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Generating sociability to drive science: Patient advocacy organizations and genetics research

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Abstract

This paper examines how patient advocacy organizations (PAOs) representing those with rare genetic disorders drive research to their concerns. The rarity of the diseases produces a basic condition of marginalization: small numbers of widely distributed disease sufferers. The lack of promise of an eventual market makes it difficult to attract the economic and biological resources necessary for sustained research. My analysis relies mainly on 21 interviews with leaders from nine PAOs and scientists involved with them, and seeks to understand how PAOs try to attract and influence scientific research. Using a comparative framework, I find that the five main mechanisms emphasized in the literature – economic resources, social movement-style mobilization, moving early, lay expertise, and organizational controls – cannot fully explain the differences in strategies and relationships among members of my PAO sample. I propose instead to show how 'sociability' – forging close relationships with scientists and orchestrating relationships among them – enables PAOs to drive research to their concerns. I show how the strategic manipulation of sociability can give PAOs substantial influence over the research process. However, the forms of sociability that yield the greatest effects are difficult to achieve, and most forms of relationship-building offer PAOs much less influence on research.

Keywords

genetics, health movements, lay–scientist interactions, patient advocacy, rare disorders, research policy

At the intersection of the sociological literatures on science, medicine, and social movements is the question of how marginalized groups can drive scientific research to their concerns. For example, studies of the AIDS movement (Epstein, 1996), the women's health movement (Ruzek, 1979), and the Association Française contre les Myopathies[1] (Callon

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and Rabeharisoa, 2003) have shown how groups struggle to transform marginalization into a positive identity that can bind a group together and enhance its ability to advocate 'rights' over the direction of research. Such mobilization also can lead groups to oppose medicalization of their conditions as both a threat to their existence and a distraction from viewing marginalization as a problem of social access and stigma rather than (or in addition to) one of 'defective' bodies, as some deaf and disability rights activists argue (Shakespeare, 1999; Wrigley, 1996).

This paper investigates a different marginalized population: people afflicted with rare genetic diseases. According to the National Organization of Rare Diseases, approximately 6000 diseases are classified as rare or orphan diseases (affecting fewer than 200,000 people in the US).[2] A substantial portion of these are known or believed to be caused by some genetic defect. The possession of one or more copies of a mutated or 'defective' gene, a deleted or repeated section of chromosome, or extra or missing chromosomes are just some of the possible genetic abnormalities that can produce developmental problems or disease. These conditions vary widely in their severity, their manageability, and the physiological system they affect. Among the best known are Huntington's disease, Down syndrome, phenylketonuria (PKU), sickle cell anemia, and cystic fibrosis.

Families of genetic disease sufferers, and sometimes patients themselves, have often formed patient advocacy organizations (PAOs) to connect with each other, serve as a source of information and support, and promote research into their particular diseases. I focus on this last set of activities.

The rarity of these diseases produces the basic condition of marginalization that these PAOs confront when seeking to generate research. A common explanation for limited research funding for rare diseases is that drug companies fail to invest in areas that lack large potential customer bases. The low numbers and broad distribution of afflicted individuals can make it difficult for researchers to locate sufficient cases to study first hand. In addition, scientists who study a rare disease may lack a community of interested colleagues, often instrumental for driving research forward. Still, rare genetic diseases often hold considerable scientific interest, because the discrete genetic alterations that often cause them can help scientists model how genes affect developmental and physiological systems. From the PAOs' perspective, this situation can be a mixed blessing, since it may direct scientists' attention toward 'basic discoveries' rather than research relevant to changing health outcomes (Terry et al., 2007). Given this situation, the question I seek to answer is: How do rare genetic disease PAOs overcome these barriers to direct scientific research to their concerns?

The core of this question may seem to be the problem of *attracting* scientists' attention, but perhaps more important is the challenge of *influencing* scientists to do research that reflects patients' interests. The literature on marginalized groups rarely separates the two tasks and seems to emphasize the second. For example, AIDS activists in the1980s and 1990s sought not only to draw funding and scientists, but also to oppose research and public health measures they viewed as homophobic and to ensure that clinical trials were speedy and spread benefits widely (Epstein, 1996). The women's health movement sought to ensure women-centered medical practices by building alternative medical institutions (Ruzek, 1979).

Indeed, the example of Canavan disease suggests the potential danger arising when a group is successful at attracting research without gaining substantial control of the situation (Greif and Merz, 2007). Dan Greenberg, the father of two children who both had Canavan disease (a fatal degenerative genetic disease), approached scientist Reuben Matalon and convinced him to work to generate a test for the disease. Beginning in 1987, affected families and two PAOs (the National Tay–Sachs and Allied Diseases Association, and the Dor Yeshorim Committee for Prevention of Jewish Genetic Diseases) donated money and tissue samples to Matalon. After a number of false starts, in 1993 his lab at Miami Children's Hospital identified the gene. Without consulting the patient groups, the hospital patented the gene and placed a restrictive license on its use. This hindered genetic testing and effectively halted research. This example highlights the dilemma for many PAOs: losing control may harm their interests, but they have limited means to exercise control and risk alienating the scientists on whom they depend.

To address the question of how PAOs drive research to their concerns, I conducted interviews with leaders of nine PAOs and 12 scientists involved with them.[3] I used these interviews to learn how PAOs and scientists interact, what they offer each other, and how they make decisions together. My research suggests that PAOs are able to direct research to their concerns mainly by fostering *sociability* among researchers and between researchers and the organization. That is, PAOs can attract and influence researchers by forming close relationships with them and coordinating them into stable and cooperative research networks.

This finding contributes to our understanding of patient influences on research in three ways. First, sociability is an important factor different from those emphasized in the previous literature on patient organizations and research. Second, it reframes the problem of those suffering from rare disorders away from issues of limited resources, inability to attract attention, and small markets, to one of generating relationships. Accordingly, it is much less sensitive to the 'numbers problem' inherent to their condition. Third, a key implication of the study is that, not only can patient groups benefit by engaging scientists, but by doing so they also can help science operate more effectively.

Data and methods

To understand the ways that PAOs seek to influence scientific research I chose to study nine different organizations with a variety of organizational characteristics and research strategies. Much of the literature has focused on single case studies of organizations with large, well known, or noteworthy research programs, so one aim of this project was to introduce a comparative perspective and study a variety of organizations.[4] My sample was designed to exhibit variation in organizational age and range of research activities as well as to compare fairly well-known examples with others that have received little attention. In my sample, the well-established advocacy groups that have undertaken vigorous research programs are PXE International (Novas, 2006; Taussig, 2005), the Autism Genetics Resource Exchange (AGRE) (Iversen, 2006; Silverman, 2008), and the Tourette Syndrome Association (TSA). TSA was selected because it was mentioned by

interviewees at AGRE as working on a consortium model (where resources are shared by a closed group of scientists to eliminate competition), which contrasted with AGRE's model (a competitive model where resources are made available to any scientist).

To select less well-known PAOs that differed by age and range of research activities, I consulted the PAO database maintained by the Genetic Alliance – an umbrella organization that helps advocate for and coordinate 600 organizations active in the area of rare genetic disorders. The American Association of Multiple Enchondroma Diseases (AAMED), the Ring Chromosome 20 Foundation (Ring20), and the Pachyonichia Congenita Project (PC Project) are newcomers (all founded in the 2000s); Cystic Fibrosis Research, Inc. (CFRI) and Foundation for Ichthyosis and Related Skin Types (FIRST) are both about 30 years old; and Parents and Researchers Interested in Smith Magenis Syndrome (PRISMS) lies in the middle of the age range. Most of the organizations perform patient/family support, but I selected them because they also engage in different types of research activity, according to their entries in the Genetic Alliance Database. CFRI, FIRST, and Ring20 engage in research primarily by making research grants. PRISMS, AAMED, and PC Project engage in a wide range of research activities, including registering and recruiting patients and linking them to researchers, tissue banking, and organizing studies and researcher consortia. PC Project was not in my original sample, but I included it because a scientist who worked with FIRST explained that it addressed a related skin disorder but took a more aggressive approach to promoting research. To my knowledge, these six PAOs have not been studied before.

