

THE ONCOMOUSE THAT ROARED:

RESISTANCE & ACCOMODATION TO PATENTING IN ACADEMIC SCIENCE*

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ABSTRACT

Academia has witnessed a dramatic rise in commercial practices including patenting. As norms and exchanges in academic science are distinctive from those in commercial science, this setting provides a dramatic example of the collision of institutional logics. The twenty-year period following the patenting of the Oncomouse in the 1980s provides a clear setting to examine scientists' strategic action and changes in exchange relationships in response to commercial forces, and the mechanisms through which the mouse community shaped far-reaching institutional change in academic science. These findings have important implications for the way that we analyze the collision between academic and commercial science, collisions of market practices with other previously protected arenas of life, and our thinking about the role of exchange in institutional change.

INTRODUCTION

In 1984, scientists at Harvard University carefully engineered a new mouse to have a predisposition to cancer, the Oncomouse. The Oncomouse represented a significant breakthrough for the mouse genetics community (the tight-knit group of researchers who used mouse models to study illness). Over the next two decades, the Oncomouse proved scientifically useful, but also became a touch point of controversy throughout the scientific community. For the Harvard researchers had not only disclosed the Oncomouse through the traditional academic means of peer-reviewed publication but also had patented their creation and subsequently licensed this patent to DuPont. The Oncomouse, therefore, became not only a significant scientific breakthrough, but also a hot commercial product named “Product of the Year” by Fortune.

DuPont attempted to use its licensed intellectual property rights (IPR) in ways that while consistent with practices in commercial science roiled those in academic science.¹ The company set a high price per mouse although researchers had long-standing norms about freely trading mice. They placed restrictions on breeding programs, although this was considered a scientist's prerogative. They demanded publication oversight, although scientists were loath to share such information with outsiders. Finally, DuPont insisted upon a share of any commercial breakthroughs made using the Oncomouse. In response to this encroachment on their daily practices, many in the mouse genetics community were outraged, raising questions about previously taken-for-granted assumptions underpinning the institution of academic science.

The Oncomouse is a prominent example of the increasingly common collision between two institutions - academic and commercial science. Since the 1980 Dole-Bayh Act gave universities the impetus to patent and license innovations created by their employees, there has been a dramatic increase in patenting rates (Owen-Smith and Powell, 2003, Mowery et al. 2001). However, the verdict on collision of market forces with the previously “protected” institution of academic science has been decidedly mixed. Many commentators have expressed deep concern

¹There are many labels to distinguish the two institutional settings in which science is practiced. For the purposes of this analysis, I use the term “academic science” to denote what some scholars refer to as the “Republic of Science” or “Open Science.” I use “commercial science” to capture the market-based logic of patents and the attendant contracts that characterize for-profit based research activities. I reject the distinction of “science” versus “technology” (Rosenberg 1974) because this presupposes that the distinction is one of knowledge, when increasingly the same idea can serve dual (scientific and commercial/technological) ends. Another typical pairing is “Open” and “Closed” science. This terminology moves closer toward an institutional distinction but the choice of language brings with it strong assumptions about the nature of disclosure and exchange which I argue are more complex.

over this introduction of market-based practices into the old institutional order of academic science. Some have gone so far as to say that patents exemplify the corruption and prostitution of pure science by commercial forces (Krimsky 2003). Legal scholars have argued that IPR will increase transaction costs of knowledge traditionally open to all and lead to the privatization of the "intellectual commons" (Heller and Eisenberg 1998). Empirical researchers assessing the impact of patenting using bibliographic data have drawn more sanguine conclusions. Measures of individual publication and overall measures of scientific progress have been little influenced by IPR (Agrawal and Henderson 2002; Azoulay, Ding, and Stuart 2005; Murray and Stern 2006). Other evidence is paradoxical: while surveys suggest that patents make no difference to scientists (Walsh et al. 2003, 2005) they are garnering more and more patents for their academic institutions (Owen-Smith and Powell 2003).

To resolve this contradictory evidence, I draw on institutional theory and take the perspective that strategic action plays a critical role in shaping institutional change. I argue that the introduction of patents into academia represents a collision between two institutions that initiates a process of transformation which can serve as a window into the mechanisms of institutional change. Building on the notion that institutions are relative stable social structures with distinctive logics, practices and considerations concerning social exchange (Friedland and Alford 1991, Scott 1995), I argue that these practices also provide the flexibility for individual and organizational strategic action (DiMaggio 1988, Granovetter 1992, Oliver 1991). Scholars have begun to elucidate a repertoire of different strategic responses to institutional collisions (and other external pressures) (Westphal et al., 1997; Van de Ven and Hargrave 2004). To date, however, the rich details of these studies have focused on single organizations or actions (Thornton and Ocasio, 1999). Our understanding of the response of a community is limited and less attention has been paid to the way in which strategic action and changing practices translate into changes in institutional logics themselves.

The collision of academic and commercial science is an opportunity for just such an analysis. Framed in this way, I argue that we can consider both these institutions as having a stable logic (Merton 1973, Schofer 2003, 2004). This logic is founded upon two quite distinctive modes of exchange (Latour 1987): publishing in academic science and patents in commercial science (Dasgupta and David 1994, Owen-Smith 2003). The potential for strategic action arises from the inherent flexibility associated with these exchanges that provide scientists with the leeway to incorporate other considerations into their choice of the currencies, exchange rates, and targets of exchange (for an explanation of evaluation in its broader context see e.g. Boltanski and Thevenot

1991, 1999; Lamont 1992, 2000; and in science see Biagioli 2000; Geison 1995; Collins 1999). Such range in existing exchange relationships means that scientists in Academia have a variety of responses to the collision of commercial science practices. What remains to be explored are the mechanisms through which new practices emerge out of the institutional collision, and the mechanisms through which new institutional logics are established.

In this paper I address these questions by analyzing the reaction of the mouse genetics community to the Oncomouse patent. This represents a particularly attractive site to explore the relationship between strategic actions taken in exchange relationships and the transformation of institutional logics: The mouse genetics community was a tight knit group that had evolved clear exchange norms. The Oncomouse provided this community with an important scientific discovery, but when Harvard patented and licensed the Oncomouse to DuPont the corporation imposed the commercial logic of IPR on academics intent on using this discovery. While this logic was costly for academic scientists, the Oncomouse was too important for them to ignore. Rather, they were forced to craft a response.

As I detail below, the story of the Oncomouse reveals a seemingly paradoxical response, and one that is unanticipated in the current literature. At the outset, the mouse community strongly resisted DuPont's claims, both at the community level and through individual acts of civil disobedience (Ewick and Silbey 2003). This resistance forced the commercial giant to retreat. Yet at the same time that they were protesting DuPont's enforcement of IPR, many scientists embraced patenting of their own work. The scientists were not as inconsistent as it appears at first blush. I show that scientists have accommodated patents into academic science but have imbued them with a new social meaning and instituted new sanctions to limit the encroachment of the commercial logic. I argue that this combination of resistance and accommodation is generated by the ambiguous role of patents as an economic resource in academic science and is resolved through the construction of new exchange practices. The institution of academic science also changed subtly as patents become a new medium for exchange and a signal for cross-boundary work with commercial partners. Of particular interest to scholars of institutional change, the Oncomouse case can also illuminate precise instances in which new exchange relationships lead to broader shifts in institutional logic; through their role in the Oncomouse debacle journal editors instituted new policies for material availability and commercial disclosure, university licensing officers created spaces for academic research outside the strictures of commercial licenses and leaders at the National Institutes of Health began to engage more closely in the dissemination and control of research, not simply its funding.

This study has implications for students of institutional change beyond the realm of science. When practices forged in one institution are injected into another, the shift in context can change the meanings of the practice. Existing exchange relationships, while reflecting an institutional logic, may be sufficiently flexible to incorporate and/or transform the practice in line with institutional logic. Just because new practices are based on norms that run counter to the institutional logic doesn't mean the institution will be corrupted or collapse or remain unscathed. Instead, institutional change of profound consequence can arise from strategic actions taken in the daily lives of individuals as they interact with one another.

CURRENT PERSPECTIVES ON THE ACADEMIC-COMMERCIAL BOUNDARY

Historians remind us that the difficulties associated with negotiating the boundary between academic and commercial worlds in science has been with us since the dawn of modern science. In making their claim for professional autonomy, scientists have engaged in social action and boundary work to define the distinctiveness of “science” (Shapin 1994, 1996; Gieryn 1983, 1995). In the early modern period, disinterestedness and truthfulness emerged as distinctive attributes of a scientist. However these features were only considered “robust” when the pursuit of science was separated from financial reward. "The gentlemanly constitution of scientific truth" therefore provided the foundation for science and the boundary between science and non-science was thus established between different strata of society (Shapin 1994).

By the late 1800s, distinctions became more strongly grounded in different types of organizations pursuing distinct objectives – applied work was pursued in the commercial setting, while academia became the setting for the pursuit of “pure” basic knowledge. The boundary work done by scientists reinforced the notion of a distinctive institutional logic for academic science, one that was unscathed by lowly economic principles (Reingold 1964). For example in an influential 1899 address, physicist Henry Rowland made an appeal for pure science: "Much of the intellect of this country is still wasted in the pursuit of so-called practical science which ministers to our physical needs and but little thought and money is given to the grander portion of the subject which appeals to our intellect alone" (Rowland (1899) in Reingold 1964). Academic science was not immune from the reciprocal charge that it might undermine Commerce. William Sewall succinctly described that: “deep thinking is quite out of place in a world of railroads and steamboats, printing presses and spinning jennies” (in Gieryn 1983 quoting Houghton 1957:114).

The contemporary debate over the impact of IPR on academics takes place against this long tradition of suspicion over the mingling of science and money. In the life sciences the stage was set for this encounter in the early 1980s when three key developments lead to an explosion in patents by academic life scientists: First, academics in the disciplines that underpin biotechnology were quick to recognize that their discoveries could potentially lead very quickly to commercial products. They found themselves in possession of dual-use knowledge valuable in both science and business that could be published and patented (Murray 2002). Second, policy shifts encouraged academics to actually file patents over their dual-use knowledge. Prior to this time, patent applications filed by universities on behalf of investigators required a case-by-case negotiation with the Federal funding agency. The 1980 Bayh-Dole Act standardized practice by assigning all patents generated with Federal funding to Universities who were also charged with a duty to license and generally facilitate their translation and commercialization (Mowery et al 2001). Finally, a critical Supreme Court decision was also reached in 1980 when the *Diamond v. Chakrabarty* case confirmed that modified organisms could be patented. In expanding the scope of patent law to cover genetically modified organisms and (later) genetically modified mammals (such as the Oncomouse), the stage was set for a boom in life science patenting in academia. Between 1989 and 1999 U.S. research universities received over 6,000 life science patents (Owen-Smith and Powell 2003). Many scientists found that the fruits of their research not only brought academic credit but also commercial interests including equity in biotechnology firms, licensing revenue from patents, and consulting (Kenney 1986, Ertkowitz 1998, Ding, Murray and Stuart 2005). At least four perspectives have reached different conclusions on this institutional collision:

Moral threats to Academic Science: The most vocal opposition to the encroachment of commercial practices into academia comes from philosophers who explore the morality of science in its social context (Krimsky 2002, Resnik 1998ab). They fear that private interests may undermine the objectivity of research by causing bias, suppression of results, and even fraud (Ziman 1996, Broad and Wade 1993, Bowie 1994). These analysts look at the norms and practices of academic and commercial science, conclude that they are incompatible, and then project that adoption of the market will cause the institutional logic of academic science to fail. They argue that financial interests will come to dominate scientific objectivity and argue that “as long as researchers have other goals besides objectivity—and many do these days and always have—then these other motivations can erode their commitment to objectivity” (Resnik 1998a). While this line of scholarship has largely focused on the impact of private funding, patents are also viewed as contributing to weakened objectivity (Blumenthal 1997, Bowie 1994, Munthe and Welin 1996).

