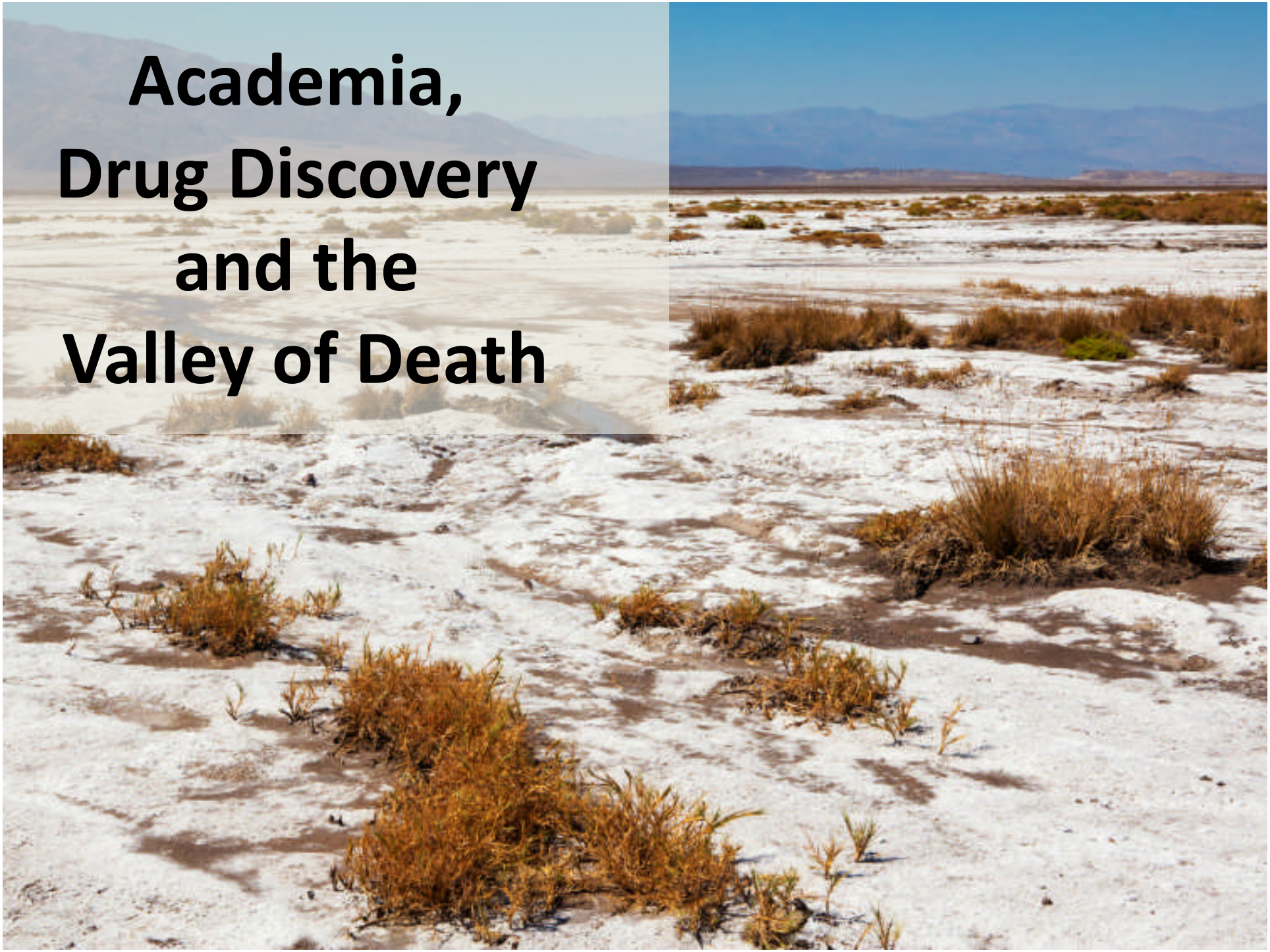
Academia, Drug Discovery and the Valley of Death