How do these PAOs compare to others in the field? The 600 member organizations in the Genetic Alliance range from very large, rich, bureaucratic organizations to very small, family operations without budgets. Some are very sophisticated about research, while others only provide patient and family support. A total of 105 organizations report budgets over US$1 million (with 19 having budgets above $10 million and five above $100 million), but more than half have revenues below $25,000 (the threshold below which non-profit organizations are not required to disclose their finances to the Internal Revenue Service). In terms of age and research activities, the median PAO was founded in 1992 (about 95% were founded after 1970) and reports 'linking patients and researchers' as its only research task – more than a third of the organizations report no research tasks. Thus, compared with the rest of the Genetic Alliance, the PAOs in my study are mostly richer and better organized than the median, but not among the richest or most bureaucratized. They have a similar distribution of ages and are much more engaged in research.

I should note that while I use the label 'rare genetic disease PAOs', some of these diseases (autism and Tourette Syndrome, in particular) may not be exclusively, or even primarily, genetically caused. Further, this paper does not explore the fascinating question of why PAOs are interested in genetics research at all, since diagnostic rather than therapeutic tools are the most likely near-term outcomes of such research. Research supported by rare genetic disease PAOs has almost never achieved its ostensible goal of developing cures or even effective treatments.[5] For this reason, the 'outcomes' on which I focus are the relationships and influence PAOs are able to establish with scientists. In the conclusion, I will reflect on the links between relationship building and PAO goals.

Table 1. PAO sample with organizational and disease characteristics*

PAO name	Interviews (organisation leader / scientists)	Disease type	US incidence	Date founded	Average total revenue (2000–2006) (US$)
AGRE (Autism Genetics Resource Exchange)	1/1	Mental disorder	Controversial, 200,000+	1997	$1.8 million†
TSA (Tourette Syndrome Association)	1/2	Mental disorder	100,000	1972	$6.6 million
CFRI (Cystic Fibrosis Research, Inc.)	1/2	Mucous affects lungs and digestive system	30,000	1975	$626,000
AAMED (American Association of Mulitple Enchondroma Diseases)	1/0	Bone tumors	Low thousands	2002	None reported, less than $25,000
Ring20 (Ring Chromosome 20 Foundation)	1/1	Chromosome abnormality, severe seizures	>100	2004	$108,000
PRISMS (Parents and Researchers Interested in Smith Magenis Syndrome)	1/2	Physical and mental development, sleep problems	600?	1993	$70,000
FIRST (Foundation for Ichthyosis and Related Skin Types)	1/2	Class of genetic skin disorders	1,000,000‡	1981	$314,000
PC Project (Pachyonichia Congenita Project)	1/1	Skin disorder	600	2004	$304,000
PXE International	1/1	Connective tissue disorder	3000	1995	$376,000

*Data on incidence come from PAOs' websites and revenue from PAO tax forms. For organizations listed in the Genetic Alliance database, the median founding date is 1992 and median income is below $25,000 – the level below which non-profits are not required to report finances to the IRS.
†This is AGRE's budget in 2008. Its parent organization, Autism Speaks, had a gross income of $69 million and reported spending about $36 million on autism research. AGRE's financial picture was similar previously when it was part of Cure Autism Now (Midgette et al., 2009).
‡FIRST derived this figure by adding together the separate incidences of all the different forms of ichthyosis; it is likely an overestimate.

The core data of the study were 21 interviews. For each of the nine PAOs, I interviewed an organizational leader with experience promoting research activities and one or two scientists they work with. I also conducted informational interviews with three other scientists and a patient advocate. Interviews usually took 90 minutes (from 45 minutes to 2 hours) and covered a range of topics. I asked PAO leaders about the history of the organization, how it became involved in research, what its research activities are, and for a description of its relationships with scientists (including the types of contacts it has, support it offers them, how it selects among them, and its oversight efforts). I also asked them to describe their goals, successes, failures, and relationships with other PAOs, and to recommend scientists with whom they had worked for further interviews. Interviews with scientists covered similar topics but with a focus on their points of view: for example, I asked about their relationships with the PAO, how their research connects to it, and their non-research responsibilities. Interviews were semi-structured and open ended, and I encouraged the conversation to flow naturally. Interviewees were asked to speak on the record, though they had the option to speak off the record or to check quotes before attribution. Except in the cases of certain well-known patient advocates who agreed to speak on the record, I have not attributed quotes to particular individuals. I also consulted published sources, especially PAOs' websites, to gain general information and to corroborate interview data when possible. However, few websites contain details about the organization and texture of research practices and relationships, so interview data were often the only source.

One purpose of interviewing both PAOs and scientists was to use their accounts to check each other and to see if they understood the structure and purpose of research relationships in the same way (though, of course, from their different positions). There were two limitations in this regard. First, I did not have the opportunity to re-interview people, so I did not go back to interviewees when others gave different information (though disagreements in my data never seemed to demand such a procedure). Second, most of the scientists were recommended by PAO leaders whom I had interviewed. While interviewees seemed to make honest efforts to discuss problems and disagreements, this sampling procedure would probably not have exposed serious conflicts or failures in PAO/researcher relationships that PAO leaders hoped to conceal.

Expectations about driving research

The literature on patient advocacy generates expectations about five factors that should either enable or constrain PAOs' pursuit of research: funding, collective mobilization, timing, lay expertise, and organizational capacity. Though I argued above that *attracting* and *influencing* scientists are likely to be inseparable in practice, I distinguish between them here because some of the expectations I discuss are more relevant to one issue or the other. Funding and collective mobilization are more relevant to attracting scientists, while timing, lay expertise, and organizational capacity are more relevant in influencing scientists. I show that these factors on their own are insufficient to account for the patterns of research strategies in my PAO sample. Rather, they enable PAOs to affect research by helping them cultivate productive relationships with and among scientists. I call this activity *sociability* and discuss it in the next section.

Funding and economic incentives

A common assumption about rare disease is that their limited frequency makes it difficult for PAOs to generate or attract the kind of funding that contemporary biomedical research requires.[6] Thus the US Orphan Drug Act of 1983 increases the incentives (such as tax credits and research grants, and a 7-year period of exclusive marking) for developing drugs whose costs would be difficult to recoup in sales because they treat diseases afflicting fewer than 200,000 people in the US (Department of Health and Human Services, 2001).

Given this basic assumption, we should expect that PAOs with more money for research should be able to attract scientists more reliably and also be able to use these funds to influence scientists toward their research interests, perhaps by earmarking funds for particular purposes, setting performance benchmarks, or threatening to withhold funds if their expectations are not met. Initially, it appears that good evidence supports this expectation. Almost all PAOs and scientists believe scarce resources limit research, and most PAOs in my sample devote considerable energy to raising money for research. An important reason PAOs become legally incorporated is to enable these financial activities. PAOs seeking to get into research often think about the task in terms of grant-making, which orients their activities toward confronting problems of limited money and generating incentives. Finally, the two wealthiest PAOs in my sample also claim to have supported the largest number of research publications.

However, it is a mistake to think that *the problem* for PAOs is their limited economic resources and inability to generate financial incentives for research. The head of one PAO that has been quite successful with driving scientific research told me:

> So, I would say that there is no lack of resources in this area, whatsoever, for any disease. I would boldly say that any good idea has the funding in a minute. And we've seen that in lots and lots of industries and lots and lots of places. And even diseases that shouldn't have any recognition whatsoever. So, resources is [sic] never the issue. The issue is how much can you inspire those around you to want to go for the cause. … Most groups … go right to 'If I only had money, it would be fine.' And that's never the case. I mean I think you could pour buckets of money into certain diseases and if you don't have the right kind of leadership, you're not going to get the results you want.

