

## Constructing Interdisciplinary Collaboration: The Oncofertility Consortium as an Emerging Knowledge Commons

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### INTRODUCTION

In 2002, under the leadership of then-Director Dr. Elias Zerhouni, the National Institutes of Health (NIH) launched the Roadmap for Medical Research Initiative (Roadmap) with the goal of “reconfigur[ing] the scientific workforce by encouraging novel forms of collaboration.”<sup>1</sup> The initiative was the result of several rounds of consultation with stakeholders, scientists, and health care providers, who were asked to identify major opportunities and gaps in biomedical research that no single institute at NIH could tackle alone.<sup>2</sup> One overarching theme emerged from these consultations: understanding the puzzle of complex diseases would require the expertise of nontraditional teams with divergent perspectives that cut across traditional disciplines.<sup>3</sup> Calling interdisciplinary science teams the “wave of the future,”<sup>4</sup> Zerhouni emphasized that assembling these nontraditional teams would require a paradigm shift in medical research.<sup>5</sup> The Roadmap initiative was launched to support this shift by identifying (and funding) potentially transformative research requiring collaboration and coordination across NIH institutes and across traditional scientific disciplines.<sup>6</sup>

Despite consensus among multiple stakeholders that interdisciplinarity is necessary to solve complex biological problems, conducting interdisciplinary team research

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<sup>1</sup> Elias A. Zerhouni, US Biomedical Research: Basic, Translational, and Clinical Sciences, 294 *JAMA* 1352, 55 (2005).

<sup>2</sup> See, e.g., Elias A. Zerhouni, The NIH Roadmap, 302 *Science* 63 (2003).

<sup>3</sup> See, e.g., Elias A. Zerhouni, The NIH Roadmap for Medical Research, presentation delivered on February 27, 2004, slide 13, [www.webconferences.com/nihroadmap/ppt/02%202-27%20RM%20webcast%20EZ%20final%20v.4.ppt](http://www.webconferences.com/nihroadmap/ppt/02%202-27%20RM%20webcast%20EZ%20final%20v.4.ppt)

<sup>4</sup> Elias A. Zerhouni, A New Vision for the National Institutes of Health, *J. Biomed. Biotechnol.* 159 (2003).

<sup>5</sup> *Ibid.* <sup>6</sup> See Zerhouni, note 2, at 63.

presents a number of important challenges related to coordination and information sharing across institutional and disciplinary boundaries – or what Frischmann, Madison, and Strandburg have called “boundary-spanning dilemmas.”<sup>7</sup> Scientists are embedded in scientific “communities of practice.”<sup>8</sup> Researchers who are part of the same community of practice usually share a common training trajectory and a set of assumptions and vocabulary to describe phenomena under study. They also interact with one another regularly, through scientific conferences, informal information exchanges, and collaborations. As a consequence, membership in a particular scientific community influences scientists’ methodological approach to problems, the types of problems that they consider important, and the background assumptions made when addressing these problems.<sup>9</sup> In contrast, interactions between research communities can be fraught with obstacles. Scientists unfamiliar with the techniques or the body of knowledge of another field may not be able to evaluate that field’s experimental designs and the quality of its results. Vested social interests in the set of skills and theoretical perspectives of their own community can lead to resistance to “outsider” approaches. In turn, this resistance can generate personal costs to crossing disciplinary boundaries, in addition to learning a new skill set, such as social isolation and loss of social standing.<sup>10</sup>

The Roadmap initiative represents an important opportunity to study the design of knowledge commons whose goals are to exchange information across disciplinary and institutional boundaries and to create new knowledge at their intersection. Fostering team science served as a guiding principle for all Roadmap grants.<sup>11</sup> But one subset of grants, the Interdisciplinary Research Consortia, was specifically designed to fund interdisciplinary research. This grant funded nine consortia for a period of seven years (2005–2012).<sup>12</sup> The consortia ranged in focus from the study of new ways to regenerate organ parts from stem cells (combining developmental biology, engineering, and computational approaches)<sup>13</sup> to research into fertility preservation techniques for young cancer patients through the Oncofertility Consortium (bringing together

<sup>7</sup> Brett M. Frischmann, Michael J. Madison, and Katherine J. Strandburg, *Governing Knowledge Commons*, in *Governing Knowledge Commons* 1 (Brett M. Frischmann, Michael J. Madison, and Katherine J. Strandburg eds., Oxford University Press 2014), at 37.

<sup>8</sup> Researchers have used different terms, such as “scientific social worlds” and “invisible colleges” to describe groups of scientists who share social networks. Importantly, these networks do not only track disciplinary lines. For example, communities can be formed around studying a particular disease, using a particular model organism, or focusing on understanding a particular organ. See Laura G. Pedraza-Fariña, *Patent Law and the Sociology of Innovation*, 2013 *Wis. L. Rev.* 839 (2013) (“communities of practice,” “scientific social worlds,” or “invisible colleges,” as they have alternatively been called, are defined by a core set of activities: accepted practices, techniques, legitimate research goals, training procedures, and relationships among a cluster of practitioners). See also Zerhouni, note 3, at slide 3.

<sup>9</sup> Pedraza-Fariña, note 8, at 838–40. <sup>10</sup> *Ibid.* at 843–47.

<sup>11</sup> NIH Roadmap Accelerates, *NIH News* (Mon. Oct. 4, 2004) (“Team science is an underlying current of the entire NIH Roadmap effort”).

<sup>12</sup> <https://commonfund.nih.gov/Interdisciplinary>.

<sup>13</sup> <https://commonfund.nih.gov/Interdisciplinary/consortia>; <https://commonfund.nih.gov/Interdisciplinary/consortia/syscode>

reproductive endocrinologists, oncologists, molecular biologists, biological engineers, and cryobiologists).<sup>14</sup>

Each one of these consortia can be analyzed as a knowledge commons, since they all seek to institutionalize the sharing of resources among members of a new, interdisciplinary community. The resources shared all involve knowledge (including novel experimental techniques at the intersection of multiple disciplines), but some consortia also share rivalrous resources such as patient samples. All consortia were designed to lower the costs of conducting interdisciplinary research by creating an NIH-supported framework for the sustained co-creation and exchange of information, research protocols, samples, reagents, and ideas with the goal of addressing a well-defined research question at the intersection of multiple disciplines. Importantly, the Roadmap grant was designed to serve as a catalyst to collaboration – providing short-term, seed funding to enable cross-disciplinary connections. Because funding for all consortia has already ended, it is possible to study whether the grant enabled new relationships among fields that continued absent NIH funding and infrastructural support.

This chapter will focus on a particular commons nested within the Oncofertility Consortium: the National Physicians Cooperative (NPC). The Oncofertility Consortium was founded to address the unmet need of cancer survivors (and in particular female survivors) for fertility preservation options at the time of diagnosis. As cancer treatments have become more sophisticated and effective, the number of cancer survivors – and in particular childhood cancer survivors – has increased worldwide.<sup>15</sup> But research on the impact of cancer therapeutics on male and female fertility, as well as research on fertility preservation techniques for females, has lagged behind. So has the availability of fertility services for newly diagnosed cancer patients: at the time of the grant, the infertility industry was structured to deal exclusively with planned in vitro fertilizations but not equipped to offer emergency procedures. And despite the rising numbers of patients living cancer free, treating oncologists seldom discussed the treatment's effect on fertility or options for fertility preservation with their patients.<sup>16</sup> This was the case despite studies showing that cancer patients rank fears of losing their fertility second only to those of facing death.<sup>17</sup> As a result, many cancer survivors were confronted with a second devastating diagnosis: that of infertility resulting from their cancer treatments. One fundamental reason for this disconnect

<sup>14</sup> <https://commonfund.nih.gov/Interdisciplinary/consortia>; <https://commonfund.nih.gov/Interdisciplinary/consortia/oncofer>

<sup>15</sup> L. A. G. Reis, M. P. Eisner, C. L. Kosary et al. (eds.), *SEER Cancer Statistics Review, 1973–1999* (Bethesda, MD: National Cancer Institute 2002).

