

COMMENTARY

I-Corps at NIH: Entrepreneurial Training Program Creating Successful Small Businesses

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This Commentary highlights the 36-month longitudinal study following the pilot cohort of the Innovation-Corps (I-Corps™) at the National Institutes of Health (NIH) program, which was launched in the fall 2014. Given the long timeline to commercialization for life science technologies, this interim evaluation provides an encouraging snapshot of I-Corps participants' progress. As these companies and their technologies mature, I-Corps learnings are applied to downstream company research and product lines, indicating that this entrepreneurial translational training provides lasting value for researchers.

It is late in the afternoon in the summer of 2016 and physician-bioengineer and entrepreneur Thomas Neumann, MD, and his team at Seattle based Nortis (an NIH Small Business Innovation Research grantee) just experienced an “A-ha!” moment after speaking to an industry expert about the company’s technology. Neumann and his team have learned that their technology, which could provide a fast and accurate test to gauge the quality of stem cells for research purposes, while being a useful tool, did not garner the commercial interest that the Nortis team had anticipated. The researchers and experts they interviewed stated that even though the Nortis technology potentially was an improvement over the current test, they did not see a need for the Nortis technology at the moment. Armed with new information, what was Nortis’s next step?

ENTER THE NIH SMALL BUSINESS INNOVATION RESEARCH I-CORPS PROGRAM

What if biomedical entrepreneurs and small businesses like Nortis could get training to gain a “real-world” market perspective on their discoveries and innovations and to cultivate important strategic alliances? Several NIH Institutes and Centers explored what techniques and learnings could help provide their Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) grantees with the necessary tools to understand where, or if, there is a potential market for their technology.

Through the Congressionally mandated SBIR and STTR programs, the Federal government sets aside funding from its major agencies to fund research and development as

well as a range of other activities to advance promising technologies toward commercialization. The I-Corps at the NIH program brings together phase I SBIR/STTR awardees and biotech domain experts from the therapeutic, device, diagnostic, and digital health sectors to provide real-world entrepreneurship training. I-Corps teaches scientific teams customer discovery techniques and trains them on how to develop scalable business models and identify commercialization paths for their NIH-funded small businesses.¹ This Commentary reflects on the process of adapting the I-Corps program for NIH SBIR/STTR grantees and the programmatic impact on translational science.

It should be noted that the NIH provides complementary resources for small businesses: the C3i program² serves phase I awardees, and the Commercialization Acceleration Program³ is for phase II awardees. C3i and Commercialization Acceleration Program are 6-month to 9-month programs providing mentoring and pitch coaching from domain experts, whereas the 8-week I-Corps at NIH program provides training in “customer discovery” activities to researchers to impart entrepreneurial skills. The I-Corps curriculum is currently available at agencies across the Federal government in coordination with the National Science Foundation (NSF); however, the NIH program is the only Federal I-Corps syllabus tailored for the life science sector with portions of the curriculum addressing regulatory, reimbursement, and intellectual property strategies.

WILL I-CORPS REALLY WORK FOR THE LIFE SCIENCE SECTOR?

The I-Corps curriculum first delivered by the NSF in 2011 was based on (i) the Lean Launchpad classroom syllabus developed by Bay Area serial entrepreneur Steve Blank⁴; (ii) Customer Development, the practice of obtaining customer insights to generate, test, and iterate ideas for products and services through interviews (i.e., customer discovery); (iii) the agile development methodology authored by Eric Ries in “The Lean Startup”⁵; and (iv) the Business Model Canvas created by Alexander Osterwalder.⁶ In the first iteration of the NSF I-Corps, the program was designed for academic researchers (at the precompany stage) in fields ranging from ecology to computer science. At its core, the I-Corps program is a structured method by which entrepreneurs

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can test and refine their business models. Initial assumptions around a proposed business model (i.e., a technology's value proposition, product-market fit, etc.) are tested by conducting over 100 informational interviews with key stakeholders and potential customers, which include regulators and payers within a given technology's ecosystem. Using information from these interviews, I-Corps participants are expected to complete a Business Model Canvas (Figure 1) outlining their business proposition, customer channels, and market segments. The content of the Business Model Canvas may validate or invalidate the initial hypothesis, in which case a pivot in the business model may be appropriate, as in the case of Nortis.