The implication (echoed directly by another PAO as well) is that effective organization and ideas attract money rather than the reverse. This statement is not false modesty or an effort to conceal success, because both PAOs with this view have devoted considerable effort to helping other PAOs succeed in research.

One reason to think that the main issue is not a lack of resources is that PAOs often mobilize scientists with very small sums of money. Interviewees in different organizations suggest that most provide scientists with grants in the high four-figure to mid five-figure range – perhaps enough to pay for some piece of equipment or fund a post-doc for a year. These seemingly small amounts of money help labs incrementally in their training, research, and pursuit of larger grants. Further, beyond their material impact,

PAO grants have a symbolic function, as they signal that a lab has community support and that its researchers are doing something disease sufferers consider relevant and important.

Influencing such research through relatively small grants can be a successful long-term strategy. According to Sue Levi-Pearl, the chief scientific officer of TSA, the organization has spent about $14 million since 1984 to fund over 200 scientists researching Tourette syndrome. They estimate that they have funded the authors of 90% of all publications on Tourette syndrome, which suggests that TSA has shepherded the field using one small grant after another to enroll researchers, who then seek funding through other research channels.[7] For researchers in my sample, TSA stands out for the quantity and duration of its financial investment in research, but the broader point is that some degree of research patronage is open to all but the smallest PAOs. Conversely, the ability to sponsor entire research programs is closed to all but the few very wealthy PAOs (Rabeharisoa and Callon, 2002; Stockdale, 1999).

The other main reason to think the economic story incomplete is that many of the resources PAOs offer scientists are not economic. The limited availability of patients is one of the significant barriers for research on rare genetic disorders. As networks of afflicted individuals, PAOs are uniquely situated to help scientists acquire the 'resource' of afflicted individuals and their families. They commonly do this is by advertising research projects to their members or more actively recruiting subjects for scientists. Often PAOs formalize this task by creating patient registries, databases of afflicted individuals that could contain information about their conditions and the treatments they received. PAOs can also supplement registries by collecting relevant biological material from patients, though preserving tissues in usable form and banking them usually involves building or contracting for infrastructure, sharply raising the financial stakes. PAOs can enhance the value of these resources by aiming to structure them so as to mitigate difficulties that arise when they are dispersed among multiple bureaucratic jurisdictions. One scientist I spoke with discussed this difficulty in terms of navigating institutional review boards (IRBs):

> It becomes prohibitively expensive to do research, and especially clinical research, if you have one patient in one institution and another patient in another. And in order to get the requisite 20 or 100 patients enrolled in a study, you have to have a hundred different IRBs review them …. And, it turns out that [PAOs] … can all work together to make the regulatory problems less burdensome. It hasn't happened yet, but I do believe that that is an area where cooperation is going to help.

PAOs may enhance the resources they control by helping promote national and inter-institutional IRBs. Another way they make their resources less bureaucratically burdened is by implementing a flexible consent procedure that makes 'reconsenting' easy when new projects or scientists come along.

In the section below on PAOs' efforts to generate sociability, I describe some of the remarkable ways they have used non-economic resources to coordinate communities of scientists. At this point it is sufficient to say that economic resources, at least in a narrow sense, are not the barrier to entry or key to success that they are often assumed to be,

because of the importance of non-economic resources and the limited funds with which PAOs often mobilize scientists.[8]

Collective mobilization and identity formation

A dominant analytic move in the rapidly growing social scientific literature on rare genetic diseases has been to show how these conditions have led to the emergence of new identities, collectives, and forms of political action (Heath et al., 2004; Rabinow, 1996; Rapp et al., 2002; Rose, 2007; Rose and Novas, 2004). Such work is broadly framed on social movements or collective mobilization, and suggests a number of ways that patients can influence research to address their concerns. One is through collectively pressuring politicians and agencies – such as the National Institutes of Health (NIH) – to fund research on their diseases (Heath et al., 2004; Rapp et al., 2002). Another is to mobilize moral authority to generate sympathy among researchers. For example, Heath et al. (1999) describe how the presence of a Marfan disease sufferer in a research lab helped motivate scientists to research the disease. A third is to support disease sufferers to develop a positive identity, so that they can see themselves as empowered rather than dependent upon doctors and scientists. Callon and Rabeharisoa (2003) document the critical importance of such empowered identity for the success of the Association Française contre les Myopathies (AFM) in maintaining decision-making autonomy in their extensive research programs.[9]

For most of the PAOs I have studied, the active assertion of a positive disease identity seems not to be a strong part of their organizational strategy, particularly for promoting research. Of course, the founding of a PAO whose mission and membership is circumscribed by a disease category is, at least implicitly, to mobilize around an identity: to put 'biosociality' into practice (Rabinow, 1996). But, compared with the parents of children with epidermolysis bullosa discussed by Heath et al. (2004: 155), who reported using 'their bloody, blistering babies like a battering ram' to mobilize support for research, the activities of the PAOs in my sample are placid. My interviewees offered essentially nothing explicit about positive identity formation, efforts to overcome stigma, or collective empowerment. PAOs generally described challenges to marginal status in terms of helping individuals reach pragmatic accommodations to the difficulties of living with disorders – for example, helping disease sufferers get letters from their scientific or medical advisors to help them claim accommodations from employers or schools. These PAOs view their missions less as a matter of self-conscious pursuit of rights or challenges to marginal status, than as vehicles for community building and pursuing research.

This finding is less remarkable in itself than in its contrast with much of the literature. Three possible explanations can be suggested. One is that sufferers of the particular diseases in my sample experience less stigma than those with other diseases. Indeed, the chief exception is the TSA, which expends significant effort trying to educate the public about the tics and behavioral patterns of individuals with Tourette syndrome. A second is that the most politicized PAOs have (unsurprisingly) drawn the most attention and that the 'average' PAO is not militant. A third is that my concern with research directed attention away from more politicized activities. I do not rank or otherwise evaluate these possibilities, but it is clear that several of the PAOs I spoke with anticipate risks when

deploying identity claims in interactions with researchers. After attempting to interest one doctor in research on her child's condition, one PAO leader was told:

> 'You're the mom', you know, 'play your role and I'll be the doctor, and I'll play my role and that's it', you know ….
>
> And I really sat and thought long and hard about how I was going to approach them, because I knew intellectually, that if I contacted somebody and said, 'Hey, I have a child, you know, and she's got this disease, what can you … .' You know, that wasn't going to work. I had to somehow make myself be known to them as somebody that was interested in their field, and coincidentally, I had a child with this disease.
>
> Interviewer: I see. Because you didn't want to open yourself up to being told ….
>
> Yep. You're just another mom …. And researchers, God bless them, they do what they do and ... their world is about science, it's not about emotion. It's about pure science. So you cannot approach the emotional front, because they don't connect with that. That's not what they're about, you know.

The perceived danger is that mobilizing sympathy will be a 'turn-off', enabling scientists to see the PAO representative as someone who does not have to be taken seriously as a partner. Perhaps because it is what scientists expect PAOs to do, wielding sympathy or moral authority risks putting the PAO in the disempowered 'client' relationship with scientists.

This is not to say PAOs never try to mobilize sympathy, but they generally try to do so within the context of an already close relationship with a scientist. As the same speaker explained:

> So your relationships with them grow on a personal level, which is also very nice, because that brings that element of emotion that I originally spoke to you about. Now you are looking at these guys face to face and saying, okay, you know, you bring your pictures just like they bring pictures of their kids. Well, you bring pictures of your kids, only your kid happens to have [the disease] …. Now you have taken these lump of cells that you have been sending them in little dry ice packages, and you have put a face to this.

Some of the scientists I spoke with explained how their senses of sympathy and solidarity were enhanced through engagement with affected patients at PAO-sponsored conferences, but these sentiments developed 'naturally' rather than in response to an explicit strategy. Sympathy, it seems, is something that can help cement relationships, but it must be used subtly and sparingly and cannot be a principal way to influence research.

