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Forming interdisciplinary expertise: One organization's journey on the road to translational nanomedicine

Sharon Ku

Office of History, National Institutes of Health

Sharon Ku: sharon.ku@nih.gov

Abstract

This paper provides a sociological account of how researchers of different disciplines become experts in translational nanomedicine. Using a case study of the Nanotechnology Characterization Laboratory (NCL) at the National Cancer Institute (NCI), the author argues that the relationship between the different disciplines involved in translational nanomedicine should be understood in the broader socio-political context of the boundary politics between the academy, industry, and government. This study suggests that the process of training the nanobio expert is not simply a process of inculcating skills; it is also a process of institution-building. In the case of the NCL, sustaining the laboratory's existence at the interface between the university, industry, and government informed how researchers practiced interdisciplinarity and cultivated their interdisciplinary expertise. It required mobilizing institutional resources through administrative/managerial strategies. Viewing the formation of a professional identity as a social process helps clarify the meaning of interdisciplinarity and provides insight in evaluating the performance of interdisciplinary collaboration and the design of nanoscience education.

Keywords

translational nanomedicine; interdisciplinary collaboration; interdisciplinary expertise; nanoscience education

Introduction

Nanotechnology: interdisciplinary expertise undefined

Back in 1997, I was working on my physics dissertation on the formation of nanoscale clusters on silicon surfaces. Most of my work took place in a lab in a dark basement away from the main campus called the "surface science characterization laboratory." It was equipped with a scanning tunnelling microscope, a low-energy electron diffraction, an ultrahigh vacuum system, and two students who considered themselves peripheral to the mainstream of industry-oriented, university-based microelectronics research.

Further Reading/Resources

For those interested in NCL's work in endotoxin-nanoparticles interference:

Dobrovolskaia, Marina, Neun, Barry W; Clogston, Jeffrey D; Ding, Hui; Ljubimova, Julia; McNeil, Scott E: Ambiguities in applying traditional Limulus Amebocyte Lysate tests to quantify endotoxin in nanoparticle formulations. *Nanomedicine* 2010, 5 (4): 555–562

For those interested in NCL's work in the relation between nanotechnology definition and institutional politics, see:

Gallo, Jason. The Discursive and Operational Foundations of the National Nanotechnology Initiative in the History of the National Science Foundation" in *Perspectives on Science*, 2009, 17 (2): 174–211

Bawa, Raj. Regulating Nanomedicine – Can the FDA Handle It? *Current Drug Delivery*, 2011, 8: 227–234

The situation changed dramatically just after I left the field. After the Clinton administration announced the National Nanotechnology Initiative (NNI) in 2000, many institutes whose previous work focused on micro, sub-micro, even atomic-scale materials science adopted the “nano” prefix. Nano-electro mechanical systems became an alternative expression for microelectro mechanical systems (MEMS); the National Submicron Device Research Laboratory renamed itself the National Nano Device Research Laboratory. And my former lab at National Chao-Tung University in Taiwan is now called the Nanoscale Characterization Laboratory. Such relabeling seemed to be motivated by a desire to accord with the shift in science policy and obtain resources.

I did not have the opportunity to convert my identity from surface scientist to “nanoscientist,” a profession that seemingly became more desirable along with the growth of nanotechnology. Nevertheless, many of my former colleagues, particularly young scholars or PhD students, mentioned their “identity crisis” in this period. My laboratory colleague expressed this self-doubt. A newly-minted PhD from the Institute of NEMS (former MEMS) with a first-authored paper published in *Nature*, he felt that his training did not form the basis of a “profession,” which he defined as practices productive of new knowledge. Rather, he regarded his own research as a hybrid constituted of bits of knowledge borrowed from different disciplines.

His experience indicates that although the NNI suggested a very encouraging future for nanotechnology, young researchers instead confronted a rather different reality. This raises the question of the meaning of “interdisciplinarity” and “interdisciplinary expertise” in nanotechnology. A good deal of evidence suggests that nanotechnology is becoming institutionalized, manifested in increasing federal resources made available for nanoscience training and nanoscience centers at universities¹ and the rapid expansion in nano-prefixed science journals since 2000.² Despite the infrastructure building which seems to stabilize the development of nanotechnology, it is still not clear that whether nanotechnology should be considered as a discipline with its core expertise and experts. While NNI advertised nanotechnology as a concrete emerging field which creates new discoveries and professions for “the next industry revolution”,³ historian of science argued that nanotechnology is merely a discursive tool of mobilizing scientific and political resources and the related expertise has been developed by different disciplines.⁴ In terms of scientific practice, Schummer’s scientometric analysis of nanoscale research revealed no particular patterns and degrees of interdisciplinarity. Rather, nanoscience/nanotechnology’s apparent multidisciplinary consists of different, largely “mono-disciplinary fields” which are rather unrelated to each other and which hardly share more than the nano prefix.⁵ Scientists like Oberdörster⁶ and Maynard,⁷ on the other hand, argued that nanotechnology not only stimulates the reorganization of traditional toxicology but also triggers the formation of “nanotoxicology” as a new discipline.