HATE
LOVE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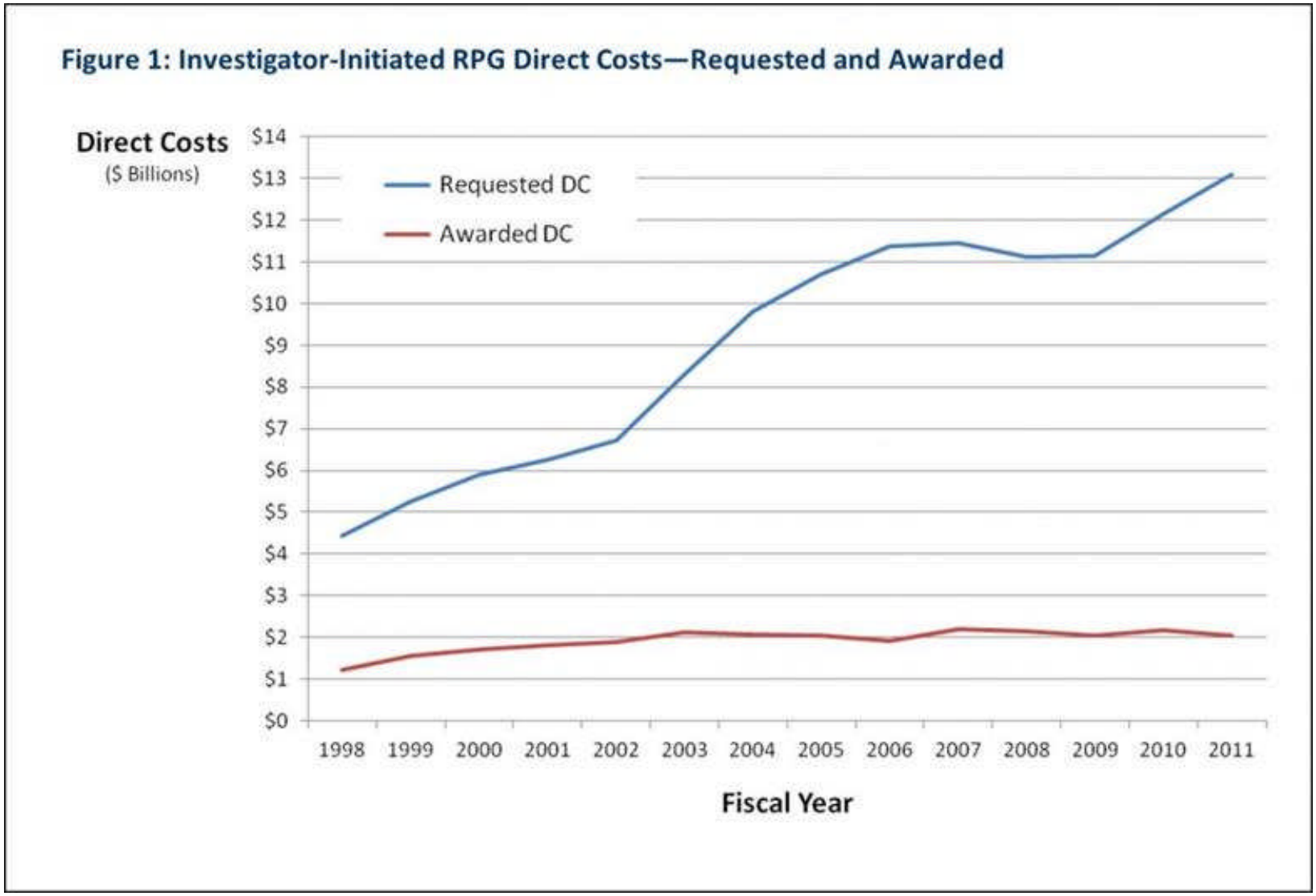


