



Teaser The Stanford SPARK program is an innovative academic–industry partnership for translating academic biomedical research. This article highlights SPARKs model, which can provide a template for other universities and institutions interested in de-risking and facilitating the translation of biomedical research.



Accelerating biomedical innovation: a case study of the SPARK program at Stanford University, School of Medicine

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Translating academic medical research into new therapies is an important challenge for the biopharmaceutical industry and investment communities, which have historically favored later-stage assets with lower risk and clearer commercial value. The Stanford SPARK program is an innovative model for addressing this challenge. The program was created in 2006 to educate students and faculty about bringing academic research from bench to bedside. Every year, the program provides mentorship and funding for approximately a dozen SPARK ‘scholars,’ with a focus on impacting patient lives, regardless of economic factors. By reviewing the detailed structure, function and operation of SPARK we hope to provide a template for other universities and institutions interested in de-risking and facilitating the translation of biomedical research.

Introduction

In this case study we profile the structure and impact of the SPARK Translational Research Program at Stanford University School of Medicine, a partnership between academics and individual experts in industry dedicated to overcoming the hurdles of translating academic discoveries into drugs and diagnostics that address unmet clinical needs. SPARK’s underlying philosophy is that academia has an important part to play in decreasing the time and cost of developing new therapeutics and diagnostics that benefit society. By studying this innovative partnership, we aim to provide a template for other universities and academic medical centers interested in launching their own translational medicine accelerators.

Academia — defined here to include nonprofit universities and scientific research institutions — is a major stakeholder that can play an important part in progressing medical development. The interactions between academia, the pharmaceutical industry and regulatory authorities are of paramount importance for ensuring the quality, efficacy and safety of drugs in clinical and

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commercial use. New models, such as that of SPARK, can facilitate partnerships among stakeholders and accelerate the commercialization of biomedical research.

Translational medicine background

The past few decades have brought tremendous breakthroughs in the fundamental knowledge necessary for understanding, preventing, diagnosing and treating many diseases—breakthroughs such as human genome sequencing, immunotherapies and gene therapies. However, the process of translating new discoveries into products severely lags behind the pace of discovery. The transition period when a developing technology is seen as promising but is too new to validate its commercial potential and unable to attract the necessary funding for its continued development has been coined the ‘valley of death’ [1]. Investors are reluctant to bear the full cost of entering the valley of death, owing to the high risk and historically low return on investment for early-stage R&D. Consequently, only 12% of active preclinical assets reside in large pharmaceutical companies [2], and 80–90% of biomedical research projects never progress to trials in humans [1].

Translational medicine is a growing field, focused on addressing this gap between medical discovery and commercialization [3]. Within the past decade, the National Institutes of Health (NIH) has made translational research a priority, forming the National Center for Advancing Translational Sciences (NCATS) and launching the Clinical and Translational Science Award (CTSA) program in 2006. Additionally, at least three journals are devoted to furthering the field: *Science Translational Medicine*, *Journal of Translational Medicine* and *New Horizons in Translational Medicine*.

The risk-averse attitude in industry opposes the culture of academia, where risk-taking is often rewarded by promotion and recognition. The essential role of academic institutions in commercial drug development calls for a better funding mechanism to reward academic contributions and a more efficient academic–industry collaboration. Although this process is complicated by the fact that academic and commercial interests are not always aligned, an evolving hybrid drug discovery model can be useful in mitigating risks and increasing productivity. SPARK provides one such example (Fig. 1).

The origin and mission of SPARK

The SPARK program was founded in 2006 by Professor Daria Mochly-Rosen, who came up with the idea while serving as Senior Associate Dean for Research in the Dean’s Office of Stanford University School of Medicine. Two years before her appointment, she had taken a leave of absence from Stanford to found her own company, KAI Pharmaceuticals, which was subsequently acquired by Amgen in 2011. From her experience with KAI, Dr Mochly-Rosen found that bridging the translational research gap was extremely challenging and not necessarily an intuitive process for academics. Recognizing the need for education and funding to help her academic colleagues translate their research into therapies, Dr Mochly-Rosen created SPARK with crucial early backing from the Dean’s Office of the School of Medicine, which allocated the funds to launch the program and continues to provide financial support. Dr Mochly-Rosen then recruited Dr Kevin Grimes, an academic internist with drug development experience, to join her as co-director of the program. Now in its tenth year, SPARK offers training, support and mentorship to academic researchers to pursue basic research with potential medical applications. SPARK’s stated goal is ‘to move five to ten new discoveries each year from the lab to the clinic and/or to commercial drug and diagnostic development’ [4].

