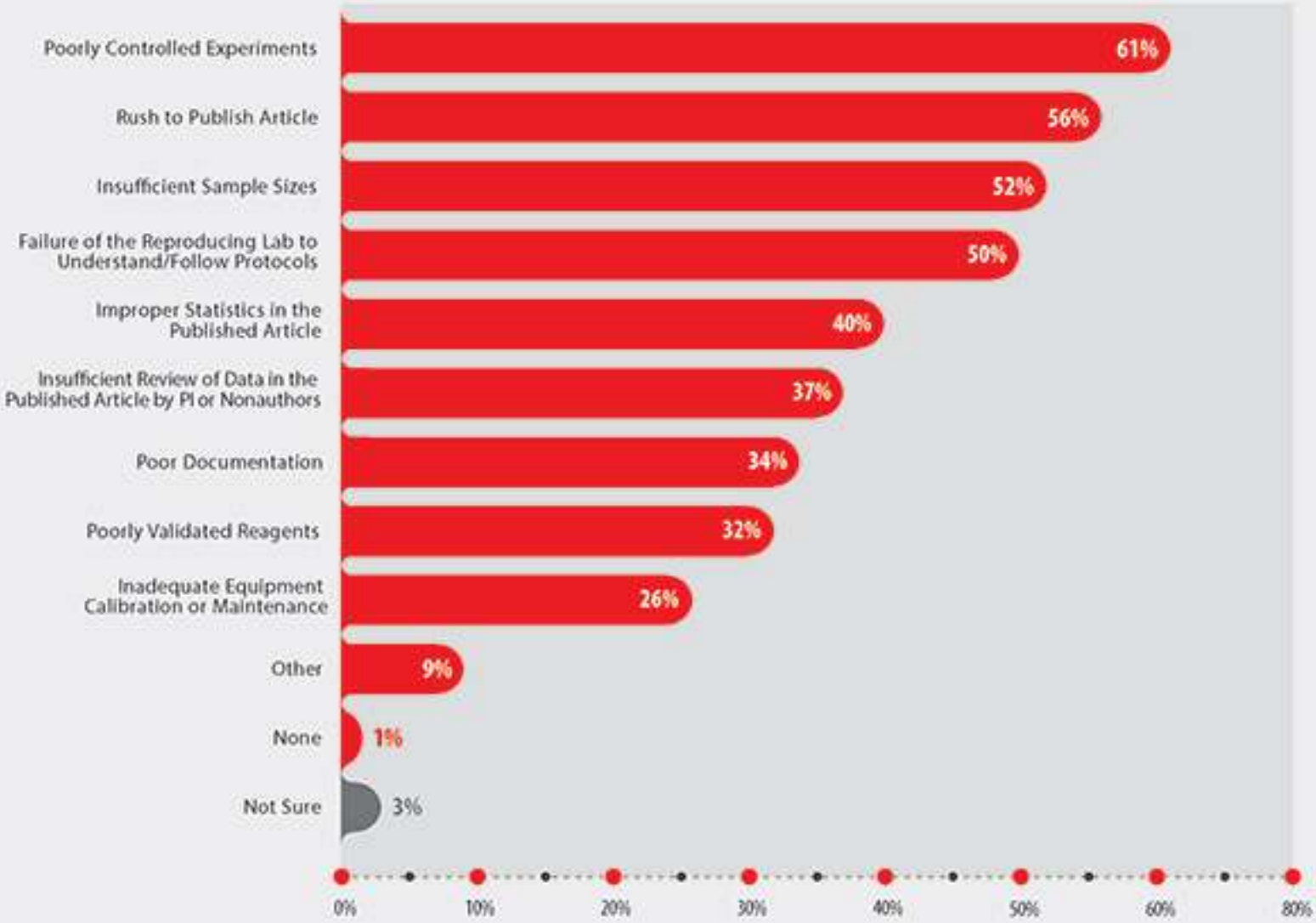
http://retractionwatch.com/2015/02/18/evidence-scientists-continue-cite-retracted-papers/

almost nothing happens: nearly 40% of scientists rarely (26%) or never (11%) checked for retractions



http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0044118




Poorly Controlled Experiments
61%
Rush to Publish Article
56%
Insufficient Sample Sizes
52%
Failure of the Reproducing Lab to Understand/Follow Protocols
50%
Improper Statistics in the Published Article
40%
Insufficient Review of Data in the Published Article by PI or Nonauthors
37%
Poor Documentation
34%
Poorly Validated Reagents
32%
Inadequate Equipment Calibration or Maintenance
26%
Other
9%
None
1%
Not Sure
3%
0%
10%
20%
30%
40%
50%
60%
80%

Believe it or not: how much can we rely on published data on potential drug targets?

- In studies for which findings could be reproduced, authors had paid close attention to controls, reagents, investigator bias and describing the complete data set.
- For results that could **not** be reproduced, however, data were not routinely analysed by investigators blinded to the experimental versus control groups. Investigators frequently presented the results of one experiment, such as a single Western-blot analysis. They sometimes said they presented specific experiments that supported their underlying hypothesis, but that were not reflective of the entire data set.
- There are no guidelines that require all data sets to be reported in a paper; often, original data are removed during the peer review and publication process.

Кто виноват?

- Dr Bohannon's sting was directed at the lower tier of academic journals. But in a classic 1998 study Fiona Godlee, editor of the prestigious British Medical Journal, sent an article containing eight deliberate mistakes in study design, analysis and interpretation to more than 200 of the BMJ's regular reviewers. Not one picked out all the mistakes. On average, they reported fewer than two; some did not spot any.

- Another experiment at the BMJ showed that reviewers did no better when more clearly instructed on the problems they might encounter. They also seem to get worse with experience. Charles McCulloch and Michael Callaham, of the University of California, San Francisco, looked at how 1,500 referees were rated by editors at leading journals over a 14- year period and found that 92% showed a slow but steady drop in their scores.

Что делать?

