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Building a Robust Research Commons: Enhancing the Precompetitive Environment

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Introduction

- **Precompetitive research: improving the tools and techniques for successful translational research (Woodcock, 2010)**
- **Current institutional and rule-based impediments to developing bioresources**
- **2 Empirical Studies:**
 - **Canadian Stem Cell Network**
 - **Mouse Models for Human Disease**

Building a Robust Research Commons



- Databases and biorepositories to *support* research
- Commons is a shared and managed resource that is vulnerable to social dilemmas
- A set of resources available to all researchers on terms that encourage efficiency, equitable use and sustainability that is managed by groups of varying sizes and interests

Thinking about the Commons



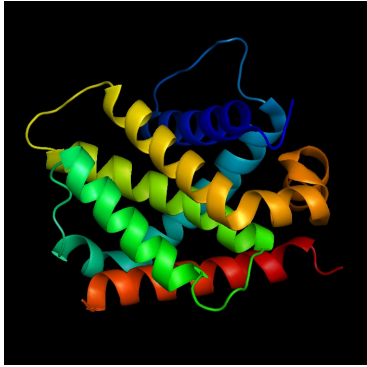
ELINOR OSTROM
2009 Nobel Laureate
in Economic Sciences

Nobel medal © © The Nobel Foundation

UNDERSTANDING
INSTITUTIONAL
DIVERSITY

Elinor
Ostrom

GOVERNING THE COMMONS



Differences between research and natural commons

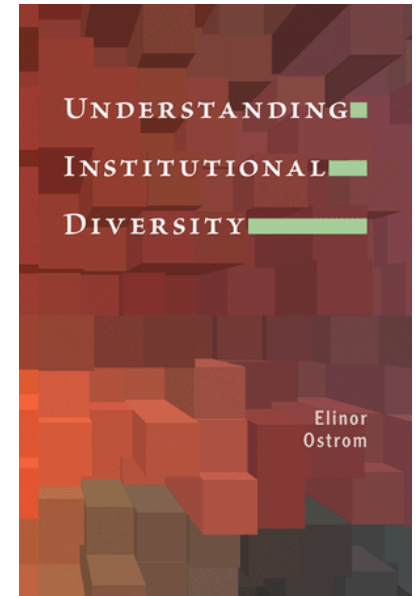
- the main issue facing research commons is under-use
- the value of a research commons is enhanced as *more* people use the resource - “network effect”
- global rather than local in scope
- a global research commons must be managed to facilitate not only use, but also re-contribution from the user community, creating a feedback loop between withdrawal, value-added research, and deposit

Rules in Use: (Focus on IP and Sharing)

- **FORMAL LAWS (IP, animal welfare, FDA)**
 - Often out of sync with new capabilities, community norms and technology
- **CONSTITUTIONAL**
 - Who may make the rules (e.g., institutional structures: PPPs, consortia, repositories, databases, etc.)
- **POLICIES AND GUIDELINES**
 - E.g., funding agencies, universities, journals, repositories, creative/science commons
- **INFORMAL RULES/ COMMUNITY NORMS/ PRACTICES**
 - Citation, attribution, reciprocity and sharing, publication,

Requirements for a Robust Commons (Elinor Ostrom)

- Cultural homogeneity
- Rules that match the structure of the community and desired outcomes.
- Active participation
- Some autonomy in rule making.
- System for self-monitoring of behaviour.
- Graduated system of sanctions.
- access to low-cost resolution mechanisms.



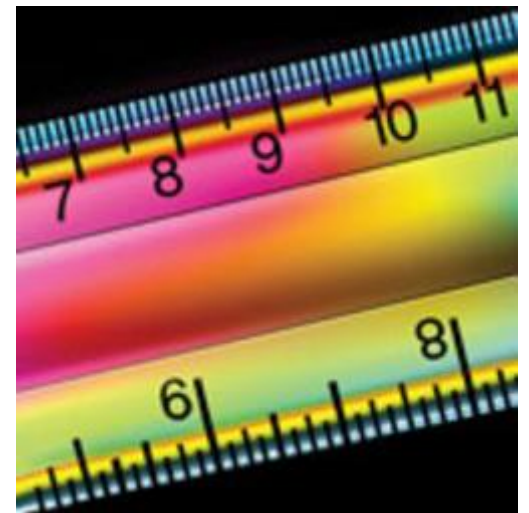
The Problem with Current Rules in Use

- **No doubt of increasing commercialization pressure on publicly funded research institutions and their researchers**
- **Mediated through technology transfer offices**
- **Patenting as a proxy for commercialization and a signal of changing values and norms of a community (of users)**
- **Impact on community norms and trust?**
- **Impact on sharing/willingness to contribute to and use a resource?**