Economic threats to Academic Science: A second line of argument builds on legal and economic thought. In an influential article, Heller and Eisenberg (1998) propose that the "intellectual commons" will collapse due to increased transaction costs leading to an "anti-commons" (Heller 1998). They argue that as patented knowledge becomes more costly to access by follow-on researchers a lower equilibrium level of on-going research productivity will result (Eisenberg, 1996). Economic theory predicts that while the scientific community as a whole may benefit from the free dissemination of knowledge, individual researchers have strong incentives to take advantage of the protections afforded by IPR. Therefore, once a few members of a scientific community have shifted towards patenting, the fragile equilibrium of the academic (open property) regime will be rapidly undermined (Gambardella and Hall 2003, 2005).

Merging of Academic and Commercial Science: A third, network-based perspective takes a rather different approach. Powell and his co-authors have used an extensive analysis of the biotechnology industry to underscore the role played by networks of shared ties between academic and industry-based life scientists in the development of vibrant clusters. They argue that these cross-institutional ties have become the dominant feature of the life sciences and are characteristic of an expanding web of innovation networks that criss-cross organizational and institutional boundaries (Powell et al. 1996; Powell et al. 2004; Owen-Smith et al. 2003; Owen-Smith and Powell 2004). While they have not explicitly analyzed the implications of the rise of patenting, this perspective would suggest a sharp decrease in the institutional distinctions made across the academic and commercial settings.

Academic Science Unscathed: Current empirical evidence for the impact of patents on academic scientists presents an alternative verdict to the literature described above. Interview- and survey-based studies have recently suggested that academic scientists pay little or no heed to patents. In a survey of life scientists, few affirmed that patenting had caused them to change research direction or incur delays in their research programs (Walsh et al. 2005). Interviews suggested that scientists are unaware of what is patented (Walsh et al. 2003). And in general across a variety of Universities it has been shown that patenting activity is often associated with the most productive scientists (Agrawal and Henderson 2002; Thursby and Thursby 2003; Azoulay, Ding and Stuart 2005). In a recent study of publications in a leading life science journal over 50% of the papers authored academic scientists were found to be associated with patents. However those patented articles showed a modest (10%) decline in publication citations after the grant of the patent implying that the incorporation of ideas into follow-on work in the scientific community was slightly hindered by IPR (Murray and Stern 2006).

ANALYTIC FRAMEWORK

One of the limitations of scholarship that focuses solely on patents and publications is that it does not attend to the institutional logic in which these “documents” are embedded. As such it is “under-socialized”. More than simply texts, patents and publications represent exchange mechanisms strongly embedded in distinctive institutional logics. On the other hand, the normative approach to the role of patents in academic science is “over-socialized” because it fails to recognize the degree to which individual scientists have the flexibility to use their existing relations and understandings to incorporate, transform, or resist new practices.

The balance between over- and under- socialized perspectives is a central challenge for theories of institutional behavior (Granovetter 1985). As a useful analytical starting point institutions can be considered as a stable set of logics, practices and exchanges that reproduce the social order (Friedland and Alford, 1991); an order that is also maintained through rewards and sanctions (Jepperson 1991). However, institutions are subject to change and transformation. As Granovetter (1992, p 31) notes about culture, institutions are "not a once-and-for all influence but an ongoing process, continuously constructed and reconstructed during interaction. It not only shapes its members, but also is shaped by them for their own strategic reasons." Following this approach, I argue that while institutional logics shape the practices of actors and their exchange, exchange processes inform new practices and transform institutional logics.

For academic scientists who confront the intrusion of patents into their daily life, their response is therefore best understood by examining the way in which patents change how individuals interact and formulate their exchanges. By focusing on exchanges between scientists, I therefore hope to capture any transformations that may be occurring in the institution of Academic Science. In particular I focus my analysis of three aspects of the evaluative routines that characterize exchange (Boltanski and Thevenot 1999). First, I explore the currencies that are used in exchange between scientists: publications, materials, tacit knowledge, and advice on the one hand; inventorship, money, co-authorship, or acknowledgement on the other. Second I attend to the exchange rates (the incentives and rewards) that operate in these relationships: How much money, material, or expertise? And in return for what – am I an inventor? Will you just acknowledge and cite me or do I warrant a co-authorship? And third, I explore whether and how these exchanges differ with different people. Do I strike a richer exchange depending on status or prior relationships? Together these constitute a central aspect of scientific life and the cycles of disclosure and reward that are critical not only in academic but also in commercial science.

For analytical clarity I lay out this analytical framework by describing the two distinctive institutional logics. Of course academic and commercial science are institutions that have been widely studied and are the subject of contentious debate. For the purposes of my analysis I focus on the central role of publications and patents in each institution, how they are formed according to their respective institutional logics, how they serve as central exchange mechanisms and how they shape other exchanges.

Publishing and Related Exchanges in Academic Science

The study of academic science has become a contentious arena; with some scholars rooted in the "strong norms" approach of Robert Merton (1973) and others following the ethnographic studies of laboratory life (see for example Woolgar and Latour 1979). Although these two perspectives have many irreconcilable differences, both sides closely consider the importance of exchange in scientific life and in what follows I argue that each side can contribute to the overall understanding of how scientists form their exchanges.

Hagstrom (1965) observed that publication practices are a form of exchange that reinforces the core institutional logic of academic science. He posits that the published paper is a gift of information made in exchange for the hope of social recognition. Publications are also the mechanism through which social recognition is bestowed. The contributor cites work he found useful, thereby signaling the value of previous contributors. After publication, the value of a discovery is determined by the number of scientists citing the work in their own publications, again reinforcing the autonomy of academic science. Merton (1973) can be credited with delineating how the fight for priority is the engine that energizes the disclosure of scientific results. For individual scientists, the incentive to publish comes from the importance of priority, and the history of science has been punctuated by acrimonious battles between scientists over who should be credited with a discovery. Considerable institutional energy is put forth determining the outcome of such fights, signaling the importance of these claims not just to individual egos, but to the functioning of the institution².

Successful claims give scientists "ownership" of their discoveries and allow them to gain a share of prestige. Institutional insistence that such claims be adjudicated fairly underlines their

² While closely associated with university research, academic science is also feasible (and profitably adopted) by private firms, including many within industries dependent on the life sciences (Cockburn and Henderson, 1996; Stern, 2004; Murray, 2002).

importance. It also motivates scientists to publish their results quickly to pre-empt the claims of others. Publication and the attendant status may be directly valued by those who engage in academic science, but it also is reinforced and translated by universities into promotion and future resources. By premising career rewards (such as tenure) on disclosure through publication, universities become virtual "outposts of disciplines" (Ben-David 1971) that give up their employment prerogatives to the collective judgment of the scientific community.

The cumulative effect of disclosure through publication and valuation through citation is to create a vast "intellectual commons" of inter-related work. For those who study science, monitoring the commons by studying publication and citation traces has become a tool for mapping differentiation in science. For example, the exchange of information for recognition through citation allows analysts to chart invisible colleges, show how scientists form special communities within disciplines to study new problems or approaches (Beaver and Rosen 1978; Crane 1969) and illustrate the degree of scientific stratification.

By reviewing the practice of publication through the lens of academic science's institutional logic, I do not mean to reintroduce a Panglossian view to the study of scientists. The practice of publication may be rooted in institutional norms and serve as the basis of a norm-based system of exchange (Fauchart and von Hippel 2006), but there are at least two major sources of indeterminacy in the practice of publishing that open up the possibility for strategic behavior embodied in a broader range of exchanges practices:

1. The terms of the exchange of information for recognition are underspecified (how much information in a given publication, what forms of recognition); and
2. The complex combination of inputs into research prior to publication requires a variety of exchanges (for resources, research materials and collaborators).

Such indeterminacy is best illustrated by one of the mouse geneticists we meet later in the study: "in general I don't think you need credit as a co-author unless you contribute materially to the new experiment but there are people who expect they'll be a co-author even if they just send you something through the mail...I don't care. If someone says only if they can be a co-author and I really want to do the experiment I say fine. Of course for pre-publication requests we do require co-authorship because we are still characterizing the mouse or the particular construct". Studies by ethnographers observing laboratory life confirm these complex, sometimes strategic practices. Knorr-Cetina (1981) reveals that the drafting of a scientific paper entails numerous strategic

decisions about how to frame findings and determine whom to cite. Collins shows that what is exchanged in a publication can vary; the information described in a publication can be more or less explicit and sometimes scientists leave out nuanced tacit knowledge that allows for precise replication (Collins 1974). Others have also described the tension that arises disclosure in a given paper that allows for validation and withholding information for future discoveries (Greif 1989), particularly in highly competitive communities (Atkinson et al. 1998; Hilgartner 2002). Scientists are also bedeviled by the proper exchange with collaborators. Is their contribution recognized by co-authorship, acknowledgement or citation?

Hilgartner (1997) has advanced the useful notion that scientists create an ongoing data-stream of techniques, findings, and resources. At the research frontier, scientists who develop a new technique may enjoy a competitive edge that provides a valuable bargaining chip in the hunt for further resources, creditability and allies, but they have to consider the strategic implications of disclosure as they formulate exchanges. They must bound elements of their data stream into discrete portions that can be traded. They have to decide on the method of disclosure (publication, lab visits, and private disclosure), the exchange partners and the credibility of what they are disclosing. Collaborations represent a particularly tricky issue since scientists have to merge two streams and sort out what is disclosed and who gets credit in an ongoing relationship. Nonetheless, strategic considerations are bounded by institutional and local practices and communities of researchers develop norms about the disclosure and free exchange of certain kinds of data and/or materials, prohibiting their use as bargaining chips (Collins 1998).

Exchange and disclosure therefore is a complicated affair in academic science. Inter-related practices relating to publication and citation are shaped by institutional logic, local order, and daily practice and an array of strategic considerations confronts scientists as they decide what is disclosed, to whom, and at what price. Together this context creates the exchanges that are central to the production, dissemination and evaluation of scientific knowledge.

Patenting and Exchanges in Commercial Science

Contrasting patenting to publishing serves to highlight how distinctive the publishing practice is to academic science. On a superficial level, scientific patents resemble scientific publications. Like a publication, a patent is a text that describes a novel idea. Patents establish priority and require citations to prior work. The practice of patenting was introduced to

commercial science as a way of encouraging disclosure of what previously were "trade secrets." ³ In spite of these similarities, patents diverge completely from publications because they are rooted in the market-based logic of commercial science.

In commercial science, institutional practices are directed at turning ideas into private property and direct economic rewards and depend on the degree to which a scientist can *exclude* others from replicating his work and thus appropriate the value created by that knowledge (Nelson 1959; Arrow 1962; Levin et al. 1987). However, recognizing that disclosure provides an important efficiency in the economy, governments have developed incentives for disclosure in exchange for the provision and enforcement of intellectual property rights through a (time limited) legal right to exclude others from practicing the same invention. Typically patents are filed by an organization (e.g. corporation) on behalf of an inventor. From the outset, the practice of patenting, therefore, is in the hands of variety of actors unconnected to science. While publishing is largely a matter for individual discretion (at least in academia), patenting (in industry and academia) is costly and is undertaken at the discretion of different constituencies beside the inventor, including lawyers, managers and investors.