Dr. Sally Rockey, NIH, *http://nexus.od.nih.gov/all/rock-talk/page/2/*

The New York Times

THE SESSIONS
NOW PLAYING

October 12, 2012

University Endowments Face a Hard Landing

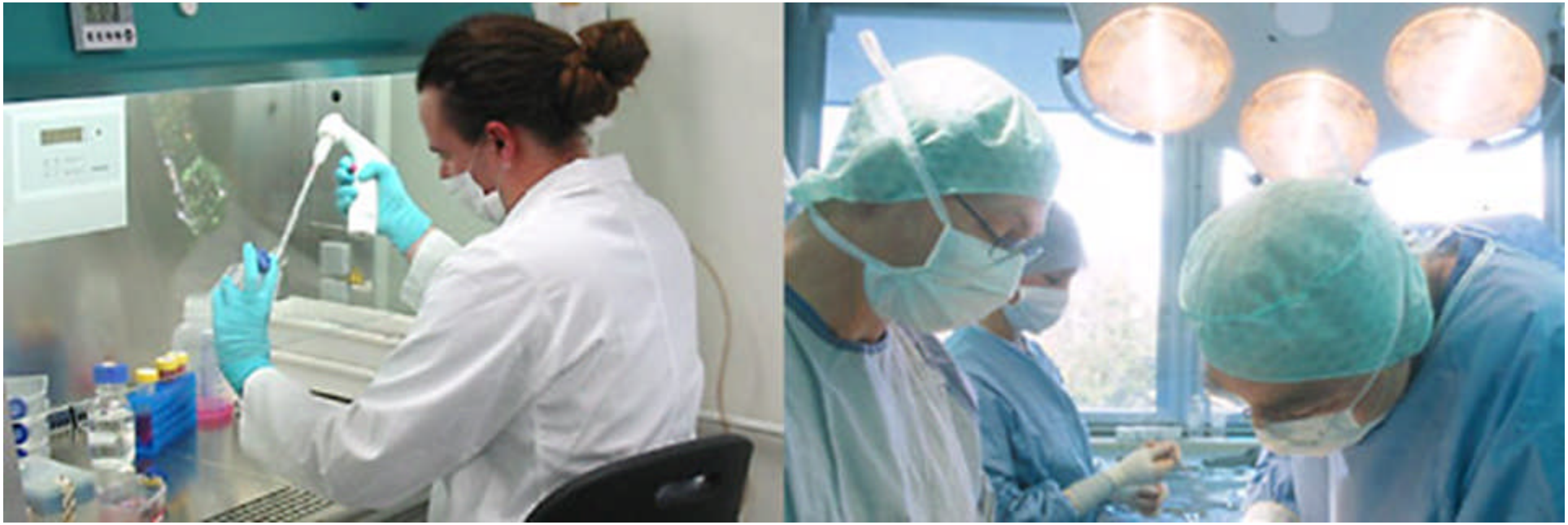
By JAMES B. STEWART

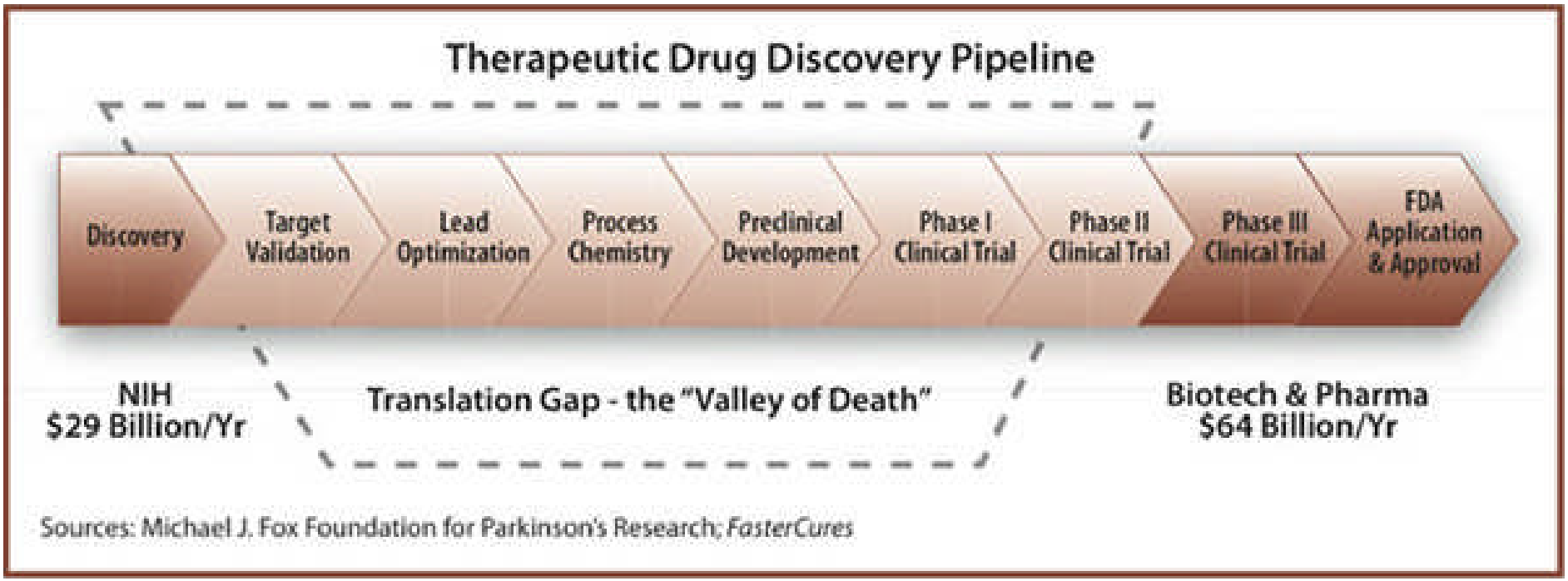
For years, America's largest, richest and most prestigious universities have been the envy of investors. They churned out double-digit returns over the last two decades, even with steep losses during the financial crisis. Harvard's endowment today is over $30 billion and has generated annualized returns of 12.5 percent over the last 20 years.

College and university endowment returns for the most recent fiscal year, which ended June 30, are starting to roll in. And in many cases, they warrant a grade of C at best, and in some cases, an F. Harvard reported a 0.05 percent loss and a drop in its endowment of over $1 billion in the same period, even as a simple Standard & Poor's 500-stock index fund gained about 5.5 percent. Harvard's endowment decline is more than the entire endowments of roughly 90 percent of all colleges and universities.

http://www.nytimes.com/2012/10/13/business/colleges-and-universities-invest-in-unconventional-ways.html