Metrics aligned with commercialization objectives

- Matched to commercialization-based outcomes
- *You get what you measure. Measure the wrong thing and you get the wrong behaviors.*

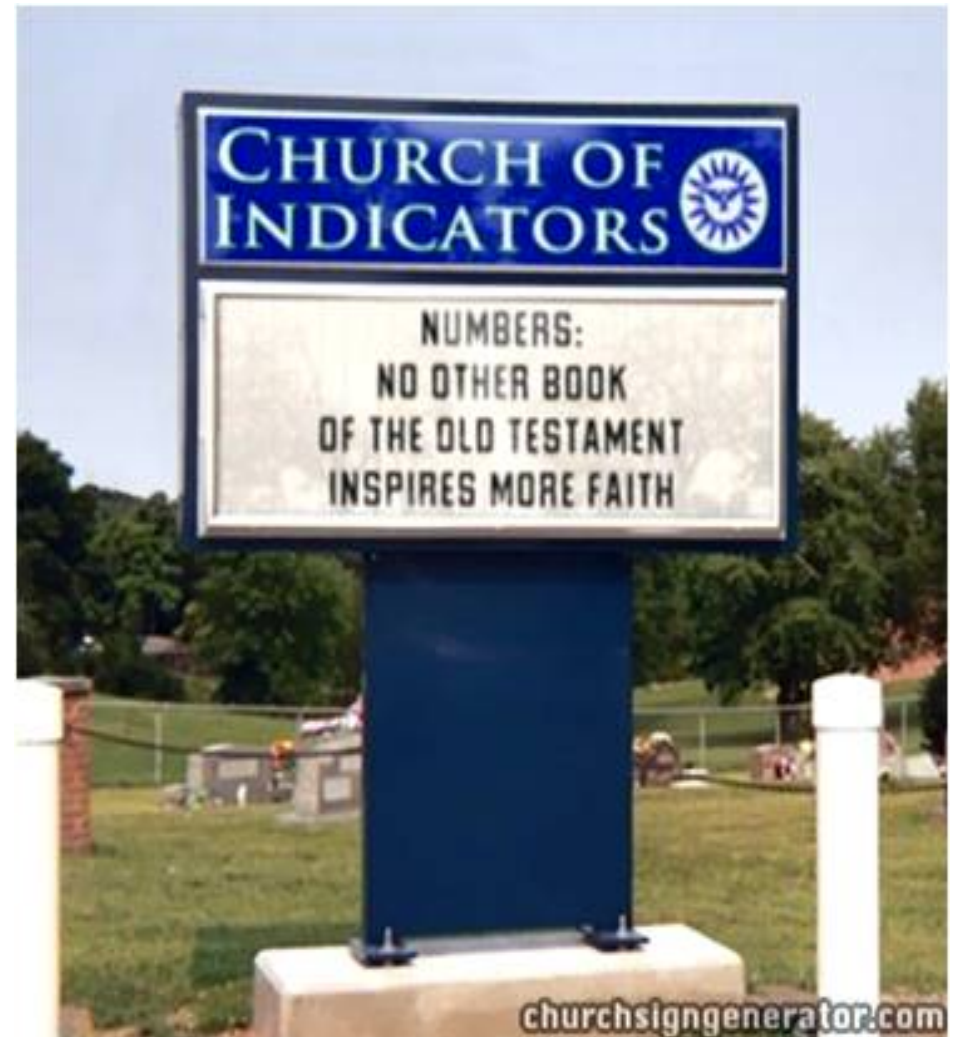
- John H. Lingle





Current Metrics

- **Economic**
 - (OECD,
 - National Stats Offices)
- **Aggregated**
- **Input/output**
- **Direct vs. indirect**
- **Correlation**
- **Simplistic**
- **Based on pipeline model**



Metrics driver

- **Association of University Technology Managers (AUTM) Metrics**
 - **Out the door**
 - Licenses
 - Spin-offs
 - **Revenue-generation**
 - Licensing revenue
 - Cashed-in equity



Encouraging Behaviours?