These different perspectives in defining expert and expertise in nanotechnology indicate that nanotechnology is still an undefined expertise and its perception relies very much on actors’ various interests. The rapid investment regarding the infrastructure building and regulatory changes seem to suggest that nanotechnology is more than a (temporary) strategic alliance for actors to claim resources; nonetheless, what can be count as the core expertise of this “inherently interdisciplinary” nanotechnology, given the significant diversity of interests and research agendas that each discipline possesses? Apparently there is a tension between interdisciplinary collaboration and discipline-based knowledge production—they both are important and have to coexist to contribute to the interdisciplinarity of nanotechnology. This brings up a set of analytical question about the meaning of discipline and interdisciplinarity, and whether they should be view as contradictory concepts or not.

Interdisciplinarity in the context of translational nanomedicine

The tension between disciplinarity and interdisciplinarity is not unique to nanotechnology. Weingart⁸ provided a generic account of viewing interdisciplinary research as a recombination of existing specialties rather than a promise of ultimate unity; interdisciplinarity and specialization are seen as parallel and mutually reinforcing strategies scientists deploy to seize opportunities of acquiring knowledge and resources for the purpose of innovation. The constructivist's approach is validated by other historical and sociological studies about the formation of discipline/interdiscipline. Golinski⁹ demonstrated that "discipline" as an established order of knowledge emerged with the modern university in the nineteenth century. Disciplinarity in that context developed as a pedagogical resource designed to reproduce expertise; it encapsulated those socio-institutional conventions necessary for training, evaluating, and 'disciplining' the student. The history of the "discipline" thus predates the history of "interdisciplinarity", suggesting that the interdisciplinary knowledge-making in contemporary science and technology development should be treated as a socio-political phenomenon derived from the specific context where "the organizational matrix of disciplines is beginning to dissolve."¹⁰ Klein¹¹ argued that World War II was a watershed of interdisciplinary teamwork. Knowledge exchange and collaborative work between different disciplines occurred in state-funded science and engineering projects such as the Manhattan Project and in subsequent enterprises of science-based industry. During the Cold War, the virtues of interdisciplinarity were urged both by defence administrators and student radicals. Bensaude-Vincent¹² argued that the heterogeneous practices constituting materials science were institutionalized by a federal government interested in developing advanced materials for the military-industrial complex. Using a case study of membrane technology, van Lente & Rip¹³ argued that a discipline consisted of strategic alliances formed in response to federal science policy, which justified projects of basic science according to their potential to yield practical benefits at some point in the future.

These researches demonstrated that discipline/interdiscipline represents a specific division of labor sponsored by certain patrons to produce the type of knowledge in response to particular sociopolitical interests. As Burian¹⁴ concisely pointed out, the formation of discipline is a process of inclusion and exclusion. There are no intrinsic elements which define the content of a discipline, as well as there is no generic formula to guide how different disciplines relate to each other; rather, the boundary conditions of disciplines/interdisciplines are negotiable and constructed under specific social context. The contingent aspects of forming a discipline have been examined by Chadarevian and Gaudillière using molecular biology as a case study.¹⁵

The social construction of discipline and the social negotiation of relationships among disciplines further indicate that interdisciplinarity has to be practiced by discipline-bound experts--the boundaries between different disciplines, though may have to be redrawn, still play an important role in interdisciplinary collaborations in order to provide resources of knowledge exchange and secure scientists' expertise and autonomy in collaborations. This reinforces the argument that disciplinarity and interdisciplinarity are not mutually exclusive ideas that emerged separately in different historical contexts; rather, they are two sides of the same coin that researchers and institutes construct and strategically mobilize to fulfil certain needs in their knowledge making.

Understanding this "essential tension" between disciplinarity and interdisciplinarity, I argue, is the key to unpack the idea of "inherent interdisciplinarity" NNI claimed. Therefore, this paper does not attempt to argue whether nanotechnology is a newly formed discipline or not. Instead, it takes the NNI's assumption that nanotechnology is going to be an influential field as a starting point, and reveals the complex sociopolitical factors embedded in