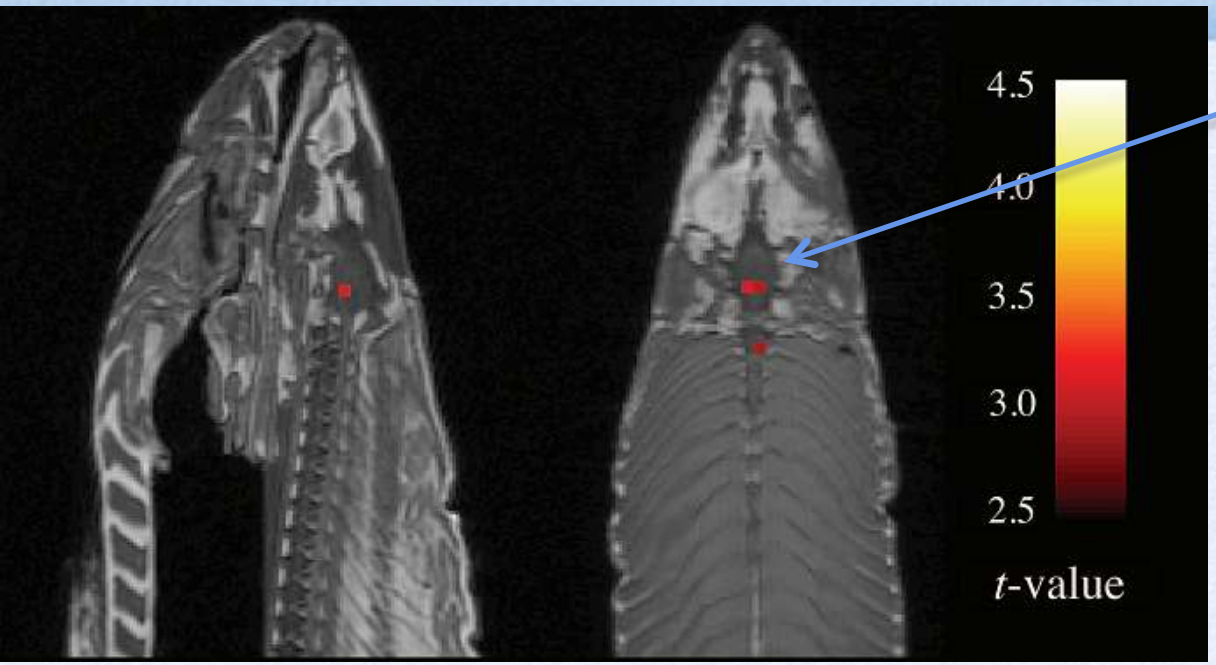
- PLoS ONE and Science Exchange have launched a programm called the Reproducibility Initiative through which life scientists can pay to have their work validated by an independent lab.
- In October 2013 the initiative announced it had been given $1.3m by the Laura and John Arnold Foundation, a charity, to look at 50 of the highest- impact cancer findings published between 2010 and 2012.

- The journal *Cortex* started offering yet another means of improving reproducibility and reducing bias. The mechanism, termed a “Registered Report,” involves peer review of an investigator's experimental design before data are collected. If the scientific question and methods are deemed sound, then authors are offered “in principle acceptance” of their article, irrespective of the study's outcome.

Общие проблемы с работами в области системной биологии

- изобилие положительных и недостаток отрицательных результатов
- размытие ответственности авторов (список авторов часто исчисляется десятками)
- большая часть данных находится в дополнительных материалах к статьям
- возможности затруднить анализ, предоставляя неполные или избыточные данные
- для проверки выводов требуется коллектив специалистов
- для проверки выводов требуется огромное количество времени
- воспроизвести результаты часто невозможно, не получив доступ к исходному оборудованию
- использование альтернативных методик может привести к противоречивым выводам

Salmon in the fMRI scanner



Brain activity detected

…there's a ton of information there, generally broken down into sections called voxels. Up 130,000 of them in a single study and contrast selection, looking at each one to see if it is 'activated' compared to the others…

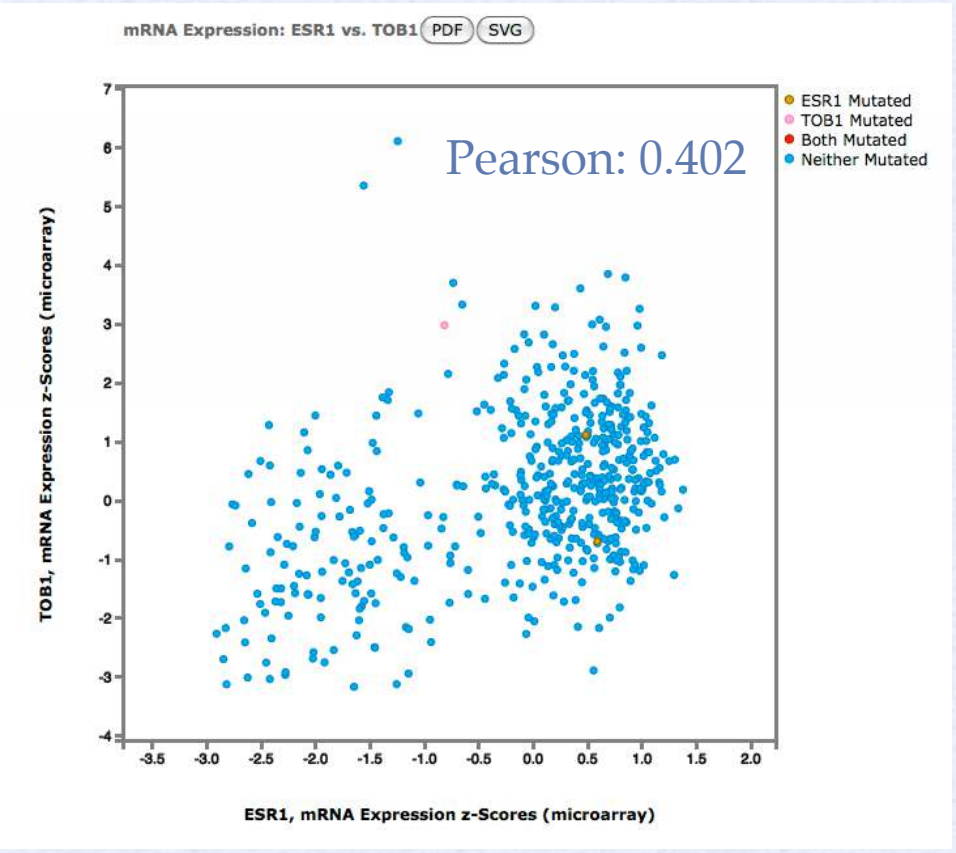
"Neural Correlates of Interspecies Perspective Taking in the Post-Mortem Atlantic Salmon: An Argument For Proper Multiple Comparisons Correction"