The nine PAOs' record on campaigns to pressure politicians, government agencies, or business is more ambiguous. None reported currently active campaigns. Some of the smaller organizations viewed 'lobbying' as a professionalized task beyond their capacities, but more importantly incompatible with their aims. The website of FIRST (www.scalyskin.org), offers instructions for members to lobby members of Congress, but

these are little more than talking points. TSA, PXE International, and AGRE's parent organization Autism Speaks, have historically engaged in vigorous lobbying of Congress and the NIH (Heath et al., 2004; Silverman, 2008). The limited degree to which it was discussed in my interviews could reflect PAOs' efforts to insulate their research from their 'political' activities. Another interesting possibility is the emergence of a broader shift in strategy among rare disease PAOs: having achieved strong recognition in Congress and at the NIH (for example, passage of the Orphan Drug Act in 1983, the founding of the Office of Rare Diseases in 1993 and its establishment by statute in 2002), many see ongoing political action by particular disease groups as counterproductive.[10]

Indeed, the PAOs I spoke with seem to go to great lengths to avoid conflict with scientists and to avoid appearing to exercise power or claim authority. This is remarkable, considering the desperation that many families must feel and the limited hope they are offered. But, such conflict avoidance makes sense in a situation where PAOs dearly value their relationships with scientists and are wary of jeopardizing them. It also is consistent with the section below, where I show how PAOs drive research by cultivating sociability.

Timing

In his work on the German Retinitis Pigmentosa Society, von Gizycki (1987) describes two ideal types of patient–scientist cooperation: the 'patient-dominated type' 'characterized by integration of research interests into the patient organization' and the 'researcher-dominated type' 'characterized by the integration of patient interests into the research organization' (Von Gizycki, 1987: 85). He claimed that the patient group will have more 'influence on the content of research' in cooperative relationships that they dominate.

Von Gizycki suggested that the patients' chances of dominating the cooperative relationship, and therefore their capacity to influence scientists, is a matter of timing: 'it is easier for a patient organization to formulate and achieve its research environment, even if its resources are small, than vis-à-vis a well-established, state-supported scientific community' (1987: 87). Following this claim, we would expect that PAOs that move first, seeking to mobilize research before scientists have generated a strong network devoted to the disease, will have greater influence over the scientists and their research. Of course, patient organizations need not (and rarely do) lead *all* research into the disease – some research must have occurred for the disease to even be recognized by medicine.

The evidence for the timing thesis is mixed among the cases I studied. The explanation works well for at least two of the PAOs – one of which, PXE International, was an early mover, and another, CFRI, which followed scientists. PXE International was founded by Sharon and Patrick Terry after their two children were diagnosed with PXE. Sharon Terry explained to me:

> We realized very quickly, within a month, there was nothing going on that was of any value to figuring out how to slow down the disease or mitigate its effects. We, in the course of our reading, realized that the medical arena was a morass. And we were shocked by that because, I think, average people expect that science is done in a systematic way with some intelligent plan. We found that that was not true.

As Sharon Terry described when interviewed by Taussig (2005: 239), she and Patrick had been able to find 400 articles that referenced PXE, but they were told by a researcher that, 'Nobody cares [about PXE] …. You have only me.' Further, two groups of researchers that did approach her family both wanted separate blood donations, and as Terry told me, they claimed it was not ordinary practice for scientists to share samples. Under these conditions PXE International sought to organize the field of research by curtailing what they viewed as counterproductive competition among scientists. They built a patient registry and tissue bank that scientists would find valuable, engaging them in close relationships (including working with some in the lab), and coordinating scientists' interactions with each other. The PXE field may not have been as chaotic as Terry describes – after all, an image of chaos helps legitimize PAO interventions into the research world (a project which Terry is very interested in promoting (see Terry et al., 2007)). But following the von Gizycki thesis, neither scientists nor patients were so organized that they were inclined to see PXE International's interventions as disrupting already established networks or patterns of practice. This relative disarray thus set the conditions for the group to organize the field to their advantage.

CFRI faced the opposite situation. When it started up in 1975 with the aim of stimulating cystic fibrosis research among West Coast scientists, cystic fibrosis research was already highly organized and the CF Foundation was the dominant patient group (Stockdale, 1999). CFRI encountered a well-organized research field, and it lacks strong influence over scientists. The research activities it supports with grants mainly involve post-docs, as it follows a formal model similar to bureaucratic government funding agencies. CFRI requests proposals which it commissions scientists to review and rank. CFRI has sought accountability among grantees through reporting procedures and scheduled meetings, but neither PAO leaders nor scientists view these as directing research. Thus, facing an already well-organized field, CFRI has assumed a traditional patron role and has not assumed the kind of close partnership characteristic of PXE International's efforts.

Other cases I am studying present a more ambiguous picture. Most PAOs and scientists report that PAOs face relatively disorganized fields from the outset.[11] Two such groups were FIRST and PRISMS. Both groups began as partnerships between patients, doctors, and scientists, with close and mutually committed relationships. But, as the PAOs sought to supplement patient support activities with serious research engagements, they did not seriously challenge researchers' prerogatives or strongly assert research goals of their own. In these cases, the timing advantage became moot because their initially close relationships with researchers worked against their inclinations to assert independence.

Another example is the TSA, which, as I noted earlier, has widely supported research on Tourette syndrome. TSA has largely followed a traditional model of autonomous science that views basic research as preceding applied or treatment-oriented research. While TSA funds clinical research, unlike PXE International, it has not pushed hard for treatment-oriented research or otherwise sought to dominate relationships with researchers. Further, as Stockdale (1999) argues, scientists dominate the CF Foundation's research agenda even though it was a leader in the field and has immense resources. Scientists, he claims, have pushed it to fund risky gene-therapy research to 'cure' CF rather than research targeting current sufferers' symptoms.

Finally, PC Project is another organization that has focused on generating treatments, perhaps even more so than PXE International, but the conditions when it began were the opposite of TSA's and PXE International's. Pachyonichia congenita (PC) is one of a large class of genetically caused skin-scaling disorders. PC is a variant of ichthyosis, which is represented by PAO FIRST. FIRST was founded in 1981, so that when PC Project was founded in 2004 it encountered a well-organized field. However, whereas scientists dominate the relationship with FIRST, the reverse is true with PC Project. As one researcher involved with both organizations said, 'I think that they [PC Project] are doing a really good job. I'm being dragged along by the tidal wave in this one. And that's what is so interesting, because FIRST – the physicians were leading it. Now, the physicians are kind of going along with it [PC Project].' PC Project has been able to exercise control over the research community, despite the prior organization of the field.

Von Gizycki suggested that the first mover gets to define the situation to their advantage. But what seems to be more important is having a confident, yet realistic, conception of such advantage. PAOs may confront a disorganized scientific field, but lacking self-confidence and clear goals it may end up simply imposing a traditional model of PAO/scientist interactions that does not offer them much power. Likewise, a PAO with confidence and clear goals need not be daunted by a preexisting situation that it can avoid or reorganize.

Lay expertise

Scientists' authority and autonomy is largely based on two interrelated aspects of their 'expertise' (Collins and Evans, 2007): first, their superior knowledge which they use to limit non-scientists' capacities to oversee or otherwise influence them, and, second, the legitimacy that expertise grants them (partly through credentials and reputation). Marginalized groups that are committed to contentious politics and unwilling to accept scientific authority at face value may attempt to acquire 'lay expertise' to gain power in their relationships with scientists. Steven Epstein's (1996) classic work shows that AIDS activists were able to have substantial impact on scientists by acquiring sufficient knowledge to interact with scientists and participate in technical decisions.