nanoscientists' daily laboratory practice to explain how interdisciplinarity is conducted and stabilized. These micro-level practices reveals how scientists in the early career stages transform themselves into nano-experts in a research environment that does not support traditional disciplinary trainings. It thus helps to understand the cultivation of interdisciplinary nano-expertise and the professional identity of being a nanoscientist. Establishing a solid professional identity matters in interdisciplinary collaboration; to be a "nanoscientist", one has to know how to use disciplinary identifiers cleverly to establish one's autonomy whilst simultaneously leaving sufficient interpretive flexibility in order to immerse oneself or engage others in forming collaborations for mutual benefit. Kurath and Maasen¹⁶ were the first to study this question in an exploration of how the rise of nanotechnology fostered identity change in toxicology. Their analysis showed that the identity of toxicologists was shaped by cognitive, institutional, and external factors. However, by treating these categories separately, their analysis overlooked the "essential tensions" between disciplinarity and interdisciplinarity manifested in nanoscience researchers' scientific practice. Although being expected as interdisciplinary experts, most nanoscientists still have to mobilize their disciplinary-based trainings to help their home institutes establish interdisciplinary nanotechnology. Understanding how individuals as both social and cognitive actors reconcile different layers of social forces in the development of nanotechnology is thus a key aspect to further clarify the idea of interdisciplinarity under the NNI policy.

The Nanotechnology Characterization Laboratory (NCL) at the National Cancer Institute (NCI) is an ideal case to explore these cross-boundary dynamics in interdisciplinary knowledge-making. It was the first federally-funded laboratory dedicated to nanoparticle characterization for translational nanomedicine, an NCI health research policy which aims to move bench nanoscience to bedside nanodrugs. Drawing from a one-year laboratory observation from March 2010 to February 2011^a and in-depth interviews with laboratory members, I contextualizing the notion of interdisciplinarity in this particular social setting, and argue that the formation of interdisciplinary expertise is not simply a process of knowledge exchange at the conceptual level. Rather, new technical and managerial skills in bridging existing discipline-based knowledge, new social relations in mobilizing resources kept in university, industry, and the government, and new forms of professional identity individual scientists cultivated in respond to these intellectual and social changes have to be invented as a package to realize interdisciplinary collaborations in the production of translational nanomedicine. The strong correlation between knowledge-making, institutional building and identity formation revealed in the NCL case study broadens the scope of interdisciplinarity from a pure epistemic concept into a series of socio-political practices, and offers solid empirical foundation for real-time reflections on the adequacy of current nanoscience education.

THE CASE STUDY OF THE NCL

Translational nanomedicine at the National Cancer Institute

The origins of the NCL can be traced to the Unconventional Innovation Program (UIP) NCI established in 1998. As the director of this wealthiest NIH center historically known for its radical approach in fighting the war on cancer, Richard Klausner advocated the idea of "tool-based, engineered biology" to improve cancer diagnosis and treatment at the molecular level, and viewed nanotechnology as a high-precision tool to realize this idea. Under the UIP, a series of pioneering nanobio projects were contracted to university principal

^aThis project is co-sponsored by the National Cancer Institute and NIH Office of History. I gratefully acknowledge the support and cooperation of the NCL staff, especially Scott McNeil and Marina Dobrovolskaia.

investigators, with the goal of testing the feasibility of applying nanotechnology to cancer therapeutics.¹⁷

It soon became clear to UIP program managers that the lack of comprehensive metrics and measurement standards to characterize nanoparticles, a vehicle for a drug payload, presented an obstacle in developing cancer nanomedicine. A typical issue was the correlation of results between disciplines. Teams made up of chemists who could synthesize nanoparticles with superior chemical functionality were not able to provide substantial biological evidence correlating the particles' bioactivities to the chemical structures. And teams organized by biologists that produced impressive results of bioefficacy did not have methods to further study the structure-activity relationship. Moreover, the NCI became aware that measurements were not always reproducible: because labs had unique experimental protocols, data were normally incomparable. Under the FDA's requirement that pre-clinical data must be of high quality and reproducible, the NCI worried that the research generated by this program might never be translated to the clinic.

The urgent demand for reliable methods to systematically produce and correlate physiochemical, *in vitro* and *in vivo* characterization set the stage for the birth of the NCL. The NCI realized that a centralized facility was necessary to help academic researchers overcome the issues of poor comparability and reproducibility in developing nanomedicine. Due to the high risk, rapid growth but unclear future of nanotechnology, NCI decided to use contract mechanism instead of establishing a permanent facility within the bureaucracy to conduct this task.

The proposed facility became more concrete and gained further justification after NIH announced the Translational Medicine Roadmap in 2003¹⁸ where translational nanomedicine was selected as one of the key targeted areas. In 2004, NCI signed the contract with its current Federally Funded Research and Development Center (FFRDC) operator, SAIC-Frederick, to create the NCL, the first government-owned, contractor-operated (GOCO) entity designated to nanotechnology in the U.S. The first five-year contract was managed by the NCI Alliance for Nanotechnology in Cancer, an office formed in 2004 under the support of the NCI Deputy Director Anna Barker. Except the NCL, the alliance program office also sponsored the other two facilities through the grant mechanism, the Centers of Cancer Nanotechnology Excellence (CCNE), and the Cancer Nanotechnology Platform Partnerships (CNTP). The reason to put the NCL together with university grantees was to make the NCL a center of translation to offer technical assistance to the academic nanobio community, developing standard characterization protocols to translate academic nanoscience to clinically-valid nanomedicine.^b However, the sophisticated social setting for the NCL to be administratively intramural but financially extramural provided the first layer of complexity in its practice of interdisciplinarity.