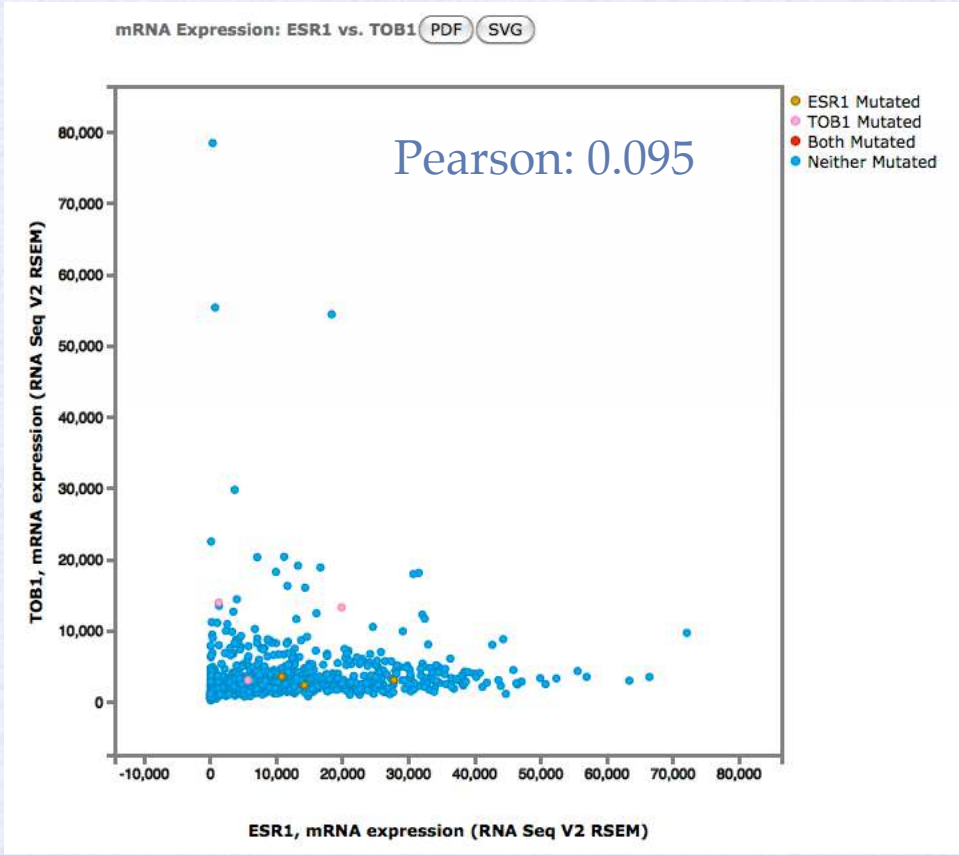
In this study, the salmon was shown images of people in social situations, either socially inclusive situations or socially exclusive situations.

IgNobel Prize in Neuroscience 2012

Общие проблемы с работами в области системной биологии

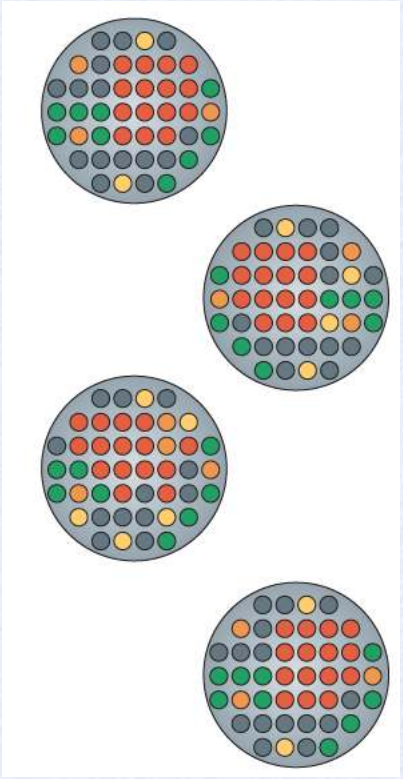
- использование альтернативных методик может привести к противоречивым выводам



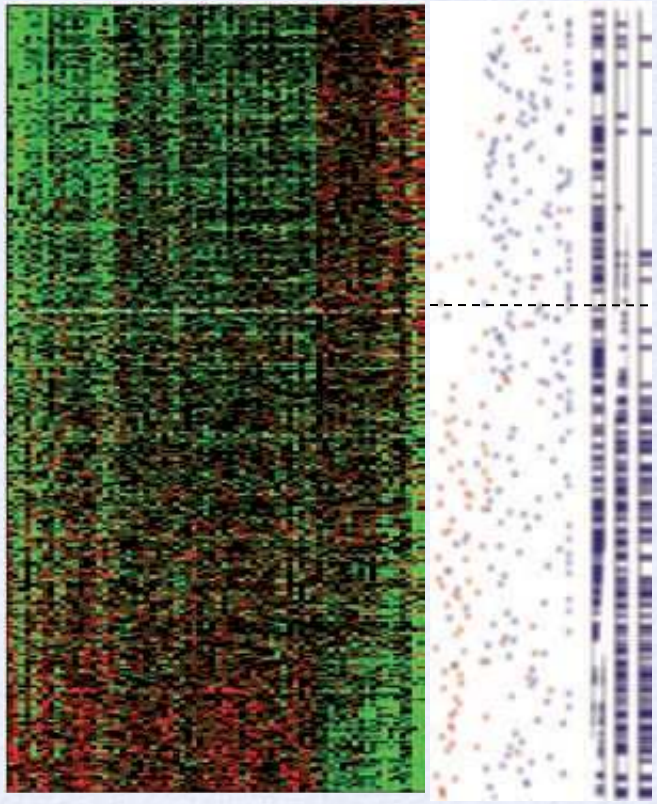


Транскриптомика на службе медицины

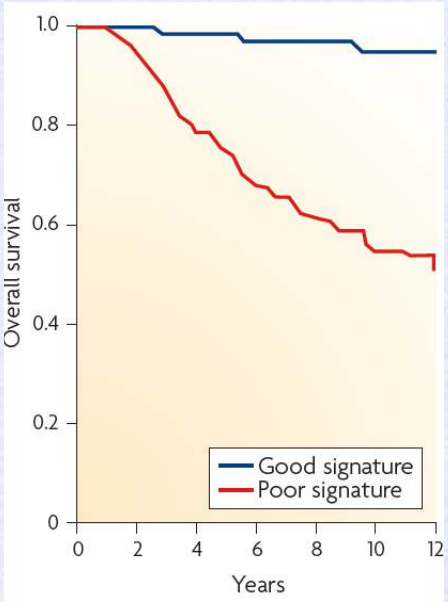
Получение большого объёма молекулярных данных путём гибридизации образцов РНК больных на ДНК-микрочипе