<sup>16</sup> Oncofertility grant, at 134, on file with author.

<sup>17</sup> Carrie L. Nieman, Karen E. Kinahan, Susan E. Yount, Sarah K. Rosenbloom, Kathleen J. Yost, Elizabeth A. Hahn, Timothy Volpe, Kimberley J. Dilley, Laurie Zoloth and Teresa K. Woodruff, Fertility Preservation and Adolescent Cancer Patients: Lessons from Adult Survivors of Childhood Cancer and Their Parents, 138 *Cancer Treat Res.* 201 (2007).

between the needs of cancer patients and research and treatment priorities was the lack of communication and collaboration between oncologists and reproductive endocrinologists. The Oncofertility Consortium sought to remedy this “information, data, and option gaps”<sup>18</sup> and “serve as an authoritative voice for research, clinical practice and training that happens at the intersection of oncology, pediatrics, reproductive science and medicine, biomechanics, material science, mathematics, social science, bioethics, religion, policy research, reproductive health law, cognitive and learning science in a new discipline called ONCOFERTILITY.”<sup>19</sup>

The Oncofertility Roadmap grant contained a series of sub-grants structured around an administrative core to support the members of the consortium by providing governance and a communication and data-sharing plan.<sup>20</sup> The NPC, funded through a P30 core grant, was an integral part of the consortium’s roadmap for addressing the disconnect between reproductive endocrinologists’ and oncologists. The NPC had several missions: first, to serve as a repository for testicular and ovarian tissue for scientific research; second, to provide a referral network and serve as a connector between oncologists and reproductive endocrinologists; and third, to serve as a forum to exchange ideas, develop and disseminate new clinical research methods and technologies for ovarian research, as well as patient education and advocacy tools.<sup>21</sup> The NPC also aimed to serve as a reproductive medicine network that enabled researchers to conduct longitudinal studies on ovarian tissue.<sup>22</sup> Ovarian tissue for basic research would be obtained from cancer patients who would be asked to donate 20 percent of their tissue for research (80% would be cryopreserved for fertility preservation).<sup>23</sup>

To succeed, the NPC needed to recruit reproductive clinics (most of which did not traditionally serve cancer patients), convince them that providing emergency procedures for cancer patients was a worthwhile endeavor, and train them in cryopreservation procedures. But recruiting reproductive endocrinology clinics was only half of the puzzle: without referrals from treating oncologists, few patients would find their way to these clinics. Thus the NPC also sought to enlist

<sup>18</sup> The grant application describes the unmet needs of the cancer-survivor community in these terms. The “information gap” refers to the lack of information regarding cancer treatment’s effect on fertility and fertility preservation options to newly diagnosed cancer patients. The “data gap” refers to the “paucity of data on the precise gonadotoxicity of cancer drugs,” and the “option gap” refers to the lack of research into fertility preservation techniques for females, including prepubescent girls. Oncofertility grant, at 137–38, on file with author.

<sup>19</sup> Oncofertility grant, at 134, on file with author.

<sup>20</sup> In addition to the U54 administrative core grant, the consortium was comprised four R01 grants for basic research into female follicles, and for addressing emerging social issues in oncofertility, two P30 cores, one educational and three training modules.

<sup>21</sup> <http://oncofertility.northwestern.edu/NPC>.

<sup>22</sup> Oncofertility consortium conference, NPC Panel, comments by Teresa Woodruff, December 2007.

<sup>23</sup> National Physicians Cooperative of the Oncofertility Consortium Letter of Agreement (“NPC Letter of Agreement”), item 6. (“With the remainder of the tissue the patient can donate approximately 20% of the remaining ovarian cortex to the NPC for research use and the remainder will be frozen for the patient’s own use.”)

major research centers with oncology providers and to build a referral corridor between those providers and reproductive endocrinology centers.

The NPC has been successful in achieving several of its main objectives. In particular, it has created a robust referral network between oncologists and reproductive endocrinologists in several of the 50 US states where none had existed beforehand; it serves as a forum to synthesize current research into fertility preservation options and research, and to provide easy access to research tools (through detailed, annotated protocols and video demonstrations). Finally, it facilitates the exchange of ideas among oncologists and endocrinologists through a series of monthly expert group meetings, and an annual conference.

My case study suggests that the following factors were key to the NPC's success. First, echoing findings from studies on successful scientific social movements, the involvement of a "high-status intellectual actor,"<sup>24</sup> in this case Dr. Teresa Woodruff, with a high degree of trustworthiness in the eyes of consortia members, and with a network of preexisting relationships that formed the core of the consortium, was crucial to the program's success and continuity. Second, the NPC transitioned from a relatively "closed" format, in which protocols, findings, and access to expertise were available only to NPC members to an "open" format. A closed format appeared necessary to generate buy-in for the initial NPC consortium members. Once the consortium was firmly established, and with a higher degree of institutionalization (as evidenced by the creation of several expert working groups, and a cadre of new medical graduates who prioritized oncofertility), the consortium became more open – sharing most of its research findings, protocols, and expertise with any interested researcher or clinician.

The remainder of this chapter is organized as follows. Section 11.1 explains the methodology of this case study. Section 11.2 explains in more detail the background context in which the NPC is embedded and the coordination and discipline-bridging challenges the NPC, and the Oncofertility Consortium more broadly, sought to overcome. Section 11.3 describes the types of resources that the NPC is tasked with administering and creating. Section 11.4 explores the NPC's transition from a closed to an open community model. This section also discusses the history of the NPC, focusing on how its founding members described the existing barriers to collaboration in the area of fertility preservation for cancer patients that the NPC sought to address. Section 11.5 analyzes the NPC's governance structure. Section 11.6 analyzes the costs and benefits of the NPC both to its members and to the public at large. Section 11.7 concludes by synthesizing a set of hypotheses about successful commons management, and comparing them to conclusions drawn through other existing studies of scientific consortia.

<sup>24</sup> See Scott Frickel and Neil Gross, *A General Theory of Scientific/Intellectual Movements*, 70 *Am. Sociol. Rev.* 204, 211 (2005).

## 11.1 METHODOLOGY

My approach follows the modified version of the IAD framework described by Brett M. Frischmann, Michael J. Madison, and Katherine J. Strandburg.<sup>25</sup>

Specifically, I did the following:

- **Conducted a literature review.** I reviewed available public documentation about the Roadmap Grant and about the Oncofertility Consortium. In addition, I obtained access to the full Oncofertility Consortium application for a Roadmap grant, and additional grants that currently support the consortium's activities. I also obtained access to the NPC Letter of Agreement, which must be signed by those who wish to join the NPC.
- **Reviewed stored video footage of all oncofertility conferences and virtual grand rounds; attended 2016 Oncofertility Conference.** The Oncofertility Consortium website makes available video footage of all yearly oncofertility conferences since the consortium was launched in 2007. It also makes available virtual grand rounds – presentations by researchers working in the area of oncofertility. I also attended in person the 2016 Oncofertility Conference.
- **Conducted a series of semi-structured interviews.** I interviewed 12 professionals involved with the Oncofertility Consortium – whom I determined to be key informants: the named principal investigators (PIs) in all of the Oncofertility Consortium grants and all past and present administrators of the NPC. Interviews were tailored to each individual's role within the consortium and structured to seek answers to the key questions in the IAD framework.

## 11.2 THE NATIONAL PHYSICIAN'S COOPERATIVE BACKGROUND ENVIRONMENT

The National Physician's Cooperative emerged out of a concerted effort by a group of basic science researchers and clinicians to meet the reproductive needs of cancer survivors. The NPC's work is thus fundamentally shaped by the background social norms and practices of four distinct groups of professionals: (1) treating oncologists who first diagnose and treat cancer patients; (2) reproductive endocrinologists who, until the consortium's coordinated efforts, largely treated cancer survivors for infertility long after cancer treatment; and (3) scientists conducting basic science research on ovarian follicles. The NPC is also nested within the Oncofertility Consortium and thus constrained by the terms of the initial Roadmap consortium

<sup>25</sup> See Michael J. Madison, Brett M. Frischmann, and Katherine J. Strandburg, *Constructing Commons in the Cultural Environment*, 95 *Cornell L. Rev.* 657 (2010), and Frischmann, Madison, and Strandburg, *Governing Knowledge Commons*, in *Governing Knowledge Commons*.

grant. Finally, the ability of the NPC to meet its goals is also influenced by the interaction among the different NIH institutes that make up the Roadmap grant.