According to the 2004 NCI Cancer Nanotechnology Plan and the NCL business Plan, the NCL was expected to collaborate with a wide range of stakeholders including pharmaceutical companies, university researchers, and government agencies, developing a set of preclinical analytical methods to systematically characterize nanoparticles submitted by these institutions. The NCL conducted three types of collaboration in its daily laboratory work, as Fig 1 illustrates. First, NCL formed a formal collaboration with the FDA and NIST (National Institute of Standards and Technology) via a three-party Memorandum of

^bIn this context I refer to "standards" and "standardization" as actors' categories expressing viewpoints on nanotechnology that are not clearly defined. The flexible usage of standardization later became a major challenge between the NCL and NIST in their collaborative project of making a certified reference material for the nanobiocommunity. For a detailed case study, see Sharon Ku, *There's plenty of room at the bottom: A sociology of nondrug standardization*, PhD Dissertation, Cambridge University, 2009.

Understanding to develop standard methodology for characterizing nanodrugs. Second, NCL offered free characterization services to industrial nanodrug developers, aiming to assist insufficiently capitalized biotech spin-offs unable to test products *and* large pharmaceutical companies interested in using nanotechnology to reformulate or improve the performance of existing drugs. Third, the NCL worked with university professors who had promising ideas in nanomedicine but who weren't necessarily familiar with the process and knowledge required in pre-clinical drug development, assisting them in transforming their test-tube materials into FDA-approved medical products. The mixture of academic, national, and commercial interests made the NCL a hybrid, planting the seeds of identity-searching among the lab and its members.

FFRDC

First established during World War II, the FFRDC is a contract mechanism developed by the U.S. government to assist federal agencies engaged in scientific research, systems development, and systems acquisition in executing their missions in support of national objectives as efficiently and quickly as possible. They can be operated by a university, nonprofit, or profit organization depending on the mission. The FFRDC thus serves as an interface between government, industry, and university. Of 38 FFRDCs in the U.S., NCI-Frederick is the only one under the Department of Health and Human Services. The mechanism was adopted in the 1970s at a time when "fighting the war on cancer" was portrayed as a national mission.

Starting from zero—Scott McNeil, a cell biologist at SAIC, assumed directorship of the NCL in August 2004. Through his interaction with higher-level managers he came to realize that although the NCI had a strong interest in translational nanomedicine, the questions of how to define "nanotechnology," how to conduct "characterization," and who to hire in a lab with a mission of nanotechnology characterization were still not clear. With five years of funding, McNeil now had to staff the project. Here he faced a number of serious challenges. The first and most obvious problem was defining expertise in this context; second, the project demanded people who were committed to the translational ideal, who would not take advantage of nanotechnology solely for the funding that came with it, and who were not concerned with building academic careers and, hence, not compete with the project's university academic collaborators. After protracted interviewing in 2005, he eventually hired three junior scientists—Steve Stern, Anil Patri, and Marina Dobrovolskaia—to lead three scientific groups: toxicology, chemistry, and immunology.

McNeil organized the project along military lines. In a style drawing from his past experience as a combat officer in the First Gulf War, McNeil informed his new recruits that time was of the essence: "action has to be taken as soon as possible." For this new laboratory, operated under the NCI contract, there was no time to warm up. It had to be equipped as fast as possible, carrying the available "weapons" in hand, whatever they were, to fight the "nano war on cancer." This created additional pressure for individuals in an unfamiliar institutional situation engaged in an undefined field of medicine.

Anil Patri, the NCL chief chemist, had previously worked as a faculty member at the University of Michigan Medical School. Having extensive experience in dendrimer projects sponsored by the NCI UIP, Patri believed the new NCI facility could help him conduct translational research with a direct impact on cancer treatment. But on his first visit to the lab, he was disappointed:

They wanted to develop physiochemical characterization, but there was no position for a chemist, only a biochemist. When I saw the small chemistry room where

hardly any piece of chemical analysis equipment could fit, I realized that they may have no idea that the tools we chemists need are not just petri dishes and test tubes, and seriously doubted that this was the right place for me.