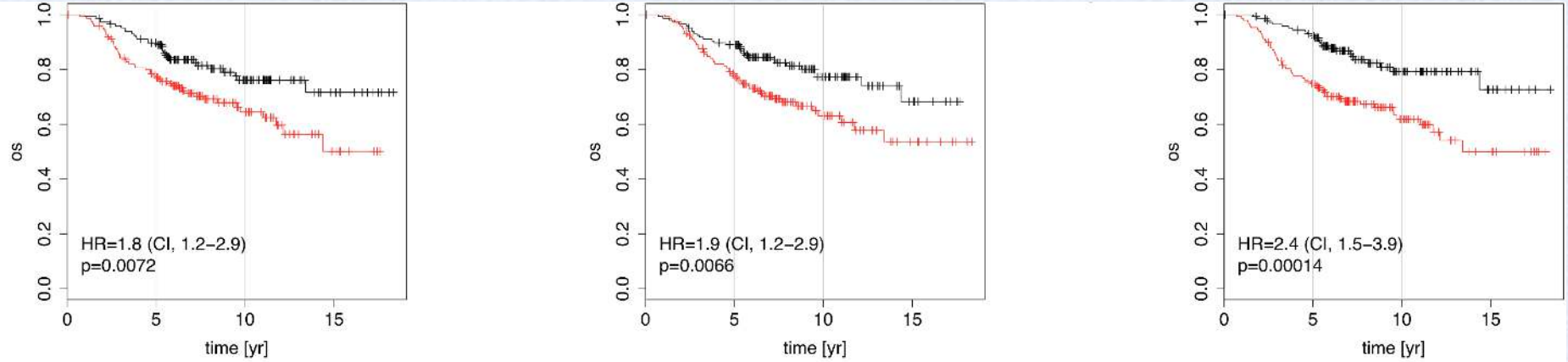
Обработка данных и построение модели



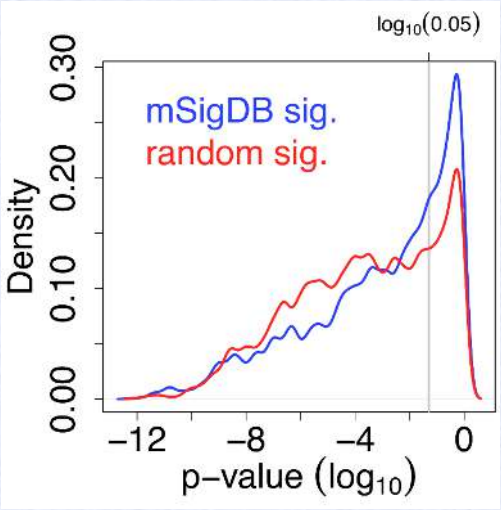
Клинически важное решение (классификация)



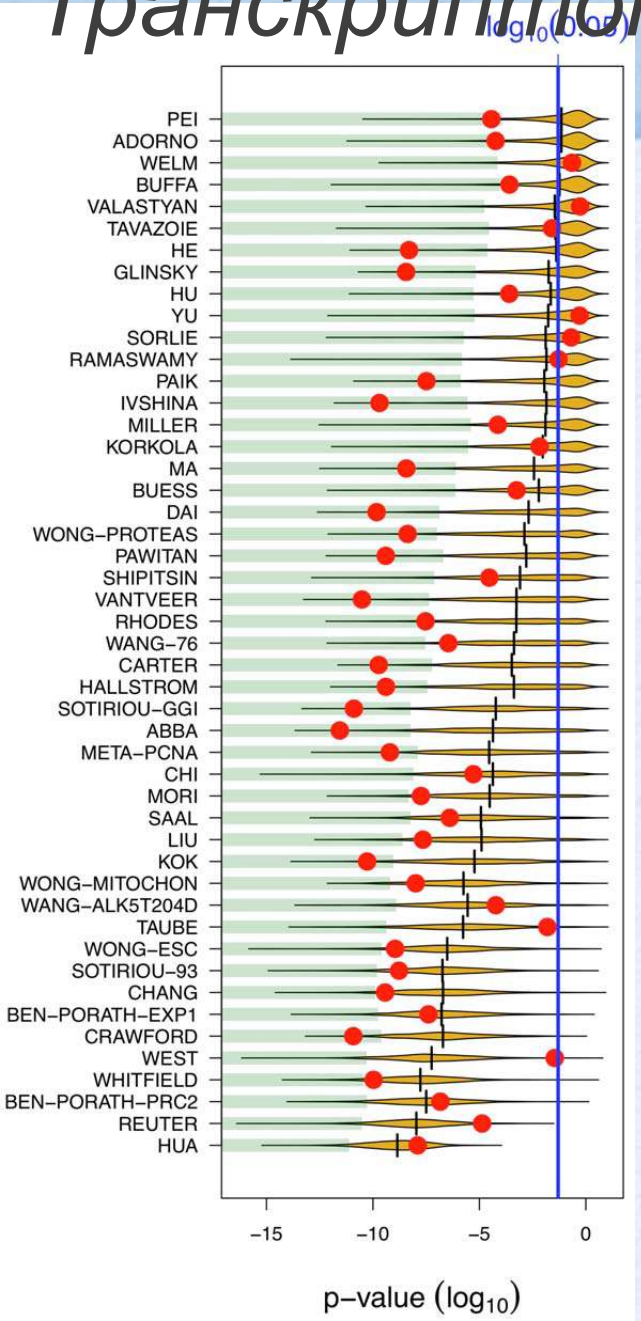
Транскриптомика на службе медицины



Association of negative control signatures with overall survival. In plots A–C the NKI cohort was split into two groups using a signature of post-prandial laughter (panel A), localization of skin fibroblasts (panel B), social defeat in mice (panel C). A–C, the fraction of patients alive (overall survival, OS) is shown as a function of time for both groups. D, The 1890 signatures examined in MSigDB c2 encompass all the fields of biomedical sciences, nevertheless we discovered that 67% of them were associated with breast cancer outcome at p,0.05, 23% at $p=10^{-5}$



