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Opinion

A Unique Approach to Business Strategy as a Means to Enable Change in Global Healthcare: A Case Study

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The focus of translational science—a multidisciplinary field of basic scientific research that is motivated to develop practical healthcare applications—is to bring intellectual property (IP)[2] developed in an academic environment into the commercial marketplace, where it can meet a need. The term "translational science" broadly refers to potential therapeutics, biomarkers of disease, medical devices, and diagnostic technologies. The NIH currently provides funding to 60 US-based academic institutions that are dedicated to clinical and translational science *(1)*. The use of academia as an incubator for ideas is an attractive method to build value and mitigate the risk that is inherent to scientific research, because the structure of academic research—multiple sources of funding for high-risk concepts, the peer-review process, and the pressure to disclose data publicly—provides a measure of security. Many ideas that leave this environment before they are developed properly will fail in the competitive industrial environment. After an idea is vetted in academia, an industrial partner is required to mature the idea into a product *(2)*. Although there are many examples of this process (e.g., IP is licensed by an established company, or a start-up company is created), the common foundation minimally requires (*a*) an important need, (*b*) a good idea, and (*c*) the funding to develop ideas into products. We present a case study that outlines a novel business strategy we have developed for bringing such products to the global economy.

Diagnostics For All (DFA) was founded in 2007 as an outlet to engineer and commercialize a biotechnology platform—cost-effective diagnostic devices based on patterned paper that are designed specifically for use in the developing world—pioneered by the laboratory of Professor George Whitesides of Harvard University *(3–8)*. Atypical of most start-ups, the goals of DFA were best embodied by those of a nonprofit organization. After incorporation, DFA applied for and was granted 501(c)(3) status, a signal that the mission of the company would be to focus on healthcare solutions that (*a*) meet a global need rather than those of its shareholders or investors and (*b*) are affordable to all, particularly those in resource-poor settings.

DFA was founded without the backing of a trust or other significant source of capital, and securing funding therefore became paramount to the success of the company. In addition to traditional funding outlets (e.g., independent government grants or foundation awards), DFA has access to sources of funding that for-profit start-ups do not have. For example, nonprofit enterprises can receive personal donations and gifts from charitable organizations. These varied sources of funding allow DFA to operate independently of the influence that is tied to capital provided by angel investors, venture capital, or private-equity firms (e.g., seats on the board of directors), and to focus on developing ideas through to completion rather than on the distractions that accompany efforts to maximize profitability. Relying on funds obtained from donations and grants alone, however, is not an advisable strategy for ensuring the long-term success of a company. We have developed an unusual hybrid business model to ensure the sustainability of our mission through royalty revenues generated by a wholly owned for-profit subsidiary, Paper Diagnostics.[3]

DFA is the sole shareholder in Paper Diagnostics, and this unique arrangement gives the nonprofit enterprise complete control over the operations of the for-profit company. By leveraging the development in the platform technology that is grown by DFA without the use of investors (e.g., nondilutive financing from grants), the valuation of Paper Diagnostics is similarly increased. Paper Diagnostics can sell shares of stock at a later date, when the company may have a higher valuation, and can then court investors to secure funding

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[2] Nonstandard abbreviations: IP, intellectual property; DFA, Diagnostics For All.

[3] The laws that regulate the relationship between a taxable subsidiary and its tax-exempt parent are complex. Certain activities or transactions may jeopardize the exempt status of the parent organization. The proper advisors (e.g., lawyers and accountants with specialization) should be consulted.

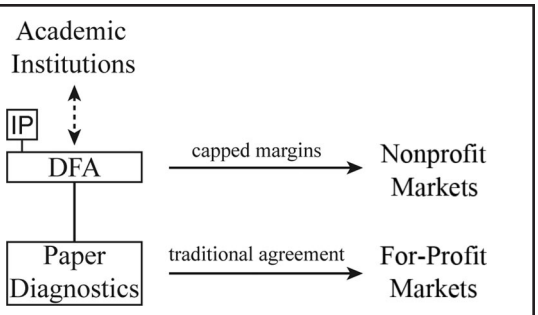

Fig. 1. A simplified representation of the DFA business model.

DFA collaborates with academic institutions to develop its technology and in-license IP. DFA supports the direct distribution of tests to nonprofit markets or with commercial partners to ensure they are provided affordably to those in need. DFA, through a license to its for-profit subsidiary, Paper Diagnostics, follows a more traditional route of partnering with companies active in markets with developed healthcare systems.

for its independent research programs. These investors would then have minority interest in the company and the direction of DFA. This model provides a near-term benefit. Paper Diagnostics, but not DFA, is eligible to receive Small Business Innovation Research and Small Business Technology Transfer funding through the NIH or the Department of Defense because it is independently owned and organized for profit *(9)*. More importantly, the long-term success of DFA is tied to Paper Diagnostics: After accounting for taxes, fees, and operating expenses, Paper Diagnostics will provide a continuing source of royalty income to support DFA and its mission.