This line of research suggests that some form of lay expertise, though not necessary to attract scientists, is critical for PAOs' to influence research. Rabeharisoa and Callon (2002) claim that lay expertise by itself is insufficient because it still leaves non-scientists in an 'auxiliary' position of choosing among scientists and delegating decisions to them. They suggest that to forge 'partnerships' with scientists in which patient groups have true decision-making power, patients need their own 'experiential expertise', independent of scientists' expertise but useful for research. As Rabeharisoa and Callon show, lay members of AFM confronted scientific indifference to muscular dystrophy by observing, measuring, and recording MD patients and then codifying this knowledge to make it a valuable resource for professional scientists.

The overall picture from these studies is that PAOs that acquire and mobilize lay expertise – technical knowledge independent of scientists' expertise – will have more influence on research. The further expectation is that PAOs that acquire some form of autonomous, perhaps 'experiential', expertise will be in an even stronger position of

influence. Consistent with this picture, all the PAOs in my sample attempted to acquire some degree of lay expertise: both knowledge of the relevant fields (genetics, physiology, and so on) and of how science works institutionally and culturally. This is not surprising, as it is hard to imagine how a PAO could seek to support research without making some attempt to acquire (or at least 'hire') expertise. They acquired such knowledge both through painstaking searches of the scientific literature and by interacting with scientists (though the most savvy do so critically). And many decided to pursue research upon learning that research on their disease was limited. An interesting question is whether PAOs that aim to support patients but not to influence research also acquire expertise.

I found mixed evidence, however, that more (or more autonomous) lay expertise, leads to greater influence with scientists. PXE International and AGRE (and its former parent organization Cure Autism Now) best fit this pattern. The founders of PXE International went so far as to work as lab technicians during a critical period in the hunt for the gene mutation causing PXE. PAO leader Sharon Terry was even listed as a coauthor on the paper reporting the discovery (Bergen et al., 2000). This experience, which I discuss later, gave the PAO the knowledge and authority at a critical juncture to nudge the research in a direction that Terry considered more patient-focused. Portia Iversen, one of the parent founders of Cure Autism Now and AGRE, reports a similar dynamic in her memoir about her quest to understand her son's autism (Iversen, 2006). In her effort to master the science of autism, she acquired such expertise that many autism researchers were willing to take seriously her challenges to their ideas, and they even tried to test some of her hypotheses (resulting in her inclusion as an author on at least six publications[12]). Some researchers offered qualified support for an autism treatment regimen she helped develop.

Other PAOs I studied acquired lay expertise – even expertise that scientists lack but find useful (as in Callon and Rabeharisoa's AFM example) – but without having much influence with scientists. In the case of PRISMS, both advocates and scientists told me that parents are an important source of knowledge about the disease. A leader of the program explained:

> And it was the parents reporting to these two researchers, who started the question. 'Now, wait a minute. We've got these kids who are all doing the same thing. There's got to be a connection. Well, we need to keep digging further.' So, they kept listening to parents describe what a parent might think is a very subtle characteristic, but was huge in the scope of things. The way that these children looked, so, that was the other thing, was to – pictures of all of the kids and putting them all together and seeing that they all did tend to resemble each other …. So that a researcher, from my point of view, can't sit in a lab and look at a test tube and figure out how to help this child. They really have to understand all of the aspects that go into it and that comes from the parents reporting.

This knowledge has helped PRISMS forge close relationships with scientists and convince them to take seriously patient and family experience. But it does not seem to have led PRISMS to view themselves as having the capability to steer the research agenda. These examples suggest that a degree of lay expertise is necessary for PAOs to engage

scientists fruitfully, but they do not support the idea that more expertise, even expertise that is independent from but potentially useful to scientists, is a reliable way for PAOs to form partnerships in which they can exert influence over research.

Organizational controls

Callon and Rabeharisoa's work on the AFM suggests that large, well-organized groups can use their formal bureaucratic structures to maintain decision-making control.[13] Accordingly, we might expect that PAOs with robust organizations are more likely to have formal tools that give them control in their relationships with scientists, such as independent boards with decision-making power, or contracts, benchmarks, and other instruments of accountability.

All the PAOs in my study are incorporated as non-profit organizations (with officers, a board, financial reporting, and so on). My preliminary investigation suggests, however, that there are two main models for using formal organizational rules and procedures. AGRE, TSA, and CFRI are committed to bureaucratic professionalism, where professional staff adhere to formal rules that they view as important for the smooth operation of their research programs. For example, one interviewee suggested that rules are important for governing the participation of science advisors in granting programs to check against potential conflicts of interest. The other model, exemplified by PC Project and PXE International, is more entrepreneurial: the organization works as an instrument of a creative and committed director, but organizational structure and formal rules are not considered important ends or means. The degree to which other PAOs gravitate toward one or the other model remains to be determined (often because they are too young or small for this to be clear).[14]

Among my cases, formal rules to govern research activities are implemented to delegate authority to scientific advisors, rather than to create oversight procedures to influence researchers. PAOs that seek to cultivate research mainly through grants emulate procedures used by other grant-making institutions: they solicit applications, and use scientific advisors and peer reviewers to review and evaluate the proposals. The scientists I interviewed suggested that they try to keep the PAOs' priorities in mind, while ensuring quality. In one PAO, the lay board of directors has formal control over approving research, but interviewees told me that the board never overrides science advisors' recommendations, though they expect them to explain how proposed grants fit the organization's priorities. Two other PAOs also cede proposal evaluations to scientific advisors, and lay members' discretion is limited to selecting among recipients when they have more high quality proposals than they can fund.

In contrast, PC Project does not rely on formal processes to make funding decisions. Describing their funding decisions, a scientist told me: '[The director] pretty much decides. And, I think she's been very generous. She has, I think, funded every legitimate person who had something to add to her organization.' PC Project uses an informal network of affiliated scientists rather than a formal peer review process. Evidently, PC Project views the discretion and relationship-building that personal, informal processes allow as more important than the advantages of formal rules (for example, legitimization, quality control, and preventing conflicts of interest).

PAOs sometimes do attempt to implement rules to make scientists accountable, but these measures usually fail. For example, one scientist explained this by contrasting PC Project with FIRST:

> PC [Project] would like to run their research program as a business, with accountability. It doesn't work out that way because science moves at a very funny pace. It goes at fits and starts. [The director] started out having quarterly conference calls with all of us. She couldn't understand why we couldn't meet our deadlines. So finally she realized that – actually, these quarterly conference calls were counter-productive, that, overall the things that she wanted were happening. But, they weren't happening on the schedule that her accountability instincts wanted to happen. So, she backed off. And it didn't take very much complaining on our part to make her realize that she was asking a little bit too much. On the other hand, FIRST has very little in the way of accountability. And this is sort of what the NIH does, too …. The problem is, who would be the one to determine accountability? You can't ask a volunteer research committee to sort of be watching over everybody's grant …. I think you can't ask somebody to volunteer that much time. So, it doesn't get done.

As this example suggests, scientists are able to resist PAOs' accountability efforts, regardless of whether they involve formal reporting procedures or project management practices used in the business world. Part of the problem is the imbalance of expertise that requires the PAO to rely on scientists to monitor one another. Another part is that scientists tend to view oversight as incompatible with research culture. The larger issue is not that accountability procedures are impossible (after all, NIH audits projects and corporate research is subject to managerial oversight) but that they tend to strain relationships with scientists; relationships that are key resources for PAOs. For PAOs, organizational capability requires connections with scientists, but formal organizational controls tend to produce less rather than more influence on scientists.

Generating sociability to drive research

Thus far I have called into question the factors that other studies suggest are crucial for PAOs to effectively direct research to their concerns: economic incentives, exerting pressure through mobilization, moving early, contesting scientists' monopoly on expert knowledge, and organizational rules to control scientists. In this section I describe a different way that PAOs can drive research: fostering sociable relationships with and among scientists. 'Sociability', I argue, is more than another factor alongside those already considered; it captures aspects of them, but it is a more of a medium through which they work to positively influence research.