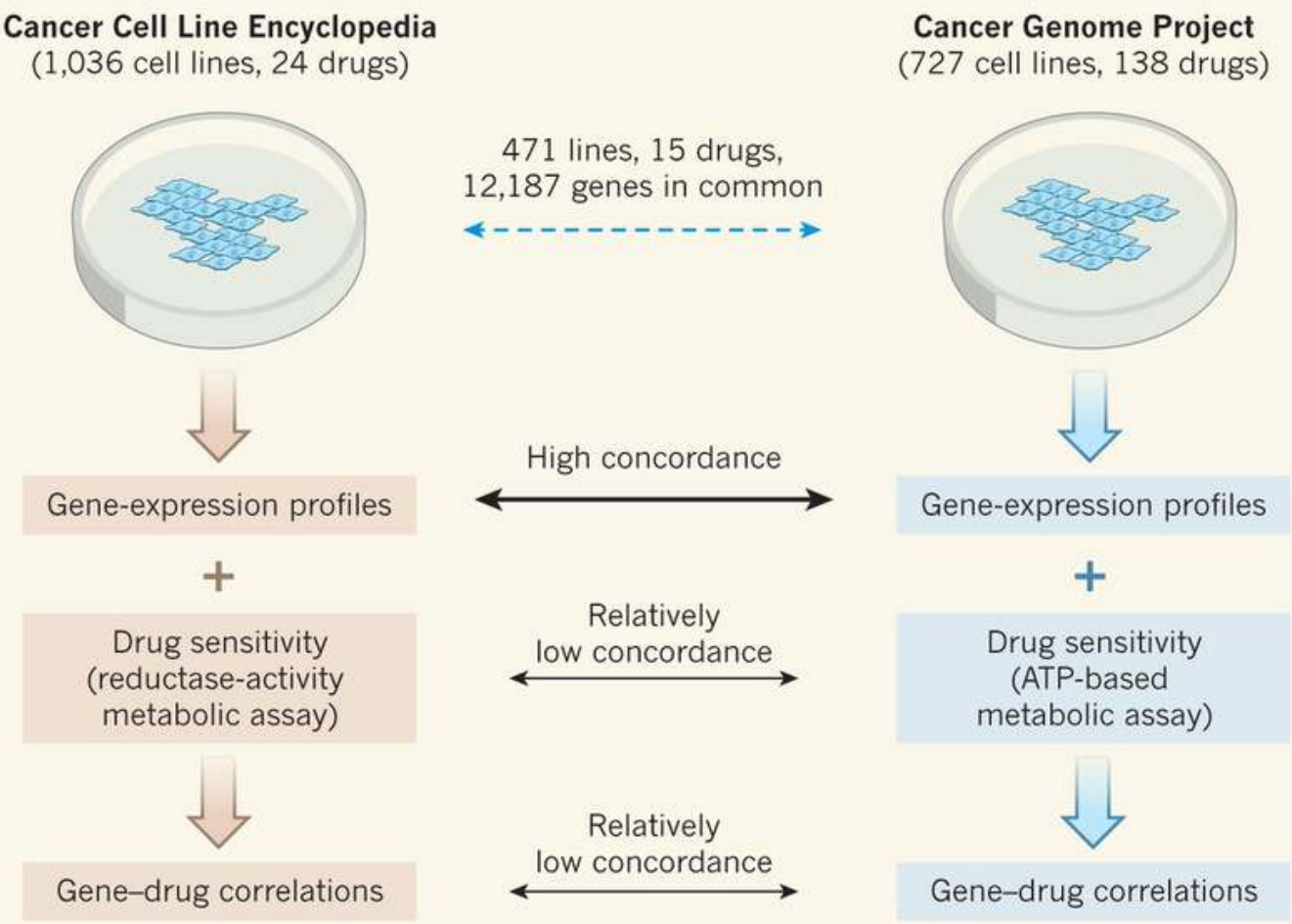
Транскриптомика на службе медицины



- We next compared 47 published breast cancer outcome signatures to signatures made of random genes. Twenty-eight of them (60%) were not significantly better outcome predictors than random signatures of same size.
- 11 (23%) were worse predictors than the median random signature.
- More than 90% of random signatures >100 genes were significant outcome predictors.

Most random gene expression signatures are significantly associated with breast cancer outcome. Venet D et al. PLoS Comput Biol. (2011)

CCLE vs CGP

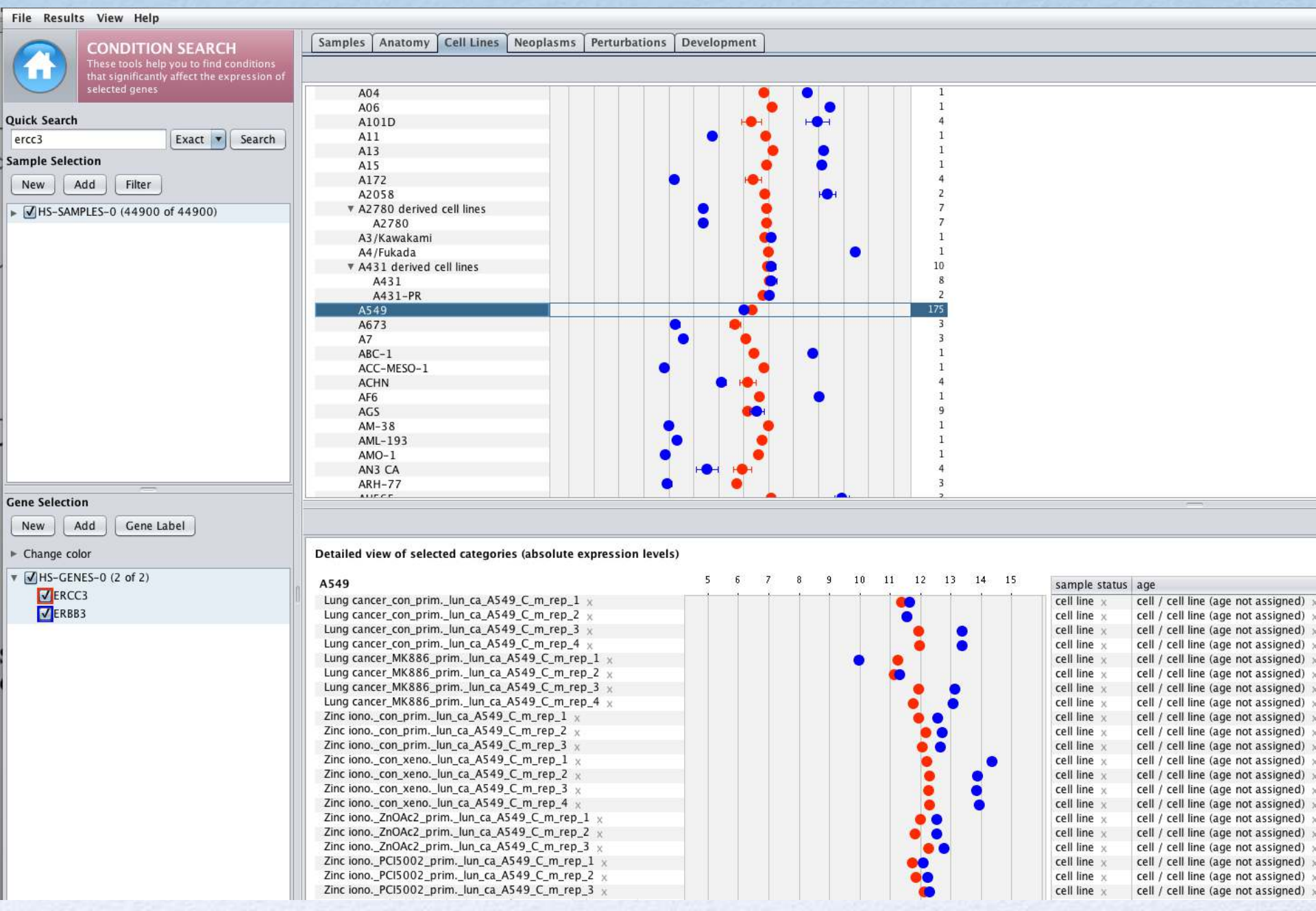


Cancer: Discrepancies in drug sensitivity
John N. Weinstein & Philip L. Lorenzi
Nature 504, 381–383 (December 2013)

CCLE vs CGP

- The pharmacological assay used by the CGP (the CellTiter 96 AQueous One Solution Cell Proliferation Assay from Promega) measures metabolic activity in terms of a reductase-enzyme product after a 72-hour incubation of cells with a drug; that used by the CCLE (the CellTiter-Glo assay from Promega) measures metabolic activity by assessing levels of the energy-transfer molecule ATP, after 72–84 hours of incubation. Both assays provide indices of the drug's activity against the cells, but they would not be expected to mirror each other across all cell and drug types, even if run in parallel (and neither may be the best indicator of cell viability).
- drug sensitivities can diverge if different batches of fetal bovine serum (which varies in its content of cytokines and other biologically active molecules) are used.
- The time and conditions of the cells' incubation before the drug is added, the coating on the plastic culture wells, intra-study batch or trend effects and other such arcane factors can all be influential.
- **Given the differences, which pharmacological assay represents the 'truth'?** The probable answer is either both or neither, depending on one's purpose*. If the aim is to predict clinical efficacy, then neither assay will be 'correct' in most cases.* The well-worn dictum “all models are wrong, some models are useful” applies with a vengeance in this context; there are too many differences between cultured cells and patients, particularly in terms of the delicate balance between beneficial and toxic effects of anticancer drugs.
- **The more appropriate uses of cell-line pharmacological data are for hypothesis generation and for elaborating on existing hypotheses, rather than for formal statistical prediction.**

Cell line identities ?