Legal guidelines define the "rules" of patenting. These laws cover not only what constitutes patentable matter but also the requirements that the ideas be non-obvious, novel and useful. The adjudication of patentability does not operate through a peer-review system. Instead a national patent office and its professional examiners make this determination, often through a series of negotiations that include the scientist and lawyers appointed by his or her organization (either other employees or external legal counsel hired for the purpose of securing the patent) (Cockburn, Khortum and Stern 2004). This negotiation of rights also continues after a patent is granted with competitors and other "interested" parties having the right to challenge the patent in formal legal proceedings (rather than through peer inventors). Patent law also provides for a precise definition of inventorship. In contrast to authorship with is a flexible construct that varies by field and which continues to be the subject of local negotiation and debate among different scientific communities (Biagioli and Galison 2003), inventorship has legal standing and the omission of inventors can serve to invalidate a patent (see Ducor 2000 for an empirical comparison). Like publications, patents also establish priority for its inventors; however, this is incidental to the powerful property rights that are conferred to the owner of a patent. First the property right gives

³As described in the U.S. Constitution "to Promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."

the right of exclusion and second they can be used to extract economic rewards from others. Other parties can be sued for damages if they practice the inventions described in the patent without appropriate contractual permission from the patent owners. This restricts others not only from practicing the invention (i.e. replication) but also from utilizing the idea as the basis for some other invention.

Patent, like publications, contain citations, but the parallel with academic science quickly breaks-down as the requirement to cite “prior art” has a legal basis, rather than serving as a status-conferring form of gift exchange. Indeed an inventor has a legal obligation to disclose any prior art that he is aware of, and the patent examiner also engages in a detailed prior art search (Alcacer and Gittelman 2004; Sampat 2005). A patent citation is a very public example of exchange and one which, while it has no symbolic value, may have economic implications if the citee is required to have a license to practice their invention.

An important feature of a patent is that it distinguishes between the inventors – those individuals who developed the ideas – and the owner (assignee) of the property rights. This separation is often explicitly defined in an employment contract in which an employee assigns his or her patent ownership rights to the employer. This means that the various rights and rewards associated with patenting are retained by an owner, even in the event of an employee leaving a firm or changing institution. Patent ownership rights can also be contractually transferred to others – i.e. they are alienable. Armed with a patent, its owners can engage in a series of exchanges with any parties who might be interested in incorporating these ideas into their own activities. IPR therefore brings considerable flexibility in crafting exchange relationships. Exchanges in commercial science take place in a market setting (sometimes referred to as the market for ideas), in which patent owners develop a series of complex, differentiated arrangements with others wanting to use their ideas. Rights can be granted and restricted in any number of ways through a complex and often sophisticated license agreement. For example, rights specified for particular geographic areas, or (in the case of biotechnology) therapeutic areas. The nature of these contractual terms and their differentiation across parties leads to the emergence of complex local orders around particular technologies or processes. For example, contractual differentiation can define the boundaries of a industry (Uzzi 1996). Indeed, the foundations of the biotechnology industry lie in a complex web of interlocking contracts that share the rights to key (patented) ideas among a variety of parties (Powell et al. 1996; Stuart et al. 1999; Edwards et al. 2003).

Moreover, there is no obligation that patent holders exchange their rights with others. Unlike academic science which is crafted around strong norms of exchange and sanctions when information is not clearly defined in a publication or additional material not exchanged, there are few (if any) norms that require exchange in the market for ideas (beyond some government “march in rights”). Indeed the patent confers a monopoly giving the owner wide ranging discretion to use it in anyway he or she prefers. Large firms with considerable resources may practice "defensive patenting" solely with the purpose of preventing others from using those ideas rather than for the active promotion of further innovation. Patents are also filed to create an impressive “stack” of patents so that in exchange negotiations with other patent holders, cross-licensing can be accomplished (Grindley and Teece, 1997).

While patents and the exchanges they engender generally follow the logic of commercial practices, social relationships also influence exchange in commercial science. Citation patterns suggest that prior employment (Kogut and Almeida 1999), shared ethnic background (Kerr 2004), alliances (Podolny and Stuart 1996) and shared membership of technical communities (Rosenkopf et al. 2001) all shape decisions on licensing and collaboration. This argues that commercial scientists may hold criteria other than strict commercial advantage when they choose their exchange partners and arrange collaboration. However with the exception of Saxenian’s work (1996) on Silicon Valley, there are few ethnographic studies to support this idea.

Taken together, this exchange-based perspective on commercial science highlights the importance of economic strategy among a diverse set of actors – scientists, lawyers, investors, and managers. Commercial science represents a mirror image of academic science. Academic science publications trade in the currency of disclosure for prestige, tempered by market-like strategizing among scientists to gain the most exposure and credibility for their "gifts." Commercial scientists trade disclosure and the right to replicate their findings on a strict economic calculus backed by the power of the state, yet these considerations are influenced somewhat by social ties.

Mixing the Logics of Exchange

The marked differences between patenting and publishing as exchange practices reflect the differences in the underlying institutional logic. However, the mingling of these practices becomes an important strategic choice for scientists (in academia or the commerce) when the ideas they generate have duality – they are both a contribution to fundamental knowledge and of practical

utility. At the micro-level, this duality gives them the flexibility to patent and publish their work and to incorporate two quite distinctive logics into their daily patterns of exchange.

Historians of science have shown that such intermingling of distinctive forms of exchange is not a recent phenomenon but has been an important element of scientific work since the dawn of modern science. Even prior to the establishment of the dominant logics of patenting and publication, scientists had ideas which allowed them to operate in dual (or even multiple) logics of exchange. For example, Biagioli (2000) analyzes Galileo's disclosure of his discovery of Jupiter's moons to uncover the famed scientist's strategizing. While seeking approval of his scientific peers, Galileo omitted detailed description of his telescopes that would have enabled others to replicate his observations. On the other hand, he dispatched telescopes to prominent individuals (who were not scientific competitors) throughout Europe. With these gifts, he succeeded in raising his status in the Medician court and maintained a monopoly on celestial observation with which to bank further claims of priority. Biagioli notes that Galileo's selective disclosure would have been less likely in the 17th century, when patent laws became more comprehensive and newly established journals regularized the publication of findings, making the exchange between disclosure and credit easier to realize. Nonetheless, as I have argued, patents and publications do not obviate the need for strategizing. Rather they channel strategic behavior into conformance with two dominant institutionalized logics, however as I have described, we have limited insights the strategic use of these logics by contemporary academic scientists as they attempt to access the full range of ideas, expertise and materials needed for each project and gain the appropriate credit.

Latour (1987) provides the most detailed account of how contemporary academics use extensive exchange repertoires to nurture their scientific enterprises, but ignores patenting and other aspects of commercial logic. He argues that scientific work takes place in ever increasing cycles of credit: A scientist exchanges resources with colleagues to build credibility, translates this to gain resources from external audiences, which can be used to gain further credibility. While observing only scientists who exchange with one another, Latour argues that: "[Their] isolation exists only in so far as other scientists are constantly busy recruiting investors, interesting and convincing people. The pure scientists are like helpless nestlings while the adults are busy building the nest and feeding them" (p156). Nonetheless, as they describe neither the practices of "adult" scientists as they cross boundaries, nor the logics that guide these exchanges, current laboratory studies provide little insight into the "inside" of academic science as "outside" practices such as patenting come rushing in.

THE ONCOMOUSE AS A STRATEGIC RESEARCH SITE

The reaction among the mouse genetics community to the Oncomouse patent is a strategic research site in which to study the interplay between the academic and the commercial logic of science. Because the core Oncomouse finding was disclosed in both a publication and a patent, it can be thought of as a “patent-paper pair.” This provides a naturally occurring experiment; we can examine exchange arrangements in the period before and after the granting of the patent (which took four years). It gives us a window into the impact of the Oncomouse under two distinctive institutional regimes (the identification strategy is outlined in Murray and Stern 2006). The case has a number of other features that allow for clear identification of the impact of patents on academic science:

- The mouse genetics community was a longstanding and tight-knit group with norms and communal resources concerning the exchange of mice, making it possible to compare exchange relationships pre and post the Oncomouse patent;
- The patent was issued early-on in the wave of academic patenting, as a result of the research funding arrangements and as such is a largely “exogenous” shock to mouse geneticists who to this point had not used of patents in their relationships;
- After the IPR was licensed exclusively to DuPont, they demanded extensive commercial terms from the academic mouse genetics community;
- The Oncomouse was recognized as an important academic idea, making the possibility of switching to a different research arena to avoid the commercial requirements a highly unattractive strategy for most researchers;
- The publicity over the patenting of the Oncomouse rippled through the entire life science community guiding subsequent practice among other researchers.

By focusing on a key event and its aftermath, this analysis provides insights into the response of academic science to market forces and more broadly, the mechanisms of institutional collision and change. When we examine “the cognitive aspects of major collective events in which large numbers of persons rapidly adopt orientations that might have appeared culturally alien to the majority of them a short time before” (DiMaggio 1997, p. 280), we discover a great deal about the social practices of the actors. This strategy is not new in the sociology of science. After all,

routine assumptions and consensus over practice are hard to reveal (Radner 2004, Scott, Richards and Martin 1990). It is often only in moments of transformation when these assumptions are challenged that scientists reveal their thinking about taken-for-granted aspects of their milieu.

I combine three types of evidence in my analysis (see Zelizer 1989 for a similar approach): (a) contemporaneous documents describing the Oncomouse controversy; (b) bibliometric research on citations to Oncomouse publications and review articles; and (c) interviews with various members of the mouse genetics community who were engaged in scientific research during the period of the Oncomouse controversy⁴. As I collected and analyzed the data, the analytical framework guided my avenues of inquiry. I explored how exchanges were struck in the period just after the Oncomouse discovery and norms balance competition and recognition prior to the patent. I then explored scientists' attitudes towards the Oncomouse patent: What understanding did academic scientists have of patenting? What was their response to the Oncomouse patent? Did they use the exclusionary tactics that are a central feature of patenting? How have scientists incorporated patents into their strategic calculus of finding collaborators, acknowledging the work of other scientists and exchanging research material? The rest of this article consists of an analytical narrative which is divided into the pre- and post- patent periods (including a brief history of the mouse genetics community prior to the development of the Oncomouse).

ANALYZING THE ONCOMOUSE I – THE PRE-PATENT PERIOD

The Mouse Club

From its inception in the early decades of the twentieth century, mouse genetics has been a tight knit community held together by intertwined social relations and organizations. Although

⁴ This article is based on the qualitative analysis of an extensive and diverse set of documentary and interview-based sources. Primary documentary sources include (1) the editorials, opinion pieces and letters from leading scientific journals *Science* and *Nature*; (2) Archives of speeches, interviews and award salutations from major scientific prize awarding organizations including Nobel and Lasker; (3) historical accounts of the mouse genetics community found in the Jackson Laboratory Archives; (4) newspaper articles and editorials (mainly the *New York Times*). These sources were supplemented with extensive bibliometric analysis based on the forward citations of two key articles describing the development of oncomice. In addition, all the leading scientific review articles of developments in oncomice 1984-1990 were examined for the references. These sources of data were combined with forty hours of interviews. Scientists were approached for interviews on the basis of their appearing repeatedly in popular discussions of the Oncomouse patenting decisions, their contribution to the Oncomouse literature and the identification on the roster of mouse genetics meetings at Cold Spring Harbor. While the precise representativeness of these sources cannot be established, the reliability is strengthened by the agreement that emerged among multiple sources, or with key events being recounted and corroborated by different individuals.

not thought of as sharing a single discipline or even sub-discipline, mouse geneticists refer to their shared sense of community and frequently act in concert (see Paigen 2003ab). Part of the reason this community has developed into such a close network is that many of today's leaders can trace their scientific lineage to a single individual, William Castle (Director of Harvard's Bussey Institute 1908-1938) who trained a cadre of students destined to become the social fabric of the field (Morse 1985). Over a thirty-year period he and one of his most influential students, Clarence Little made mice the object of their research, developed mouse genetics from an activity for hobbyists into an important scientific activity based on a model experimental system for the study of cancer and other diseases, and laid the U.S foundations for the systematic analysis of genetics (Castle 1903). One key experimental strategy that was to shape the field and its social relationships was the use and exchange of a few inbred lines of mice from one key supplier - retired school teacher, turned fancy-mouse breeder, Miss Abbie Lathrop. Some of today's most common lines of inbred mice originated on the Lathrop farm and have been exchanged and bred by generations of scientists (Morse 1981).

