ÉCONOMIE DE LA SCIENCE

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PARTIE 1: OF MICE AND ACADEMICS EXAMINING THE EFFECT OF OPENNESS ON INNOVATION

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GENERAL QUESTIONS

- (Why) are academics needed?
- What distinguishes academic research from industrial research?
- Are there downsides to using patents to reward research?

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IN PARTICULAR

- Does openness help or harm basic research?
- How does increased availability of research inputs affect the flow and nature of subsequent research and innovation?

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TWO ALTERNATIVE VIEWS ON OPENNESS

- Appropriability view
- Control rights view

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APPROPRIABILITY VIEW

- Two research stages: basic and applied
- Research line pays out only when applied stage is completed
- Applied researcher can hold up basic researcher …
- … unless patent system protects basic researcher
- Thus here openness benefits more applied research, and it discourages basic research and innovations !

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CONTROL VIEW

- Openness helps match ideas with researchers …
- … This is more valuable in academia than in private sector as academic research is more free, thus less focused and more diverse

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THUS increasing openness …

- Should increase the overall flow of subsequent publications
- Should increase the diversity of researchers involved in follow-on innovation
- Should increase the diversity in the new lines of research that are being pursued

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PART 2 : THE OPENNESS EXPERIMENT

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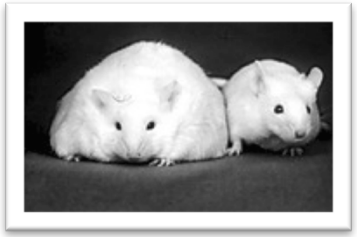
THE MOUSE REVOLUTION AND THE OPEN ACCESS CRISIS



Over the past century, specialized research mice have become a central research tool in life sciences research

- Particular mice strains, many bred from "spontaneous" mutations, were collected, classified, and distributed through institutions such as the Jackson Laboratory

Over the past twenty years, a genetics "revolution"

- Mice could now be "engineered" to have a particular gene inserted or removed to mimic a disease e.g. cancer or diabetes
- Over 13,000 specialized mice published in scientific literature
- 2007 Nobel Prize in Medicine to Mario R. Capecchi, Martin J. Evans and Oliver Smithies for "gene modification in mice"

While specialized research mice have the potential for application across many areas, exploiting these mice for a new "line" requires access

- Costly and time-consuming to develop from scratch

Notably, two key tools – the Oncomouse and Cre-Lox – received broad patents controlled by DuPont, who then imposed stringent licensing restrictions and substantial reach-through royalty payments, even for academic researchers

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RESEARCH UNDER LIMITED OPENNESS

- Spontaneous and Knock-Out mice would be freely available
- Oncomice available informally for research purposes….but using them for more applied projects would contravene DuPont's licensing requirements
- Cre-lox mice only available at very high transaction costs

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TWO OPENNESS SHOCKS

- We now describe two ”natural experiments” that significantly shifted openness on genetically engineered mice

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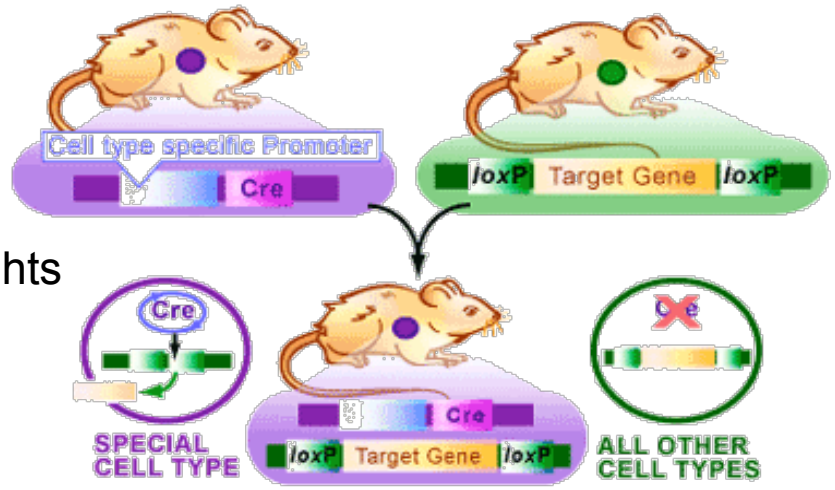
CRE-LOX SHOCK

Cre-lox tool developed by DuPont to create genetically engineered mice with a target gene "turned on or off" in specific tissue

Powerful tool providing greater selectivity & insights into the role of genes in disease….