'Sociability' refers to social relationships with a particular set of characteristics: coordination, usually achieved through cooperation, trust, and commitment. Sociability is facilitated by stable, long-term relationships characteristic of a community. But this 'community' need not be self-conscious about its existence. Indeed, it probably is uncommon for scientists and patients to think of themselves as a community, in the sense of being members of the same social unit, and yet they frequently interact in stable, mutually committed, cooperative, and trusting ways.

Simmel (1949 [1910]), and later Goffman (1974), used the term 'sociability' to refer to modes of social interaction that are irreducible to instrumental or value rational relations. They often associated it with pleasurable, playful dimensions of interaction (gossiping, flirting, just hanging out), in contrast to formal organization or 'society' in the structural or totalizing sense. This kind of direct interaction is one aspect of the sociability I discuss here – members of many PAOs build personal, friendly relationships with scientists, to talk 'like a couple of Joes', beyond any interest in 'how they can help' through research. But sociability can also refer to more formal arrangements (such as biobanks and conferences) or patterns of interaction (such as the 'switchboarding' described below) that also create conditions for trust, interaction, diffusion of ideas and materials, coordinated action, and, importantly, opportunities for PAOs to develop and assert their interests. Actor network theory (Latour, 1987) frames such matters in an instrumental language of network extension and obligatory passage points, but sociability suggests that patterns of interaction, affiliation, and commitment affect the course of innovation as well. PAOs may steer research by establishing themselves as obligatory passage points for researchers (for example, by establishing a biobank), but their capacity to shape that research as it passes through their 'doors' can depend on the relationships they establish.

Previous studies of PAOs' effects on research have touched in passing on sociability (for examples, see Epstein, 1996; Taussig et al., 2003: especially 63–64; Wexler, 1995: especially ch. 13). However, they tend to leave sociability implicit in their discussions of other issues. Generating sociability is important for PAOs to counteract the depersonalization associated with scientific competition and ideals of pure science and ethical neutrality, and to encourage commitments to the afflicted. PAOs often encounter poor sociability, and anomie more generally, when they first confront the scientific world. As Sharon Terry of PXE International described the situation:

> Competition [among scientists]. Ineffective methods of data sharing. Lack of resources, but mostly because people wouldn't share. Lack of infrastructure. Lack of coordination. Lack of anybody standing outside a one-lab or two-lab kind of arrangement and saying to themselves 'If instead of doing research, you wanted to solve the problem of finding a treatment for PXE' – which is a very different problem than most researchers are engaged in – 'then what we could do [is this].' So, the unique part was that nobody had stood apart from the research and said 'What if you are going to try to solve this disease?'

PAOs can hope to intervene in this situation by coordinating scientists and committing them to seeing research problems as simultaneously intellectual challenges and lived conditions.

Techniques for cultivating sociability

PAOs generate sociability with networks of researchers in many different ways. Holding small workshop-style conferences is one of the most common. These conferences' connect potential researchers and get them to concentrate on questions the PAO cares about. NIH even has a program to support PAO grants for such conferences. One scientist

explained how attending PAO conferences improves research beyond enabling connections with patients and scientists:

> [Without PAO conferences] we certainly wouldn't be as informed about what is really affecting these individuals' lives and we wouldn't be as aware of the phenotype, I think. Because we would otherwise only see these children in a clinic. And being able to see them at a support group meeting where you have the kids kind of in a comfortable situation, it's really nice to see them. And it's very educational, from a geneticist's perspective too. I personally think that if I didn't have [PAO name] that it would have been very difficult for me to have done the research that I've done. Because I've been very much dependent on samples from these families and for their support and their information.

It may not be surprising that the experience of interacting with patients in a non-clinical setting can be a powerful means for de-objectifying patients' problems and committing researchers to their cause, but, as the scientist explains, such contact can enrich the research as well.

In addition, at these conferences PAO members can subtly and informally advance their interests in research. As one explained:

> And we do what we call, you know, 'elbow to elbow,' and we go out and, you know, we have very formal dinners at very nice restaurants, and … see you take them out of the lab and you sit them down at a table with a meal and you're talking and it's like so you say, 'So, Jeff, listen, all right, what's the deal with this random spontaneous mutation? Why can't they figure out what it is?' You know, you don't have to sit and be formal and, you know, write a big long email or a big long paper to get their attention or, you know, to get them to, um, converse with you. You just sit and it's what I call 'elbow to elbowing.' You're just sitting there talking like just a couple of Joes.

This kind of setting helps PAOs overcome some of the barriers to communication with scientists. Although disadvantaged in the formal realm of scientific communication, PAO can 'talk science' and nudge scientists in a direction they prefer.

Grant-making is an important way to foster sociability, but this is less likely to occur if PAOs conceive grants on the traditional project-focused, RFP (request for proposals) model. Through funded projects, scientists not only engage with a particular problem, but they also build research networks by investing emotional energy, enrolling collaborators and assistants, and publicizing the work. But research grants are expensive and PAOs usually cannot fund full programs and renewals. Treating their money as 'seed' grants is double-edged, because fuller funding by NIH and similar agencies sustains the project but dilutes the PAOs' financial influence. In addition, project grants on their own are a 'thin' way to build sociability and networks, especially if it is only possible to fund one or two projects. If the larger grant application fails, progress can be stymied if there are no alternative means to keep a project alive. For these reasons it is problematic for PAOs to drive research by thinking of themselves as traditional grant makers – their own actions can exacerbate the problem of raising research money, by forcing the PAO to over-commit to a fundraising role. A PAO leader explained this by recalling the

realization that it is more effective to conceive of grants primarily as a means of building relationships:

> I thought you funded a researcher, you gave them x-dollars per year and they went and found it. [Scientist] was the one that taught me that will never work …. That $50,000 is not going to what you think it's going for. It's going to fund what their next grant application is. If you don't have their hearts. If they're not part with you – the people that were funded by our grants are still working on the things they're working on three years later, four years later. You don't fund and get scientific results. That's not how it happens.

Instead of encouraging scientists to run the gauntlet of grant writing, reviews, revisions, and so on, this PAO leader suggests that by modestly funding almost every plausible proposal, the PAO can bring its agenda present to researchers' attention:

> So, a lot of what's going on is going on without direct funding from us, it's going on with funding. But people have [our disease] in the back of their minds. That's my goal. Is that everybody who's working in [other diseases] has [ours] in the back of their minds …. So, they're doing their experiments [on other topics] and they're thinking [the PAO head] might want to know about this. … So, piggy-backing and getting people so that your disorder is piggy-backed on ones that are funded.

In contrast to acting as just another funder (and a minor one at that), this PAO conceives of grants as *gifts*, which foregrounds their sociability-building function. The PAO also presents scientists with other personal gifts (novelties, handicrafts, and so on), which symbolize the personal relationships it is forming. As Mauss (1990 [1924]) and others have long claimed, gifts create relationships with bonds of commitment that extend beyond the exchange itself, unlike a fee-for-service model, in which the commitment ends with the transaction.

Compared with the limitations of trying to build relationships through funding, PAOs are in a strong position to create research infrastructure, such as patient registries and tissue and data banks, which can become central nodes around which to assemble enduring research networks. PAOs can effectively build and maintain these relationships because of their intrinsic interests and bonds with patients. In contrast, for scientists such infrastructures make up an immediate resource: they are inclined to structure them for their own needs and to monopolize them; and they have less interest in maintaining them beyond their immediate use. The scientists with whom I spoke also suggested that individual labs can be very disorganized in their handling of materials, especially over the long term, whereas PAOs can structure their data and materials for broader research purposes and outsource them to specialized organizations.

Eight of the nine PAOs in the sample have developed such resources, and at least five of them treat them as important research tools. Perhaps the most impressive example is the Autism Genetics Resource Exchange (AGRE) of the PAO, Autism Speaks (formerly Cure Autism Now). According to interviewees associated with AGRE, autism genetics research was hindered by the small sets of samples individual labs were able to assemble.