Traditional focus of industry funding



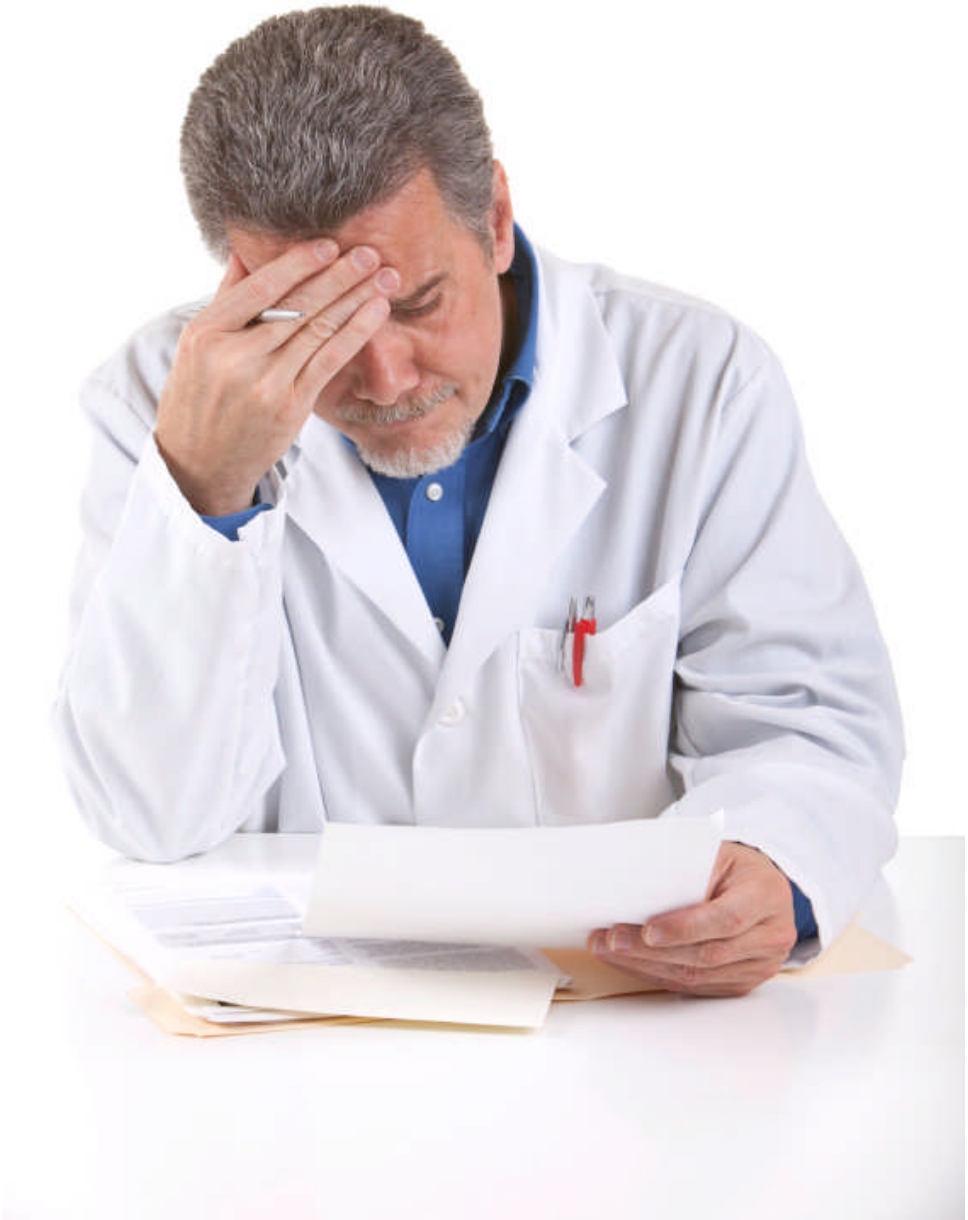

Therapeutic Drug Discovery Pipeline
Discovery
Target Validation
Lead Optimization
Process Chemistry
Preclinical Development
Phase I Clinical Trial
Phase II Clinical Trial
Phase III Clinical Trial
FDA Application & Approval
NIH
$29 Billion/Yr
Translation Gap - the "Valley of Death"
Biotech & Pharma
$64 Billion/Yr
Sources: Michael J. Fox Foundation for Parkinson's Research; FasterCures