DuPont's IPR (#4,959,317) covered any mouse made using Cre-lox - used to control mouse distribution & follow-on use



SHOCK

July 1st, 1998: A **Memorandum of Understanding** between DuPont, JAX & the National Institutes of Health allowing JAX to distribute Cre-lox mice with a simple license

THE EXPERIMENT

Pre 1998 mice made & published using Cre-lox could not be shared without a costly license from DuPont which included arduous terms & conditions– no JAX distribution

Post 1998 Cre-lox mice available for all researchers at non-profit institutions for internal research via JAX who make mice available & manage the simple licenses

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ONCO SHOCK

Oncomice developed at Harvard in 1984 by Leder & Stewart by inserting an oncogene to give the mouse susceptibility to cancer

Powerful approach providing greater insights into the role of genes in cancer….

Harvard's patent (was ambiguous) but seemingly covered any mouse made using an oncogene – licensed to DuPont who use to control mouse distribution & follow-on use

SHOCK

1999: **MoU** between DuPont, JAX & NIH allow JAX to (continue to) distribute Onco mice with a simple license that had to be signed by universities

THE EXPERIMENT

Pre 1999 Onco mice made & published could not be used without a costly license from DuPont which included arduous terms & conditions but JAX distribution went ahead

Post 1999 Onco mice available for all researchers at non-profit institutions for internal research via JAX who make mice available & manage the simple licenses

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RESULTS : KEY FINDINGS

- A significant increase in the rate of follow-on citations for “mouse-articles” impacted by the NIH MoU agreements in openness
- Boost in follow-on research is driven by
  - Contributions by “new” authors or institutions (reprint authors or institutions that had not previously cited the original mouse-article)
  - More diverse types of research (articles using previously unused keywords or published in journals that had not previously cited the original mouse-article)
- An increase in both basic and applied research

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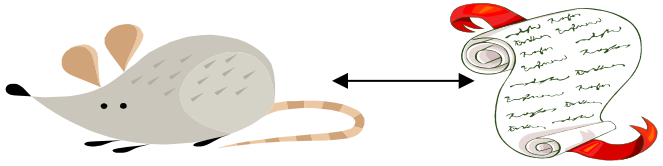
EMPIRICAL APPROACH



- Start from “Mouse-articles” - Sample of scientific research mice linked with specific scientific research articles – Cre-lox, Onco, Knock-Out& Spontaneous
- Then look at citations to mouse-articles in other scientific publications observed over time
  - Citations are specific – unlikely to cite a mouse article unless one is directly using that mouse or providing an comparison with the results from a particular mouse model
- Exogenous institutional “shocks” – natural experiments - to the openness of Cre-lox (1998) & Onco (1999) mice
  - Shocks shift the degree of openness associated with treated(Cre-lox & Onco) mouse-articles, after the article has been published
  - We also observe (Knock-Out & Spontaneous) control mice – who experience no change in openness subsequent to their initial publication
- We look at rate and nature of forward citations to Cre-lox and Onco mouse-papers before and after the openness shocks, also including untreated mouse-articles in regression exercise

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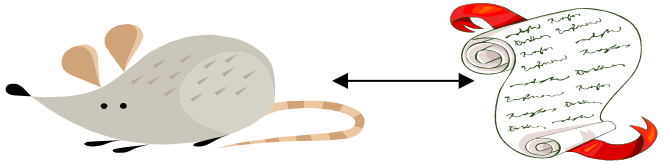
EMPIRICAL APPROACH



Data Sources

- Mouse Genome Informatics (MGI) database catalogs over 13,000 mice & links each mouse to an original publication in a scientific journal – mouse-articles
- PubMed for information about mouse-articles & ISI Web of Science SCI for citations

Sampling Strategy

- Identify universe of MGI mouse-articles published 1983-1998 sample on four types of mouse-articles (2171 total mouse-articles)
- Cre-Lox (28), Oncomouse (102), Knock-Out (1895), Spontaneous (146)