Steve Stern, the NCL's toxocologist, was puzzled by the facility's ambiguous role and unsure of the work that he was expected to produce. Trained as a medical toxicologist, he was interested in pharmacotoxicology of small molecule-based drugs. His initial motivation was the prestige of being part of the NCI, the biggest research funding agency in cancer research, and the excitement of being part of the nanotechnology frontier described by the NCI in its business plan. With no prior knowledge of nanoscience, he soon found the reality dramatically different. In contrast to the well-defined work flow and expertise he received in his past training, he found the situation in NCL chaotic:

I was expected to design toxicological tests for nanomaterials. In medical school we just start the toxicological studies using materials with given physiochemical properties, without questioning this information...But when I presented the toxicological data based on particles with certain sizes, chemists kept questioning: where did you get these particles? How were they synthesized? What instrument was used to obtain the number?

The NCL's complex and ambitious mission—blurring the boundaries between analytical chemistry and medical toxicology and combining the institutional functions of government-supplied standard characterization services with research-oriented academic science—frustrated the young toxicologist fresh from the academic environment.

Among the three chief scientists, immunologist Marina Dobrovolskaia was the only one who had laboratory experience with pharmaceutical companies. Coming from a Contract Research Organization, she was an expert in *in vitro* drug testing. Nevertheless, she experienced the greatest professional identity crisis of the three:

Both Anil and Steve could more or less justify their expertise as a chemist and toxicologist who provide physiochemical characterization and toxicological studies to meet the FDA's requirements. However, traditionally immunology in oncology comes into play at later stages, and I couldn't find my role in the lab.

The confusion and insecurity experienced by the NCL scientists provides an alternative image of the "nanoscientist," one that contrasts starkly with the glowing image projected by the NNI. Underneath the interdisciplinary discourse lay many questions about interdisciplinary expertise. The NCI Nanotechnology Alliance Program Office had provided generous support in establishing the NCL, enlisting scientists with various types of expertise. Yet a crucial ingredient was missing—guidelines for practicing interdisciplinarity and becoming an interdisciplinary nanomedicine expert. The truth was that no one clearly knew what to do. With no formal rules or model to guide them, McNeil and his team decided that they had to construct their own.

The story of the NCL immunologist and her endotoxin test

Although Dobrovolskaia was hired as the NCL immunologist, she did not fully understand the correlation between immunology and nanotechnology, or how to pursue interdisciplinary studies on this subject. After several weeks surveying the literature, she was hesitant to propose any research project because the directions taken by the immunology community seemed to be too "academic" for the NCL. She then decided to do something "not fancy, but at least useful to the lab"—developing protocols for sterility tests, the most basic and routine assays for drug testing. One marker of sterility is the level of endotoxin, which is associated with bacterial contamination that can lead to fever or induce cytotoxicity. "At the beginning, when I received the task of detecting endotoxin, I told Scott, 'it's easy--it is textbook

knowledge for every biologist; there are commercially available kits on the market to do the measurement; there's even a FDA guideline on endotoxin.”

However, in December of 2005, she noticed high endotoxin levels in various nanoparticles, regardless of the purification method she applied. Checking with the particle submitter, the instrument providers, and other groups who reported similar observations, the team later decided that there was a great deal of interference between nanoparticles and the endotoxin assay. Measuring endotoxin levels was no longer possible through a simple experiment. Understanding the mechanism of endotoxin response required further study in order to enable scientists to discriminate between endotoxin toxicity and the potential toxicity of nanoparticles *per se*, and whether nanoparticles modulated endotoxin responses.

The interference of nanoparticles with bioassays complicated the whole process of characterization and data interpretation in NCL. However, this was good news for the anxious Dobrovolskaia, since working on the problem provided a means of understanding immune responses triggered by small particles and offered a unique way to define the interface between nanotechnology and immunology while contributing her expertise to the lab.

She dug into the problem more deeply. Working closely with Stern and Patri, she systematically purified and controlled variables at each stage of sample preparation, comparing the *in vitro* results with toxicity tests and physiochemical characterization. The team confirmed that the interaction between nanoparticles and endotoxin could lead to false-negative and false-positive responses in the traditional Limulus Amebocyte Lysate (LAL) assay. This empirical assumption illustrated in Fig 2 changed the meaning of endotoxin measurement from a standard yes-or-no test into a series of much more complex judgments. Scientists had to carefully compare data obtained from three test methods—gel-clot, chromogenic, and turbidimetric—in order to tell whether the positive reaction was caused by nanoparticles, endotoxin, or endotoxin plus nanoparticles, and which number was the most reliable to represent the system.

Dobrovolskaia's efforts transformed endotoxin measurement in nanoformulations from a routine laboratory practice into a sophisticated research subject. As a result, not only did the endotoxin protocol become part of the NCL assay cascade¹⁹ and a screening method for all particles submitted to the NCL, her experiences working on the interference problem also stimulated the design of more immunology-based *in vitro* assays in the NCL cascade. Dobrovolskaia created a connection between nanoparticles and immunology by using endotoxin, a very common substance found in almost every received sample, as a proxy to consolidate this relationship. In so doing, she contributed substantial content to the practice of “nano-immunology” in the NCL.