### 11.2.1 *Three Distinct Communities of Practice: Oncologists, Reproductive Endocrinologists, and Basic Research Scientists*

#### 11.2.1.1 Oncologists

Oncologists are the first group of practitioners who encounter cancer patients. Because they drive the referral pattern to reproductive endocrinology clinics, the oncology community is a key component of a successful oncofertility program. Despite advances in cancer treatment that dramatically increased the odds of surviving cancer, and in particular childhood cancer, oncologists seldom discussed fertility with their female cancer patients prior to the creation of the Oncofertility Consortium. The reasons for this are manifold, but three in particular represent a common thread across all interviewees. First, oncologists' *research priorities* into cell proliferation and cell death (the hallmarks of cancer) meant that there was scant research into the fertility effects of cancer chemotherapeutic agents for different populations – and thus little information to give patients as to the effect of chemotherapeutic drugs on their fertility.<sup>26</sup> There was also a widespread assumption in the oncology community that hormones that would be used to stimulate egg production for fertility preservation were counter-indicated for women with cancer. For example, a PI in the oncofertility grant described a key hurdle to getting oncologists interested in fertility preservation as follows: “Oncologists thought hormones cause cancer. So, there was this notion that hormones are bad. And, they're not. And they're not causing cancer. This was just this kind of zeitgeist.”<sup>27</sup>

Second, oncologists had developed particular practice styles and protocols that had become entrenched. Fertility preservation required a significant modification of these established practice routines. For example, a clinician member of the NPC remarked,

There are individuals who have styles of practice. The issue for oncologists is living or dying. From the outset you see patients for cancer, the team says so and so has this cancer, and it's very hard and you don't know how much they have to live . . . My colleagues in oncology, they are so busy and they are so much dealing with living and dying issues. How to treat the cancer, what kind of cancer is it. They are getting pulled in all different directions about taking the cancer out. Talking about fertility preservation is not in their agenda. They are not trained to do it. The questions that are going to come out they are not ready to answer.<sup>28</sup>

<sup>26</sup> “[M]edical oncologists are not aware of the precise reproductive threats of their treatments on reproductive outcomes and clinical reproductive endocrinologists do not routinely treat cancer patients.” Oncofertility grant, at 137, on file with author.

<sup>27</sup> Interview with Oncofertility Grant Principal Investigator, basic sciences track.

<sup>28</sup> Interview with Oncofertility Grant Principal Investigator, clinical track.

Finally, oncologists held particular ideas about their patients' priorities, which did not include a focus on fertility preservation. A PI with a background in endocrinology described her experience speaking with oncologists as follows: "they would tell me, we don't worry about [fertility], [the patients] should really think about that later and they are not married so they are not even thinking about that."<sup>29</sup> Another interviewee similarly remarked:

These physicians had in-bred biases about how to deliver care to these patients. And those biases ran again from "Don't bother her, she's got enough on her mind right now, my focus is on getting her well. Don't worry about the esoteric stuff, she can't afford this. Don't even bring it up," to my favorite "Adoption is always an option," which we knew from our research was not the case. But they had all these biases that came from old school kinds of treatment and the fact that they hadn't re-calibrated their thinking to the fact that these were diseases that killed people in the last generation so we didn't have to worry about them.<sup>30</sup>

#### 11.2.1.2 Reproductive Endocrinologists

While oncologists drive the referral pattern for cancer patients to receive fertility preservation, endocrinologists must also be equipped to provide fertility preservation to cancer patients for a successful oncofertility program to emerge. And prior to the creation of the Oncofertility Consortium, the practice styles of reproductive endocrinology programs were built around healthy, informed patients – not sick patients with limited knowledge of fertility treatments. This meant that reproductive endocrinology centers were not set up for performing emergency procedures. They were also, according to several interviewees, "used to patients who are the smartest medical consumers on the planet"<sup>31</sup> because "they've read everything that they can read about infertility for the most part, they've already maybe even gone through some procedure."<sup>32</sup> In contrast, oncology patients "think they're going to die. No matter how good the prognosis is. So, reproductive endocrinology is not used to having that kind of complexity."<sup>33</sup> As a consequence, prior to the formation of the Oncofertility Consortium, reproductive endocrinologists only came in contact with cancer patients long after the completion of their cancer treatment, when damage to their fertility was often already irreversible.

#### 11.2.1.3 Basic Research Scientists

The Oncofertility Consortium also sought to bring together several communities of basic scientists to work on developing techniques for maturing eggs *in vitro* (a

<sup>29</sup> Interview with Oncofertility Grant Principal Investigator, basic research track.

<sup>30</sup> Interview with Oncofertility Grant Administrator.

<sup>31</sup> Interview with Oncofertility Consortium Patient Coordinator. <sup>32</sup> *Ibid.* <sup>33</sup> *Ibid.*



technique that would allow fertility preservation for prepubescent girls). To do so, it brought together engineers, biologists working on primate models of ovarian development, reproductive scientists, and cryobiologists. Although these groups did not traditionally work together, the particular individuals who made up the initial oncofertility grant all had preexisting relationships with Woodruff, the PI who spearheaded the Oncofertility grant. In particular, a number of both clinicians and basic scientists were part of an NIH group that brought together scientists who studied the ovary. Despite knowing one another, and one another's work, these scientists had not previously collaborated to address the key research questions posed by the oncofertility grant application: how can we mature follicles *in vitro*? How can we best understand follicle dynamics? Interviewees uniformly attributed this previous lack of collaboration to the entrenched practice styles of basic science researchers that develop early in a doctoral student's career, and to an 'unspoken' penalty for this type of collaboration in basic research. For example, one PI remarked:

So, you use bench science, you write the paper, your students . . . do their work, they get their grant, their PhD, you get a grant and you repeat and it's a vicious cycle, but it's the cycle that we've all established to be the way we're going to increase our fount of knowledge but the problem is that doesn't allow you to escape that gravitational force and move into broader spheres . . . Now, there's kind of a penalty for collaboration; it takes a little more from everyone and it takes a lot more from one person. Whoever is leading the effort, there's more of a kinetic energy loss. So, you have to put more in and I think that's okay, because I think that's when you succeed, that's when the program can go ahead. So, if you don't put that loss in, if you don't put that extra kinetic energy in, everything can really then fall apart, because there is no center; there is no gravitational force. Everybody will go back to doing what they do.<sup>34</sup>

### 11.2.2 *The Roadmap Grant and the NIH Institutes*

The Roadmap grant sought to fund interdisciplinary team research projects that required a trans-NIH funding mechanism where multiple NIH institutes would work together. Indeed, according to several principal investigators involved in the Oncofertility Consortium, it was particularly hard to obtain individual investigator grants (or Rzero1 grants) for work at the intersection of reproductive endocrinology and engineering because it did not fit squarely into the work of any one NIH institute.<sup>35</sup> The Oncofertility Consortium sat at the intersection of the National Cancer Institute (NCI), which funds cancer research; the National Institute of Child Health and Development (NICHD), which funds fertility research; the

<sup>34</sup> Interview with Oncofertility Grant Principal Investigator, basic sciences track.

<sup>35</sup> For example, one PI explained: "[We] were doing these projects together that were really striving to make momentum and the first time we sent our grant in, the NICHD said: 'Well this is really good, but it's really cancer' . . . We fell through the cracks, our work just couldn't really go anywhere."