clarus Ventures

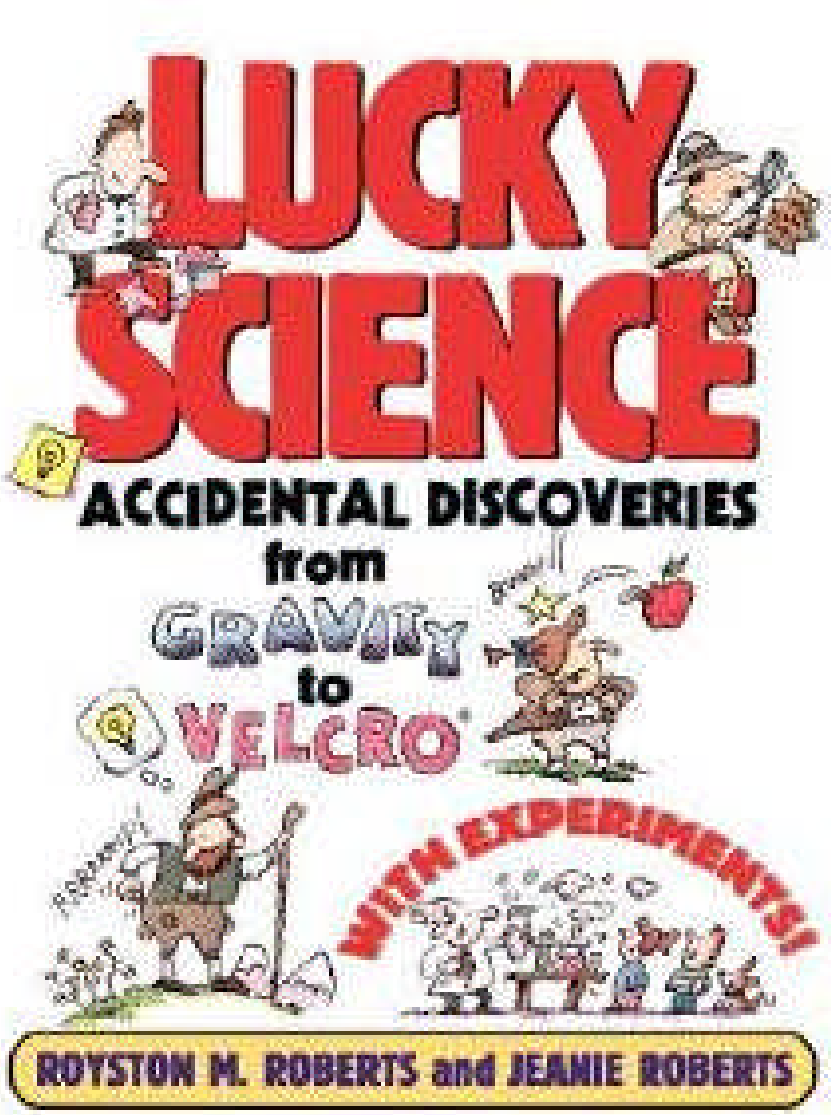
POLARIS VENTURE PARTNERS

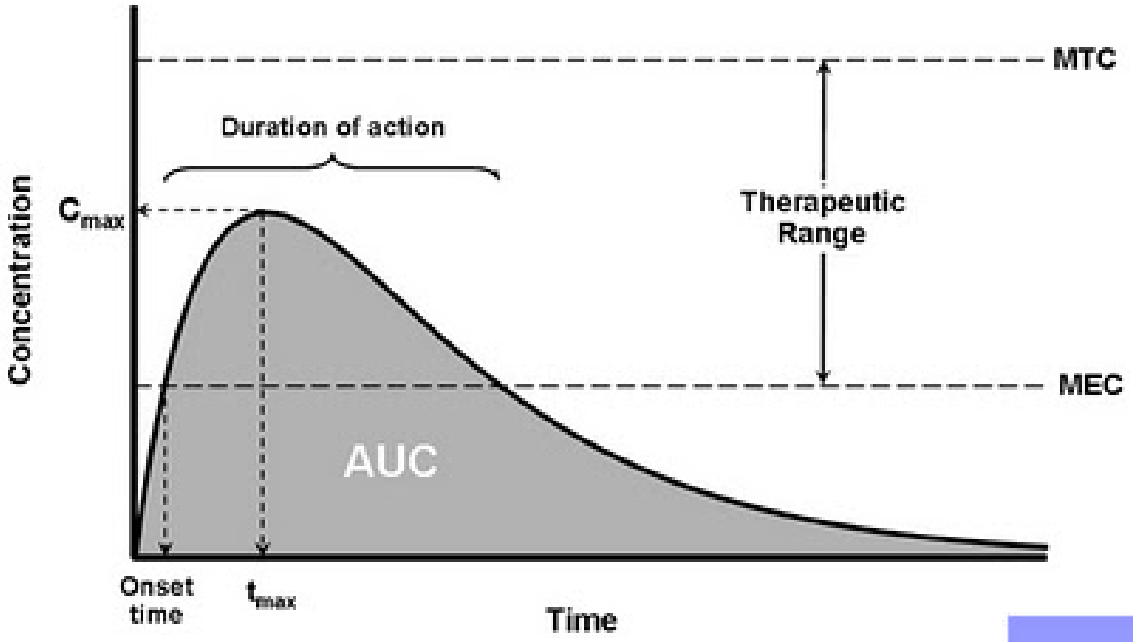
ATLAS VENTURE

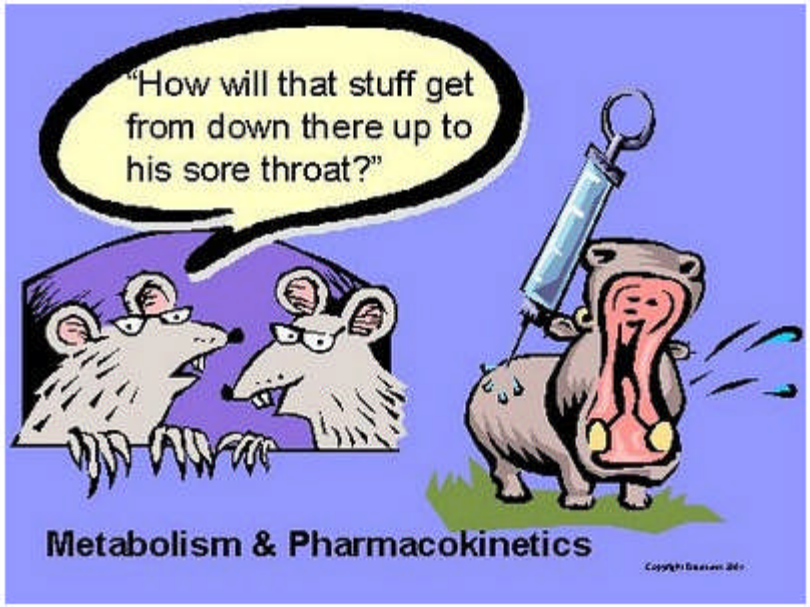
HealthCare Ventures LLC



- Knowledge
- Resources
- Robustness
- Tech Transfer


LUCKY SCIENCE
ACCIDENTAL DISCOVERIES
from
GRAVITY
to
VELCRO®
WITH EXPERIMENTS!
ROYSTON M. ROBERTS and JEANIE ROBERTS


MTC
Duration of action
Therapeutic Range
Concentration
C_{max}
MEC
AUC
Onset time
t_{max}
Time