Dobrovolskaia's story shows that the disciplinary priority suggested in the FDA's preclinical guideline—that chemistry and toxicology should be considered at an earlier stage of drug development than immunology—was reversed at the NCL. This indicates that the practice of interdisciplinarity was context-dependent. It heavily relies on intense social negotiations among the lab members in order to achieve a given mission. As Dobrovolskaia indicated, “I wouldn't be able to recognize nanoparticle interference on my endotoxin assay if I wasn't working side by side with toxicologists and chemists. We sometimes fight with each other on whose assays go first to screen the submitted particles, but it is by these back and forth confrontations I learned how to defend and modify my assays to fulfil the collective goal.”

Through reinventing the meaning and usage of the endotoxin assay from a routine test to a collaborative research subject, Dobrovolskaia successfully convinced her team that nanoparticle-induced immune effects should be considered earlier in the process of

nanodrug development and that the testing protocols should be incorporated into the NCL assay cascade. As a result, this young immunologist, who joined the NCL with no prior knowledge of nanotechnology, found a way both to make nanoparticles visible in the immunological world and make her professional position recognizable in the social world.

Tensions between academic, industrial, and translational science—Over time, NCL scientists gradually realized the ineffectiveness of using their original disciplinary labels to define their roles in the laboratory. But they refused to use “nanotechnology” and “nanoscientist” to categorize their expertise. Dobrovolskaia made an interesting statement regarding her professional identity:

I won't call myself a nano-immunologist since no such field exists at this moment.
I identify myself as an immunologist with experience in nanoparticles, since I was trained in immunology and that discipline is where my expertise lies.

Dobrovolskaia's ambiguous self-portrait illustrates her personal struggle between her past academic training and her current translational research in a government-owned laboratory. It thus indicates another dimension of interdisciplinarity in the translational context: the tension between academic, industrial, and translational science.

Despite internally the NCL scientists adjusted their original disciplinary training tuned themselves into the mode of highly interdisciplinary team work, a lot of time they still faced the challenge from their academic or industrial collaborators who carried distinct perspectives on what translational nanomedicine should be. These external pressures had great impacts on the experiment design and content the NCL produced, as the mission of the lab was to “work with”, not “compete with” their clients. It further suggests that to fully understand how interdisciplinarity was performed in the NCL, we need to situate these micro-level practices in the broader social and political arena where different stakeholders interests were negotiated and contested.

The promotion of the NCL's endotoxin test from the lab to other research and regulatory domains provides a vivid example to reveal the tension in translation. The NCL viewed this assay as a bridge connecting bench science and the bedside medicine, as it helped to select the right candidates from the pool of academic nanotechnology for further preclinical characterization. However, this view was not shared by most of the NCL's collaborators. Most university PIs who paid more attention on the novelty of nanoparticles tended to overlook this background substance. Even the NCL listed endotoxin measurement as a sterility test to make sure the “cleanness” of nanoparticles, materials scientists who performed the synthesis were still confused when they were informed that their nanoparticles were contaminated with high levels of endotoxin. From their experiences if every procedure was taken in cleanrooms where level of contamination can be reduced to few particles per cubic meter, their nanoparticles should be very “clean”. In addition, for many academic labs which used graduate students instead of professional technicians to conduct countertop synthesis, NCL's endotoxin report always created tensions between the lab and its university collaborators due to their different criteria of quality control of sample preparation and labor training. Academic researchers argued that what really mattered were the nanoparticles themselves and that the rest of the system (including endotoxin) should be a future problem for companies who might license the technology for commercialization.

Pharmaceutical companies viewed the endotoxin test from a different angle. Most drug manufacturers were very good at validating the bacterial endotoxin test for their products. Nevertheless, their knowledge about endotoxin focused more on how to eliminate it through standard GLP measures such as sterile injected water, proper reagents, and well-disciplined personnel, but less on treating it as a research subject. For these experienced companies, the

real challenge of nanodrug invention was to find the right nanoformulation to enhance efficacy and reduce toxicity; endotoxin was just an easily-resolved issue separated from the nanoformulation that most companies did not even bother to mention it while interacting with the NCL.

The FDA's attitude was crucial, as it dictated the evaluation of nanodrugs. As a regulatory agency which reviews thousands of products, the FDA tends to provide a general direction rather than specific instructions to explain its regulatory principle. According to its *1997 Bacterial Endotoxin Test Guideline*, any LAL technique can be used to test endotoxin. And in many practical situations, the gel clot method is still the favored assay.¹⁹ This approach was not consistent with NCL's experience that these three techniques were not interchangeable and had to be carefully selected based on the type of nanoparticle formulation. However, from a regulatory viewpoint, changing the existing rule requires not only significant evidence, but also the consensus of industry to make the guideline applicable. Because the interference between nanoparticle and endotoxin was only reported by NCL scientists, the FDA did not use it as its regulatory reference.