When I-Corps was initially designed, it was not thought to be a good fit for life sciences technologies due to the recognized and perceived complexities around regulatory affairs in health technology and the limits for established companies to pivot. However, after observing the early success of the I-Corps program at NSF, the NIH recognized the potential for a modified version of I-Corps to positively impact the development of early stage biomedical businesses. Although phase I SBIR and STTR grants are designed to foster proof-of-concept or feasibility work and phase II grants support continued research and development for a technology, it is widely recognized that the "Valley of Death" between research and development and commercialization in the life sciences field is a huge chasm. I-Corps at NIH aims to equip companies to anticipate the barriers (e.g., adoption, regulation, and finances) surrounding early stage technologies.

Toward that goal, the NSF and NIH collaborated to modify the I-Corps curriculum to better address the needs of biomedical companies. In the NSF I-Corps program, academic teams are comprised of a research Principal Investigator, an Entrepreneurial Lead (e.g., student or postdoctorate), and

a business mentor. The NSF team's technology or innovation may not be fully developed but rather a nascent idea. By contrast, the NIH program is working with small businesses that have somewhat more mature ideas and technologies. Participating companies enter the program with three-person teams: C-Level Corporate Officer (e.g., CEO), Principal Investigator, and Industry Expert. By design, the NIH program's team structure incorporates the titles and roles of individuals with decision-making authority within the company.

During the course, these teams receive training to effectively conduct Customer Development interviews. Each week focuses on various aspects of the Business Model Canvas (Figure 1), beginning with Value Propositions and Customer Segments. Teams conduct in-person interviews, distill key learnings from the conversations, then present them to the class and receive feedback from the instructors. Throughout the course, the continuous process of conducting informational interviews allows the teams to simultaneously refine their business models and explore their technology ecosystem. The focus for each week's interviews progresses through the right-hand side of the canvas, to the left-hand side, and culminates with the bottom components of Cost Structure and Revenue Streams.

Because the NIH cohorts address life science technologies, it was equally important that the NIH teaching team reflect both domain expertise in the life sciences (e.g., therapeutics, medical devices, diagnostics, and digital health areas) and competency with delivering the I-Corps curriculum. A key resource for building the teaching team is the National Innovation Network, a national pipeline of collaborators, mentors, and partners that was developed by the NSF. I-Corps at NIH learnings are applied directly to each company's technology or product under development, so the teams are vested in practicing what they learn during

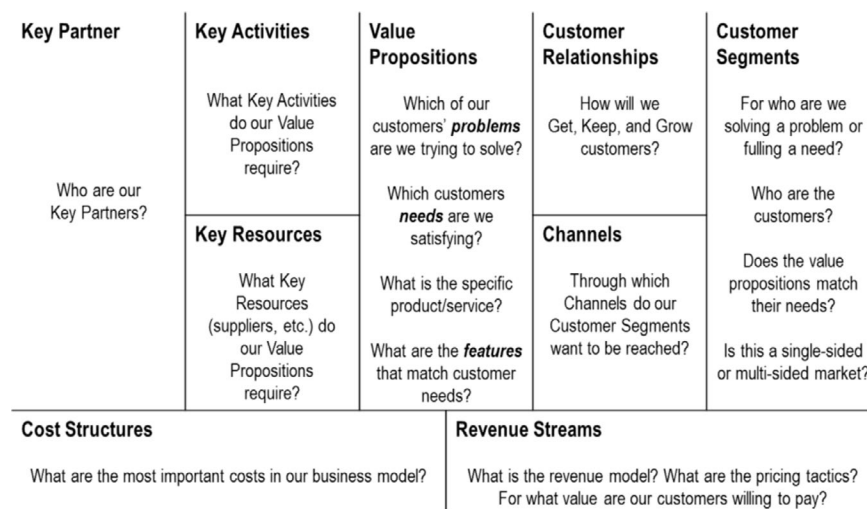


Figure 1 The Business Model Canvas is a framework tool utilized to help Innovation-Corps (I-Corps) teams understand and describe the ecosystem surrounding their potential product. The right-hand side of the canvas focuses on the customer and the left-hand side focuses on the business. The I-Corps curriculum addresses each of the nine components, starting with Value Propositions and Customer Segments (right side) and progressing later to Revenue Streams and Cost Structures (left side). Image adapted from Strategyzer AG. The Business Model Canvas, Alexander Osterwalder, and Business Model Foundry AG, <<https://www.strategyzer.com/canvas/business-model-canvas>>, CC BY-SA 3.0 <<https://creativecommons.org/licenses/by-sa/3.0/>>.

their customer interviews and making necessary changes and pivots. These learnings are not restricted to the duration of the course but are applied throughout their entrepreneurial careers. These teams are also being taught how to cross the threshold from the clinical or academic medicine settings to those of the world of business and eventual commercialization:

“We have a very complex market that we deal with in life sciences,” says Bob Storey, an I-Corps at NIH instructor and medical device domain expert. “There are lots of stakeholders, lots of conflicting and complimentary needs in the marketplace. I-Corps at NIH provides the opportunity to look at the entire patient management process from start to finish. It helps [the teams] see how the ecosystem overlays and understand how they’re going to either disrupt or add efficiency to that process. That complexity in the market is what we really dive into in this I-Corps process.”