Competition and uneven diagnostic and data quality standards inhibited cooperation among these groups. According to one of its organizers, AGRE was established in 1997, and since then has been amassing standardized clinical data, statistical genetic data, and cell lines for genetic lab analyses. Currently it has samples from about 1900 families, comprising some of the most valuable data in autism genetics (Midgette et al., 2009). All qualified researchers can use this resource as long as they acknowledge AGRE and redeposit their data (for example genotyping) into the repository for others to use. Scientists thus cannot use these data in a proprietary way, and proprietary datasets will have diminishing value as this freely available source grows. AGRE seeks to encourage 'productive' intellectual competition by decreasing inefficient resource competition, and to draw in more researchers by lowering barriers to entering the autism genetics field. The threat of being scooped (which is decreased when research groups can monopolize data sets) can spur researchers to work faster. To date, more than 130 articles have used AGRE's data (Midgette et al., 2009).

Although there are other successful examples like AGRE, PAO-established resources do not automatically facilitate research. One scientist I spoke with prefers not to recruit patients using a particular PAO's registry, because the group has put consent requirements on it that the scientist considers onerous and overly restrictive. Another scientist told me of a patient and tissue registry a PAO helped build that hardly has been touched by researchers. Still another PAO built a remarkable registry with 2700 patients, each of whom completed a 13-page medical questionnaire and consented to donate tissue samples whenever they had operations for their condition. While the PAO rightly considers this to be a definitive resource, no more than three researchers have been seriously interested in using it. What makes such a resource attractive is not always clear: the first registry did not accommodate the needs of researchers; the second was insufficiently promoted; but the third registry never gained much traction despite major efforts by the PAO. These are issues for future investigation.

PAOs can also influence research by coordinating scientists' activities. These efforts can be very active. For example, one PAO inserted itself in the daily conduct of a network of researchers, in a way the director likened to a telephone 'switchboard operator' from years ago:

> So, [Scientist #1] has an idea and he's got something working and he needs reagents and so he calls me and so I conference him to [Scientist #2] … [who] has them on his shelf and he's shipping them out to him today. And that happened about, it was probably midnight.... So, we put it together, it's done. Anybody can call me at any time and I'll get in touch with whoever else. [Scientist #2] needed mice. I called [Scientist #3] who doesn't collaborate with anybody, and he shared his mice with us. Because I've adopted him and I've told him he's mine. So, that is much more interactive on a very frequent basis.

This PAO facilitates research by easing and speeding exchanges among scientists. Rather than setting itself up as a 'center of calculation' it performs a service that is humble and hardly visible, yet no less essential, to the functioning of the network.

In still another example, TSA helped organize Tourette genetics researchers into a consortium, which in this case is a closed set of 11 different research groups that had

agreed to collaborate and pool resources. TSA coordinated these efforts in at least four ways: first, by hosting conferences and other events to bring scientists together; second, by performing 'switchboard' efforts to connect scientists, though at a much less intense level than in the previous example; third, by helping produce a Memorandum of Understanding (MOU) for the group that sets the terms of data use, authorship credit, intellectual property, and so on; and, finally, by assuming formal ownership of the tissues and data that undergird the genetics research. The last two factors deserve further comment. In the previous section, I discussed organizational controls as one way in which PAOs try to influence research. This and other MOU examples suggest that formal agreements are less useful as tools of accountability than as means to broker trusting relationships. TSA's formal ownership of the consortium's data suggests another way to broker trust among scientists. Unlike AGRE, which built a resource and then invited researchers to use it, the TSA consortium came together when geneticists agreed to collect data that the PAO would 'hold', so that none of the groups would gain advantage over the others.

These examples return us to the notion of sociability. What enables these PAOs to coordinate scientists is that they can help set rules of interaction and generate relations of trust that scientists have difficulty establishing on their own. Indeed, scientists can be quite surprised at PAOs' capacities in this regard. As one explained:

> [The director] insisted that all of the people who were involved with this [PAO] would collaborate. This is pretty unusual. She said 'I'm going to help you guys out as best I can either financially or emotionally or whatever, but you have to agree, up front, that if you have anything, it's available to anybody else who's in this project.' So, that's been quite remarkable. And that's true [that sharing occurs] …. In other areas of science this could happen, but it rarely does happen, because she's made it so easy and it's otherwise generally difficult.[15]

Usually these PAO-driven rules of interaction are about cooperation and sharing, but not always. In the AGRE example, the PAO sought to leverage competition among scientists by making the resource open access and requiring them to redeposit data. AGRE researchers must work fast, because another group might pursue the same analysis. We normally think of cooperation as demanding intentional coordination of trust, but that competition is self-organizing. The AGRE model suggests this is not true. Without the rules they established, and the sociability that resulted, it is likely that secrecy and monopoly tactics would undermine effective competition among scientists.

Sociability and PAO effectiveness

I have argued that many PAO activities for promoting research generate sociability. But does fostering sociability enable PAOs to be more effective at driving research to their concerns? In the cases where PAOs assembled networks of researchers, the answer is fairly clear: there is now research where little or none would likely have existed. Fostering sociability does more than simply 'attract' researchers because, in some cases at least, it also involves establishing the material and normative conditions for their productive interaction.

Let us turn to the issue of PAO 'influence' on scientists. Some of the practices that PAOs use to attract and coordinate scientists can give them power over the products and even the direction of research, both of which are usually at the discretion of scientists. A key example is PXE International's patient, data, and tissue registry. As in other cases, this group was able to require scientists to cooperate with each other. When the gene mutation causing PXE was discovered, the PAO spearheaded the patent application and was able to get scientists to sign over their intellectual property rights.[16] More interestingly, the group also used its leverage to push lab work in a direction it preferred. When the PXE mutation was linked to a particular chromosome, researchers realized this was an unexplored part of the genome and they were eager to map the entire region rather than just isolate the particular mutation. The PAO was able to dissuade them from this approach, as Sharon Terry explains:

> Basically, because they were using our blood and tissue samples, and our clinical data, we said 'Sure. You definitely want to go off on all of those tangents and find those other genes, but we really need you to pay attention here.' And because we supplied this resource, and we were also supplying labor at that point, as well – reading gels and stuff – we directly asked them, 'Would you please focus on the ones that … could potentially be the right ones?' And they reluctantly agreed.

This degree of influence is remarkable (and rare), and it is worth noting that it depended on two things. First, the resources the group provided gave it clout, and second, its close involvement in the process enabled it to intervene at the appropriate moment. Terry agreed that group members' lay expertise enabled them to intervene at this juncture, but she also suggested that this expertise was not essential: 'But, I think if we didn't understand it, we would have found someone to understand it. Because it isn't that we didn't trust these guys along the way. We just knew that their interests were different and we needed to stay focused on our end goal.' This suggests that the fundamental conditions for their effective intervention were their close relationships and involvement with the scientists and an understanding (and respect for) competing interests.

There are other ways that sociability enables PAOs to influence research. Examples are the patient/scientist conferences discussed earlier, which increase contacts between two parties and thus give patients more chances to meet and work with scientists. The PAO director who works as a 'switchboard' is an even more direct example. This PAO's mediating role enables at least three sources of influence. First, the PAO gains up-to-the-minute information on research progress and problems. Second, unlike a telephone company switchboard operator, PAO representatives can 'join the conversation' and nudge scientists with suggestions. Third, it can also enable the PAO to better articulate how patient needs relate to evolving research possibilities; that is, what patients need and what science can deliver are not preset but are 'co-constructed'. The potential for influence is increased not only by more intensive contacts between the PAO and scientists, but also through the PAO's key position as a hub in the research network. Here sociability decreases social distance between the PAO and scientists, enabling it to slip beneath barriers of authority and expertise that ordinarily keep patients and other non-scientists at arm's length.