Breeding and exchange had already come to characterize the community in the 1920s. Lionel Strong began raising mice in 1919 while still a graduate student at Columbia and later moved with his collection to the Bussey Institute. He had been spurred on in his mouse development project by the prohibitive cost of tumor-ridden mice: "a single mouse with a spontaneous tumor was selling for \$300 in the laboratories on the eastern seaboard" [in 1920]. In 1922, Strong was advanced \$200 for his research program in exchange for 800 mice and by 1925 had created one of the first inbred cancer prone strains (C3H) (Strong 1978). However, the mouse work was time and resource intensive (Figure One).

-- Insert Figure One about here--

Strong's description of the problems he faced in meeting demand for mice by other researchers closely echoes concerns voiced by today's mouse geneticists. His research interest in cancer was endangered by the time mouse breeding was taking:

Work toward stabilizing the inbred strains, and a half dozen experiments involving them, continued amidst a rising clamor from other investigators who wanted the mice for their work. When possible, a breeding pair was sent to anyone requesting them. Memorably, one of the first such pairs was a gift to Marie Curie. Keeping up with the demand, however, was far beyond the capabilities of my small laboratory (Strong 1978).

Strong's comments argue that in the 1920s the exchange of mice was guided by collegial reciprocity and that refusing to exchange mice could endanger one's reputation. He described his dilemma in the following terms:

When it was impossible to fill requests for the mice, there were grumbings that Strong was uncooperative. A few even complained that I was trying to restrict scientific material for my own selfish use. These charges were never justified. Few people realized that the inbreds had been created in the first place as a means of opening my own scientific line of inquiry into the cancer problem. I was glad to share the mice, but I had no intention of abandoning my career in cancer research to become a supplier of laboratory animals for others (Strong 1978).

In order to keep up with demand in mice and protect his reputation, Strong joined Little and colleagues to create a center to serve as a communal resource for researchers – the Jackson Laboratories (the lab became popularly known as JAX). A modern mouse man explained the value of JAX: “there will always be two kinds of people – those who oppose sharing and those who do not. You are basically obligated to send a mouse even if it’s onerous...keeping mice is a pain but that is the expectation. That is why we try hard to make sure that the mice are elsewhere, managed by others”. In continuous operations for the sale of mice since 1933, JAX maintains many strains of inbred mice and sells more than two million mice annually. As Rader describes in her history of the Laboratory, JAX mice have developed into “standard research organisms...and iconic symbols of the value of standardization within our culture” (Rader 2004, p. 7). Castle and his students went on to build several important organizations to support their validation of inbred strains of mice as a research tool. In 1939, an International Committee on Standardized Nomenclature for Mice was founded and tasked with establishing the rules for mouse genetics nomenclature and developing key protocols, a practice that continues with the naming of mouse genes, mutations etc. (Lyon and Searle 1989, Silver 1995).

Leading members of the community also established a variety of associations and other forms of research infrastructure, helping solidify the structure of the mouse community (see Schofer 2003 for a similar analysis in geology). In the 1920s, Little was a central figure in an informal but elite group comparable to an invisible college (Crane 1969) within the mouse community called the "Mouse Men of America," whose one hundred or so members “exchanged information and mouse stocks and got together at scientific meetings” (Russell, 1978). In the 1960s, *The Mouse Newsletter* allowed members of the mouse community to keep track of each other's activities, with more than sixty contributing institutions. This publication served a quite different purpose to the peer-reviewed publications; it was a forum for announcing new strains and mutations that were being bred around the world.

These strong ties led to norms that encouraged researchers to think of mice as a communal resource. Researchers traded specialized mouse stocks not available from suppliers (Silver, 1995). The mouse community's norms had substantive scientific implications. The mouse became as important as the fruit fly or worm as a “model organism”. Its genetic likeness to humans (99% homology) made it particularly central in the study of cancer (Boguski, 2002). The shared resources and relationships allowed researchers to identify do-able problems, gain faster results, and build a consensus on their meaning (Fujimura 1996, Kohler 1994; Rader 2004).

Oncomice – Published & Patent Applications Filed

The 1970s was a pivotal decade across biology. Molecular biologists developed new tools that had a dramatic impact on the field, transforming not only the practice of science, but the do-ability of questions and the importance of certain inquiries (Judson 1996, Morange, 1998). Mouse genetics was among the many communities to be rocked by the power of molecular biology. Paigen, a Director of JAX described events that ended the “classical period” in mouse genetics:

Then, at the end of 1980, in a period of a few months, an entirely new era in mouse genetics began, with the creation of the first transgenic mice, initiated by the abrupt and then continuing entry of molecular biological techniques into what had, until then, been a classical genetic system. What ensued was an explosion of knowledge when a myriad of new biological and molecular insights appeared over the following years. Although certainly built on the past, the new science quickly developed a life of its own and deserves its own chapter (Paigen 2003a).

In the winter of 1980, in a classic example of multiple discovery (Merton 1973), five teams published the development of transgenic mice. They described that when foreign DNA (a so-called transgene) was injected into mouse eggs which were then transplanted into female mice, the genes were incorporated into the offspring creating a “transgenic” mouse⁵. These transgenic methods solved an important methodological gap in whole mammal biology - they allowed the insertion of a known gene into a mammal allowing researchers to monitor its function in the whole organism.

Among the first to recognize the potential of these mice were scientists studying cancer. During the classical period of mouse genetics, cancer researchers relied upon chemical and radiation-based methods to induce cancerous mutations in mice. Creative experimentalists used such mice to reveal insights into cancer biology, but the entire program suffered from a lack of

⁵ The groups included Ruddle at Yale (Ruddle et al. 1980), a collaborative effort between Brinster and Palmiter at the University of Pennsylvania and the University of Washington (Brinster et al. 1981), Constantini (Constantini and Lacy 1981) at Oxford (later Columbia), Beatrice Mintz at Fox Chase Cancer Center (Wagner et al. 1981), and T.E. Wagner’s group (Wagner et al. 1981).

precision. During the 1970s, cancer biologists had responded by shifting their focus to the cellular level where they identified an intriguing class of cancer-related genes – so-called oncogenes⁶. However, while oncogenes had been analyzed in cell lines “their action in a living organism is, at best, incomplete” (Stewart et al. 1984, p. 627). In an example of scientific advance produced by combing insights from different “data streams”, it occurred to biologists that oncogenes could be introduced into mice via transgenic methods to produce a valuable “Oncomouse” – a mouse model for the study of cancer. But only a few groups actually attempted these experiments in the early 1980s because of the methodological challenges.

The techniques required practice and skill (Collins 1985) and had not, as yet, been reduced to simple "kits" (Fujimura 1996). To create an Oncomouse, one needed to have “magic hands” (Hilgartner 1993). Even under the best conditions, the uptake of cloned genes into the embryos was only 10-25% efficient (Cory and Adams 1988). In addition, development of reliable breeding lines that continued to transmit the transgene required an array of traditional mouse genetics skills. This is how one of the leading researchers described the challenges of training someone:

“With X we didn’t have to spend much time perfecting the technique. But that was because he was very good. You need someone with good hands and a good observer – that was X for you. Off the bat he started getting successful cases. I’ve tried to teach a succession of people and it’s not a teachable skill – some catch on right away and some never do a good job. X was just a natural.”

One collaborative team that was working on an Oncomouse was the Palmiter and Brinster labs (among the first to develop transgenic mice). Another was headed by Philip Leder. A leading cancer biologist, in 1981 Leder had moved to Harvard from the National Institute of Health (NIH) to head the newly established Department of Genetics. In the 1970s, Leder, had focused on genetics at the cellular level, using mouse cell lines rather than mice themselves and was well-known for leading the first team to clone a mammalian gene (Tilghman et al. 1977)⁷. He also had more than a passing interest in oncogenes, spending several years studying one (“myc”) implicated in a rare form of Lymphoma. The Leder lab had not pioneered transgenic methods. Fortunately, Timothy Stewart, a co-author on one of the first transgenic mouse publications (Wagner et al. 1981) who had been trained by leading embryologist Beatrice Mintz, applied for a position in his lab. With Stewart’s expertise, Leder’s group created a viable mouse that carried a myc oncogene and therefore had a predisposition for cancer.

⁶ This discovery would bring Harold Varmus and John Bishop the Nobel Prize.

⁷ Leder was elected to the National Academy of Sciences in 1979 in recognition of this accomplishment.

The labs published the results of Oncomouse experiments incorporating different oncogenes within a few months in the prestigious journal *Cell*; Palmiter and Brinster in June 1984 (Brinster et al. 1984) and Leder and Stewart in October 1984 (Stewart et al., 1984). The *Cell* article was not the only way in which Leder wrote-up his Oncomouse discovery. Two months before submitting the manuscript, on June 22, 1984 Harvard filed a patent application on the Oncomouse. This decision can be traced to late 1983, when Leder approached the Harvard Office of Technology Licensing at the Medical School to discuss the patentability of his research (Kevles 2002). DuPont was also involved in these discussions as Leder has described:

The work that we did was supported, actually, by an industrial concern, Dupont. They made a significant investment in that research and this is one of the products that could emerge from it, and did emerge from it, and they are incentivised to make further investments in this process by virtue of the return that they will receive [from the patent]. That is our system. You may like it—you may not like it. (Lasker Foundation 1987)

Between 1981 and 1984 DuPont had awarded Leder over US\$6 Million in grants which, together NIH awards, supported his research⁸. DuPont’s funding was made under an agreement that ensured no restrictions be placed on Leder’s freedom to publish or discuss his research. Nonetheless, DuPont required that Leder have any new discoveries assessed for their patentability. The other Oncomouse team (funded by NIH, NSF and a graduate fellowship from SmithKline Beecham) did not file patents, although under the terms of the Bayh-Dole Act they were free to do so⁹. The patent application recognized the Oncomouse as a dual advance: an important step for academic science, and a high potential tool in commercial science with which to create novel cancer drugs. But for the moment, the patent application was confidential.

Response in the Pre-Patent Period

With the patent application known to only a few people, and its future implications unimaginable by all, we have no reason to assume that the future patent affected the diffusion of the Oncomouse into the academic community. This was not an “idealized” period of openness. Analysis suggests that exchange in this period followed the broad norms-based exchange

⁸ Grants from the NIH included Grants1Z01HD000074-4—74-11 (data from the NIH Crisp Database, accessed from <http://crisp.cit.nih.gov/> on April 22, 2005).

⁹ In this period (1982-1984) academic patenting was still relatively unusual: the top twelve universities in terms of biotech patent applications (ultimately granted) (as defined by US codes 800/001; 435/172.3; 435/240.1; 435/240.2; 435/240; 435/317.1; 935/032; 935/059; 935/070; 935/076; 935/111) were the University of California (14 patents), Columbia (8), MIT (6), University of Texas (6), Harvard (5), Stanford (5), Caltech (3), Wisconsin (3), Cornell (2), Johns Hopkins University (2), New York University (2), and State University of New York (2).

principles established by the Mouse Club, interwoven by strategic exchanges. Scientists built more complex exchanges than those required for in-bred mice because of the inherent instability of Oncomice in this period, the difficulties with breeding, and the competition engendered by the academic value associated with the mice.