For each mouse-article collect information about the forward citations

- 432,083 total citations (from pub year thru 2006)
- Aggregated up into 22,265 citation-years

For each citing article code key article/author characteristics

- **New/Old Last Author**: new if last author never appeared as last author before in citations to the mouse-article in prior years, old otherwise. **New/ Old Institution**:…**New/Old Key Words**:…**New/Old Journal**….**Basic/Applied**: Basic if journal of citation scores 1 or 2 on CHI Research journal basicness score, Applied if journal scores 3-4 on the CHI journal basicness score (see Lim 2004)

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RESULTS

Overall Impact of Openness on Level of Scientific Research

Negative Binomial	Annual Forward Citations		
Post Shock	**1.302*** **		
Post Shock (Short Term – shock +3)		**1.220*** **	
Post Shock (Long-Term – 4-6)		**1.429*** **	
Post Cre Shock			**1.467*** **
Post Onco Shock			**1.267*** **
Conditional Fixed Effects for Article, Age & Calendar Year, Window Effects			

Coefficients reported as incident rate ratios (percentage relative to 1.0)

After the MoUs, a significant uptick (~ 20%) in the total level of citations to mouse-articles

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RESULTS

New or Old Researchers?

Negative Binomial	Overall Shock		Short-Term v Long-Term	
	Annual Citations with New Last Author	Annual Citations with Old Last Author	Annual Citations with New Last Author	Annual Citations with Old Last Author
Post Shock	1.379***	1.135		
Post Shock (Short Term)			1.276***	1.064
Post Shock (Long-Term)			1.537***	1.224**
Conditional Fixed Effects for Article, Margin-Age and Margin-Calendar Year, Window Effects				

The impact of both MoU agreements shocks is concentrated in citations by "new" last authors

Robust to "New Institution" v."Old Institution" or broken down by Cre v. Onco

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RESULTS

New or Old Researcher lines?

Negative Binomial	Keywords		Journals	
	Annual Citations with New keywords	Annual Citations with Old keywords	Annual Citations in New Journals	Annual Citations in Old Journals
Post Shock	1.260***	0.925	1.381***	1.201**
Conditional Fixed Effects for Article, Margin-Age and Margin-Calendar Year, Window Effects				

The openness shock results in a significant increase in articles with new keywords

- Robust to short-term versus long-term, and dividing out by Cre and Onco shocks

The impact of the openness shock is concentrated in citations in journals which had not previously referenced the mouse-article

- Short-term impact on journals is very big, and there is a modest long-term effect for new and old (perhaps because of "induced" repeats)

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RESULTS

Robustness Tests for a Pre-shock Trend

Negative Binomial	Overall Citations	New vs. Old Author Citations		New vs. Old Keyword Citations	
	Annual Forward Citations	Annual Citations with New Last Author	Annual Citations with Old Last Author	Annual Citations with New Keywords	Annual Citations with Old Keywords
Post Shock	1.145*	1.117	1.034	1.127	0.984
Treatment Group Overall Time Trend	1.003	1.014	1.000	1.001	0.997
Post Shock Change in Trend	1.050**	1.052**	1.046*	1.053**	1.045
Conditional Fixed Effects for Article, Margin-Age and Margin-Calendar Year, Window Effects					

The coefficients on the Treatment Group Overall Time Trend are never significant.

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CONCLUSION : KEY FINDINGS

A significant increase in the *rate* of follow-on citations for "mouse-articles" impacted by the NIH MoU agreements in openness

Boost in follow-on research is driven by

- Contributions by "new" authors or institutions (reprint authors or institutions that had not previously cited the original mouse-article)
- More diverse types of research (articles using previously unused keywords or published in journals that had not previously cited the original mouse-article)

An increase in both basic and applied research

- Horizontal exploration effect is greatest in "pure" experiment when IP & material rights limit access ex ante, i.e for Cre-lox
- Vertical exploitation effect dominates for Onco, where access possible but ex post threat of hold up makes downstream research "risky"

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CONCLUSION : NEXT STEPS

- Our results suggest that IP rights may impose limits on the diversity that would otherwise be pursued by follow-on researchers
- Future research
  - Reassess Bayh-Dole
  - Wikinomics

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