National Institute of General Medical Sciences (NIGMS), which funds basic approaches to cellular mechanisms; and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), which funds basic and applied biomaterials and tissue-engineering research. The Roadmap grant sought to combine the work of all of these institutes by creating an administrative core whose purpose was to “reduce barriers, encourage research, solve problems, maintain documents and provide a robust intellectual environment with shared vision and an altruistic approach to credit and results.”<sup>36</sup>

### 11.3 RESOURCES

The NPC creates, manages, uses, and shares a number of resources, ranging from tangible patient samples to an intangible referral network. These resources can be organized into three distinct categories: (1) patient samples; (2) research tools, reagents, and experimental protocols (including Institutional Review Board (IRB) approval protocols), and related know-how; and (3) referral network and brand name. While the three categories are related, each one has specific characteristics and presents particular types of social challenges that warrant individual analysis. The Oncofertility Consortium also receives monetary and infrastructure resources crucial for its sustainability from the NIH in the form of grants, and from multiple research institutions in the form of office space and administrative support.

#### 11.3.1 *Patient Samples*

One of the main goals of the NPC is to serve as a repository for the ovarian tissue of cancer patients. Patients who chose to have ovarian tissue cryopreserved had the option of donating 20 percent of their tissue for research purposes, and keeping 80 percent for their own fertility preservation.<sup>37</sup> The cryopreserved tissue could later be thawed and transplanted into the patient – a technique that at the time of the grant had resulted in live births but that carried the risk of reintroducing cancer cells into the patient.<sup>38</sup> The portion of the tissue reserved for research was meant to provide samples to support consortium research projects. In particular, the bulk of the research samples was used for studies on *in vitro* follicle maturation funded by the consortium Rzero1 grants, that is, how to take immature follicles present in ovarian tissue and transform them into mature eggs.<sup>39</sup> Mature eggs could then be used for *in vitro* fertilization. Unlike tissue transplantation, this technique did not run the risk of reintroducing cancer cells into the patient. Tissue samples were also used to optimize new cryopreservation techniques. NPC members could apply for access

<sup>36</sup> Oncofertility grant, at 159, on file with author. <sup>37</sup> NPC Letter of Agreement, note 23.

<sup>38</sup> Interview with Oncofertility Consortium Principal Investigator. <sup>39</sup> *Ibid.*

to research tissue by submitting their own research proposals for consideration by the steering committee.

Because any individual reproductive endocrinology clinic sees only a handful of cancer patients, developing a national repository for ovarian tissue and for patient information is a key step to gathering sufficient data to make important discoveries regarding the impact of chemotherapy and the success of fertility treatments on different patient subpopulations. Tissue samples are an inherently rivalrous resource; as a consequence, the largest challenges facing the NPC regarding these samples was how to collect sufficient tissue to carry out research, and how to prioritize distribution of the tissue among NPC members who wanted to carry out research studies. Recruiting fertility centers required that the centers be willing to apply for (and obtain) approval from their institution's IRB and set up a cryopreservation protocol at their institution. Because ovary tissue must be cryopreserved shortly after extraction, participating centers also needed to learn and apply standardized tissue cryopreservation techniques, using consortium-approved freezing media and protocols to ensure reproducibility.

The NPC was extremely successful in recruiting reproductive fertility centers to donate tissue to the repository, quickly exceeding its initial goals. The reason for its success lay in the lack of interest on the part of most reproductive fertility centers to carry out their own research projects (thus diminishing concerns about allocation of scarce tissue resources) coupled with the ability of the NPC to trade access to tissue for other resources of value to reproductive fertility centers. In particular, *access to know how and reputational benefits* were both crucial elements in obtaining buy-in from fertility centers. For the first three years of the consortium's existence, core members provided training in tissue cryopreservation, as well as access to cryopreservation media – critical know-how in the field – only to NPC members. One NPC administrator who personally delivered lectures and training modules to several NPC allied centers explained: “[Learning how to do] tissue freezing and the possibility of being part of research was a big one. We also had a commercial company manufacture all of the media and freezing solutions. And we provided that to them for a charge. So, they were getting the secret recipe that no one else was going to have. That set them apart.”<sup>40</sup> In addition, being an active participant in oncofertility research, as well as being associated with the consortium, provided a reputational boost to fertility clinics. As a NPC member explained: “Some of these people [at reproductive endocrinology clinics] had an interest in research but they couldn't do it because they were in practice. People were part of this Oncofertility Consortium that had this cache of being academic science and research.”<sup>41</sup> Similarly, a former NPC administrator noted:

A lot of IVF in this country is done in small IVF centers. Those people don't do enough clinical work to generate research [but] they would really love to be

<sup>40</sup> Interview with Oncofertility Consortium Administrator.

<sup>41</sup> Interview with Oncofertility Consortium Principal Investigator, clinical track.

involved in research. And so, we were able to go out and appeal to these people and say, look, if you'll take the ride with us and go through the IRB process . . . you'll be involved in the research side of things simply by having contributed.<sup>42</sup>

Finally, to capture the expertise and clinical data of those centers that were interested in following their own protocols for ovarian tissue cryopreservation and keeping their own tissue for research, the NPC developed the "clinical membership" tier. Clinical members had access to know-how developed by the Oncofertility Consortium and were also able to contribute their own experience to the common knowledge pool through participating in NPC monthly and annual meetings. An NPC administrator explained the rationale for the different membership tiers as follows:

Just in the last handful of months we've had a call where it's a center interested in joining the NPC, but saying "we already have an ovarian tissue protocol open, that's been open already for five years and it's been successful, can we still be a member?" So in that case that's fine because otherwise if we say, "Oh well, you have to switch to our protocol," then we're going to lose them as an NPC member and we're going to have no data that we're gathering from them. Whether it's a survey study or participating in meetings. So that was a way to have another membership tier so we're not shoving people away. . . [We tell them that the NPC] is always here as a resource, if this is something that you would like to switch over to someday, we can discuss it. You're in the fold already. In that case, there's not been too much pushback.<sup>43</sup>

### 11.3.2 *Research Tools, Reagents, Experimental Protocols, and Related Know-How*

The core members of the Oncofertility Consortium (i.e., the named principal investigators in the original interdisciplinary research grant) pioneered a series of experimental protocols to grow follicles in 3-D matrices,<sup>44</sup> to translate technology developed in vitro and in mice to primates,<sup>45</sup> and to freeze ovarian tissue.<sup>46</sup> Although several of these experimental protocols were published in peer-reviewed journals, many required in-person training to be carried out successfully. In addition, while protocols were continuously refined, those improvements were not always reflected in printed publications. For example, at the NPC launch in 2007, Woodruff explained the informational benefits of NPC membership:

<sup>42</sup> Interview with Oncofertility Consortium Administrator.

<sup>43</sup> Interview with Oncofertility Consortium Administrator.

<sup>44</sup> This technique resulted from a collaboration between Dr. Teresa Woodruff, a reproductive biologist and Dr. Lonnie Shea, a bioengineer. See, e.g., L. D. Shea, T. K. Woodruff and A. Shikanov, Bioengineering the Ovarian Follicle Microenvironment, 16 *Ann. Rev. Biomed. Eng.* 29 (2014).

<sup>45</sup> Oncofertility grant, at 151, on file with author. <sup>46</sup> *Ibid.*

The key is that there is a lot of real knowledge that is embedded that has not come out in vetting some of these tables [from published papers]. And as we go forward, as people are really looking at this in a new and different way, we are going to be able to substantively change those documents. We'd like to get not only those pdfs but we'd like to annotate those pdfs. Getting your paper and having you annotate that, and then saying, what we now need to know is X. Now you may have the opportunity to study 100 more patients.<sup>47</sup>

Through its website, the NPC created a library of up-to-date, annotated protocols and videos of key procedures.<sup>48</sup> These protocols were only available to NPC members during the first three years of the consortium. In addition, core members of the Oncofertility Consortium would often travel to new NPC sites to show them how to perform key procedures in person.<sup>49</sup> Finally, cryopreservation media was, until quite recently, available only to NPC members. Access to both know-how and key reagents was an important draw of the NPC – and one that, as described in the previous section, was often sufficient to incentivize centers to contribute research tissue to the Oncofertility Consortium. One NPC administrator summed up the importance of the informational resources aggregated and created by the NPC as follows: “You got access to all this information. You got support, so when you had your very first case, we would fly someone out to you, to show you how to dissect the tissue and how to freeze it appropriately. And we also pay for all of your media. So we send you all the media that you're going to need. It's totally free, you don't have to pay anything.”<sup>50</sup> Another NPC member and administrator similarly remarked: “The interesting thing about it was there was a lot of training that they got. It was a lot of intangibles, but there was very little money exchanged . . . Unlike a drug study where money is usually the motivator, this was more, well, I'm on the waiting edge of something cool.”<sup>51</sup>

A key social dilemma that would be expected to arise in a data-sharing commons, especially one that involves sharing of know-how that cannot be easily gleaned from publications, is that members of the NPC who were not actively generating data or important know-how would free-ride on this knowledge, potentially using it to make competing discoveries or disclosing it to active research competitors. This concern was somewhat mitigated by the fact that most NPC members were not themselves actively engaged in research, and that Oncofertility Consortium members were getting something in return – valuable research tissue for their exclusive use. Nevertheless, interviews reveal that researchers were certainly worried about the dangers of disclosure. In fact, although annotated protocols and know-how were

<sup>47</sup> Presentation at NPC Launch, Dr. Teresa Woodruff.