Researchers in cancer biology –those in the “Mouse Club” and molecular biologists, recognized the Oncomouse as a breakthrough: “the creation of transgenic mice carrying specific cancer-promoting genes opened an exciting new era in oncology” (Cory and Adams 1988). Citation analysis of both Oncomouse publications and contemporaneous reviews identified sixty peer-reviewed article using oncomice between 1984 and 1989 and reveals that the authors had only been able to publish because of a series of intricate exchanges to access and assemble the requisite materials and methods, forming an "invisible college" around the originating labs (Crane 1969). These labs maintained their "competitive edge" despite the fact that they held (as yet) no IPR on oncomice and their publications laid out their methods clearly. Their normative advantage came largely from the difficulty in mastering the techniques and the shortage of individuals with requisite skills. One leading scientist from that period commented:

“At the start I was accused of not being forthright in outlining my methods. [Aside: I knew they were saying this because mutual friends told me] But of course people spoke too soon. Of course you can’t do this sort of work if you’re clumsy. In the fullness of time my detractors came to realize that I was right. It was just a question of having the prior background.”

Furthermore, transgenic mice themselves were fragile, and the breeding lines had not been stabilized. Therefore, the usual system of exchanging mice was not initially practical. One scientist who had managed to make oncomice in the late 1980s recalled:

“I had a few requests for mice and offers of co-authorship. But I did not send them the mice. I send a long and detailed explanation of the implausibility of the request. The mouse line died very young. Over the period I was having to slow my own work down because they were breeding very poorly and so it was impossible to ship them around.”

As a result, the currency that was traded was the skill in building an Oncomouse rather than the mice themselves. Methodological expertise became an important source of prestige and advantage (Hackett 2005) which was exchanged either through lab-to-lab collaboration (and co-authorship) or via individual mobility. For scientists who entered the field with no prior expertise in mouse genetics, collaboration and co-authorship was the most common “price” for access. Embryonic manipulation, maintaining strains of mice and breeding new generations were skills not typically available to cancer biologists (who either worked purely on a molecular level or who relied upon JAX for inbred strains). In return they brought knowledge of molecular biology. One

such collaboration (later to become infamous in a case of scientific misconduct) was struck between David Baltimore at MIT and Frank Constantini (an early transgenic pioneers) at Columbia. As part of the exchange, Baltimore sent Constantini the gene and he in turn created the mice. The mice were sent to Baltimore's lab where two students were tasked with their nurturing. The faculty co-authored their publications (Weaver et al., 1987). At times exchanges might fail. One scientist explained how he had sent a colleague some material with explicit instructions as to how it should be used and maintained. His colleague "totally violated all the stipulations I had made, then published an outrageous paper. It does have my name on it but that's because when I saw the first draft I told him he should do the experiments differently and I felt that made me an active participant....but this is not collegial behavior."

Exchange could also be established through the movement of people. Leder himself had built the Oncomouse with the expertise from a highly-trained post-doc. Steward's rare talents brought him first authorship on important publications and later a sought-after position at Genentech. Other labs also brought in students trained at the benches of pioneering transgenic experts. One lab with expertise "got an uptick in applications from people wanting to do post-docs and learn the methods so they could take them elsewhere and gain fame and fortune." Some of these post-doctoral students had enough experience to set-up independent labs (taking mice with them) and build their own stream of research, exchanges and reputations around oncomice (e.g. Scangos and Cory from the Ruddle lab). All of these exchanges could be difficult to negotiate. As one expert noted: "Nothing activates the baser form of human nature than the possibility that they can claim more fame if they say they did it all themselves and this was truer in these mice than in most other areas I've worked in." Not everyone was as sanguine about sharing their mice under any exchange rate. Leading cancer biologists such as Weinberg commented that "the public did not invest in these things to accelerate my career but in order to move the field forward" (quoted in Cohen 1995), but other scientists were less generous and were reluctant to give up their mice, as an informal "poll" documented in the leading journal *Science Magazine*¹⁰.

By the late 1980sm as the mice started to stabilize, informal channels constituted another type of exchange for expertise. Acknowledgements in the period (see McCain 1991) note the

¹⁰ MIT Nobel Prize winner Tonegawa was described as one such individual. From a list of 15 researchers he claimed to have given mice, journalists reported that three received them a year later from a post-doc after he established an independent lab, one was denied as a direct competitor, four received mice with the stipulation of direct collaboration and six said they had never in fact approached Tonegawa because of his reputation, going instead directly to his post-doc (Cohen 1995).

advice of an embryologist but the exchange rate did not include co-authorship. Oncomice also began to travel more frequently, but this traffic was limited and was often accompanied by a co-authoring graduate student (Slaughter et al. 2002). However the appropriate norms of exchange remained in flux. Some called for “internationally acceptable and consistent guidelines” to remedy the difficulty scientists were having establishing their own exchange practices. Most scientists recognized that one of pre-requisites for more extensive, normative mouse exchange was organized, efficient breeding, as Strong found in the early Mouse Club days. In the words of one scientist, “we needed an ambitious and well-supervised operation”. In 1989, discussions were opened with JAX to promote the breeding, exchange and standardization of these mice for cancer biology. At precisely this moment, DuPont appeared with the Oncomouse patent and scientific life changed dramatically for the entire mouse genetics community.

ANALYZING THE ONCOMOUSE II – THE POST-PATENT PERIOD

Granting the Oncomouse Patent

On April 12 1988, U.S patent office granted Harvard Patent 4,736,866 property rights over the Oncomouse and other transgenic mice and mammals. But the arrival of the Oncomouse in the commercial world was more widely signaled when *Fortune* named it “Product of the Year” and DuPont placed a full page ad in *Science* heralding the arrival of a “potentially disruptive and radical” new research tool. For the general public, the patent proved controversial because it was the first to be granted on a mammal.¹¹ However the controversy in the scientific community was Harvard's exclusive license giving DuPont the right to “make and have made, to use and have used, to sell and have sold, the Oncomouse, and to fully exploit the patent rights”. In other words while they did not own the IPR, they had an exclusive license to broad rights that DuPont interpreted as sweeping coverage of the transgenic landscape¹².

If scientists expected DuPont to play a role similar to that of JAX, they were mistaken. DuPont set out to establish a commercial science-style market for industry and academic research scientists and laid out new terms of exchange, based on principles practiced in commercial science.

¹¹ The Oncomouse patent has a complex legal history outside the United States which might provide additional insights into the differences in scientific behavior in nations with and without patent rights. However this “experiment” is not the subject of the current paper.

¹² The first patent claim reads: A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant activated oncogenes sequence introduced into said mammal...at an embryonic stage.

As they attempted to strike a richer exchange with academics it became clear that standing on the shoulders of the Oncomouse would come at considerable cost (Blaug et al., 2004). In the market that DuPont envisioned, the Oncomouse would no longer be exchanged for prestige or co-authorships. Instead the prevailing currency would be financial. The actual cost of the mice was high – the \$50 price tag was ten times the price of a JAX mouse (Anderson, 1988). DuPont sought three additional terms which applied to any Oncomouse, bought, exchanged or bred:

Limits on informal exchange of mice - DuPont would not allow scientists to follow their traditional practices of sharing mice or breeding extensively from the mice. This was true for scientists who had bought a “sanctioned” Oncomouse from DuPont but was also true for scientists who generated oncomice (with any oncogene not only “myc”) on their own.

Contractual control of scientific disclosure - DuPont imposed forms of contractual control on scientists, most notably a requirement that they fulfill annual disclosure requirements; this was not a strict prohibition on publishing but a requirement that scientists using an Oncomouse would provide an annual research report on their published findings.

Reach through rights on future discoveries made with an Oncomouse - DuPont required that scientists give them rights to future inventions made using oncomice. These so-called reach-through rights give the licensor of a patented technology a share in any proceeds from a product even though the original technology is not incorporated into the end product. These rights are not an integral part of patent law but instead emerge as part of a negotiation over the terms of conditions of a contract to make use of a technology – they are part of the price of use. While common in the contracts between biotechnology and pharmaceutical firms, this was the first time a company had sought to impose such a provision on academic scientists.

RESISTANCE – the Initial Post-Patent Response

The Mouse Club responded strongly to the encroachment of commercially-based exchange into their community. The annual *Mouse Molecular Genetics* summer conference at Cold Spring Harbor became a central organizing point for the resistance. According to observers, “the grumbling reached insurrection proportions after a meeting at Cold Spring Harbor” in August 1992 (Anderson, 1993). In an impromptu session led by Harold Varmus (by then a prominent member of the community and Nobel Prize winner) over three hundred researchers stayed on to share their grievances. Their concerns over restrictions on the use of oncomice were heightened

because GenPharm International, a biotech firm in California, had emulated DuPont and placed similar restrictions on the new and innovative “knock-out” mice – a cousin of transgenic mice.

Scientists raised objections to each of the conditions set out by DuPont concerning use of the Oncomouse. They had both practical and philosophical problems with DuPont's restriction on sharing mice. At least as the rules were interpreted in the early 1990s, if a scientist whose transgenic mouse infringed the Leder patent wanted to share strains with colleagues, not only did he have to complete a DuPont Material Transfer Agreement (MTA) every time a colleague requested a mouse but he was also required to keep DuPont informed of the nature and progress of each project. In the words of one scientist: “It was an enormous obstacle to free and open distribution of information and materials....it was a whole new way of doing science...it really affected the way the mouse research community works” (Rajewsky quoted in Jaffe 2004). Another commented: “When DuPont was making a noise about IP and there were schools with licenses and some without those who’d signed couldn’t send a mouse to you if you were at a school who hadn’t signed. It did start to create tension and a schism in the community.”

The requirement to submit annual reports of the oncomice research was also highly inflammatory to many academics. Issues of secrecy, the “gagging” rights of companies in cases of corporate sponsored research, and publication delay had already been a topic of considerable concern at Harvard in the debate over significant research sponsorship from Monsanto in 1974 (Cooke 2001). However, DuPont's conditions on the Oncomouse went beyond this. They were claiming rights without providing funding or any negotiation. If a scientist did not acquiesce to these conditions they could not carry out the experiment (whatever the source of funds).

For scientists in the mouse community, the notion of commercial reach-through rights was particularly disturbing. On the one hand this is perplexing; scientists have long negotiated something akin to these control rights when they negotiate the complex expectations of authorship versus citation as the currency for a resource exchange (Biagioli and Gallison 2003). However, these claims were quite nuanced and weakened over time as ideas and methods became more widespread. In contrast, the imposition of rights to an on-going “research” stream on the basis of intellectual property rather than continued collaboration was an alien concept which was antithetical to both local and more universal scientific practice. As one scientist put it:

“In science we always try and appreciate a new idea and give credit. People with something new hold onto it for a while and we collaborate with them but over time these rights weaken and ideas become mainstream. No-one monopolizes them forever. If they do, they are just won’t reach the sort of widespread acceptance that is so vital to our field”

“Sometimes firms that sponsor our work come in and try and negotiate the right to an authorship on every paper that we write. I always have to explain that authorship is not for sale....you have to make a real contribution. There is no automatic credit in our field”

DuPont countered all these criticisms by taking on only the practical issues of time and financial cost. They claimed that the licensing terms were not burdensome: the license was “free” and that the firm could “turn around a license to an academic user in two days to a week” (Townsend, Associate Director DuPont Intellectual Asset Business, quoted in Marshall 2002). However for many scientists it was not the pure transaction costs (Heller and Eisenberg 1998) that were at stake. Rather it was a matter of the normative costs associated with the conditions.

The scientists were in a bind. Most could not simply drop Oncomice from their research agenda. “By the time the patent was granted the method had become well-established and so even if you weren’t using it before you still would choose to continue and start to use the mice – it was so obviously a good idea.” As the success of the research line over the prior four years had shown, oncomice were a valuable tool and provided a growing stream of new insights into the role of cancer in whole mammals. They featured in the research of Nobel Prize winners and were gaining acceptance as an important research model in cancer.