"How will that stuff get from down there up to his sore throat?"
Metabolism & Pharmacokinetics

18 Months From the Clinic

- Knowledge
- Resources
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- Tech Transfer

FROM THE ANALYST'S COUCH

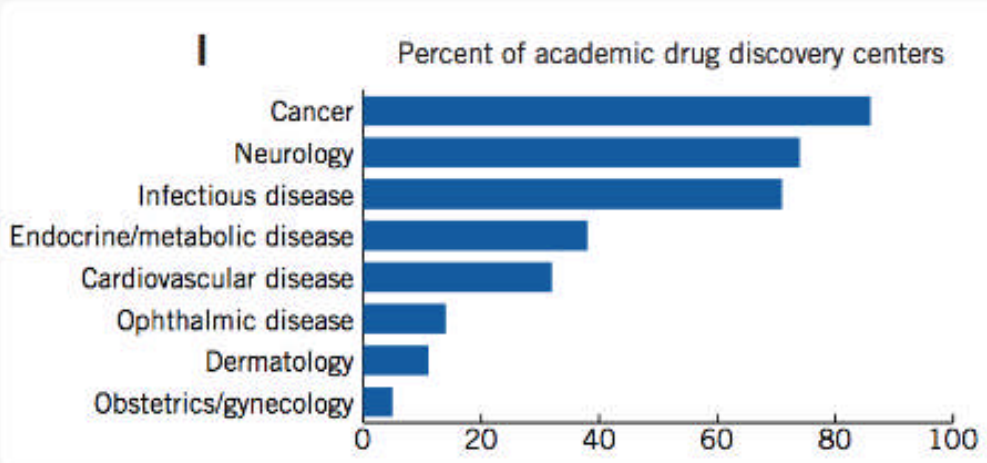
US academic drug discovery

Stephen Frye, Marina Crosby, Teresa Edwards and Rudolph Juliano

There has been substantial investment in the past decade to provide academic institutions with the capabilities for early-stage drug discovery, such as high-throughput screening (HTS) of large compound libraries and

Research portfolios and capabilities. A broad range of therapeutic areas are included in the interests of the academic drug discovery (ADD) centres (FIG. 1a). Cancer and infectious diseases are the most

According to a recent *Nature Reviews Drug Discovery* article, there are 78 small molecule–focused drug discovery centers at universities or nonprofit research organizations in the US. The report discussed some interesting stats:



- **2/3** of the drug discovery centers have high throughput screening infrastructure
- **2/3** have hit-to-lead medicinal chemistry expertise
- **1/2** have *in vivo* efficacy capabilities

http://www.blogoup.com/blog/2011/8/15/academic-drug-discovery.html

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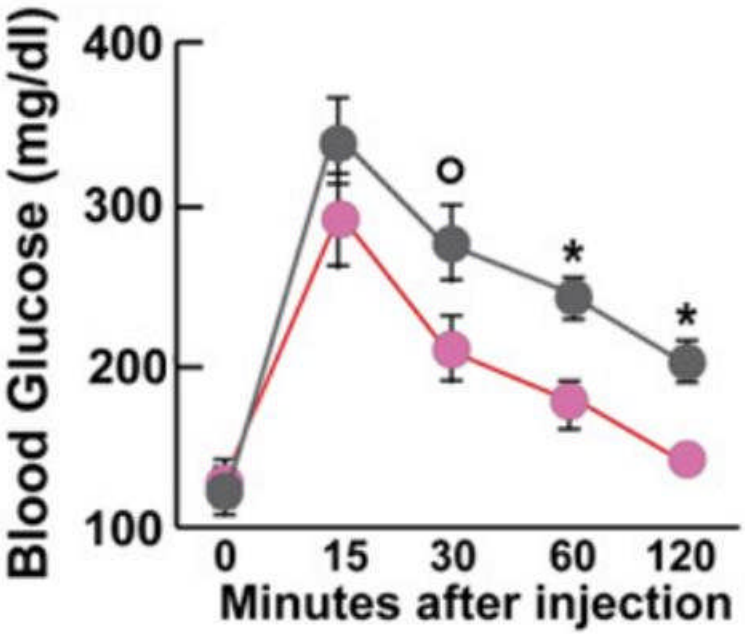

Blood Glucose (mg/dl)
400
300
200
100
0
15
30
60
120
Minutes after injection
o
*
*

Raise standards for preclinical cancer research

C. Glenn Begley and **Lee M. Ellis** propose how methods, publications and incentives must change if patients are to benefit.