<sup>48</sup> See, e.g., video coaching on how to prepare ovarian tissue for transport, <http://oncofertility.northwestern.edu/media/prepare-human-ovary-for-fresh-transportation>

<sup>49</sup> Interview with Oncofertility Consortium Patient Coordinator.

<sup>50</sup> Interview with Oncofertility Consortium Administrator.

<sup>51</sup> Interview with Oncofertility Consortium Administrator.

certainly widely shared, ongoing and unpublished research findings were only discussed among a small core group of oncofertility researchers – namely the principal investigators named in the initial grant (and members of their laboratories) who held monthly virtual meetings. As will be explored later, these researchers were part of a preexisting social network and enjoyed high levels of trust in one another.

### 11.3.3 *Referral Network and Brand Name*

A final type of resource created by the NPC was a referral network whereby oncology providers (and others whose patients required treatment that could endanger their fertility) could be readily put in contact with local IVF centers that could perform emergency ovarian tissue-freezing protocols. In addition, the Oncofertility Consortium has developed a brand name with positive reputational externalities attached to it. Indeed, as the consortium's website states, "the Oncofertility Consortium<sup>®</sup> logo is a trademarked advocacy ribbon that reflects the growing concern for the reproductive future of cancer patients."<sup>52</sup> Branding materials (including the Oncofertility Consortium's logo, and PowerPoint presentation templates) are available to all NPC members, and generally available to download from the Oncofertility Consortium's website. As with any trademark, the consortium faced the possibility of its logo and name being used by NPC and non-NPC members in a manner that would not be consistent with Oncofertility Consortium goals, or to claim credit inappropriately for discoveries made by the consortium as a whole.

## 11.4 TRANSITION FROM A CLOSED TO AN OPEN COMMUNITY: THE ROLE OF PREEXISTING SOCIAL NETWORKS, TRUST, AND PATENT RIGHTS

A key attribute of a research commons is whether the resources that it creates and manages are available to the larger public or whether they are kept within the commons. As of this writing, the NPC shares many of its resources with members and nonmembers. But this was not the case when the NPC was founded. This section places the history of the NPC's creation within the larger context of the Oncofertility Consortium's history and goals, charts the NPC's transition from a relatively closed community to an open access structure, and addresses the factors that contributed to the initial decision to restrict access to NPC members and those who influenced its transition to an open infrastructure. It also places the NPC's structure within the broader framework of the Oncofertility Consortium, analyzing how information sharing took place in the consortium as a whole.

The idea for applying for an NIH interdisciplinary grant to form a consortium to address fertility preservation in cancer patients originated with Teresa Woodruff. Herself a reproductive endocrinologist, Woodruff was, in 2001, the director of

<sup>52</sup> <http://oncofertility.northwestern.edu/branding-materials>

basic sciences for the Cancer Center at Northwestern University. Through her work as a center director, Woodruff came in regular contact with cancer researchers and oncologists. As she describes it, her conversations with oncologists – who downplayed fertility preservation concerns for cancer patients – did not resonate with her experience with cancer survivors. Prompted by this gap between oncologists' and patients' views of fertility, Woodruff began work on trying to close that gap. Seeking to address a key hurdle in fertility preservation for women at the time – the inability to transform immature follicles into eggs in vitro – she began a collaboration with an engineer who also worked at Northwestern University, Dr. Lonnie Shea.<sup>53</sup> Woodruff explains how she brought together the core grant members, and the crucial role that the Interdisciplinary Research Consortium grant played in advancing the project:

Lonnie Shea and I were doing these projects together that were really striving to make momentum . . . [Our project] was very good, but then the grants would fall between the cracks because the portfolio for the NIH had no way to understand fertility in a cancer setting . . . It fit neither under the NCI nor the NICHD . . . Zerhouni decided with the Roadmap grant . . . to take that common fund and . . . ask the biomedical community, tell us what your most intractable problems are and how will you solve them using teams. And I thought that that was the best thing ever because what that said was that we could take something like oncofertility, which didn't fit and just make it an unmet need. And it was an intractable problem because there were no women, zero, who were getting fertility counsels at the time.<sup>54</sup>

Following the request for applications (RFA) for the interdisciplinary consortium grant from the NIH, Woodruff brought together the researchers who would become the principal investigators in the grant. At the time of the RFA, Woodruff and several of the principal investigators in the oncofertility grant were members of the Specialized Cooperative Centers Program in Reproduction Research (SCCPRR) – a program that fosters translational research projects in the reproductive sciences. This program also provided a venue for interaction with other programs around the nation that focused on reproductive research. One such venue was the Ovarian Focus Group Meeting, which took place every six months. In one of these meetings in the fall of 2005, Woodruff brought up the idea of putting together an application for an interdisciplinary consortium grant that would focus on oncofertility. As explained by Dr. Richard Stouffer:

<sup>53</sup> This initial interaction between Dr. Teresa Woodruff and Dr. Lonnie Shea was mediated by Dr. Steven Rosen, the then-Director of the Cancer Center at Northwestern University. Dr. Rosen also recognized the option gap for cancer patients, and for the pediatric population in particular. Interview with Dr. Steven Rosen.

<sup>54</sup> Interview with Dr. Teresa Woodruff.

At the end of our focus group, Teresa said, “Let’s talk about this” and she also invited [an] NICHD representative. So at that point, we had a person there, Teresa Woodruff, who had been working on follicle development, primarily in rodent models. She and I had collaborated some before (in fact we had one patent at one point when she was with Genentech). I was working on the monkey ovary, so I was using a primate model. Christos Coutifaris and Jeffrey Chang were both clinicians, who were working with infertility patients – polycystic ovarian syndrome, etc. So, we sat around and talked about that area and various aspects and how to treat it and several of the options came up . . . The two interdisciplinary aspects that were added was one that Teresa was aware of at Northwestern, which was with Lonnie Shea, who was a bioengineer, where she had the suggestion that it was possible to take small follicles out of the ovaries of rodents, put them into these alginate-type beads, basically Jello-type beads, and grow the follicles until a point that you could get a mature egg. So, Lonnie Shea was added to develop matrices and to consider ways that we can improve matrices to allow follicles to grow in vitro. But we realized of course that probably the best way to do this would be as patients determine that they have cancer that they would either decide to bank their eggs [or freeze ovarian tissue] . . . It’s very difficult to freeze individual eggs, although we’ve made quite a bit of progress in that . . . So we decided we needed to add a second interdisciplinary person, which was a cryobiologist.<sup>55</sup>

One element in the composition of the original group of researchers that stands out is that most of them were part of a preexisting research network. Several of the founding members of the Oncofertility Consortium had known one another for a long time and held high levels of trust (both in their individual integrity and in their scientific abilities) and in Woodruff, the principal investigator who spearheaded the grant. Several had also collaborated prior to the consortium grant.<sup>56</sup> For example, one of the principal investigators, Dr. Mary Zelinski explained her relationship with Richard Stouffer and Teresa Woodruff as follows:

Because of our interest in follicles we had known of Teresa’s work for a very long time . . . And then if you’re in a similar area, you get invited to give presentations at their home institution. So, we had all done that. Dick and I at Northwestern earlier and Teresa had been at our Primate Center. Well, since the very beginning of her career in science. So, we had known her for a long time.<sup>57</sup>

Similarly, Lonnie Shea remarked:

<sup>55</sup> Interview with Dr. Richard Stouffer.