Scientists resorted to civil disobedience. They chose to flaunt the law “and simply breed their own oncomice, effectively boycotting the company” (Anderson 1993). This form of widespread infringement is consistent with recent survey results asking scientists whether they consider patents in designing experiments (Walsh et al. 2003). However the Oncomouse was a case of more mindful insurrection rather than a benign neglect of the details of patent law.

“I knew there was a patent on the use of isogenic DNA but I did not think about getting a license. I suppose that every once in a while we heard from DuPont or our TTO but it was rare that a patent holder challenges an academic institution so in practice we didn’t think twice about just going ahead”.

Others attempted to circumvent the patent and operate in the shadow of the law. In a classic example of the role of patent scope in shaping the response of follow-on innovators (Scotchmer 1996), some scientists tried to “invent around”. However the patent was extremely broad; covering all oncogenic mice, if not all oncogenic mammals. The scope of the patent and its restrictions was particularly damaging for Palmiter and Brinster who had created their Oncomouse at the same time as Leder. Because they had not filed patents, they were subject to the same patent restrictions as any other researcher in the field.

DuPont's restrictions also curtailed discussions with JAX about distributing transgenic mice, since JAX would not share mice that had complex contracts associated with them. This delayed the adoption of the Oncomouse as a lab standard for studies in cancer. While scientists who infringed the Oncomouse patent developed their own breeding and transgenic programs, given the difficulty (and at times illegality) of sharing, the “home grown mice” approach incurred a number of costs: it was time consuming, it restricted research to a smaller number of people with the requisite expertise and most importantly it undermined the tradition of standardization so critical to the establishment of early mouse genetics (Rader 2004). By each using their own mice, scientists were unable to compare research results and start to develop these tools into replicable and verifiable research system. One researcher active during this period stated:

“I won't reject a mouse because of complex conditions but it slows the process down and if there is a choice well sometimes its easier to do it yourself if you possibly can and this is exactly what happened with DuPont, we just kept doing things ourselves and that made it much more difficult to compare our work and I think it really slowed down the adoption of mice by industry too because just at the time we should have been generating all the basic information to make this a standard model we were slowed down.”

Some scientists sat down with DuPont directly, explaining their position and their own interpretation of what they considered the appropriate scope of the patent:

“I objected to the license on the grounds that DuPont's interpretation of the patent was too broad. In their view it covers any germline manipulation of the mouse. I sat with their lawyer who told me this was all about enablement...I am not sure about that but what I do know is that the claims have never been challenged. I explained my view of the appropriate claims and won't sign anything for uses beyond that. They told me ‘you are in violation of the law’ but there you are.”

They also lobbied their own Technology Transfer Offices (TTOs) to ignore the broadest strictures of the DuPont terms:

“Most of our scientists did not want us to sign and in fact we [in the TTO] had a lot of reservations too. We could not use the mouse for sponsored research...because that was commercial and continued to be an issue for us with DuPont and a point of contention particularly if the sponsor of our research did not have a license already. We were trying to negotiate with DuPont but they were not very keen on negotiating with us. We also worried about the obligations that came with signing a license. One of the issues is that by signing you have to undertake due diligence, you need to be vigilant about who the mice are sent to – you are now responsible.”

But DuPont's exchange tactics placed some faculty at odds with their TTO. One noted: “certainly we did butt heads with the TTO both with respect to incoming and outgoing stuff and the details of the stuff we'll send”. University administrators had different reactions to the notion of foregoing patent protection and licensing streams on mice. The scientist continued “I will sometimes scream and shout but I'll give up with the TTO many times because I am worn down

and it takes months...I delegate to post-docs or a lab manager but they are inexperienced". For universities, a letter saying that a faculty member was in violation of a patent and exhorting the university to sign a licensing agreement came as a surprise and could ignite acrimonious debate (Marshall 2002). But while some faculty were vocally resisted the restrictions and proceeded with their research without any adherence to DuPont's requirements others lived with a cloud of fear (Smaglik 2000) and chose not to use the mice, turning instead to other projects (Jaffe 2004).

Whatever their response at the lab bench, scientists could also try and place informal "sanctions" on DuPont. Some commented on the fact that DuPont was an "outsider" to the Mouse Club, with no prior experience in how the community was organized, its norms and practices. While they regarded that an excuse (or explanation) in the early days, over time scientists "got tired of their repeated insistence that their practices were justifiable and appropriate". Some also countered that this approach made poor business strategy:

"I mean, I think it was a stupid business practice. Why didn't they simply recognize that people weren't buying and so they should lower the cost, whatever those costs might be. I mean I know the cost to industry kept firms from adopting the mice because they would tell me and this is unfortunate because cancer drugs were inhibited and that is unfortunate"

Within their own community scientists could always sanction their colleagues for behavior that fell outside their expectations:

"It is hard to explain. You knew who those people were and you made sure to not be very helpful with them. To do the minimum and to be very careful with your ideas around them"

For DuPont, these sanctions had little bite. But scientists had an alternative recourse – to discourage their students when they completed their post-doctoral or doctoral studies from joining DuPont. Of course the supply of well-trained life scientists did not dry-up at DuPont, but some of the leading laboratories were less connected to DuPont's own fledgling biotechnology activities in this period. For Leder himself (also an outsider to the Mouse Club), there was no sanction. Scientists voiced surprise over Leder's decision to patent: "he took out a patent much to the shock of the rest of us. Anyone who makes any kind of mouse is financially beholden to Phil and that was a very odd situation". Another commented; "I doubt it caused people to think Phil [Leder] is a bad person". Others sympathized with Leder and described this, and the similar events in knock-out mice, as an "unintended consequence" of patenting. One commented that he "wouldn't criticize Leder because my concern is breadth [of the patent] and that is a US Patent Office decision and I also fault DuPont for their interpretation of the claims and their business

practices.” Like Leder they believed that patenting was an obligation under the recent Bayh-Dole Act. Many in fact echo Leder who described his patenting decision in unproblematic terms:

One of the elements of the creation of these mice--these animal models of human disease--was that it coincided with a time that the Supreme Court had just decided that life forms could be patented. And as an obedient employee of Harvard Medical School, Tim and I reported this invention to our Office of Technology Licensing as an invention and a discovery, which we disclosed to them and which potentially would be patentable. They consulted with a patent attorney and it was patented. (Lasker Foundation 1987).

Any fault, scientists argue, lay with Harvard for “naïve licensing” or with DuPont for “aggressive practices that clearly misunderstood the nature of academia”. A few people did voice their concern with Leder:

“He was already a rock star by this time” but “his attitude towards faculty and students going to industry was a bit hypocritical – after all he was so involved but thought others dropped their IQ 50 points in they moved”

The long-standing sense of community among mouse geneticists allowed them to confront DuPont as a coherent and powerful group. The annual summer meetings at Cold Spring Harbor became an important forum for orchestrating resistance. Scientific journals became another outlet in which to debate the Oncomouse patent and to criticize DuPont. Some scientists tried to work together to bring a law suit against DuPont to invalidate or narrow the scope of the patent:

“I have been contacted over the years by two or three lawyers on behalf of other academic labs who wanted me to join them to challenge the patent so that they could avoid the licenses and void the patent. I didn’t join them- it just seemed like an exercise that would be costly and time consuming. I preferred to get on with what I was doing, breed my mice and ignore the patent.”

Commenting on the possibility of a law suit, another scientist said “I wish there had been a suit filed against DuPont but I am afraid if you do the calculation of how much that would cost compared to the US\$1-2 million the license might cost a firm, its good business strategy not to sue and no university will take this on.” But these actions were never able to gain adequate momentum. Instead, scientists used their most powerful and prestigious institutions to pressure DuPont. A prestigious National Academy of Sciences (NAS) panel was convened on the topic in 1993. At that NAS meeting, GenPharm announced that researchers could pay for the option to breed as many mice as they want for an annual fee of \$1000. Scientists had made some progress defending the boundaries of their practices from encroachment, but as Tyler Jacks put it:

“The community’s lobbying is a success story, to the extent that it’s made an objectionable policy much more palatable...But I’m still not convinced we’ve reached the optimal solution” (quoted in Anderson 1993).

Therefore, in 1995, Varmus who by then had become the Director of the NIH, opened up discussions with DuPont. Through a series of protracted negotiations, he held onto the principle that DuPont should not infringe upon academic science and that the boundaries of patent law should not restrict research in academia. By late 1999, after four years of negotiations, DuPont and the NIH signed a Memorandum of Understanding under which academic scientists (when funded by the NIH) could use oncomice without cost, providing they were not using them for any commercial purpose, including research sponsored by a commercial firm. While much of the press coverage at the time announced that researchers could now freely exchange the mice (Smaglik 2000), the MOU explicitly stated that an MTA was required for exchange with colleagues at another non-profit institution. If scientists planned to distribute mice to a for-profit organization, they had to alert DuPont (DuPont 1999). One TTO commented on this change in strategy:

“Eventually we went into negotiations and signed. I had a lot more PIs who wanted mice from JAX but they were on hold until we signed the license – JAX wouldn’t send mice to them until we were on the list of institutions. This was really the point at which the business decision changed for us. We can now received the mice from other academic institutions and send it to other academic institutions under a simple MTA. But there are still problems. They did not want us to send to send any mice we make that are covered, to a company. We could do that but not for consideration [financial reward] which makes no sense if the company was willing to pay.”

In the aftermath of the agreement, Varmus recognized the role of commercial science when he is quoted as saying that ““it will be a great relief for many people to know they are not violating the law” by sharing animals with a colleague down the hall” (Marshall, 2000). And in a reciprocal acknowledgement of the importance of academic science, DuPont’s corporate intellectual property manager describes how DuPont “deeply appreciates the importance of wide dissemination of tools for basic research and is committed to making [Oncomouse] available to the academic community” (quoted in Marshall 2000). Thus an accommodation is reached and the ceremonial recognition of both institutions made.

ACCOMODATION – A More Surprising Post-Patent Response

Commercial science made inroads into the Academy and imposed a wide-reaching (if short lived) set of market requirements that highlighted the power of IPR s to disrupt academic science, just at a time when academia was set to embrace patenting (after the Bayh-Dole Act). In responding, academic science defended its boundaries and in doing so reaffirmed its own commitment to its independence and its core norms and values. If the story were to end right here, this would be a reasonably conventional account of the strength of institutional logics.

However, the reality is more complicated. Inside the institution of academic science changes were taking place. Academics far away from the power brokers in Washington were incorporating and accommodating IPR into their work routines (the reciprocal is true but for the remainder of this analysis the transformation inside commercial science will be put to one side). Many of the same mouse scientists who were furious at DuPont for patenting what they had here-to-for considered a common resource, began patenting their own work. One mouse geneticist remembers:

“I was chairing yet another session on the problems of patenting in mouse models [the meeting took place at Cold Spring harbor in the late 1990s]... Everyone was complaining about the patent restrictions, what the licensing requirements were, how arduous they were and how they stopped them from acting independently... Then I asked 'Would all those in the room with a patent please stand up' suddenly half the room stood up.”

One might accuse the Mouse Men of hypocrisy, or of trying to beat back a competitor so that their own patents would be worth more. But that would hardly be the case; the outrage over DuPont was real and the scientists' dismay at the way IPR was interfering with their work was considerable. Many of those who were now patenting worked hard to spoil the market not only for DuPont, but for all subsequent patent holders who sought to exclude others from using vital research tools and methods. The agreements that reached with DuPont reduced the economic value of any patent and made it difficult to launch a viable business around research tools.