The diverse interests of the collaborators and scepticism of the NCL's endotoxin assay raised doubts about the NCL's role in assisting drug developers to carry their nanoparticles into clinics. Clients and collaborators wondered why they didn't detect the same level of endotoxin as reported by the NCL; they framed the problem in terms of the lab's measurements rather than their products. When informed that their nanoformulations were contaminated by endotoxin, they wondered why the NCL didn't choose the technique that showed no endotoxin, since the FDA's guideline allowed the proof from any of the three techniques.

Doubts from these sophisticated collaborators provided an early "trial by fire" for the NCL. In addition, the lab's ambiguous social status--it was neither a university-based laboratory devoted to research-driven science, nor a regulatory agency with legal authority, nor a profit-making organization that could spend all its resources solving the endotoxin problem for one specific nanoproduct--made establishing its credibility even more difficult.

We are known as a team, not as individuals!—The challenge that the NCL scientists encountered can be viewed as a general issue in building the interdisciplinary expertise—how could one claim to be an expert when he/she knew less about one field comparing with other experts in that field although he/she might know more in other fields. Particularly in the translational setting where all the players were either serious biotech companies who have put huge investment on their products, or reputational academic research teams selected by the NCI, finding a way to establish a credible professional identity at the nexus of universities, industry, and government became the NCL's primary task, its institutional ethos, its "rule of survival."

This had been McNeil's intention at the outset, but the principle proved much more difficult to implement in practice, as NCI required the NCL to act as a "helper" rather than a "competitor", in order to reduce nanodrug developers' resistance of submitting their particles and revealing their intellectual properties to the NCL. As a result, NCL was explicitly instructed to avoid producing scientific papers, patents, or anything that could help the lab to establish their credibility in a more direct way.

For this fledgling laboratory, credibility thus had to be derived from collectivity, not competitiveness. During the first three years, he and "the NCL trio" established a very close professional bond. They discussed experiments, published data, and attended meetings and conferences together in attempting to frame the NCL as a well-unified and highly-integrated

entity instead of just a center hosting various individual projects. Nonetheless, the real challenge was internal management. Creating such a team proved a painstaking process, since myriad details had to be coordinated. Tim Potter, a senior technician and one of the first hires, recalled hours-long discussion of “seemingly” trivial matters during group meetings:

The first two years were a nightmare, we could not understand each other’s language; we did not know how to listen and talk to get ideas across. We argued about almost everything, even how to name the nanoparticles—whether to name them by numbers, by particle types, or both? What about different batches of one particle? What about if each group has to dilute their samples to suit the requirement of their instruments...

Behind these simple questions lay the inertia of disciplinary tradition. The process of selecting the proper measurement unit was instructive. Researchers engaged in prolonged discussion over a consistent format expressing the concentration of testing samples: biologists relied on the pipette as a tool of quantity measurement, and so preferred volume concentration (ml/l); chemists tended to use the electronic mass scale, and so were more comfortable with mass concentration (mg/g). Although theoretically these two expressions are mutually convertible, in practice their use was guided by tacit disciplinary knowledge.

Such subtleties may lead to insurmountable boundaries. As “conventions,” they are easily ignored, difficult to identify, and impossible to be judged by logical methods. However, the NCL staff had no choice but to make Interdisciplinary collaboration work. For university researchers, this approach might be advantageous, but was not obligatory. Yet for a contractor assigned to perform interdisciplinary research, this was a serious issue. As Christopher McLeland, the lab’s technician manager, remarked memorably, “We were like a bunch of sailors on a small boat, sailing on the big ocean with no clear clue about where to go; the only thing we knew is that if we don’t collaborate, the boat will sink and no one benefits.”

Leadership played a crucial role in navigating the boat in the right direction. Expected to achieve the mission of translation in five years, McNeil intentionally created a very strong inward-looking working environment for the NCL members to prevent distractions and assure productivity. Military-style terminology (“action,” “mission,” and “prioritization”) was constantly invoked in this managerial plan. With more than twenty ongoing collaborative projects characterizing distinct types of nanoparticles, McNeil requested that each be assigned to a scientist as a given “mission;” technicians received “prioritized action,” meeting weekly to negotiate and decide priorities and discuss progress. In short, the practice of interdisciplinary collaboration in the NCL occurred not by amorphous interaction, but via a social order allocating labor, materials, information, and research direction.