<sup>56</sup> See, e.g., S. A. Pangas, H. Saudye, L. D. Shea, and T. K. Woodruff, Novel Approach for the Three-Dimensional Culture of Granulosa Cell-oocyte Complexes, 9 *Tissue Eng.* 1013 (2003); J. D. Brannian, T. K. Woodruff, J. P. Mather, and R. L. Stouffer, Activin-A Inhibits Progesterone Production by Macaque Luteal Cells in Culture, 75 *J. Clin. Endocrinol. Metab.* 756 (1992).

<sup>57</sup> Interview with Dr. Mary Zelinski.



I like to think that I have a good lab and Teresa obviously has a great lab as well. And I think we happened to hit a situation where two people with great labs came together and I think it bought us some really exciting science and some really exciting progress. And I think that, ultimately, it's the people that connect. And the ability for those people to work together. And Teresa and I have just been incredibly fortunate that we've just both had the same vision for the long-term goals and really stuck to it.<sup>58</sup>

None of them, however, had embarked on a collaboration of this magnitude, or held a focused discussion on how to address fertility preservation questions in a concerted manner prior to applying for the Oncofertility Consortium grant.

Within this original group of collaborating principal investigators, raw data was shared with an openness that many noted was "uncharacteristic" of their field. All of the interviewees in this core group credit this uncharacteristic data sharing with both accelerating the speed of discoveries and enabling different types of discoveries. Stouffer describes the level of data sharing and its impact on his research as follows:

I think what made it so exciting was we had monthly virtual lab meetings . . . We could sit there every month and show our data to the rodent people, and say, "Look, you can grow these follicles in 14 days. But look, it takes us 5 weeks." What we found for example was that some of the follicles would actually just sit there and just look at you . . . And then you had others that would grow over the five weeks and turn into these beautiful, gorgeous antral follicles. And you'd sit there and say, "You know, what's this heterogeneity? Do you see this in the rodent?" And they would go, "No" . . . But then you sit there and think, "Well, so how does this relate to follicles from humans?" For example, we found if we took follicles from young, reproductive age monkeys, what would be considered 20 year olds in humans they did really well, would give us a lot of those large growing follicles. If we took them from animals that were over 15 years of age, we didn't . . . And we thought, "Well, what did this mean for the cancer patient that's 40 or 35 as opposed to 20?" . . . It made us think on a much broader scale and made us think that immediately because we were having these tremendous and exciting virtual lab meetings every month.<sup>59</sup>

Others similarly remarked that the combination of unusual data sharing with high levels of trust among researchers became "infectious," giving rise to a virtuous cycle of more openness and collaboration:

What I loved about it was the openness of the sharing of data. You can't make advances unless you can share what you found and Teresa is a perfect example of that. [She would often say] "Oh here's what we can do now. We'd love to see if it works in your system and we'll help you in every way." And then that is infectious

<sup>58</sup> Interview with Dr. Lonnie Shea. <sup>59</sup> Interview with Dr. Richard Stouffer.

among people who share a similar science personality and it makes it very, very fun as a part of your career and also is critical for advancing the field.<sup>60</sup>

Beyond this core group of researchers, members of the NPC – but not the public at large – also received broad access to resources (including know-how developed by core members). Indeed, according to some interviewees, having privileged access is what prompted NPC members to join the cooperative. A former NPC administrator explained the decision to restrict access to NPC members as follows:

Everything was closed . . . because I felt that we had to create an exclusive club, in order to get people to want to join it . . . For the first three years, anything that we provided was for members only. We had an 800 number where any patient or provider in the United States could call and they would be triaged to a local IVF program that was staffed and set up at Northwestern. But only members of the NPC got the benefit of those referrals. The training was only provided to NPC members. The ability to get access to reagents and so on [was] only [for] NPC members. We had a password-protected website. And only the members had the passwords and all of the documentation that they would need to take care of their patients, best practices and so on. We went beyond that, we had templated letters that they could use for the insurance companies. So, it was all an integrated whole that was seen as very beneficial. But many of them still would ask, “Are you going to do this for my competitor across-town?”<sup>61</sup>

After spending its first three years as a closed community, the NPC eliminated its password-protected feature and transitioned to a more open structure. This transition was likely enabled by a combination of factors. First, the pull exerted from the basic science research norm of openness in sharing protocols and reagents played an important role: whether to make data and resources freely available to the general public was a source of disagreement among several core group members, many of whom thought closeness was “against the spirit of research.”<sup>62</sup> In addition, once the NPC became an established group with a core membership and recognized reputation, exclusivity lost its importance in achieving buy-in from potential members. Rather, being part of a recognized network provided a reputational boost sufficient to encourage membership. In fact, NPC administrators report a surprising increased interest in membership when protocols were made widely available. This likely happened for two reasons: first, the annotated protocols and videos served as a *signal* of the worth of the cooperative; second, some of the benefits of membership reside in acquiring important know-how and being part of a reference network – all of which are still more readily available to NPC members. As a current NPC administrator remarked: “People if they find our protocols, they’ll reach out and they’ll say, ‘You know, I saw these protocols. What do we need to do if we want to be a member? How

<sup>60</sup> Interview with Dr. Mary Zelinski. <sup>61</sup> Interview with Oncofertility Consortium Administrator.

<sup>62</sup> Ibid.

do we get this implemented? Is this something you can help with?"<sup>63</sup> Finally, not all resources are accessible to non-NPC members. Access to research tissue is open only to NPC members. And although some non-NPC members have been given permission to purchase culture media (necessary to freeze ovarian tissue) from the NPC's commercial manufacturer, media is much more readily available to NPC members.

Oncofertility Consortium research led to several patents, owned by different combinations of principal investigators. For example, principal investigators Lonnie Shea and Teresa Woodruff are co-inventors on patent applications regarding methods for growing follicles in engineered alginate beads.<sup>64</sup> Researchers had an ambivalent relationship to patents. On the one hand, most found patents important both for commercializing technological developments in oncofertility, and for securing credit for their inventions. On the other, researchers worried that patenting their inventions would send the wrong signal to patients that they were profiting from their contributions to the NPC. Because none of the technologies patented by Oncofertility Consortium researchers has yet been licensed to a commercial company, it remains to be seen whether and how the NPC and named inventors would address disputes over potentially conflicting objectives (e.g., profit maximizing vs. wide access).

### 11.5 GOVERNANCE STRUCTURE: TWO NESTED GOVERNANCE REGIMES

The governance structure of the NPC can be best understood as composed of two nested governance structures. The first is the largely informal governance structure of the Oncofertility Consortium and the NPC. The second is the formal administrative structure at the NIH that was put in place to manage interdisciplinary consortia grants, and the specific NIH institutes that were required to work together to monitor and manage the Oncofertility Consortium.

#### 11.5.1 *Managing the NPC: Informal Structure and Reliance on Social Norms*

At the NPC, the Oncofertility Consortium's Steering (or Leadership) Committee is in charge of all major decisions, including allocation of resources and membership criteria. The committee was first constituted following consortia grant guidelines. It included principal investigators from each project, as well as a survivor advocate and a bioethics representative. Since then, the committee has expanded to include what, through experience, current committee members have identified as key stakeholders including patient liaisons (usually nurses or physicians' assistants) and physicians or researchers involved with specific subpopulations (such as pediatric patients). When the Leadership Committee was first constituted, decisions were often made

<sup>63</sup> Interview with Oncofertility Consortium Administrator.