Why then did the mouse men patent? And why did they not feel that their patenting contradicted their outrage? In short, they redefined the meaning of their own patents. Whereas DuPont had exercised its IP rights to derive economic rents from a valuable asset, the mouse men had stripped many of the direct economic implications from the idea of patents. Using the inherent flexibility in patents and the fact that, like publications, exchange using patents is underspecified in commercial science, they developed a complex new repertoire of practices using patents to build new types of exchange. In the hands of academic scientists patents took on new meaning: they gained a new symbolic status; they could be used to further the traditional aims of academic science; they were a potential bargaining chip in arranging collaboration with other scientists; and scientists also used them to establish a new local order with industry. Scientists also started patenting defensively and publishing not just to gain prestige but as a quasi-political act. To be sure, mouse geneticists could (and did) use patents strategically to further their own economic interests, but practices also developed to check the degree to which patents could be used as currency. I take up each of these transformations in turn.

1. Patents took on new symbolic meaning. Publications have long been the certification of priority. However when Leder patented the Oncomouse, filing for IPR was still an unusual faculty decision in the life sciences. Over the past 20 years, patents have emerged among some mouse geneticists as another channel through which to trade information for prestige. To gain a patent established priority and importance of a particular idea in a different sphere and with different judges. As one scientist noted: “A patent is different from consulting. You see it’s really more like a publication. It has to meet certain hurdles and there is a high bar I think (I’ve never tried it but I would like to). You know, you have to be inventive and useful and someone really has to think that it’s new.”

Even the patent office recognizes the symbolic importance of patents; you can mail order a wall-mounted patent plaque (gold or silver). It comes with a “prestige” mount for an additional \$15. A large patent portfolio has also come to be regarded as a symbol of commercial savvy and awareness. One colleague was described (with a combination of awe and trepidation): “X is just a patent machine but he certainly understands the business side of things.” While this would have been regarded as insulting in 1988, by the late 1990s this and similar comments were high praise.

While gaining patents might be a source of pride, and producing useful products was what really brought prestige not just from peers, “but also from friends and family, and from the outside world” and “enormous personal satisfaction.” Many mouse geneticists saw patents as a “necessary evil” or an “important step” in the prestige and satisfaction of seeing a product at the bedside. This fulfilled a sense of obligation held by many mouse geneticists – that their “research has a long term impact on health, on diseases like cancer, and on finding a cure.” When findings were in the commons, they argued companies would be leery of investing money in developing something over which they would not have exclusive control. A patented technology was more commercially viable. Leder noted:

I remember it used to be the policy at the National Institutes of Health--it no longer is--but to pursue patents on their discoveries, and then to dedicate the patent to the public domain. Now that sounds terrific. What could be better than that? The government has achieved a patent, and it has then dedicated it to the public domain so anybody can use that. The problem with that, as I have encountered it, was that nobody was interested. Unprotected by patents, nobody was ready to make the investment in the utilization of that technology. I wish the world were different, but that is what it seems to be like. NIH has changed that policy and that has made a tremendous difference, because I think in no field has there been a more dramatic change in transferring technology to the public good than there has been in biology over the last 20 years. (Lasker).

Thus patents expanded the calculus of credit and reputation as scientists used patents to disclose innovations, have then commercialized and gain recognition. At the same time, academic

scientists have checked the degree to which patents could replace publication as *the* currency for establishing reputation within academia. In most of the top-ranked research universities, the tenure decision still relies on publications and impact – measured through citations and letters from other academic researchers. While patents (and licensing) would now typically be reported as part of a tenure case, when asked about their place in the tenure decision, most scientists noted that there were neither a plus nor a minus (Ding, Murray and Stuart 2006).

2. Patents as an alternative currency in building cycles of credit and prestige. Patents provided a novel means to craft exchanges which could engage industry in generating prestige for academic scientists. Many scientists recognized the role that firms might play in move ideas into widespread (academic) circulation by alternative and complementary routes, which in turn might bring them greater credit. Once again, the role of IPR could be critical element in rewarding firms who stabilized, engineered, and distributed their scientific tools or novel compounds for a wider audience (although they often objected to the way those firms went about reaping their own commercial rewards from such an activity). As one TTO officer outlined the logic:

“Most of our scientists really want their ideas to be developed and especially if they have new tools they realize that industry can play an essential role in making these tools more stable, better validated and more easily available. When this happens, they get the satisfaction of seeing their work much more widely disseminated in academia.”

Thus, by articulating new exchanges with industry, based on patents, academics could further their traditional rewards of prestige and reputation. What was challenging about these new practices was making the careful calculation over when something should be patented to ensure its dissemination (and the associated prestige) and when it would be better exchanged only through publications. More than a few mouse geneticists confessed such differentiation was a delicate and the impact of different choices hard to anticipate:

“I suppose I should have a better philosophy about what I patent. I think that enabling materials should have broad access and you could argue that any price is too high for these materials. We rarely patent – we mainly choose a number of non-exclusive licenses and we are given the leeway by the university to do that but these are subtle and complex decisions. Are we the best people to make them – probably not.”

3. Patents became a way of shaping collaborative networks of scientists. Having patents became signal to other scientists that you were a valuable exchange partner and therefore worthy of co-authorship. Scientific collaboration was never entered into indiscriminately but under the commercial regime, a patent became a way of signaling your value to other scientists and co-opting them in your bid for prestige and reputation. The precise exchange rate is hard to gauge

but most fields have developed a market for credit, as illustrated in the pre-patent period of the However, in the shadow of patent rights, the exchange rate altered.

The changing role of Phil Leder provides a central example of the incorporation of IPR as a strategic asset in collaboration. DuPont's response had put a chill on the Oncomouse field. But as the inventor, Leder had an exemption and could freely use his mice. He also had a perfect alibi in refusing to send them to others – he was no longer a strategic opportunist but rather a scientist beleaguered by legal constraints. One mouse scientist criticized by colleagues in *Science* for his track-record in mouse exchange lamented that “everybody and their brother would like to get my mice, and if they don't get it in three months, they badmouth me” (Cohen 1995). He went on to argue that an Amgen lawyer has to approve every exchange so he was in a difficult position when it came to compliance. Thus collaboration provided scientists with a (gracious?) way out of this dilemma and gave patent holders greater control over their resources. For some this was a competitive benefit, for others, an unfortunate outcome of clumsy licensing, but it was difficult for the mouse community to make this judgment and to sanction those who used patents for personal benefit. One geneticist complained:

”They [mice] should be part of our communal resources. Patents on mice cause problems for the community and just make bad people worse and they seem to make the rich get richer if you know what I mean – not so much financially – I mean how much could Phil have made on the mice but they do give him power”

By increasing the control that an inventor (and his or her institution) has over key scientific resources, patenting has the potential to reshape social relationships between scientists, re-centering them on scientists with patents. The features that define IPR - strong control rights and the legal rights to exclude others - shift the balance of competition versus cooperation in academic science towards a stronger and legally sanctioned form of competition.

Again institutional practices to check the ability of scientists to use patents strategically to avoid collaboration have emerged. The experimental-use exemption has become a key aspect of negotiations around the licensing of transgenic mice, other research tools and is expanding to other types of academic patents. While controversial, this seeks to carve out a protected arena in which these more strategic forms of action become less viable and the shadow of the law recedes.

4. Patents as the basis of a new social order at the academic-industry boundary. Patents emerged as a way of clarifying relations with commercial concerns and extracting appropriate exchange rates with industry, as well as signaling which ideas might have commercial application

and which scientists had the “savvy” to work with industry. Patents therefore have become an important instrument in creating clarity and “social order” across the academic-commercial boundary. As one patent lawyer commented “its as if the scientists were reinventing the entire area of patent and contract law for themselves – eventually they came to see that patents could actually be useful to them”. For example, the strict legal notions of inventorship have allowed scientists to define the contribution of industry partners more precisely. One scientist noted:

At least we know who owns what, who invented what... Industry always tries to get on our publications, in fact they even tried to write that into our sponsored research agreement – what nerve (!) But they don't try and do that over patents and so that really helps us keep everyone honest.

Patents also clarified issues of ownership, defined boundaries of collaboration, and spelled out areas over which control could and should be exercised. With patents at stake, academic scientists could engage in differentiated exchanges with commercial scientists more easily. Over time, the mouse genetics community built-up a repertoire of rich commercially-oriented contractual arrangements (such as Material Transfer Agreements) some based on patents and some not. These exchanges also allowed scientists to ensure that industry paid what they believed was “a fair price for a sophisticated mouse”. Boundary work at the academic-industry nexus in mouse genetics (and beyond) became increasingly associated with the commercial practices; to such an extent that some firms complained about the legalistic and market-oriented nature of academic exchange. And in this process, universities have come to be increasingly sophisticated in their use of patents and other mechanisms that structure local order and that ensure appropriate exchange rates between academia and industry. And one veteran TTO officer said:

“We don't usually patent a mouse model any more. Times have really changed. We can normally license a mouse model non-exclusively to a company and get over \$10,000 even without a patent because we have the model. It takes a lot of work, and validation to have a published and accepted model and so we don't need to patent. We can patent but we can't make money out of it. But every institution has had to sit down to figure this out.”

5. Academic scientists patent and publish defensively to protect the "public commons". The boundary skirmishes over the Oncomouse made many mouse geneticists much more sophisticated about the role of publication as a form of priority and public commons, and conversely that of IPR in both encroaching and defending the commons. Many geneticists cited Heller and Eisenberg's article in *Science* as providing a powerful image of a public commons that they felt should be defended (ironically, the article argued that the commons was doomed). The mouse club took to patenting defensively, but not to keep others from replicating ideas (as in industry).

Rather, following the commercial science logic of using patents to exclude others, academics found that they could use patents to exclude unwanted commercial interests or to prevent one's own exclusion by others and so establish a commons.

Some patented their work to ensure that they themselves could keep working on what they had discovered. In interviews, the plight of Brinster often arose as a touchstone in explaining this strategy: Both teams (Leder and Brinster) received equal academic “credit” for their work but the patent allowed for no such multiples. Brinster’s research did not “trump” the Leder patent because he had not filed for patents, and was not willing (able?) to bear the costs of a legal suit to establish priority. Not surprisingly, he (and Palmiter) were among the first in the mouse community to file patents in the following years and others followed. One geneticist described:

We really struggle with patenting decisions. We want our stuff to get out and we want people to use it so we often choose to avoid patenting but on the other hand at times we decide to patent defensively. I mean if we are doing a series of experiments and we develop some methods, we don’t always describe them in detail in the publications so at least in theory someone else could come along and patent and scoop us and then we wouldn’t even be able to use our own stuff. I am sure that’s how the early transgenic guys [Brinster and Palmiter] felt”.

Other geneticists traced their decision to patent directly to the idea of keeping commercial interests from controlling the public commons in science. A scientist explained:

“I did take out a patent once, but not for a mouse, for a method. Why? Well frankly to keep any number of companies from using the technique and making money doing that. I didn’t want any company to make money doing that and I didn’t want to make money myself.”

The decision to publish took on new meaning as well. Prior to the rush to patent, publication was a reflexive phenomenon. With the role of patent disclosure beginning to crystallize for mouse geneticists, publication took on new meaning as a public good. It, therefore, was seen as quasi-protest against patents. Klaus Rajewsky at the University of Cologne used an important mouse conference to publicly announce a list of mice that would be freely available from his lab and to comment on the importance of a very public (both freely available and widely known) commons (Cohen 1995). Acts like these shifted publishing from its exclusive role as a channel through which to built personal reputation towards an action that, at the very least, was as a comment on what should be left in the scientific commons.

”I think that when we look back at some of these major academic projects and the way in which they have rubbed up against industry we will realize that industry forced us to think and reflect about what it means to disclose and share. These situations have challenged us to be more public and less competitive with our work and so perhaps in the long run they have been good for science.”