Nevertheless, maintaining a focused, ordered, but flexible working relationship required not only a chain of command, but highly coordinated action at the micro level. Designing which experiment should run first, what quantities of nanoparticles each group could use given the limited submitted quantities, and correlating data and representation between chemistry, immunology, and toxicology were tedious and contingent processes determined not by administrative discipline or scientific argument. Instead, the NCL researchers had to cultivate a collective spirit to constantly tune their discipline-based knowledge and skills to accommodate others’ needs. There was no fixed permanent hierarchy of disciplines in the NCL; toxicology did not always trump chemistry, just as chemistry did not always dominate the research direction. Rather, the NCL members deliberately constructed a dynamic pattern of interdisciplinarity practice based on the projects they received and the consensus

negotiated on a weekly basis. It was this chain of coordinated action—"the rule of survival"—that informed the technical content of nanoparticle characterization, professional nanobio expertise, and the NCL's institutional identity in translational nanomedicine. Cultivating the coordinated collaborative ethos was so central to McNeil's strategy that he even created a position called "data coordinator," one university laboratories usually do not have. All e-mail exchanges with clients, all signed documents, and all data produced by each division (measurements, papers, reports) had to be reviewed, edited, and distributed by the data coordinators in the name of NCL, not any individual.

NCL's strong collective identity was created not just for the purpose of responding to external pressures. It also became the source of professional identity. Although designated as a national center of translational nanomedicine, the lab was located away from the NIH main site at the Army's heavily-guarded Fort Detrick. The multiple roles NCL scientists had to play (government contractors interacting closely with other government agencies; researchers collaborating intensively with university PIs on highly research-driven projects; industrial partners working closely with biotech companies and handling proprietary business information) ultimately granted them a special social status, moving them away from their original academic discipline and differentiating them from their NCI intramural colleagues and their industrial collaborators. All these factors allowed members to generate strong empathy and mutual reliance on each other, which later became a source of confidence. As Patri described:

We all know that if we three groups separate from each other, we cannot compete with those labs which have spent twenty years in immunology, chemistry, or toxicology. Our niche is that we are forced to collaborate due to the NCI's policy and we have to be successful since our jobs depend on not losing this contract. In these years we learned how to combine and synergize each other's expertise through measuring over 200 particles submitted by our clients. There is no individual identity, only a collective NCL identity.

Interdisciplinary expertise: a boundary existence

This highly coordinated group dynamic ultimately stabilized the NCL's boundary existence at the interface of the university, industry, and government. Dobrovolskaia illustrated this point:

I gradually realized that I may not be the best immunologist, but I found my uniqueness. The best immunologist wouldn't be able to pick up the immunology we practiced in the NCL, since our work requires not the best disciplinary training, but interdisciplinary skills...standing among the government, industry and academia, which used to be a negative to me, is where my strength comes from.

Finding a way to maintain this marginal but essential existence was the most important lesson learned by the NCL scientists in developing interdisciplinary expertise. As the case of endotoxin shows, social confrontation was part of the process of establishing this profession, as institutions often rejected the boundaries the NCL set in its collaborations. With no prior training in nanomedicine, NCL scientists crafted their interdisciplinary expertise through highly coordinated laboratory practice. For them, "nanotechnology" was no longer a conceptual debate, a political discourse, or hype, but particles and protocols they tested daily in routine social interactions with colleagues, clients, and collaborators.

From this perspective, what NCL produced was not only characterized nanoparticles but also social interactions that supported the credibility of its scientific characterization. Interdisciplinarity practiced under the translational setting, thus is more than knowledge exchange between different well-defined disciplines; instead, disciplinary boundaries are

constantly redrawn and renegotiated during the process of exchange based on various institutional interests.

Conceiving the cultivation of interdisciplinary expertise as a socio-political boundary-making process further clarifies training issues in nanoscience education. Although industrial representatives sometimes frame this problem as one of “a shortage of nanotech talent,”²⁰ the story of the NCL shows that the process of forming interdisciplinary nano-expertise required carefully designed organisations to establish a disciplinary order capable of focusing resources, knowledge, and labor to bear on specific problems without being diverted by diverse interests.

The socio-political dimension of building interdisciplinary expertise in nanotechnology raises the question of scientific accountability, the problem of how cross-boundary activities are justified and evaluated. Current metrics evaluate “final products” (numbers of papers, patents, citations, and science and engineering personnel) and cannot capture the dynamics, content, and crucial “practice” of realizing abstract concepts in a deliberately constructed social infrastructure. More collaboration between science and social science in documenting and analyzing laboratory practices at different nanotechnology centers I believe, can compensate for this shortcoming. Nanotechnology under this framework is not just a technical term, an impersonal policy claim, but social and human struggles about how individuals and institutions reorganize themselves to catch up with policy changes. These empirical studies thus offer a foundation for better judgements and realistic expectations in planning nanoscience policy and education.

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Figure 1.
The operational principle of the NCL (Source: NCL)

Figure 2. Schematic diagram of how the endotoxin and the interference between endotoxin and nanoparticles formulation is studied in the NCL.