How SPARK operates

The SPARK program is centered on its researchers. Selected project leaders, called SPARK ‘scholars,’ receive ~US\$50 000 annually for two years, in addition to extensive educational mentoring from SPARK advisors. Every year, SPARK selects a class of 10–15 scholars that remain in the program for a two-year cycle. Since SPARK started accepting open applications in its fourth year, over 400 projects have been submitted for consideration in the program. The SPARK scholars are required to attend interactive weekly Wednesday meetings that include lectures from industry experts and project updates that occur on alternate weeks. Although funding is limited to the selected scholars, every university member is welcome to attend the Wednesday meetings and engage in educational sessions. Currently, ~100 individuals, including scholars, Stanford community members and SPARK advisor network members, attend regularly.

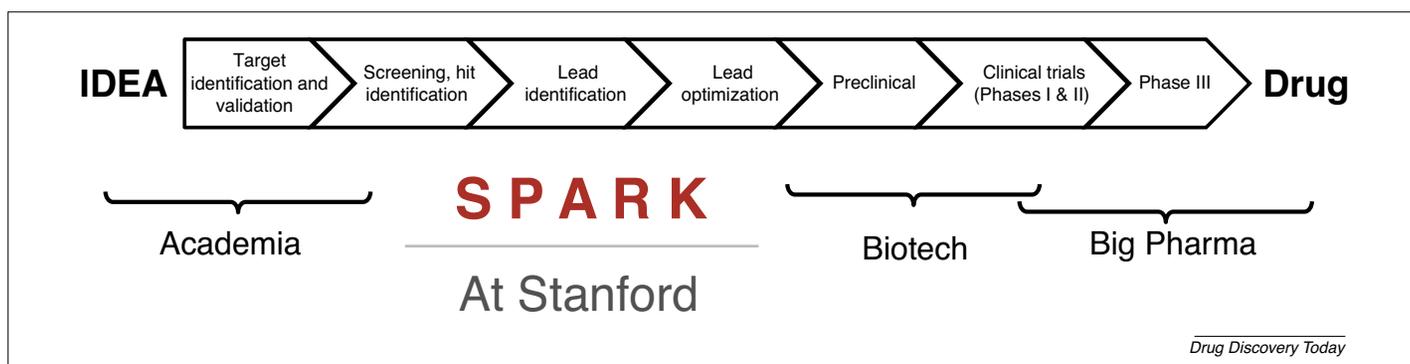


FIGURE 1

SPARK fills the gap between academic discovery and industry.

Throughout a scholar's SPARK tenure, funding is distributed as project milestones are met. Once a milestone is achieved, additional funds can be requested for the next stage of development. Any unused funds revert back to the general pool of funds, managed centrally by SPARK. Access to Stanford's infrastructure, facilities and resources helps to maximize use of the US\$50 000. One key to SPARK's success is its ability to tap into the medical school's resources, providing academic researchers with access to clinicians to better understand the clinical implications of their research.

A key element of the SPARK training is teaching investigators to think using a translational approach. The scholars learn to identify the unmet clinical need of the patient and to understand the problem in tandem with product development. In other words, they are trained to 'keep the end in mind' throughout the process. SPARK uses project management tools such as target product profiles and project timelines to help teams plan and identify key milestones, necessary endpoints and crucial decision points.

Management

The SPARK program, currently led by Drs Mochly-Rosen and Grimes, operates with a management team of five individuals that oversees communications with project teams, runs its weekly meetings, oversees SPARK funds and otherwise manages operations. Although the majority of the funds for SPARK comes from the Dean's Office, the program operates independently within Stanford University and is managed solely by the SPARK team.