Efforts over the past decade to characterize the genetic alterations in human cancers have led to a better understanding of molecular drivers of this complex set of diseases. Although we in the cancer field hoped that this would lead to more effective drugs, historically, our ability to translate cancer research to clinical success has been remarkably low[1]. Sadly, clinical trials in oncology have the highest failure rate compared with other therapeutic areas. Given the high unmet need in oncology, it is understandable that barriers to clinical development may be lower than for other disease areas, and a larger number of drugs with suboptimal preclinical validation will enter oncology trials. However, this low success rate is not sustainable or acceptable, and investigators must reassess their approach to translating discovery research into greater clinical success and impact.

Many factors are responsible for the high failure rate, notwithstanding the inherently difficult nature of this disease. Certainly, the limitations of preclinical tools such as inadequate cancer-cell-line and mouse models[2] make it difficult for even ▶

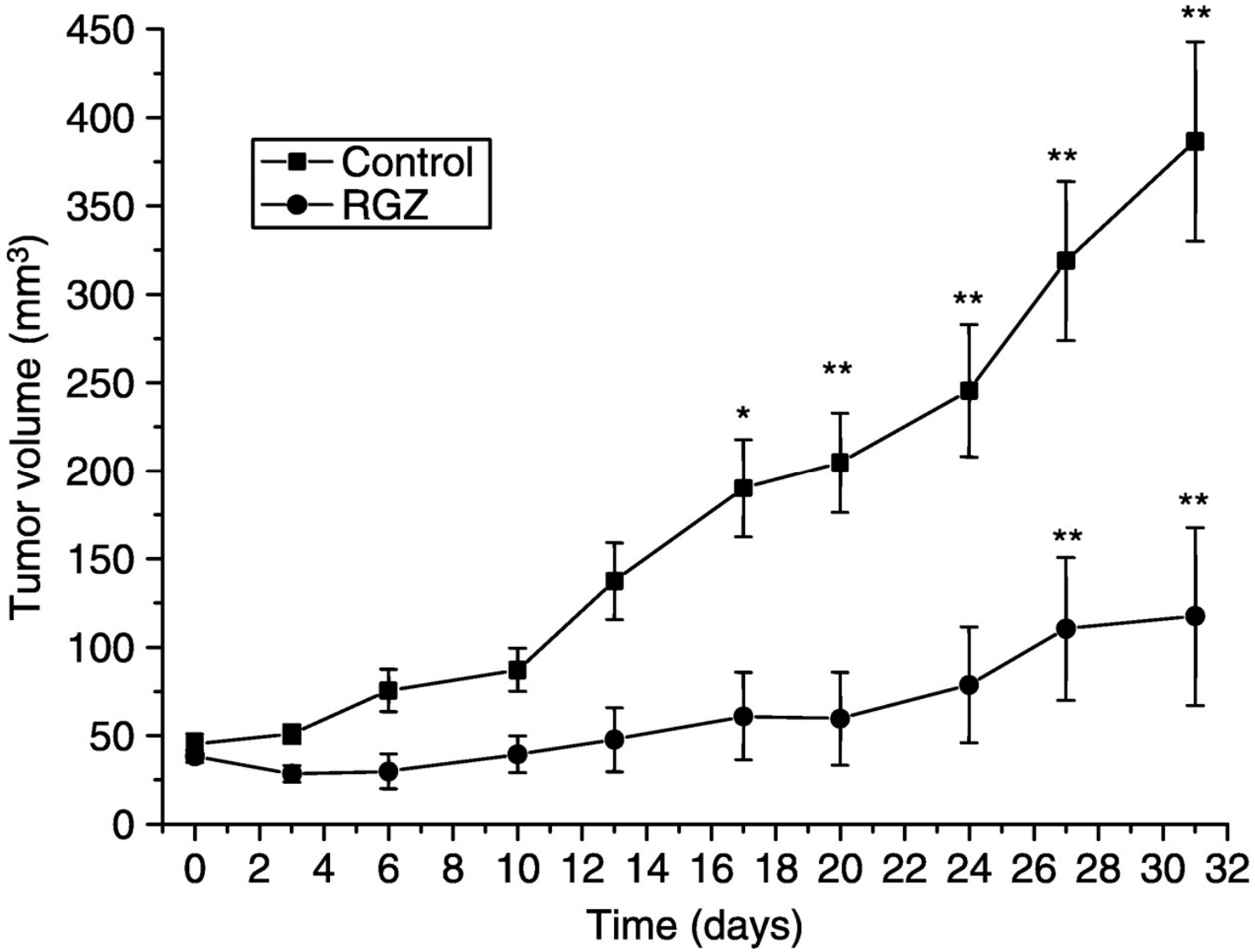
CORRESPONDENCE

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

Florian Prinz, Thomas Schlange and Khusru Asadullah

A recent report by Arrowsmith noted that the success rates for new development projects in Phase II trials have fallen from 28% to 18% in recent years, with insufficient efficacy being to 'feasible/marketable', and the financial costs of pursuing a full-blown drug discovery and development programme for a particular target could ultimately be hundreds of millions of

Nature Reviews Drug Discovery **10**, 712 (September 2011)