- Patenting
- Licensing for revenue generation
- Start-up Creation

Impacts?

- Patent Thicket
- Culture of Science
- Access / Clinical Application

= Institutional and systemic inertia





-Universities are actively patenting
research tools
(Langford et al., 2006)

-Most patents are worthless and useless
(Kirsten, 2005)

-Most gene patents held by universities
and small biotech companies (not big
business)

(Scherer, 2002; Adelman, 2007)



PRECOMPETITIVE SPACE

Upstream:
Main

Coping Strategies???

MASS INFRINGEMENT!

Downstream:
Limits to Access
Increased Costs
But tradeoff of patent
system

Impacts on Science Culture

CASE 1: Stem Cell Network

(Bubela *et al.* Cell Stem Cell, 2010)

- **Examine the impact of patenting and startup company involvement on academic collaborations measured through coauthorship**
- **Networks of Centres of Excellence (NCE)**
 - to facilitate networking, research excellence, and commercialization of network funded research

Conclusions of SCN Study

(Bubela *et al.* Cell Stem Cell, in press)

- **SCN researchers exhibit a high degree of collaboration both nationally and internationally.**
- **Some collaboration patterns were best explained by institutional affiliation, research quality and seniority.**
- **BUT Patenting negatively impacted collaboration.**
- **Collaboration/commercialization may be antagonistic.**
- **Field will require significant incubation in academia before it is ready for primetime.**

2. Creating Bioresource and Data Research Platforms – Lessons from The Mouse Commons

- **New multi-stakeholder collaborations need to be supported by data and bioresource sharing institutions and infrastructure.**
- **Explosion in mutant mouse strains, in part the product of a coordinated high-throughput community project, the International Knockout Mouse Consortium (IKMC)**
- **Traditional modes of sharing data and bioresources are no longer adequate to the scale or nature of the task required**

NorCOMM – EUCOMM - KOMP

- Public Resources established to provide public and private research communities with a source of Knockout Mice and Embryonic Stem cells
 - Knockout Mice lack two copies of a specific gene and therefore do not produce the protein the gene encodes
 - Embryonic Stem cells are used to produce Knockout mice



Research Question

- Does the legacy of basic research patents created under current laws and practices hinder the establishment of public sector resources?