Cell line identities

Genetic Profiling Reveals Cross-Contamination and Misidentification of 6 Adenoid Cystic Carcinoma Cell Lines: ACC2, ACC3, ACCM, ACCNS, ACCS and CAC2

Janyaporn Phuchareon, Yoshihito Ohta, Jonathan M. Woo, David W. Eisele, Osamu Tetsu

We performed DNA fingerprint analysis on six ACC cell lines using short tandem repeat (STR) examinations and found that **all six cell lines had been contaminated with other cells**. ACC2, ACC3, and ACCM were determined to be cervical cancer cells (HeLa cells), whereas the ACCS cell line was composed of T24 urinary bladder cancer cells. ACCNS and CAC2 cells were contaminated with cells derived from non-human mammalian species: the cells labeled ACCNS were mouse cells and the CAC2 cells were rat cells.

Leuk Res. 2014 Aug;38(8):999-1001. doi: 10.1016/j.leukres.2014.05.003. Epub 2014 May 23.

Cell line cross-contamination: WSU-CLL is a known derivative of REH and is unsuitable as a model for chronic lymphocytic leukaemia.

International Cell Line Authentication Committee (ICLAC).

Gynecol Oncol. 2012 Oct;127(1):241-8. doi: 10.1016/j.ygyno.2012.06.017. Epub 2012 Jun 16.

DNA profiling analysis of endometrial and ovarian cell lines reveals misidentification, redundancy and contamination.

Korch C[1], Spillman MA, Jackson TA, Jacobsen BM, Murphy SK, Lessey BA, Jordan VC, Bradford AP.

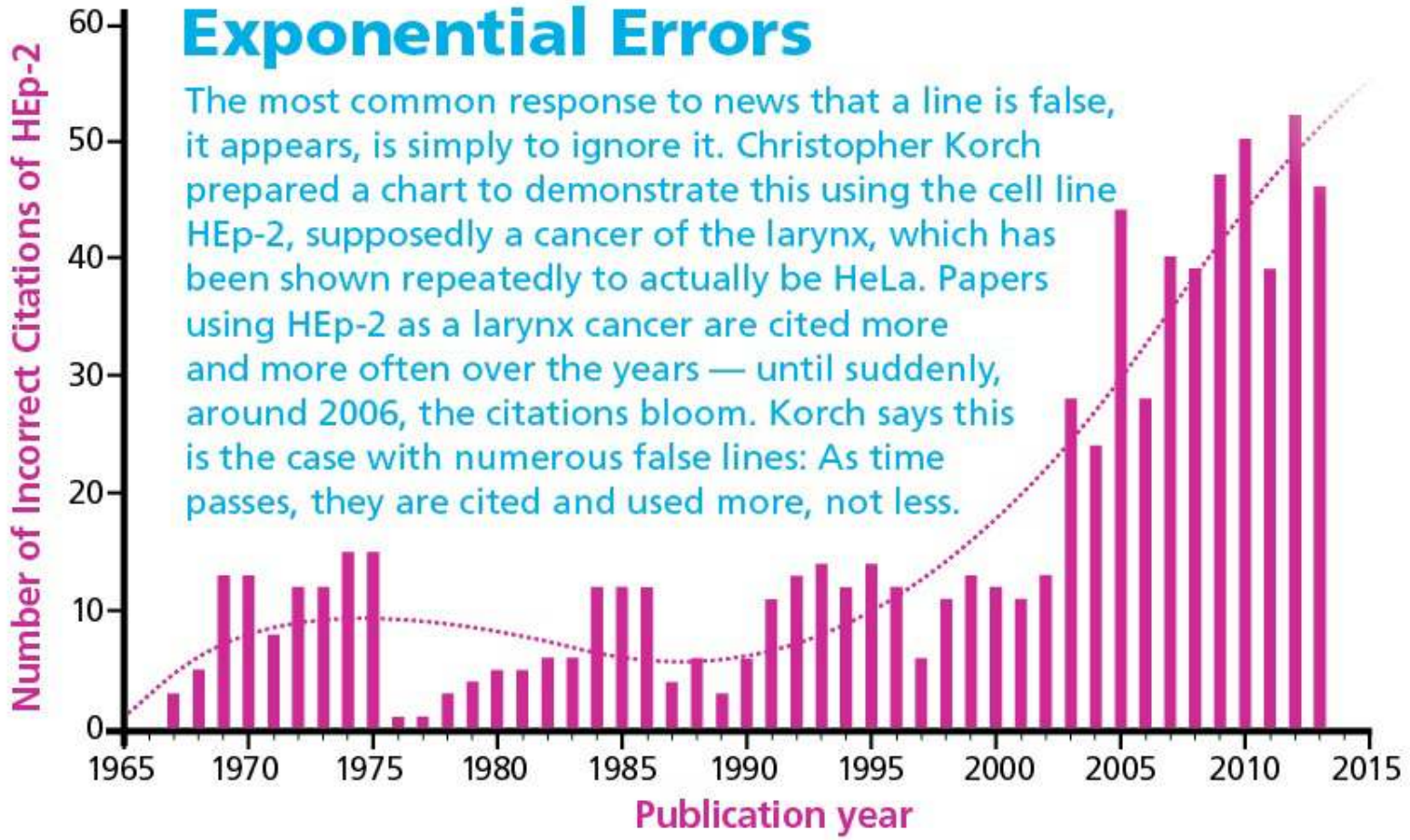
RESULTS:

Fifty-one ovarian cancer lines were profiled with **ten** found to be redundant and **five** (A2008, OV2008, C13, SK-OV-4 and SK-OV-6) identified as cervical cancer cells. Ten endometrial cell lines were analyzed, with RL-92, HEC-1A, HEC-1B, HEC-50, KLE, and AN3CA all exhibiting unique, uncontaminated STR profiles. Multiple variants of Ishikawa and ECC-1 endometrial cancer cell lines were genotyped and analyzed by sequencing of mutations in the p53 gene. **The profile of ECC-1 cells did not match the EnCa-101 tumor, from which it was reportedly derived**, and all ECC-1 isolates were genotyped as Ishikawa cells, MCF-7 breast cancer cells, or a combination thereof. Two normal, immortalized endometrial epithelial cell lines, HES cells and the hTERT-EEC line, were identified as HeLa cervical carcinoma and MCF-7 breast cancer cells, respectively.

Christopher.Korch@ucdenver.edu
Division
Title: **Th** **s**
a big in

Abstrac
Cell line
commo
that the is
problem
another w
and rep as
a false s,
tissue,
results
that are
contam
examine

Analysi
publish
identity,
and is e e
problen
analysis



"Equi donati dentes non inspiciuntur."

St. Jerome
The Letter to the Ephesians, circa AD 400.