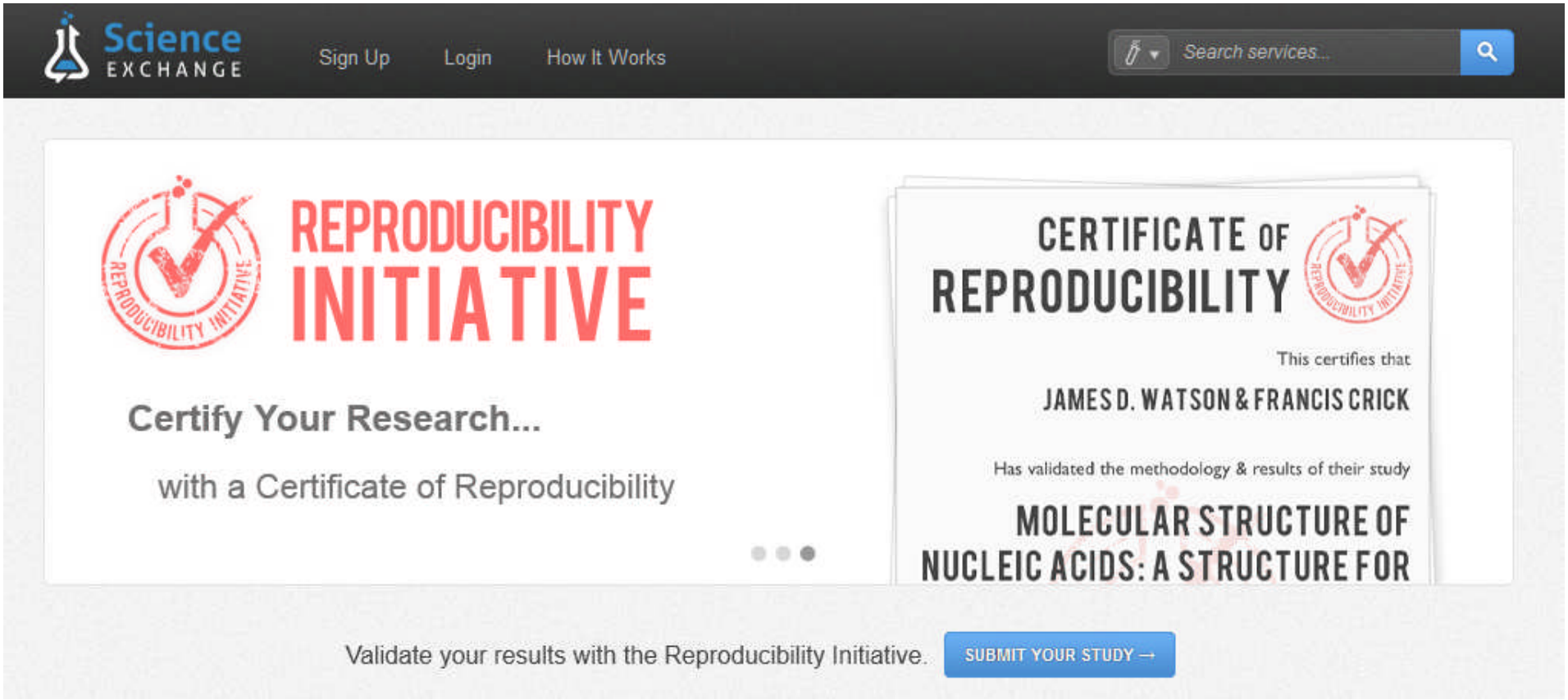
Endocr Relat Cancer March 1, 2010 vol. 17 no. 1 169-177

Importantly, **how are venture capitalists who invest in biotech supposed to engage on cool new data when the repeatability is so low**? Frankly, most VCs don't do early stage investing these days, and this resistance to fund early academic spin-outs is in part due to the insidious impact of the sector's high failure rate with academic reproducibility (a.k.a. 'bias'). But for those of us who remain committed to early stage investing, I'd suggest there are at least two key takeaways for VCs:

- **Findings from a single academic lab are suspect.** If other labs haven't validated it in peer reviewed literature, it's very high risk. It's probably bleeding edge rather than cutting edge. If it's only a single lab, it's likely only a single post-doc or grad student who've actually done the work. Given the idiosyncrasies of lab practices, that's a concentrated risk profile. Wait for more labs to repeat the work, or conduct a full lab notebook audit.

- **Repeating the findings in an independent lab should be gating before investing.** Don't dive in with a Series A financing prior to externally validating the data with some real "wet diligence". Sign an option agreement with an MTA, repeat the study in a contract research lab or totally independent academic lab.

Bruce Booth, Atlas Ventures, http://lifescivc.com/2011/03/academic-bias-biotech-failures/



https://www.scienceexchange.com/

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There are other implications of this problem, more than I can discuss here. But one is around the role of tech transfer offices. Although many TTOs are keen to start "seed funds" to spin-out new companies, this seems like a waste to me. **I'd argue that the best use of these academic "seed" funds would be to validate the findings of an investigator's work in a reputable contract research lab** that industrial partners and VCs would trust. If a TTO could show 3rd party data supporting a lab's striking findings, the prospects for funding would increase significantly. This is the type of de-risking that TTOs should focus on.


Harvard Catalyst Profiles