<sup>64</sup> See, e.g., US Patent Application 13/382709, Interpenetrating Biomaterial Matrices and Uses Thereof.

informally, involving the NPC administrator and the lead PI Teresa Woodruff. Indeed, all key stakeholders interviewed were satisfied to delegate decision making on many administrative matters to Woodruff and her administrative staff. The governance structure evolved, however, to become more formalized and to include a series of subcommittees that meet once a month. The leaders of each subcommittee also sit on the Leadership Committee, which meets quarterly. The subcommittees evolved organically – out of NPC annual meeting break-out panels. For example, the NPC now has a pediatric subcommittee, and a male fertility subcommittee.

Decisions regarding who should sit on the NPC Leadership Committee, when and how to seek expert external advice for a particular decision, whether to put an issue up for a vote from the entire NPC, or when to seek advice from all of the NPC members are still made informally, that is, on a case-by-case manner by members of the Leadership Committee. For example, an NPC administrator described discussions regarding NPC Leadership Committee membership as follows:

Once we've identified the leaders of the subcommittees, that streamlined our NPC leadership meetings. We have thought about asking for either votes or nominations for people to spearhead parts of the annual meeting . . . So people can throw out names and then we can ask for . . . other input and then invite so and so to be the chair of the meeting or participate in the panel or be a keynote or something like that, and at some point maybe if they're really participating in the subcommittee maybe they can sit in on some of the NPC Leadership meetings. So there is some room for working your way through the layers of the meetings and somehow making it to the NPC Leadership table. But it's not a formal nomination . . . It's very informal.<sup>65</sup>

Similarly, the decision to put a particular issue to a vote to the entire NPC membership or to rely instead on a vote of the Leadership Committee alone is made by the Leadership Committee on an ad hoc, informal basis:

We've done it a few other times where we've put it to a vote to the NPC overall: all of the centers, all of their support staff, their research coordinators, their nurses, their admins, their physicians, lab scientists, things of that nature and had them all vote for different topics. So it depends on what the topic is in terms of, whether it's worth having, or more or less waiting, to get responses from 600 people versus [deciding by Leadership Committee vote alone].<sup>66</sup>

In contrast to the relatively informal process for NPC governance, which became progressively formal as NPC membership increased, the process of becoming an NPC member was more formal from its inception. Prospective NPC members sign a letter of agreement that forbids them from sharing “Oncofertility Consortium<sup>®</sup>” documents,

<sup>65</sup> Interview with Oncofertility Consortium Administrator. <sup>66</sup> Ibid.

protocols, procedures, logos, promotional materials, reagents, formulas”<sup>67</sup> with anyone outside of the NPC. NPC research members also agree to contribute research ovarian tissue to the consortium and to delegate decisions regarding research use of the tissue to the Steering Committee.<sup>68</sup> Some interviewees attribute this early formality with helping enroll initial NPC members:

We had early success in getting cooperation and getting help because we behaved more like a business and less like a scientific project in the beginning. We learned that if we put forward an organized and templated approach . . . that people saw that as appealing and they wanted to be involved. So, we put together procedure manuals that were written. We put together training programs.<sup>69</sup>

Interestingly, Leadership Committee members interviewed perceived the role of the formal contract more as a tool to make membership appealing and to streamline the onboarding process than as a document that provided safeguards against disclosure of NPC research findings or protocols. Committee members spent little time considering what to do if an NPC member failed to live up to its obligations, or considering enforcement mechanisms – assuming it would be impractical to enforce the contract, and that breaches would be rare if they happened at all. Their most important concern was that “people would use [the Oncofertility Consortium name] as a branding mechanism.”<sup>70</sup> Indeed, only a single instance involved improper credit allocation. At that time, an organization that carried out its first ovarian tissue freezing had a “big media splash and made it seem as though they were the people that were driving the grant.”<sup>71</sup> This misapprehension was handled informally: “we just had to gently remind them to please correct that impression.”<sup>72</sup>

Informal norms can develop in at least one of two ways: first, they can emerge in a decentralized manner, from the “bottom up,” reflecting the informal consensus of a particular group. This is the case with scientific social norms. Second, they can emerge in a hierarchical, “top-down” manner. This appears to be the case with NPC governance: the strong leadership of the NPC was ultimately in charge of creating new norms as novel situations emerged. This informal, centralized norm creation appears quite important in the success of the NPC: it allowed board leaders to act nimbly as new situations presented themselves. These informal norms functioned effectively, however, because they were consonant with and relied upon the underlying social norms of the research and clinical community.

<sup>67</sup> NPC Letter of Agreement, note 23.    <sup>68</sup> NPC Letter of Agreement, note 23.

<sup>69</sup> Interview with Oncofertility Consortium Administrator.

<sup>70</sup> Interview with Oncofertility Consortium Administrator.    <sup>71</sup> *Ibid.*    <sup>72</sup> *Ibid.*

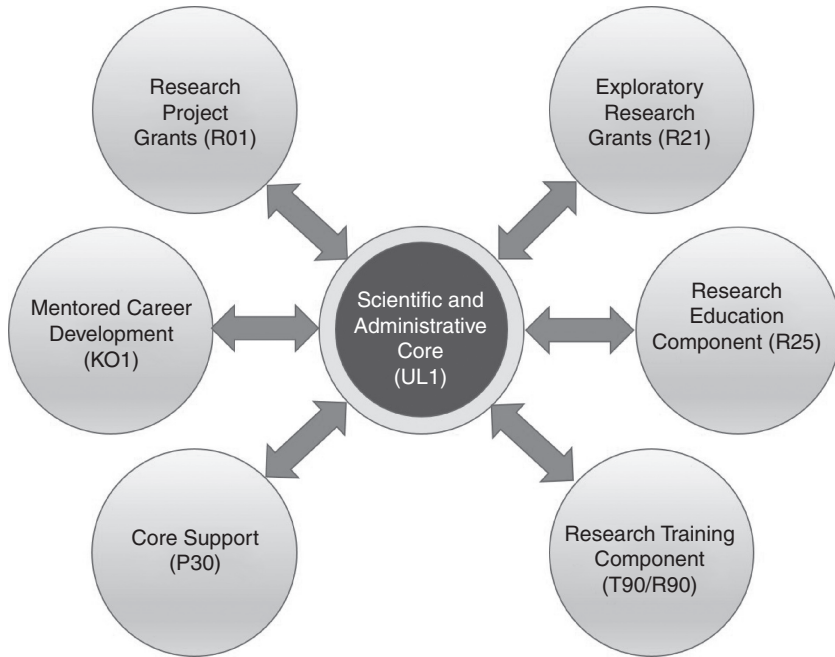


FIGURE 11.1 Grant structure of interdisciplinary research consortia (adapted from <https://commonfund.nih.gov/Interdisciplinary/consortia>).

### 11.5.2 *The NIH Governance Structure – Formal Structure, Expertise, and Coordination Challenges*

The basic structure of the interdisciplinary consortia grant is illustrated in Figure 11.1. The Oncofertility Consortium consisted of several individual NIH grant mechanisms, brought together through one administrative core funded by a U54 grant. The role of the administrative core was to organize and support the interdisciplinary team, develop scholarship on team interaction and function, and provide governance and a communication and data-sharing plan.<sup>73</sup> In addition to the administrative core, the Oncofertility Consortium contained four research grants given to specific principal investigators (Rzero1 grants), two P30 core grants – one to fund the NPC directly and a second one to fund a biomaterials core – one R25 grant to fund an educational module, and three “training mechanisms” (T90, R90, and K01 grants) to train oncofertility specialists.

Successful grant administration required coordinating the work of disparate communities at two distinct locales: first, within the Oncofertility Consortium and the NPC and, second, within the NIH itself. The latter required multiple

<sup>73</sup> Oncofertility grant, at 159, on file with author.