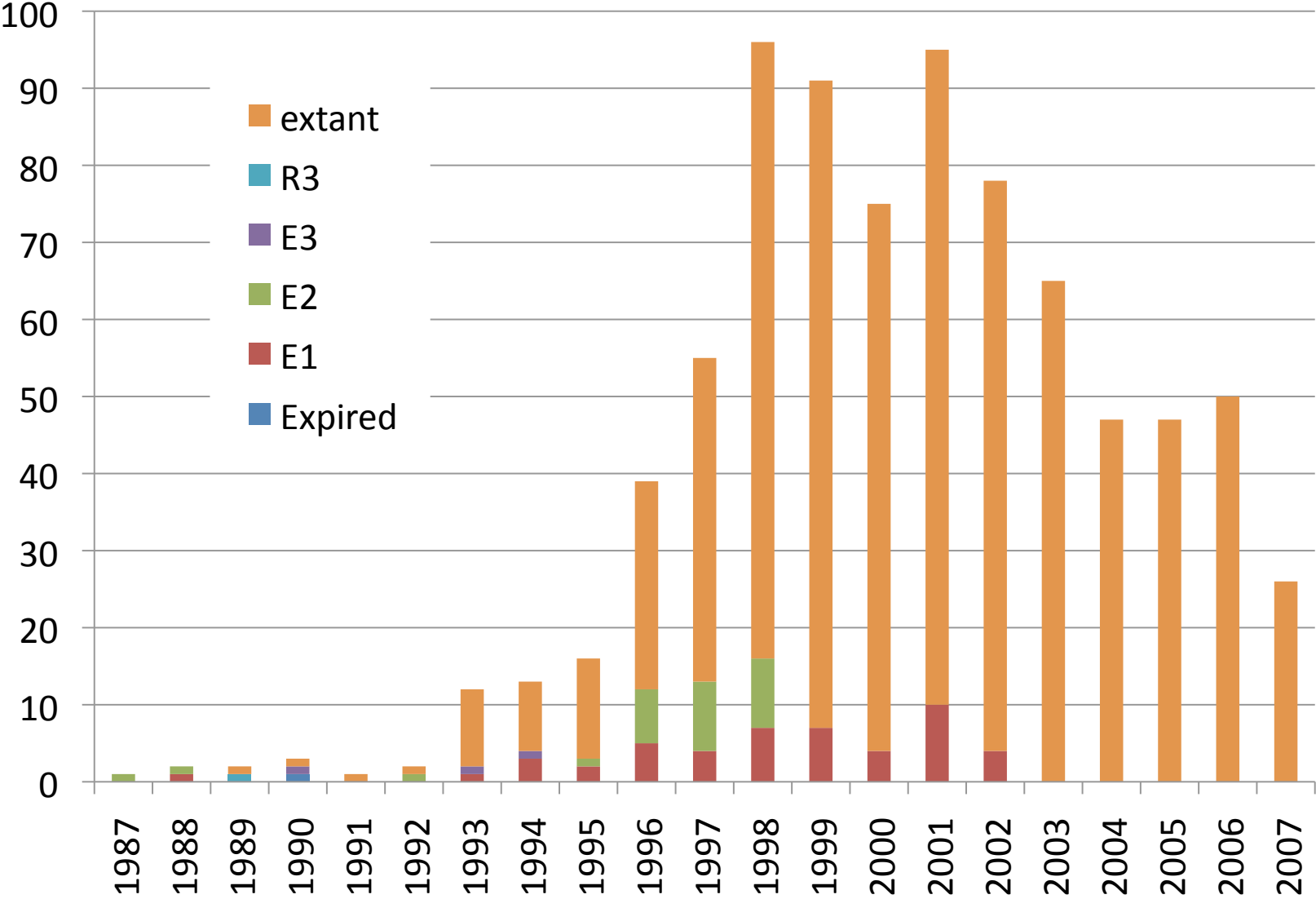


Mouse Patent Landscape:

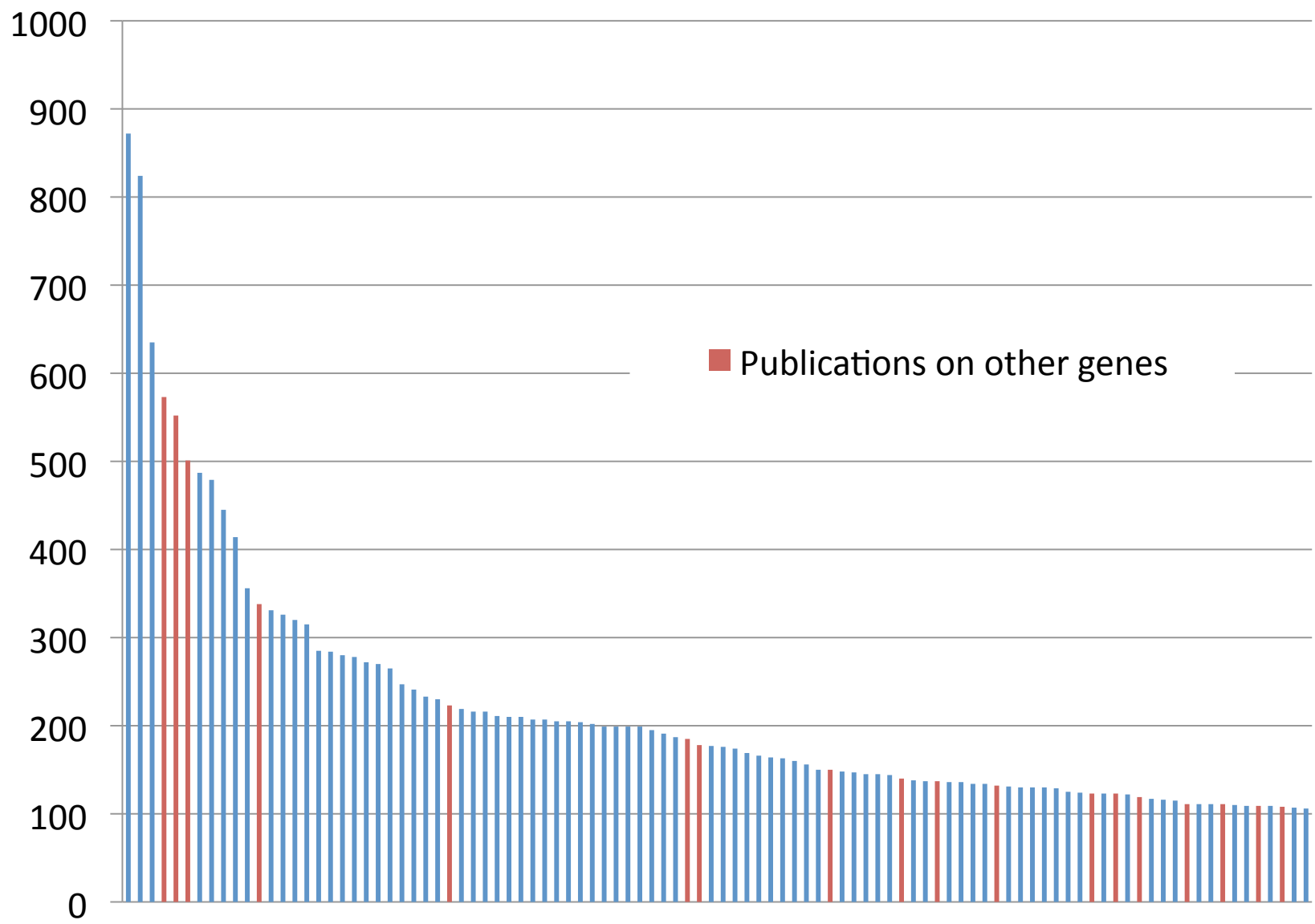
Method

- **Delphion search US Granted Patents**
 - Patents involving DNA (modified Cook-Deegan search algorithm)
 - AND Mouse search terms in claims
 - AND NOT Plant*
- **Resulted in 6,979 patents**
 - Examined claims of each patent
- **Coded each 'accepted' patent (2,373 – 34%)**
- **952 patented genes identified through Blast analysis**

Status and filing date of 816 Mouse Gene Patents (US)



Publications (>100) associated with patented versus unpatented mouse genes



METHODS PATENTS CODING

Problematic for construction of resource

- Coding frame developed with experts
- Include product
- Broad/specific method

- BAC
- Positive/negative selection
- FLP/FRT Recombinase
- Isogenic DNA
- Recombineering
- Electroporation
- PhiC31

- Cryopreservation
- Gateway Technology
- Cre/Lox
- inverse PCR
- F0/F1mouse
- Vector
- Homologous Recombination

- Method used in Gene Trapping/Targeting
- Total = 105 Patents coded**



Litigation: A sure way to destroy trust

- **Current litigation:**
- 2010 Markman Hearing: THE CENTRAL INSTITUTE FOR EXPERIMENTAL ANIMALS, a Japanese corporation, (Plaintiff) v. **THE JACKSON LABORATORY**, a Maine corporation (Defendant)
 - "NOD/Shi Mouse" and "NOD/Shi-scid Mouse"
- 2010 Demand for Jury Trial: Alzheimer's Institute of America, Inc (Plaintiff) v. Elan Corporation, PLC, Eli Lilly and Company, ANASPEC Inc, Immuno-Biological Laboratories, INC., Invitrogen Corp., **The Jackson Laboratory**, and Phoenix Pharmaceuticals (Defendants)
 - Swedish Mutation, etc.