The advisors

One of the most important keys to SPARK's success is the advisor network, thanks to its strength, expertise and engagement. Advisors volunteer their time to work with SPARK projects, attend the weekly meetings and participate in evaluating potential projects. They have no ownership or rights to any inventions or intellectual property from the program. As of 2016, SPARK had over 100 advisors with significant entrepreneurial or industry expertise in drug development, generally in a specific therapeutic area. On occasion, advisors are organized into working groups, focused on areas such as medicinal chemistry, biologics, financing and venture capital, business development and clinical trial design.

To alleviate concerns about the disclosure of scholars' research and assets at the Wednesday meetings, SPARK mandates confidentiality agreements for all attendees and has worked to create a culture of trust and sharing within the program. Advisors remain engaged because of their interest in the core science behind the projects and the opportunity to remain part of such a strong network of industry experts. Mentoring is an opportunity for these advisors to have an additional impact on drug development in a low-risk environment and continue to use the expertise and skills gained from their industry experience. Further, working with a mission-driven program dedicated to translational medicine offers an opportunity to help bring impactful products to market, which might not have been the primary focus of the advisors' former for-profit industry employers. The advisors' commitment to furthering scientific knowledge without financial compensation maintains the integrity of the process and the mission of the SPARK program.

Funding

The SPARK program is funded primarily through the Dean's Office within the School of Medicine, with additional support from nonprofit organizations and the NIH. SPARK receives no revenue from its projects. Since 2006, ~US\$7.1 million has been spent, covering staff salaries, scholars' research expenses and other program expenses. Additional funding for the program comes from the Children's Health Research Institute and goes toward research projects with a pediatric focus. It is a key element of the program to operate on funds that are not tied to commercial incentives. The program has always turned down funds from for-profit companies because of differences in incentives. Whereas for-profit companies are often driven by profitability, SPARK is primarily focused on addressing unmet medical needs. Accepting funding from for-profit companies such as big pharma could dilute the mission and create real or perceived conflicts of interest.

Project selection

A significant factor contributing to the SPARK program's accomplishments is the rigorous project selection process, conducted by a handpicked committee each autumn. The committee typically consists of the SPARK management team, two-to-three Stanford faculty members and a dozen SPARK advisors. The three primary criteria for successful applications are that the project addresses an unmet clinical need, uses a novel approach and has the potential for the SPARK program to improve its licensing and/or clinical trial prospects over the two-year cycle. Notably, commercial potential is not a factor in the selection process (See Supplementary material online for further details on the project selection process).

Program results and benefits

The SPARK program has a unique and rigorous success metric. A project is deemed successful only if it enters a clinical trial, is licensed or transferred to an existing biopharmaceutical company, or leads to the founding of a new startup. In the 10 years since SPARK was founded, 74 projects have graduated from the program. Of these, 24 were licensed to startup companies, eight were licensed to existing companies, four have been transferred to industry without licenses and 31 are in clinical trials (ten without licenses). Together, this amounts to a success rate of 62% (Fig. 2) (See Supplementary material online for an analysis of the unsuccessful or "failed" SPARK projects).

Additionally, although the SPARK project selection process focuses on unmet medical needs, the SPARK program generates significant follow-on grants and funding to support further research for Stanford. Thus far, SPARK has generated nearly US\$38.7 million in additional grant funding, ~4.95-times the amount provided by the Dean's office over the same period (Fig. 3). Because follow-on grants were generally received in the second year of SPARK participation, this multiple was calculated using a discount rate of 5% and a funding interval of two years.