NIH institutes, with their own set of priorities and ways of organizing work, to come together to make joint decisions to evaluate Roadmap grantees' success. This proved very problematic. And although every single key informant interviewed highlighted how the grant process and award itself was crucial to the success of the consortium, each also emphasized the lack of coordination among NIH institutes as a key hurdle. One interviewee commented that NIH program officers did not fully incorporate the transdisciplinary goals of the consortium to their day-to-day operations: "they were still set in 'I'm in cancer and I'm in this department' and they just were very stuck to the rules of the ordinary road. It meant that we had a bunch of program officers that had different ideas about how the grant should be run."<sup>74</sup> Interviewees also pointed to the lack of expertise on the subject matter of the grant on the part of NIH officers in charge of making funding decisions as a constant source of friction between oncofertility researchers and NIH administrators. For example, one interviewee remarked: "they brought together program officers from different institutes at NIH, who had never touched anything like this before and were from backgrounds that really had no business overseeing some aspects of this grant. But they had to bring money together from different institutes within NIH to do these specialized grants."<sup>75</sup>

Many attributed this lack of expertise in reproductive endocrinology to an inflexible reading of what types of experiments could be performed under the terms of the grant. One member of the board of directors characterized his experience as follows:

The overall project leader for the grant knew nothing about reproductive health and clinical medicine. And it showed when we had our meetings. At our oncofertility directors' meeting there were at least two or three people there from the NIH. One from NICHD who was aware of the reproductive health issues and was helpful but all decisions were made higher up. We would often get comments back like, "Well, those studies that you're doing are not in the grant. You can only do what's exactly in the grant." Well, you know, that's not the way research works. And you may put in there you're going to do this particular study. [But] we may culture follicles one way and it doesn't work, so we culture them in a different way. They basically expected us to follow the letter of the grant for everything we did. And it was a struggle.<sup>76</sup>

Another similarly described the relationship with some NIH officers:

[The NIH officer] was very stuck in whatever was written in the original grant. It's what you were supposed to do and you could do no more. And I kept arguing that "this was a brand new field, what we wrote at the outset was what we thought we would do, but as soon as we started working together, there were many more things that came out of it." And those other things were not off target. They were on a trajectory that we could see, but we couldn't tell you what would be in there. So they

<sup>74</sup> Interview with Oncofertility Consortium Principal Investigator, basic research track. <sup>75</sup> *Ibid.*

<sup>76</sup> *Ibid.*

were really stuck on the notion that, and I called it the old testament, that all we could do was what was in the old testament or the original constitution . . . So, that took a lot of my time just justifying the kind of science that was happening because science was happening very fast.<sup>77</sup>

Researchers who study when communities and individuals resort to formal, inflexible rules to reach a decision, as opposed to contextual, flexible standards, emphasize that novices in a field are much more likely to rely on rules to ground their judgment.<sup>78</sup> It is likely that a lack of familiarity with the subject matter of the grant gave rise to inflexible, textual decision making from NIH officers that hindered cooperation. This formalism in decision making stands in sharp contrast with the informal process used within the Oncofertility Consortium.

#### 11.6 THE NATIONAL PHYSICIANS' COOPERATIVE: COSTS AND BENEFITS OF MEMBERSHIP

The major benefits of NPC membership accrue both to NPC members themselves and to the public at large. By pooling patient samples collected through standardized protocols, the tissue bank has the potential to generate reliable, reproducible data on patient populations that, as a result of the small size of patient tissue samples that could be collected at any one NPC site, would be impossible to generate otherwise. At a 2007 conference launching the NPC, Teresa Woodruff described the potential public benefits of the NPC as follows:

We do fellows projects, for a short period of time, with available cohorts either through a computer database or whom they see in an 18-month rotation. But I think what that does is that cuts off the data on its knees and we get publications and abstracts that are not in the format where we can get authoritative data. The idea is that we will be that reproductive medicine network that allows us to do that kind of studies. We're hoping you all buy into the fact that we need to get our patients into this database. This will allow us to do longitudinal studies in a way we couldn't before.<sup>79</sup>

An additional benefit both to the public and to NPC members is the creation of an information exchange and clearinghouse – serving both to coordinate and to centralize data sharing. Through the NPC, members can quickly exchange information regarding best practices, and participate in discussions regarding important research questions that should be addressed by research consortium members. Because the website is no longer password protected, the public at large has the ability to access that information online.

<sup>77</sup> Ibid.

<sup>78</sup> See, e.g., Laura G. Pedraza-Fariña, Understanding the Federal Circuit: An Expert Community Approach, 30 *Berkeley Tech. L.J.* 90, 114–16 (2015).

<sup>79</sup> 2007 Oncofertility Conference, NPC Panel, <http://oncofertility.northwestern.edu/media/npc-panel>.



Finally, the NPC has created a bridge along two axes: first, it provided a mechanism for treating oncologists to refer their patients to reproductive endocrinologists who were equipped to perform emergency fertility preservation protocols. Second, it has fostered communication between basic scientists and clinical researchers and practitioners. This communication, in turn, influenced how basic scientists conducted their work. As a principal investigator remarked: "Then you get to this consortium where you have access to all of these people in different areas and even outside of the science . . . you get to hear from the people who are helping [the patients] make decisions about using your science. These are things you never get exposed to so in depth while you are doing your work."<sup>80</sup> According to several interviewees this in-depth, constant interaction with the clinicians who were seeing the patients who would ultimately benefit from their research not only motivated them to work but also influenced the types of questions they asked.

Despite this impressive set of benefits, one major cost to creating interdisciplinary research consortia is that a large monetary investment is required to bring them about. Creating infrastructure to facilitate coordination is costly, but creating infrastructure to facilitate coordination across entrenched practice styles and persistent boundaries is even more so. Indeed, interdisciplinary consortia grants given to each individual principal investigator were much larger than what those researchers traditionally obtained through the NIH's Ro1 mechanism. One factor, however, may mitigate this large upfront investment: several of the benefits described earlier have continued past the initial grant support, as the consortium gave rise to new and unexpected avenues of collaboration. For example, one researcher credits the consortium with starting a collaboration between cryobiologists and reproductive endocrinologists working on rhesus monkeys that dramatically advanced the field of ovarian cryobiology.<sup>81</sup>

## CONCLUSION

As measured against its own stated goals (and those set forth in the Oncofertility Consortium grant), the NPC has been highly successful along at least two axes: creating a pathway for cancer patients to receive fertility counseling and treatment prior to starting cancer treatment, and advancing research on follicle development. The following six features of the NPC appear to have been important for its success. First, the core group of researchers and clinicians who spearheaded the NPC were part of a *preexisting social network with high levels of trust*. This enabled the core researchers to openly share raw experimental data and create a culture of openness that diffused to the broader NPC. Second, all of the researchers interviewed emphasized the importance of *monthly face-to-face research meetings* to maintain a high level of trust and excitement, and to sustain the fast pace of research

<sup>80</sup> Interview with Oncofertility Consortium Principal Investigator, basic research track. <sup>81</sup> *Ibid.*

that characterized the research arm of the NPC. Third, having a *relatively closed infrastructure*, where information and know-how were accessible only to group members, was important for the NPC to recruit members in its early stages – as it was trying to develop a reputation and a research culture. Once the NPC became an established commons, opening its protocols and know-how to the public at large did not negatively impact membership; to the contrary, it could rely on its reputation to attract more members. Fourth, the NPC employed a *hierarchical, centralized and informal governance structure* that was highly successful in large part because its decisions were consonant with and relied upon the underlying social norms of the research and clinical community. Fifth, the external, formal management structure of the NIH often clashed with the informal structure of the NPC leadership team, revealing a *particular type of coordination struggle involving nested governance structures*. Finally, the continued involvement of a *high-status intellectual actor* vested with a high degree of trust from the community, - Teresa Woodruff, was crucial to the success and cohesion of the project.

Several of these features echo findings made by Strandburg, Frischmann, and Cui in their research of the urea cycle research consortium.<sup>82</sup> In particular, both the NPC and the urea cycle research consortium have a close-knit core research group, strong principal investigator leadership, monthly research meetings, and an informal but hierarchical governance structure. Future studies of scientific research consortia are needed to establish whether these four key features are hallmarks of successful research commons governance.

<sup>82</sup> Katherine J. Strandburg, Brett Frischmann, and Can Cui, The Rare Diseases Clinical Research Network and the Urea Cycle Disorders Consortium as Nested Knowledge Commons, in *Governing Knowledge Commons* 155.