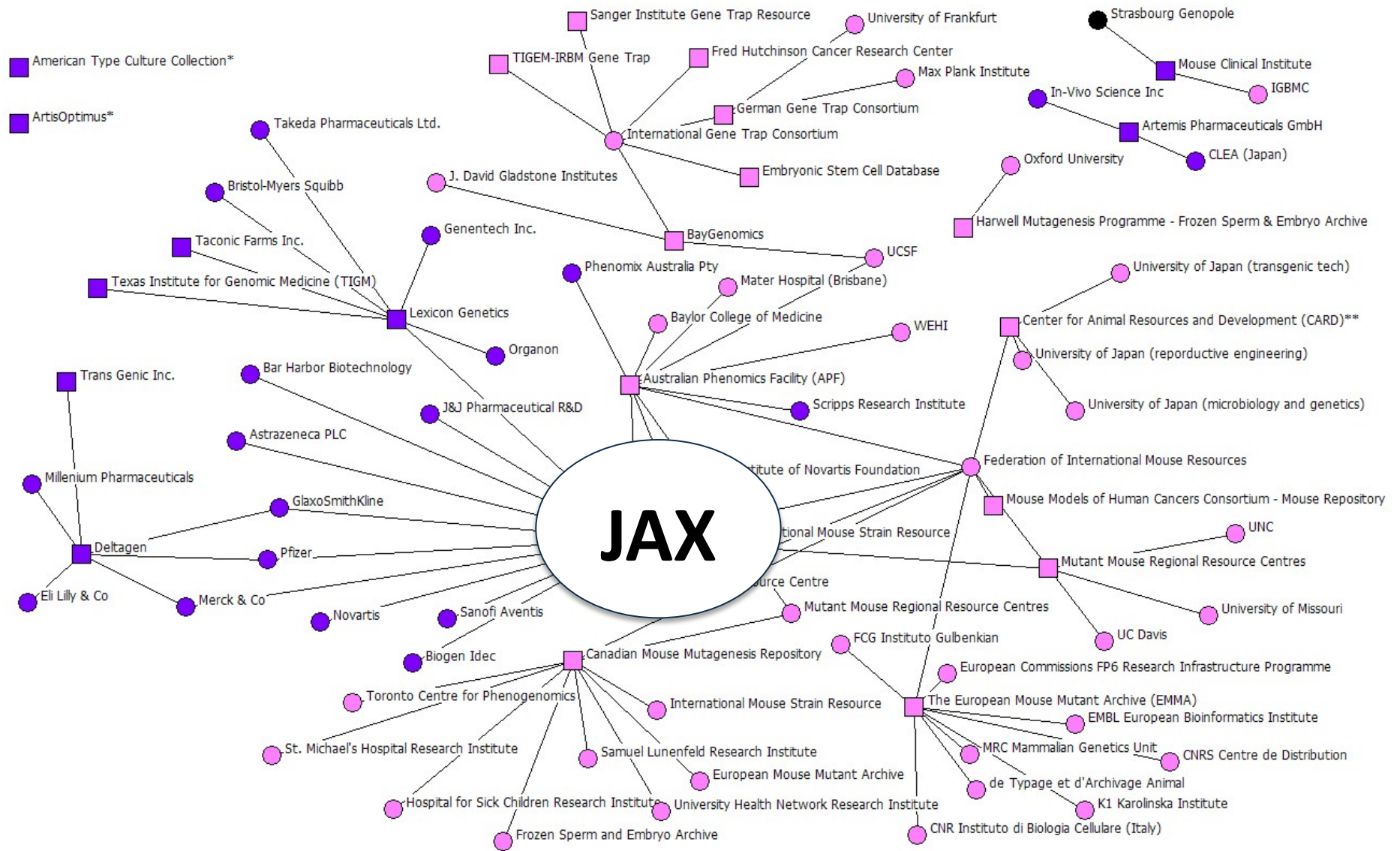
Conclusions on IP



- Large number of overlapping patents both on products and methods.
- Most gene and DNA patents held by public sector, most cell lines and mice by private sector.
- Methods patents may be more of a blocking problem in the long-term than product patents
- Public resources are being established, however patents may impact on repositories and users, especially as research moves towards clinical application.
- **Utility of maintaining and EXPENSE of public sector patents on research tools?**
- **Most important is change in CULTURE, collaboration, sharing ethos, competition and trust**

Community identified problems with rules in use

- **Material Transfer Agreements identified by the community as a substantial disincentive to accessing and providing materials**
- **Researchers should be free to breed mice for research purposes and cross-breed them to produce new strains (added value back to commons)**
 - **Rome Agenda *Schofield et al. 2009 Nature***



4. Mouse Repository Network – Actors by Institutional Type



The Rome Agenda:

Post-publication sharing of data and tools

Schofield, Bubela et al. *Nature* 461, 171-173

- Access to data and materials
- Licensing and patenting
- Data and resource-sharing infrastructure
- Standards and tool development
- Attribution and reward
- **BUT: policies are one thing and enforcement another**

Conclusions

- **The movement to implement a true science commons based on community norms has gathered considerable momentum.**
- **A combination of existing community norms, rule development, incentive structures, and adequate enforcement will all contribute to a research commons.**
- **Influencing the other actors in the game, the funding agencies, research institutions, TTOs and journals is the next major challenge.**
- **Industry, through use of the resource, can only enhance the value of the resource and add to potential sustainability**



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