"When you get a cell line, you have to look that gift horse in the mouth ? there's up to a 40 percent chance it's a Trojan horse, not what it says it is."

Christopher Korch,
University of Colorado Cancer Center

Misidentified and contaminated cell lines lead to faulty cancer science

http://proceeds-lambent.blogspot.com/2012_06_01_archive.html

Nobel winner declares boycott of top science journals

Professor of Cell and Developmental Biology at University of California, Berkeley

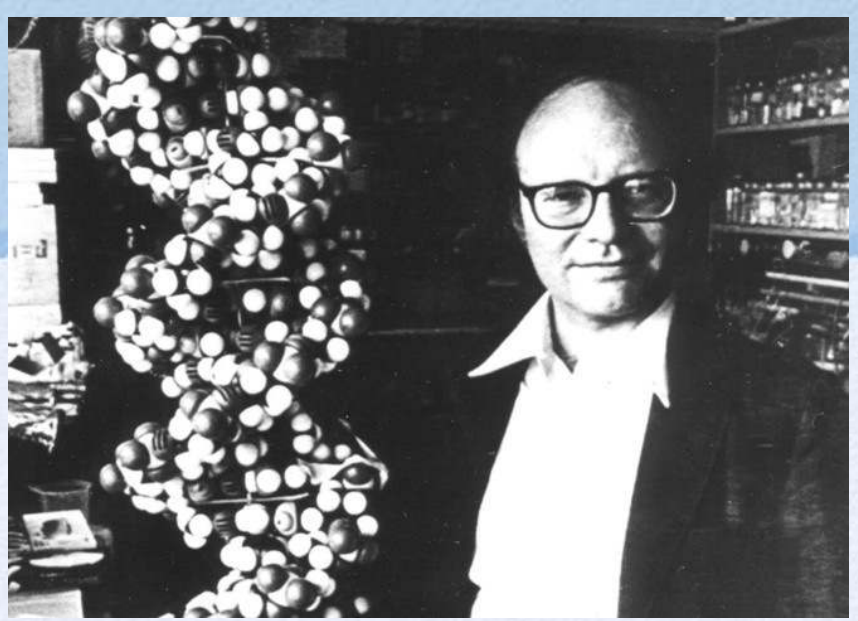
2013 Nobel prize in physiology or medicine

Randy Schekman says his lab will no longer send papers to Nature, Cell and Science as they distort scientific process

"These journals aggressively curate their brands, ***in ways more conducive to selling subscriptions than to stimulating the most important research***. Like fashion designers who create limited-edition handbags or suits, they know scarcity stokes demand, so they artificially restrict the number of papers they accept. The exclusive brands are then marketed with ***a gimmick called "impact factor"*** – a score for each journal, measuring the number of times its papers are cited by subsequent research. Better papers, the theory goes, are cited more often, so better journals boast higher scores. Yet it is a deeply flawed measure, pursuing which has become an end in itself …"

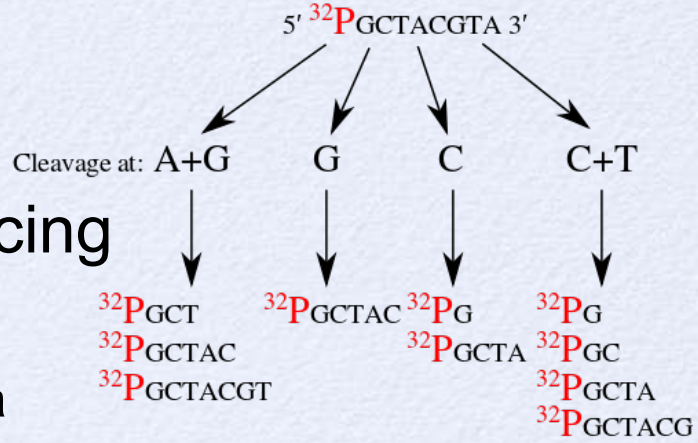
"…science must break the tyranny of the luxury journals."

http://www.theguardian.com/commentisfree/2013/dec/09/how-journals-nature-science-cell-damage-science
https://theconversation.com/how-to-break-free-from-the-stifling-grip-of-luxury-journals-21669

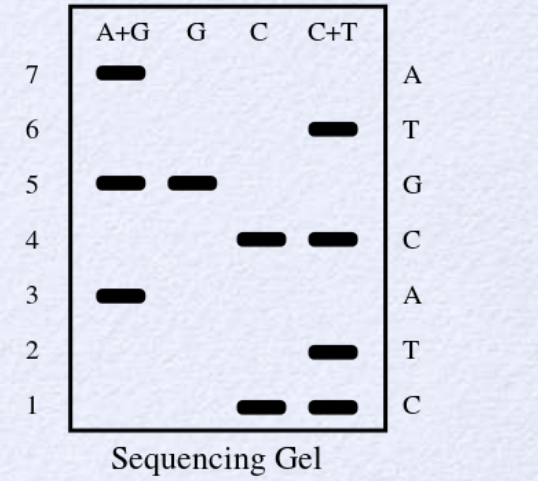


Walter Gilbert

Nobel Prize in 1980 in Chemistry



Maxam–Gilbert sequencing



Research findings

- **Together with Allan Maxam, Gilbert developed a new DNA sequencing method, using chemical methods developed by Andrei Mirzabekov**
- **Achieved the first synthesis of active insulin using recombinant DNA technology (cloning)**
- **Gilbert first proposed the existence of introns and exons and explained the evolution of introns in a seminal 1978 "Nature" paper**
- **In 1986, Gilbert proposed the RNA world hypothesis for the origin of life**

September 23 2014, 1.20am EDT

Nobel Laureate: big data and full-genome analysis not all they're cracked up to be

What are your views on "big data"?

Big data promises to collect large sets of data and find associations between genes and diseases. There's definitely something useful in the data collected, but the danger is that ***we have no clue how to interpret it***. Also, you must remember that all statistically significant things are not biologically significant. So, it is definitely not a panacea.

What problems does science face today?

Another major problem is the ***explosion in scientific manpower that has not necessarily led to the betterment of science, especially in biology.*** In fact, bad material that gets published has increased. **In biology, the top journals – Cell, Science and Nature – have created a mess.** They tell the authors "give me the headline, not the data".

What advice would you like to give to young scientists?

Do not blindly believe whatever you read. I often used to give my students papers that said opposite things and then tell them to explain to me how they were consistent, if at all.

http://theconversation.com/nobel-laureate-big-data-and-full-genome-analysis-not-all-theyre-cracked-up-to-be-31992

Скандал с клиническими испытаниями в медицинском центре Duke University

- изучение профилей экспрессии генов позволило (якобы) оптимизировать лечение больных раком лёгких (2006, Nature Medicine and NEJM)
- получено $10 500 000 на клинические испытания

Что такое! -- сказал вдруг Балаганов...
-- Три часа уже пилю, а оно все еще не золотое.