MAKING CONNECTIONS

A defining feature to the I-Corps program is the customer discovery process. For many teams, conducting those first 100 interviews is just the beginning, and the rippling effects of network building are not seen until after the 8-week course ends. For team GigaGen, the process of conducting 163 interviews during the pilot cohort in 2014 was critical to differentiating everyone from end users to buyers and decision makers. GigaGen’s platform provides a service for the custom generation of personalized or rare antibodies. Jennifer Keller, GigaGen’s Head of Marketing, filled the role of Industry Expert and reflected, “When we first started I-Corps, I thought our customers would be doctors. As we went through the process, we talked to doctors, we talked to patients, we talked to manufacturers, we talked to regulatory specialists—basically everyone across the whole touchpoint of how our business would be delivered.” By July 2017, the team’s investment in understanding their ecosystem had paid off in a big way. The company had secured a multimillion dollar private financing and co-development deal with a strategic partner. David Johnson, GigaGen CEO, also noted that the government’s investment in these programs brings dividends, “Normally, a company might raise tens of millions of dollars to achieve such a milestone, but we only spent \$225,000 of NIH money.”

LEAVING THE BUILDING

I-Corps participant Raj Singh is no stranger to getting out of his comfort zone. Formerly a research assistant professor at the University of Alabama at Birmingham, Singh licensed his invention and created spin-off company Vivo Biosciences (VBI). As VBI President and CEO, Singh successfully navigated the company through multiple SBIR and STTR grants and contracts to develop a three-dimensional material for growing cells and tissues for research use. As

part of the pilot I-Corps class of 2014, Singh and his team focused on identifying key partners and activities necessary to translate their technology to market. As a result of those customer discovery activities, VBI increased its network of connections and ultimately was acquired by LifeNet Health of Virginia in 2017 with a strategic focus on expanding the technology to oncology, personal diagnostics, and regenerative medicine applications. Singh reflects:

“At Vivo Biosciences I did that ‘multi-hat’ role all these years—but now I’m a Chief Scientist at LifeNet Health. I have come from a 5-employee company to a 1000-employee company. LifeNet has internal R&D funding programs, so I’m not going to need to apply anymore for SBIRs. I’ve graduated from SBIRs, and I’ve found a new strategic partner via mergers and acquisitions (M&A). Moreover, I am continuing with my scientific pursuits, and applying the I-Corps practices to my innovation-driven research ideas.”

In the case of Nortis, Neumann and his colleagues were also surprised to discover that they needed to adjust their product plan to meet customer needs because there was little interest in the product they were proposing. Nortis had planned to use their tissue chip technology to create a human tissue environment that allowed them to study stem cell quality, but after interviewing over 100 potential customers they learned that there would be no market for their product. In conversations with their I-Corps instructors and their NIH Program Officer, Nortis researchers discovered that there was a need for a tissue chip with a stem cell-based model to study kidney function. When Nortis polled potential customers again, they found a very different response: 99% of interviewees were interested in such a tissue chip.⁷ The new product would deliver a steady source of stem cell-derived kidney cells and allow researchers to test the effects of drug concentrations on the kidneys⁷—a very important pivot for the company. The Nortis case study is a theme observed repeatedly in I-Corps at NIH with platform technologies. There are many possible directions to pursue, and I-Corps helps teams focus and make a data-informed decision prior to pursuing their chosen option.