Keys to success

The keys to SPARK's success include the strength of its structure and management, collaborative culture, focus on its mission and, in particular, its network of advisors. The combination of Stanford-affiliated researchers and industry advisors leads to a distinctive and necessary diversity of interests and experiences. Other pro-

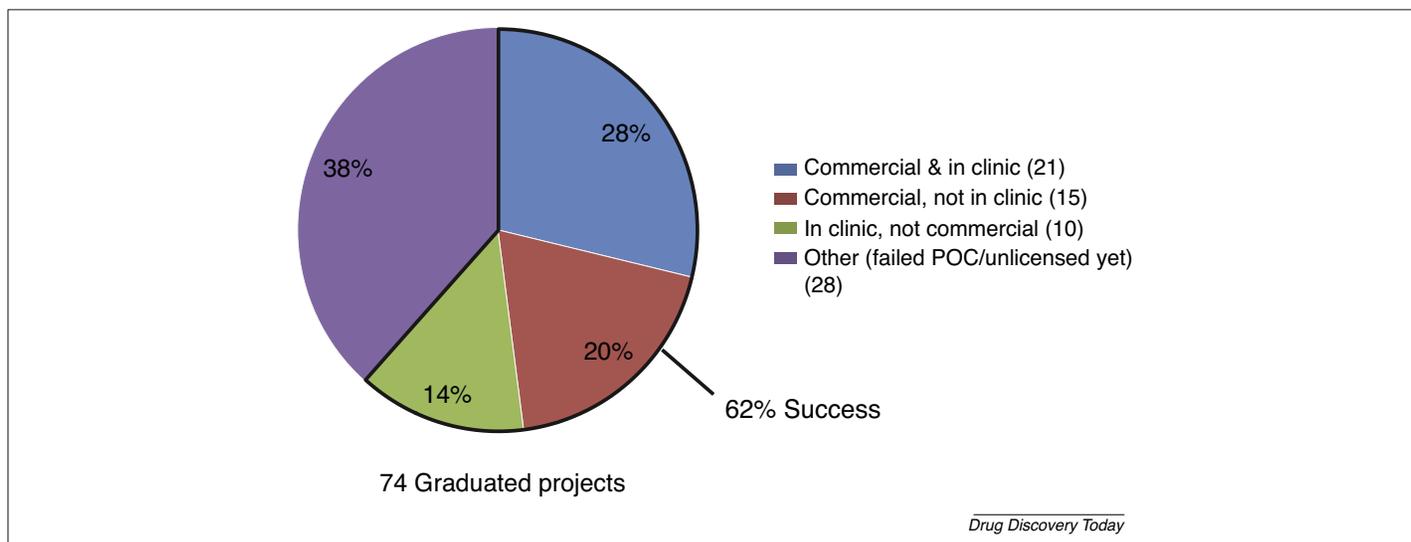


FIGURE 2

Distribution of graduated SPARK project outcomes.

grams comprising just academics could have a narrowed perspective, whereas programs that have a single or few advisors lose the checks and balances provided by a larger network. SPARK advisors receive no financial compensation; they remain involved with the program because they see value in SPARK’s model and mission.

Challenges and future plans

Financing

One major challenge for SPARK is to procure sustainable funding for the program. Currently, the program relies heavily on institutional funds, mainly from the medical school’s Dean’s Office, as well as grants from nonprofit and government agencies. The program takes no equity stake in projects, and receives no royalties from its projects’ revenues or license deals, because profiting from the projects’ commercial success would not align with SPARK’s core educational and social mission. As it currently stands, the program needs US\$2–2.5 million a year in funding. Ironically, according to the Dean’s Office, many donors find this too small of an investment. Going forward, ways that SPARK might finance itself include a long-term endowment or an annual allocation in Stanford’s budget.

To expand SPARK’s impact, the program’s founders would like to support projects further into the development cycle. Some projects need more funding to reach a value inflection point; for example, an antibody therapeutic cannot move forward without humanization of the antibody—an endeavor that costs much more than the typical SPARK investment of US\$50 000–100 000. However, expanding the program will require significantly more funding than the program currently deploys.

Institutional support

Another key consideration is that SPARK’s longevity relies on the continued partnership and support from the Stanford University School of Medicine. Programs such as SPARK need institutional buy-in, especially in the alignment of the broader university with their key values. For such a partnership to thrive, institutions cannot expect substantial revenues or rewards—although universities do benefit from increased success in commercializing intel-

lectual property. Institutions must recognize the significance of the less tangible benefits, such as the creation of a strong institutional memory and infrastructure. For example, Stanford University benefits from the successes and engagement of former scholars who find industry positions with the help of SPARK and continue to remain involved in SPARK.