- 2007 – 2009: независимой проверкой выявлены многочисленные ошибки и нарушения
  - **в основной таблице все результаты были сдвинуты на одну строчку по сравнению с идентификаторами**
  - **положительный ответ был обозначен как отрица**

~2000 часов работы!!!

- 2011: все клинические испытания (3) остановлены
- отозвано 10 статей (Nature Medicine, NEJM, JAMA , и другие престижные журналы)
- идёт судебное разбирательство

More responsibility?

https://www.genomeweb.com/scan/repercussions?utm_source=SilverpopMailing&utm_medium=email&utm_campaign=Scan%20Blog:%20Fraudster%20Gets%20Jail%20Term,%20This%20Week's%20Nature,%20Americans'%20Views%20of%20Scientific%20Issues,%20more%20-%2007/02/2015%2001:10:00%20PM

genomeweb

Ilya Serebriiskii

Business & Policy | Technology | Research | Clinical | Disease Areas | Applied Markets | Resources | Enter your keywo

Home » The Scan » The Repercussions

The Repercussions

Jul 02, 2015

A former Iowa State University researcher has been sentenced to **four and a half years in prison** for making false statements in research reports, according to the Associated Press. Dong-Pyou Han must also **pay $7.2 million back** to the US National Institutes of Health.

At the *Des Moines Register*, Retraction Watch's Adam Marcus and Ivan Oransky note that prosecution for research misconduct is quite rare and say that Han isn't even one of the worst offenders. Still, they argue that "**if Han's stiff sentence serves to deter future would-be fraudsters, that would be an example worth setting**."

NCI Sets Rules For Omics Studies

- Availability and quality of appropriate clinical specimens
- Requirements for the analytical performance of the omics assay
- Methods for omics data pre-processing
- Development of the mathematical predictor model and assessment of its performance
- Clinical interpretation of the test result
- Design of the clinical trial
- Ethical, legal, and regulatory issues

Правила проведения широкомасштабных ("-omics") исследований

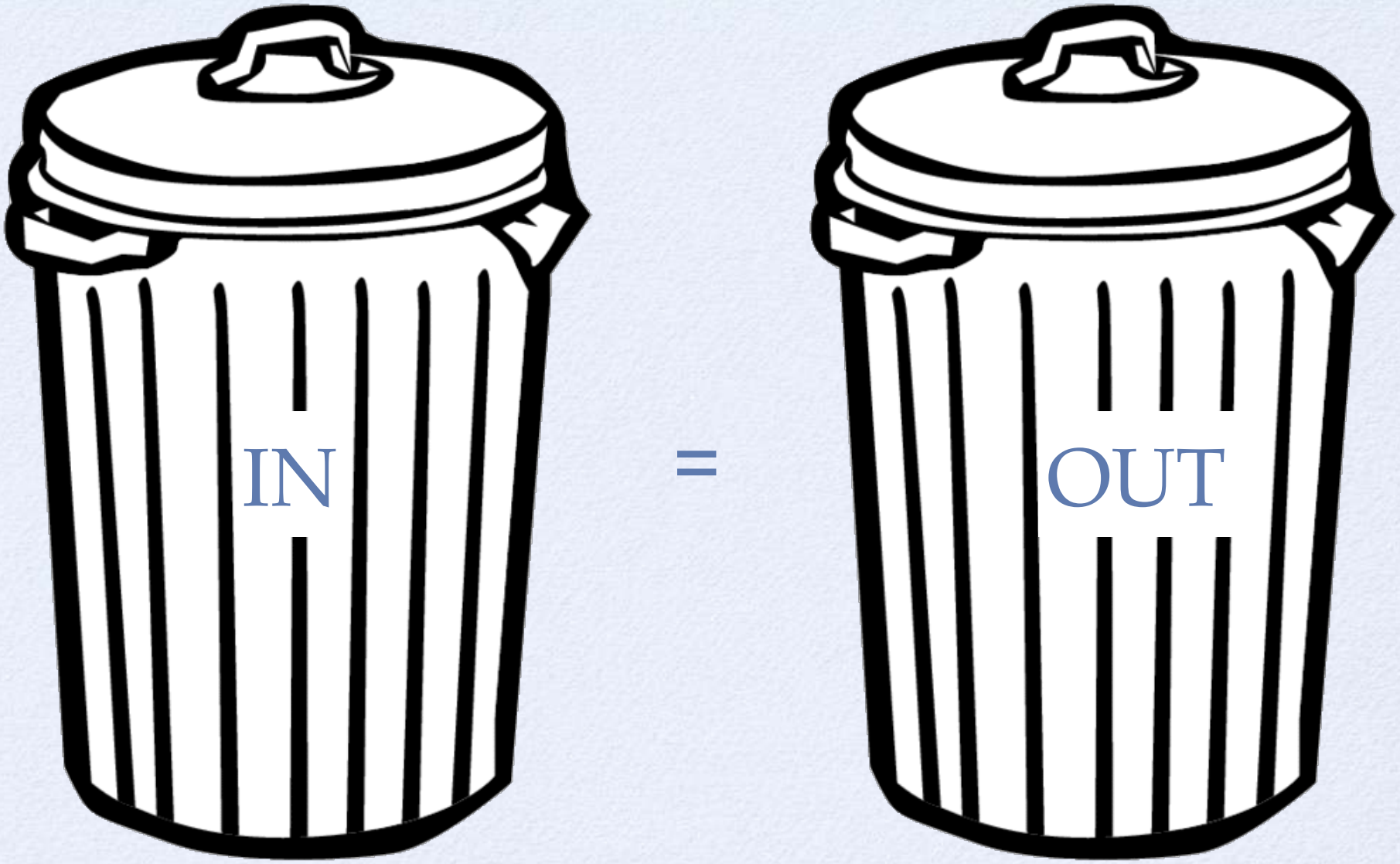
Руководство из 30 пунктов, регулирующее:

- Доступность и качество соответствующих клинических образцов
- Требования к качеству соответствующих аналитических процедур (omics assay)
- Методы обработки данных широкомасштабных экспериментов
- Построение математической модели и оценку её предсказующей способности
- Клиническую интерпретацию результатов тестов
- Принципы организации клинических испытаний
- Этические, юридические, и административные правила

NIH Presses Journals to Focus on Reproducibility of Studies

June 6, 2014 By Paul Basken

- A group of leading medical-journal editors, convened by the National Institutes of Health, this week endorsed a set of guidelines intended to tackle the widespread problem of scientific findings that cannot be replicated.
- About 40 editors, representing journals that include Science and Nature,reached a "general agreement" about what they must accept as their responsibility for ensuring the reproducibility of their published findings, the NIH director, Francis S. Collins, said on Thursday.
- Dr. Collins, addressing a semiannual session of his advisory committee at the agency's headquarters, in Bethesda, Md., gave only limited details of the agreement, and the NIH did not release a copy of the text. Officials atScience declined to authorize a release, saying the principles were still regarded as a draft.
- As one element, however, Dr. Collins said the journals discussed the need to publish articles that identify reproducibility problems with studies they previously published.


IN
=
OUT