What can be said about the relative effectiveness of the two basic strategies for influencing research in my sample – the intensive model where sociability is a self-conscious project, and the RFP model where it is more of an afterthought? Moderate successes are possible on the RFP model, since PAOs get the research they pay for, more or less. The intensive model seems to have greater upside and downside potential. Some groups are able to exert disproportionate control over scientists' research agendas while others seem to have very little ability to mobilize scientists. Money is probably crucial to the question of effectiveness. This is obvious in the RFP model, but can be important in the intensive model as well. PC Project and PXE International, the two PAOs in my sample that foster sociability most effectively, lack the resources to pay for research outright, but they have enough to fund a robust range of activities, and make strategic grants or gifts at moments critical for the research. Intensive sociability can be considered as a multiplier for research investments, and having some money to invest is necessary to take advantage of that effect. However, productivity or efficiency is not the only issue, because the most effective PAOs use sociability to focus research on what might help patients, and not just the bulk accumulation of knowledge.

Discussion

This paper has shown how rare genetic disease PAOs drive research to their concerns by generating sociable relationships with and among scientists. I conclude by reflecting on some different manifestations of sociability and their effects.

First, though I have discussed sociability as a single concept, it is clear that it involves different orders of relationship and has diverse effects. For example, the groups PRISMS and Ring20 formed close relationships between members and scientists, but did not effectively transform relationships among scientists. AGRE, in contrast, forged close relationships with a set of scientists, but the impact of its open data resources (arguably) has been much greater for establishing cooperative and competitive relationships among scientists.[17]

Cooptation is another issue to consider. The CF Foundation has successfully raised and distributed hundreds of millions of dollars in grants in line with the RFP model, but as Stockdale (1999) argues, the scientists coopted its research agenda and directed it toward their own, rather than patients', interests. Stockdale and Terry (2002) suggest that relationships (related to what I call sociability) are a bulwark against such cooptation, but this might not always be the case. AGRE, for example, has effectively coordinated autism researchers and formed tight relationships with many, but now is pressured by scientists who take its growth and openness for granted to keep expanding its costly biobank and data repository (Midgette et al., 2009). Even without these financial obligations, PAOs that fail to set independent goals or become too close to scientists may lack the ability to push scientists, and their efforts may devolve into genial ineffectiveness, if not actual cooptation. For all these reasons, pursuing a sociability strategy is no panacea for PAOs.

Future research could investigate dimensions and consequences of sociability only hinted at here. My findings suggest that robust sociability can facilitate research and better align it with patients' interests. It would be fruitful to test these ideas with a larger sample of PAOs and less subjective measures of research outcomes. Do PAOs cultivating

different forms of sociability spur more research or generate more clinical interventions net of other differences? How do sociable relationships with PAOs affect scientists' careers, and are there costs? Do different strategies for pursuing sociability constrain PAOs' capacities to pursue their support or advocacy functions, especially radical action? And why do PAOs adopt the RFP or the intensive strategy for pursuing research? None of the factors I considered seem sufficient to explain this; rather, something like the entrepreneurial creativity of the PAO leadership seems important. The topics of leadership and creative agency would be new directions for the literature.

Several implications of this study can be spelled out. As I showed above, the factors suggested by the literature – resources, mobilization, timing, expertise, and organization – are insufficient for understanding how PAOs influence research if they do not take account of sociability. Still, while sociability is analytically distinct, it is clear that it works in concert with other factors, and that outcomes, whether they involve configurations of relationships or PAO influence on scientists, are the product of complex interactions. For this reason, further research on these and related mechanisms should situate them within relations of sociability. Such relations are not limited to PAOs. Consider, for example, the exercise of lay expertise generally. Collins and Evans (2002) have argued that differences in the success of AIDS activists (Epstein, 1996) and Cumbrian shepherds (Wynne, 1996) reflect differences in the extent of interactional expertise they wielded. But my research suggests that expertise and cognitive barriers might be beside the point, and that relationships organized around trust and goodwill might eliminate or render trivial the need for a distinct expert capacity of translation. The configuration of social relationships is a crucial dimension of all knowledge production and consumption contexts.

This study could have policy implications as well. Rare disease PAOs may effectively overcome their marginalization by inserting themselves into research networks and respectfully 'interfering' with scientists, rather than respecting scientists' autonomy. Further, policy makers can promote research on rare diseases and even patient-oriented translational research by encouraging such relationships. This would entail tolerating, and even supporting, greater power and freedom of movement on the part of lay people than is customary in scientific institutions. There certainly are many questions to be answered about the conditions and effects of different forms of sociability, but aside from the benefits for PAOs, the prospects for scientists are that they can develop stronger research networks and better productivity through PAO-driven sociability. By ceding authority though robust lay participation, the legitimacy of science more broadly may also improve.

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Notes

1. The French Muscular Dystrophy Association.
2. See http://rarediseases.org/
3. I use the term 'drive' not in the sense of operating a car or powering a machine, but more like driving cattle. Rather than a mechanical relationship of control, this suggests the PAO

'drivers' use different means to pull and prod scientists, whom they lack the power to control, along an untraveled route to an unknown destination.

4. For example Novas (2006), Rabiharisoa and Callon (2002), Rose and Novas (2004), Rapp et al. (2002), Stockdale (1999), Terry et al. (2007), von Gizycki (1987), and Wexler (1995). A notable exception is Heath et al. (2004), who compares several PAOs and their activist strategies for promoting research.
5. See Pearson (2009) and Stockdale (1999) on cystic fibrosis and Wexler (1995) on Huntington's disease. Dor Yeshorim has drastically cut the rate of certain genetic illnesses in Orthodox Jewish communities, not with 'cures' but with genetic tests and arranged marriages (Wailoo and Pemberton, 2006). The value of the celebrated parent-developed treatment for adrenoleukodystrophy, Lorenzo's oil, has been controversial (Moser et al., 2007). This ambivalent legacy has led Novas (2006) to suggest that these organizations' main product is hope.
6. See Goozner (2004) on the costs of drug development and criticisms of the high estimates of those costs.
7. TSA views itself as a small player with limited means, compared with organizations such as the Cystic Fibrosis Foundation and the Muscular Dystrophy Association, whose annual budgets are in the hundreds of millions of US Dollars. However, it is far wealthier than the median rare disease PAO.
8. In the future, I hope to evaluate the incentives thesis more fully by assembling organizational and financial data about PAOs. It seems likely that severe poverty can be very limiting for an organization, but past a certain threshold financial resources matter much less.
9. One might predict that patient mobilization would be most effective in situations where patients attempt to resist research or medicalization (Conrad, 2007) or where they aim to intervene in a scientific controversy on behalf of one set of scientists against another (Epstein, 1996), but Callon and Rabeharisoa (2003) argue that mobilization around an identity actually is also effective when PAOs seek to form partnerships with scientists.
10. One PAO leader told me that many groups are upset at autism advocates for hogging attention and money. Sharon Terry (2010), head of PXE International and the Genetic Alliance, has called for an end to disease earmarks.
11. This suggests that a fuller evaluation of von Gizycki's (1987) thesis demands a clearer account of 'disorganization', a task I will not take up here.
12. See http://www.portiaiversen.com/index.php?page=biosketch
13. See Callon and Rabeharisoa (2003), Rabeharisoa and Callon (2002), and Rabeharisoa (2003).
14. Two or three PAOs might follow an implicit third model which is that organizational structures are largely pro forma.
15. In the TSA example, the sharing agreement is secured by an elaborate MOU, but in this example, the personal relationship between scientists and the PAO director seem to be effective.
16. Other PAO representatives I spoke with did not view pursuing intellectual property (IP) rights as a way to shape relationships with researchers, though they may have viewed ceding these tasks to researchers as a way to signal cooperation and non-interference. PC Project has applied for patents on treatments it is developing with researchers, perhaps with the aim of protecting them from third parties.
17. More than 200 researchers have accessed AGRE's data (Midgette et al., 2009), far more than the number with which the organization has close relationships. In addition, interviewees claim that AGRE's policies have influenced NIH data-sharing rules in the autism field and beyond.

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