WIDESPREAD TRANSFORMATION OF INSTITUTIONAL PRACTICE

The proliferation of patents, the new meaning of patents and their role in scientific exchanges evolved through the daily interactions of scientists. At the same time, those touched by these (and related) events came to initial widespread change in the broader academic science community. Longstanding academic practices and organizations were transformed to reflect the resistance and accommodation that geneticists were dealing with on an individual level. Some of these transformations have already been noted such as "academic exemptions" for patented research material. Others deserve comment since they help illustrate how the change filters-up and is codified in new institutional practices and new institutional logics.

For mouse geneticists, one of the most important changes was that JAX stepped in and shifted its policy to allow the lab to accommodate not only Oncomice but a range of transgenic and knock-out mice to be shared under a wide range of different licensing agreements. In the whirlwind of controversy around transgenic and knock-out mice licensing, the NIH released a request for proposals for a transgenic rodent facility that would distribute frozen embryos at low cost to researchers. In order to continue serve the mouse genetics community, JAX, in part under pressure from Varmus and also given its desire to maintain a central role in the mouse community overcame its resistance to supplying material that was the subject of IPR¹³.

At the same time, Varmus reconsidered the NIH's role in the dissemination as well as the funding of research. While the organization had traditionally allowed scientific communities broad autonomy in shaping their dissemination strategies, the Oncomouse experience caused Varmus to rethink his position. In 1999 the NIH released a set of guidelines for the patenting of research tools (Marshall 1999). In doing so, the organization found itself at odds with the Bayh-Dole Act, but nevertheless promulgated these ideas in the interest of promoting academic science in the new patenting environment. They underscore the lessons Varmus himself learned in the

¹³ Transgenic mice are now available through JAX with specific conditions of use pertaining to each of the mice, depending on the intellectual property position. For Oncomice a provision is described under the "terms and conditions" that "The recipient of the animal(s) is NOT authorized to breed, cross breed, reproduce, transfer possession of or otherwise make ANY use (including use for research purposes) of the animal(s) or biological material derived there from (including without limitation cells, eggs, or embryos,) without first obtaining a license from DuPont. Any making, using, offering to sell, or selling the animal(s) or any biological material derived there from without an appropriate license to the OncoMouse technology will be considered an infringement of the patent rights by DuPont. There is a caveat on the site directing researchers to the NIH-DuPont Memorandum of Understanding.

wake of the Oncomouse as they enjoined universities whose academics develop tools to follow four principles that together argued for much more limited use of patents and exclusive licensing (Marshall 1995)¹⁴. The announcement met with a mixed response. Some scientists wished the NIH would do more: “Whenever the word patent is mentioned, they still try and run away and talk about Bayh-Dole but this is changing slowly and it has to.” Others felt that the move away from the newly crafted order with industry and the clear ownership provided by patents was a mistake. Small biotech firms were upset because patents provided a key basis for competitive advantage in businesses build on research tools and the tension that has long characterized the academic-industry boundary was obvious in the words of one biotech executive who described the changes as an “unmitigated disaster” (Marshall 1999).

Universities also began reconsidering their response to Bayh-Dole. Under pressure from academics, TTOs went from promoting patents in all forms to insuring patent restrictions did not impinge on researchers. Most U.S. universities adopted licensing clauses that provided a limited research exemption – to an inventor, the University or a more widespread exemption across a large number of Universities. And at least for mice, fewer and fewer patents were filed. Instead, Universities evolved a series of practices based on Material Transfer Agreements. Joyce Brinton who had been head of the TTO at Harvard at the time of the Oncomouse license was instrumental in developing the Universal Biological Material Transfer Agreement (UBMTA) which was outlined in the Federal Register. The Association of University Technology Managers (AUTM) served as the official repository of signatories of the UBMTA. The organization also engaged its members in widespread discussions of Oncomouse licensing and issues around transgenic mice in its journal (in 2000) and at its annual meetings in 2001 and 2002. Again these events were led by Hinton and Abrams at MIT who had extensive experience with another cancer-related mouse, and Einhorn at JAX (see Abrams and Kaiser 2000). As a result they issued new guidelines for licensing research tools in their AUTM TTO Manual:

“There are new guidelines from AUTM and we try and say to companies that we follow these and NIH guidelines for research tools. So in general, we do not do exclusive licenses for tools any more. The early licenses were not like this and so Harvard would have had no choice in the way they set up their sponsored research with DuPont. Now we have changed so that we keep the rights to use

¹⁴ The four conditions were i) to ensure academic freedom in their relationships with companies; ii) to use patents and exclusive licenses appropriately and rarely in the dissemination of research tools; iii) to minimize the impediments to academic research by minimizing the use of reach-through claims; and iv) to encourage the dissemination of NIH-funded research tools on generous terms to non-profit and profit-making research organizations (Marshall 1995).

any research tools and disseminate them through a non-exclusive and also have academic exemptions. If it is exclusive we try to put the language in that our scientists have the right to continue to do research, but at times there may be push back. Not every TTO can do this, especially smaller institutions. We always try to make sure that there are exemptions, due diligence terms to try and avoid cases like the Oncomouse.”

Academic journals were also changing to protect the public commons. Journals put into place requirements that scientists divulge their commercial interests, thus helping readers and reviewers place the knowledge exchange into its appropriate commercial context. One scientist described how institutional practices would shape an exchange:

“One of my junior colleagues requested a mouse strain recently from a PI (principal investigator). It had been published the previous year and so he was obligated to send the mouse. He refused on the grounds of competition – he said “we are going to do that experiment” but my advice was you should challenge this person and threaten to report them to the journal- and the NIH. The journal policy makes it easier to sanction these days”.

As a result of another NAS Panel and report on “Sharing Publication-related Data and Materials” (NAS, 2003) whose executive summary highlighted (but was not limited to) transgenic mice exchange, a number of leading journals also instituted policies insisting that data and materials described in an article be made widely available. This policy too would have far-reaching influences on scientific exchanges well beyond the reach of the mouse men.

CONCLUSION

Patenting of the Oncomouse occasioned a number of seemingly paradoxical responses from the mouse genetics community. A vibrant scientific community rose to defend their practices from major encroachment by a commercial outsider, DuPont. The social arrangements the community had used to distribute resources and information were put to use to orchestrate resistance. On the individual level, many mouse geneticists also engaged in active and knowing civil disobedience. However while collectively decrying commercial practices, the mouse geneticists rushed to file their own patents. There was no widespread move to reverse the trends initiated by the Bayh-Dole Act. Instead, over a two decade-long period, scientists incorporated patents into their repertoire of behaviors, but on their own terms. They changed the meaning of patents to better fit with the institutional logic of academic science, but they also subtly shifted the ways they exchanged information and regarded their other normative behaviors such as publishing. In order to accomplish their daily work scientists in the mouse club came to master a more complex calculus of the appropriate currencies, exchange rates and partners that included patenting.

Perhaps the most important lesson scholars of institutional change can draw from this episode is not so much that patents did change academic science, but rather that the way in which patents shaped laboratory life was determined by scientists themselves and scientists' own organizations and leaders, not by the law courts. As a window into the collision between a market-based logic and one based on strong normative practice, this study should inform scholars concerned with commoditization and the imposition of economic logic within institutions that were previously considered privileged and immune from market forces. Kuttner describes how "realms that used to be tempered by extra-market norms and institutions are now being marketized with accelerating force" (Kuttner 1997: 55, quoted in Zelizer 2005). Scholars have characterized these economic forces as capturing and corrupting institutions, social structures and practices previously defined by an alternative logic of action.

This study suggests a number of lessons for institutional theorists examining the growing power of the market and a broader set of institutional collisions. Most centrally, this case highlights that individuals outside the market, with a strong network of social ties, organizations, and shared norms can resist and shape the encroachment of even a powerful corporation armed with strong IPR. They did so in such a way as to maintain the boundaries and logic of their institution. This does not mean there is no institutional change or accommodation, but rather that individuals, through collective and strategic action, are a powerful force in shaping change.

Moreover, we should take from the history of the Oncomouse the power of institutions to shape meaning. Intellectual property rights are social constructions that were forged in the realm of commercial science. When this social construction is transplanted into the realm of academic science, the context shifts and the meanings become changed. The transplantation changes relationships within the institution but not in the way that many predicted on the basis of how IPR functions in the commercial world. This observation may be salient for scholars concerned with commercialization and the imposition of economic logic within other institutions that were previously considered privileged and immune from market forces. While scholars may characterize these economic forces as capturing and corrupting institutions, they should also remain vigilant to the way institutions fight back and change the meanings of commercial practices.

For those interested in the details of the academic-commercial collision in particular, the findings of this study should lead some to (at least) reconsider their positions. Most have argued that academic science's normative order was but a slender reed that could easily be overcome by the forces of commercialization. Economists have posited that the open commons of academic

science is hard to maintain. They argue that with one defector, the entire community will shift to a commercial system (David 2001ab, 2003; Gambardella and Hall 2004). While it is true that patenting did beget patenting, the nature of patents shifted as well. Academic scientists adopted the practice but not all its attendant commercial implications. Social theorists who worried that scientific collaboration would wither in the face of commercial sciences should also be mollified. Arms-length transactions did not increase and collaboration continued apace. Indeed, mouse geneticists developed a new respect for their community and their intellectual commons.

Other analysts who have concentrated on the growth of networks of innovation have suggested that the boundary between academic and commercial science would wither and transaction would become seamless (Powell et al. 1996). However, this study suggests that scientists themselves like the boundary and will push back on industry when it overreaches. While networks of collaboration may indeed be crucial in the movement of ideas, maintaining and shaping a boundary remains important to academic scientists. Patents have come to facilitate some interactions, as have social relationships and prior academic affiliations, but as one commercial scientist put it: “Now I am on the other side its clear I am no longer one of them...I am not treated in the same way.” The view from the Academy is one of defending distinctions.

However, those analysts who suggest that the introduction of IP produced no change (based on publication records) should recognize that while overall productivity may not change IP can influence underlying patterns of collaboration and stratification. As patents become important in determining exchange, those with more limited access to patents may be excluded from core networks. The impact of IPR may not be felt through academic research agendas and individual productivity, but patents can change the resources needed to compete in a field, and therefore influence the mechanisms of attainment. It is for this reason that we should not be lulled into thinking that the lack of impact on individual productivity is the final word.

Academic science has changed. As an institution it has gone through major transformation in the past several decades. However at its core it had a recognizable logic. This logic is flexible and has adapted to the new economic reality – there are forms of property rights other than prestige and priority at stake. They can be incorporated and co-opted into Academic Science and become a source of value without undermining the fundamental logic of the institution. Patents have become part of every day scientific life. But they play a symbolic and strategic role in shaping exchanges, rather than as a property right to merely impose on one's colleagues.

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Table One

Taxonomy of differences between the logic of Academic Science and Commercial Science

	Logic of Academic Science	Logic of Commercial Science
Producer of knowledge	Author – defined by convention & negotiation	Inventor – strict legal definition
Ownership of knowledge	All rewards for knowledge inalienable to the author	Rewards for knowledge held by Assignee and can be traded
Additional knowledge beyond documented disclosure	Yes- materials, tacit knowledge, expertise etc.	Yes- materials, tacit knowledge, expertise etc.
Adjudication of claim	Peers	Patent office/Court
Rights granted with “accepted” disclosure	Priority rights	Intellectual property rights
Rewards	Priority leading to recognition and status	Provide for exclusion and the right to appropriate economic rents
Requirement to trade/exchange	Strong normative requirement (under different terms)	No obligation to trade
Market for exchange	Some flexibility – collaboration, citation (gift), acknowledgement	Highly differentiated & flexible – complex variety of contractual elements
Exchange partners	Homogeneous – other scientists	Heterogeneous – many types of firms & other actors
Sanctions	Normative, self-governing	Legal, external actors
Link to prior ideas	Citations – gift – also establish & strengthen claims	Citations – legal requirement can weaken value of claims