EMPOWERING ENTREPRENEURS

Because the leading reason for startup failure is lack of market need, validating or verifying a technology’s product-market fit should be a top priority for businesses and their investors. However, for entrepreneurs in the biomedical arena, such skills and learning that are critical to translating innovations to patients are not taught in medical school. After running seven successful cohorts, early analyses have shown that I-Corps at NIH fills a need for small businesses with early stage projects and provides biomedical entrepreneurs with the tools necessary to evaluate and translate technologies in a market ecosystem. Teams that conducted customer discovery interviews report a range

of lessons learned: (i) how to pivot to address new market opportunities or new customer segments and (ii) how to pivot because a change was needed in the product's value proposition. Specifically, for these NIH SBIR/STTR grantees, some of the pivots necessitated refinements to their business model, which also needed to be captured in their NIH SBIR/STTR phase II grant submissions. From the NIH perspective, we believe this is one of the most important outcomes of program—getting out of the laboratory and meeting with customers (which include regulators and payers) sometimes necessitates a pivot that creates a translational path for their innovation that can ultimately benefit patients. Teams that have gone through the training also observe other benefits in the later stage of their small businesses' development.

To assess the impact of I-Corps on companies and entrepreneurs, a combination of market analyses, electronic surveys, and telephone interviews were conducted 3 years postcourse with pilot program participants. I-Corps strengthened the companies' management teams to help them expand networks, identify new commercialization opportunities, and add new personnel (Table 1). Of the 19 teams that participated in the pilot, 13 respondents provided feedback to evaluators (12 respondents plus 1 partial respondent). I-Corps led to synergistic and strategic partnerships for eight responding teams. Market data for all teams show that the companies in the pilot cohort raised more than \$78M in funding after I-Corps (> \$53M in non-Federal funds). After considering opportunities for pivots and validated market needs, 18 patents related to the I-Corps technologies were filed or issued and two companies reported revenue generation from licensure. Academic pursuits remained active, as 24 publications resulted from development of the I-Corps supported technologies. Two companies had a spin-off that was a result of their I-Corps technology; one company was acquired; and 108 new jobs (32 full-time, 17 part-time, and

59 contract workers) were added to the workforce since 2014.

LESSONS LEARNED AND NEXT STEPS

The greatest revelations witnessed by the NIH are that the customer discovery process and I-Corps curriculum do work for life science technologies with teams from small businesses. The NIH approach to I-Corps is an experiment in pivoting the focus of the program from academic teams to established small businesses. Through customer discovery activities (i.e., interviews with past participants and others), the NIH has validated the positive impact of I-Corps on small business grantees and continues to offer the program with an eye to expand to non-SBIR teams.

Quantitative lessons learned reveal that I-Corps at NIH contributed to the progression of technologies toward commercial products and services, and also had important economic impacts in job and company creation. Qualitatively, completion of the 8-week course serves to educate researchers and empower entrepreneurs. In reflecting upon their experiences during I-Corps, course graduates recall a valuable learning experience in applying I-Corps principles to refine their work, evaluate their target clinical population or research focus, and learn how to best translate their discoveries by proactively reaching out to the right people—whether it be an experienced CEO or a strategic partner.

The most impactful revelations are less calculable but rather cultural. The sustained practice of conducting Customer Discovery persists years beyond the I-Corps course, as the mindsets shift within small businesses in approaching translational research. Although many commercialization assistance programs provide some measure of mentorship, I-Corps at NIH stands out in building an enduring ethos for entrepreneurs.

For Thomas Neumann, the Lessons Learned from I-Corps continue to help push Nortis's innovations forward into the next as well as the "final frontier":

"We knew we would never get a perfect product without understanding the user space. During I-Corps, we talked to so many people and really learned about how our technology could address the unmet needs of potential customers. Back in 2012, we had a prototype device, but it wasn't until after going through Customer Discovery that we were able to launch our fully commercial ParVivo product in 2016. The principal idea behind the chip did not change, but the devil was in the details.... In addition to refining product value propositions, at Nortis we've identified partners and avenues for new research activities. We've launched collaborations in partnership with NIH and NASA, and recently Nortis chips were selected for experiments on the International Space Station. So, it's not just people getting out the building—it's the technology, too."

Table 1 Longitudinal metrics collected from pilot I-Corps participants

Activity ^a	Metrics
Attributed I-Corps activities and network to synergistic and strategic partnerships	8 companies
Follow-on funding secured	\$78M (more than \$55M in non-Federal funds) ^b
Patents issued	18
Revenue-generating licensures	2
Publications based on I-Corps supported technologies	24
Spin-off company generated	2
Acquisition/merger	1
Jobs created	108 new jobs (32 full-time, 17 part-time, and 59 contract workers)

I-Corps, Innovation-Corps. ^aCompany Activities, with the exception of *Follow-on funding secured*, collected from 13 respondents (of 19 teams) ranged from December 2014–April 2018. ^bFunding data for all 19 teams sourced from Pitchbook.

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