Measuring success

Drug development and the translation of research is a lengthy endeavor, hence the long-term impact of SPARK is still unclear. Although SPARK’s current success metric matches the contemporary landscape, in moving forward SPARK will need to pinpoint the right metrics and implement the necessary processes to track the direct impact of its projects. Similarly, SPARK would benefit by measuring the impact of the indirect benefits of the program to the university, such as increased education and job placement in industry.

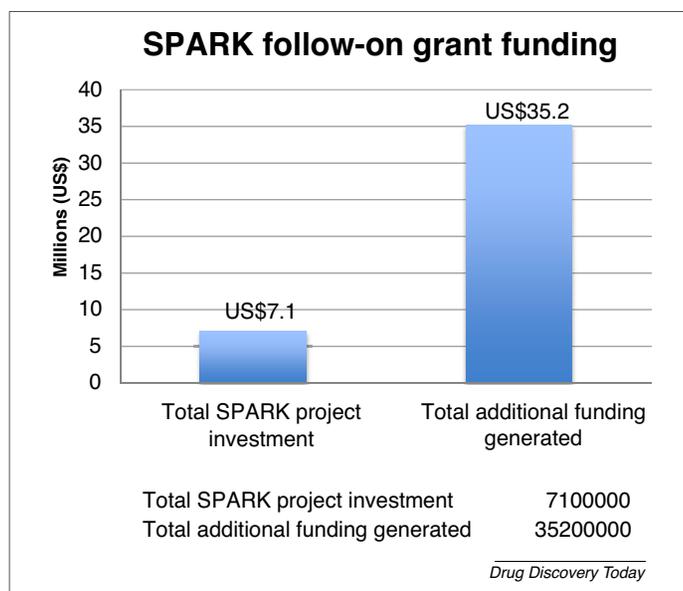


FIGURE 3

SPARK has generated significant follow-on grants from 2007 to 2015.

Replicating the program

In the recent decade since its launch, the program has learned many things about the challenges of drug development, some of them unique to academia. Projects are generally successful when physician-scientists can identify a strong medical need, and when they are based on strong science. Furthermore, a clear or identifiable pathway to patients is crucial for development.

SPARK has made significant progress in bridging the valley of death, but its scope is currently limited to Stanford. Although some might argue that SPARK is uniquely positioned to succeed given the strength of Stanford University's resources and its Silicon Valley location, the SPARK founders envision SPARK-like programs at universities across the USA and abroad playing a larger role in systemically affecting early-stage translational efforts. SPARK-like programs have already been started in the USA and in 24 universities in eight countries abroad [5]. These replication efforts rely on an institution's ability to obtain backing from the local academic and biopharma communities, to create a strong advisor network, to collaborate with technology licensing offices and to maintain a strong biomedical research program.

Concluding remarks

SPARK has achieved remarkable success in translating biomedical discoveries thus far. However, for SPARK to be an attractive model for other institutions, the program will need to further articulate success metrics and collect data from past and current scholars to inform future decisions. Similarly, an understanding of project failures can provide valuable information for future projects. Because many benefits from SPARK cannot be easily quantified, such as educational and professional enrichment, one challenge SPARK faces is meaningfully capturing the impact of the program, including total grants received, prestige of the program, impact on university recruiting and the future successes of graduated SPARK scholars.

Finally, stakeholders across the board, including the Dean's Office of the Stanford University School of Medicine, agree that SPARK has the potential to initiate a critical conversation among numerous stakeholders about the need for systemic change in translational medicine. Such a conversation would not only reduce the barriers to drug development and increase the efficiency

of the entire biopharma industry but could get more life-saving therapies into the hands of doctors and patients sooner.

Conflicts of interest

E.K. and P.O. declare that they have no competing interests. A.W.L. reports personal investments in BridgeBio Capital (also an adviser), ImmuneXcite, KEW, MPM Capital, Novalere, Royalty Pharma and Visionscope, and is a director of Roivant Sciences and the MIT Whitehead Institute for Biomedical Research.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drudis.2017.03.015>.

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