Although intimately associated by their mutual goal of enabling affordable healthcare for those in need, DFA and Paper Diagnostics are designed to operate independently with all transactions between the 2 entities being at arms length and at fair market value (Figure 1). DFA itself has 2 options to pursue the manufacture, distribution, and sales of diagnostic devices in the developing world: (*a*) independently or (*b*) through the use of agreements with third-party commercial partners. By working with DFA, our partners enter into distribution and sales agreements with capped margins. These agreements ensure that our mission for affordable healthcare for the developing world is not compromised. Paper Diagnostics focuses on providing diagnostic solutions for established healthcare systems in developed economies, as well as working with current regulatory agencies and the infrastructure of insurance providers. To facilitate their role, Paper Diagnostics can enter into traditional agreements with commercial partners, in which profit margins are less restricted. Paper Diagnostics is thus a vehicle for DFA to provide diagnostics for all in need. As we develop the platform technology, entry into additional markets (e.g., agriculture, food safety, and animal health) is planned.

A solid patent portfolio is absolutely required for a biotechnology company—this criterion applies to both for-profit and nonprofit entities—to enter into agreements with partners, to attract investors, and to conduct business in a global marketplace. DFA acquired the freedom to implement its mission through exclusive license agreements for IP from academic partners. In addition to the exclusive rights to major patents that protect the core technology, a number of nonexclusive licenses strengthen and support the platform. Importantly, DFA is active in the development of its own IP. As a subsidiary, Paper Diagnostics has access by license to those patents whose rights are held exclusively by DFA and eventually will be expected to generate and manage its own IP.

The best example of our unique business model—the translation of an idea from the academic realm into industry and the separate roles of nonprofit and for-profit entities—has been the development of DFA's lead product—a rapid, simple point-of-care test for liver function.

Blood tests for monitoring liver function are a standard part of medical care in developed nations. In particular, patients undergoing treatment for infections with potentially hepatotoxic drugs are at the highest risk (e.g., patients with tuberculosis) *(10)*. The relative expense and logistical concerns of these assays (e.g., tests must be performed in centralized laboratories) often limit their implementation in resource-limited settings. A low-cost point-of-care test for liver function would have a substantial impact on patient care in the developing world.

We developed a proof-of-concept test for liver function in collaboration with the Whitesides group at Harvard University *(11)*. The liver function test is fabricated from ubiquitous and inexpensive materials; layers of paper patterned with reagents, plastic, and adhesive produce a functional device. As the industrial partner, we then took the next steps to develop the test into a field-ready prototype (Figure 2) by (*a*) evaluating clinical samples in collaboration with Dr. Nira Pollack at Beth Israel Deaconess Medical Center in Boston, (*b*) modifying the chemistry of the enzymatic assay to improve stability for long-term storage, (*c*) using focus groups to optimize the design of the device and the interpretation of the results, and (*d*) performing inter- and intralot variability studies to prepare for a regula-

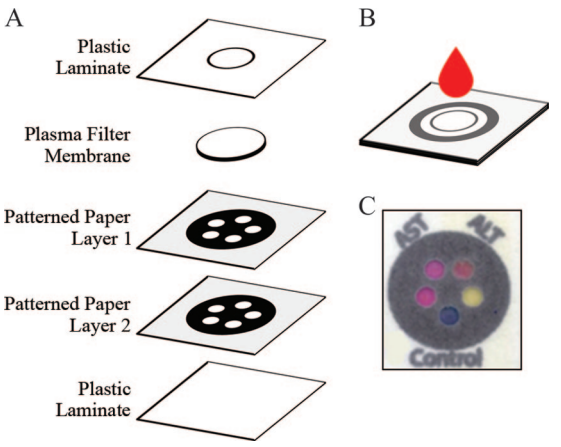

Fig. 2. A DFA paper-based liver function test.

(A), The device that performs the liver function test is fabricated from simple materials: plastic laminate to seal the device, a plasma-filter membrane, and 2 pieces of patterned paper impregnated with reagents. (B), The individual layers of the device are assembled, and a drop of blood is added to the opening in the top of the device to activate the test. (C), After a predetermined period of time (minutes), the results of the test—the activities of 2 enzymes and a set of control markers—are interpreted easily from color changes that appear in the zones of patterned paper on the bottom of the device. AST, aspartate aminotransferase; ALA, alanine aminotransferase.

tory audit of our manufacturing protocols. These liver function tests can be fabricated in moderate volumes by means of sheet-fed processes (thousands of devices per week), but the use of paper and plastic as materials affords the straightforward transition into high-throughput reel-to-reel manufacturing procedures (e.g., similar to those used to produce newspapers and magazines). Paper Diagnostics will then license this technology from DFA and generate a sustainable source of royalty revenue from devices sold in markets that are unaddressed by DFA. Using this particular organization, we can provide an outlet to serve all people who are in need.

We believe that we will succeed in our goals by virtue of (*a*) our innovative technological platform and (*b*) our innovative business model. Using patterned paper, we can produce diagnostic tests that provide clinically actionable information for multiple biomarkers from a single biosample. This information comes at little cost or no cost to the end user, because the bill for materials is essentially zero. Our approach is fundamentally different from other solutions for low-cost diagnostics that, to reduce costs, rely on subsidies from governments (whose programs can run out or be cut) or that provide information on only 1 or 2 markers per sample. Likewise, our product is not a stripped-down version of a test traditionally performed in clinical laboratories that has been repackaged for the developing world. Our unique business model—forming Paper Diagnostics, a for-profit subsidiary—will help the mission of DFA succeed by providing a sustainable source of royalty revenue to complement the capital generated through grants and donations.

The approach we have embarked on with DFA provides a new business model that could lead to benefits for the healthcare of people worldwide, regardless of economic status.

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