BioCrossroads®

Profiling Independent Biosciences Research Institutes in the U.S.

Summary Compendium

2013

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PROLOGUE

Over the past decade, Indiana's big stake in the bioscience industry has finally become obvious. As *The Economist* noted in 2009, "Though every state wants to be a hub for life sciences, Indiana really is one … Life sciences accounted for 23% of all [Indiana] job growth from 2001 to 2007." That growth has continued over the past five years at an average annual rate of nearly 15%, even as other employment indicators in Indiana and elsewhere have gone in very different directions.

There is now an abundant body of consistent third-party data (see BioCrosssroads' comprehensive 2011 report, *Indiana's Life Sciences Industry 2002-2010*) that our State is indeed home to leading academic assets across Indiana University, the IU School of Medicine, Purdue University and the University of Notre Dame. Over the past decade, Indiana's research universities have captured hundreds of millions in both federal and private philanthropic grant dollars to advance bioscience and biomedical research. Overarching these university assets, of course, Indiana is also home to one of America's largest portions of a highly diversified and desirable life sciences industry, featuring both strong R&D and intensive development / manufacturing and production capabilities in companies such as Eli Lilly and Company, Cook Group, Biomet, DePuy, Zimmer, Roche Diagnostics, Dow AgroSciences and Covance. Since 2004, these companies alone have invested, collectively, well over $3 billion in expanded operations and facilities, adding more than 17,000 new jobs in the process. In BIO's 2012 survey of life sciences business activity across all 50 states, Indiana is one of only five (in the company of California, Massachusetts, New Jersey and North Carolina) ranked "First Tier" for *every single significant indicator* of life sciences industry strength—including both concentration and total number of companies and total number of bioscience industry jobs.

It all adds up to a uniquely strong (and nationally significant) Indiana economic asset, a rising industrial sector that today represents a third of the State's $29 billion in annual exports (2011) of manufactured goods and delivers a total $50+ billion economic impact for Hoosiers every year.

Still, challenges remain. Some of these challenges involve global competition, volatile national and international capital markets, and changing federal regulatory policies — issues that range far beyond Indiana's borders or, in most cases, control. But some of these challenges are also ones we can effectively address right here at home. Among these, probably most important is the fact that industry leadership of Indiana's growing life sciences sector is still not sufficiently connected to — or advanced through — everyday

collaborations for research and development of innovative products and technologies at Indiana's premier research universities. Another, even more recent BioCrossroads report, prepared by the Battelle Technology Partnership Practice in May 2012, *Advancing Indiana's Life Sciences Competitiveness and Strategic Collaborations Among Industry, Universities and Academic Health Centers*, makes the case for why these collaborations can matter so much to Indiana's industry, universities — and economy:

"It starts with industry and research institutions sharing their insights and concerns about the problems to be researched and then finding ways to work together to move new research discoveries through proof of concept, preclinical development and clinical research. The research must be of both academic interest and directly responsive to industry problems. Other states and regions are working to find their own tailored solutions, and Indiana must also raise its ability to effectively meet this commercialization challenge. This is also (and certainly should be) of great concern to the state's governmental leadership—how to maximize the potential for high quality job generation in Indiana by leveraging the state's life sciences capabilities."

Meeting these challenges is not a uniquely "Hoosier" problem. Our counterpart (and competitor) states and regions with strong life sciences sectors have faced similar challenges in forging more productive university-industry relationships, and building wider support around shared promising opportunities. But as the 2012 Battelle study also illustrates, many of those other regions (e.g., San Francisco, San Diego, Boston-Cambridge, Kansas City, St. Louis) have begun to take the big steps, and make the major investments necessary to promote lasting and potentially game-changing university-industry, public-private partnerships that can fuel further development. Where the right resources have come together, a vibrant "bio-economy" has often flourished. Frequently, regions with life science prominence and promise have sought to capture leading opportunities and talent in this science-driven sector through the establishment of new kinds of research collaborations and institutes. The Broad Institute in Cambridge, the Danforth Plant Science Institute in St. Louis, the Florida sites for the Burnham and Scripps Research Institutes, and the Stowers Institute for Medical Research in Kansas City are all leading examples of these new types of institutes for innovation, even though all are very different from one another in origin, structure and focus.

Over the past year, and since the publication of the Battelle study, BioCrossroads has engaged in intensive discussions with Indiana's leading bioscience stakeholders, who clearly believe that now is the time for a defining project to catalyze the opportunities and overcome the challenges that this study documents. One provocative idea that has surfaced and continued to gain traction is the possibility of pursuing Indiana's own version of an applied biosciences research institute, as recently proposed in public comments by Indiana Governor Mike Pence and detailed further in a later speech by Dr. John Lechleiter, Chairman and Chief Executive Officer of Eli Lilly and Company. Such an institute—

organized in a uniquely Indiana model that is led by industry — holds the potential to be the catalyst for collaboration spanning medical device companies, pharmaceutical companies, agricultural science companies, research laboratories, medical schools, and research universities; for attracting and engaging leading scientific minds from around the country; for strengthening our economy; and for improving the lives of our citizens here in Indiana and people all around the world.

To explore the possibilities for an applied, industry-driven life science research institute in Indiana, BioCrossroads has helped to organize a steering committee of some of the State's most engaged life science industry leaders. In support of the steering committee's efforts, BioCrossroads has once again retained the Battelle Technology Partnership Practice to conduct a benchmarking and "best practices" study of several of the leading independent life science research institutes around the country. The following report summarizes Battelle's findings from each institute and, taken together, begins to establish an important foundation of knowledge and "lessons learned." These findings can assist Indiana's public, private and university leadership in better understanding how similar opportunities have been pursued elsewhere, and could begin to be considered here — even though such opportunities are typically defined not by universal models but through highly opportunistic enterprises that reflect the particular features of their surrounding communities, assets and investments.

Hence, this report is only a background for our own, further, energetic discussion of Indiana's possibilities. As such, it sets the stage for the latest chapter in BioCrossroads' eleven-year story of advancing effective dialogue among leaders from Indiana's life sciences corporations, research universities, philanthropic foundations and government. Once again, as we learn from best practices in other states and regions, we are made aware that we have all indeed done well in advancing our own life sciences sector, as one of Indiana's brightest opportunities for further prosperity and growth. And we are likewise made aware that we can all still do better — and much more — together.

Sincerely,

David Lawther Johnson
President and CEO, BioCrossroads
January 2013

OVERVIEW AND SUMMARY

Overview

Battelle was retained by BioCrossroads to provide day-to-day technical assistance, facilitation, and policy development services to BioCrossroads and a Steering Committee created to consider the feasibility of and conceptual design of an Indiana Bioscience Research Institute (IBRI).

Under the guidance of the IBRI Steering Committee, BioCrossroads asked Battelle to gather and analyze information on best practices at similar institutes and centers, drawing a benchmark set from a list of candidates prepared by BioCrossroads in consultation with Battelle. This report represents a summary of those findings.

After completing in-depth interviews with leaders of the benchmark institutes, backed up by extensive secondary research, Battelle summarized for the IBRI Steering Committee the "lessons learned" about what works in the world of independent research institutes. We also made suggestions on best practices that could form the core of IBRI's design. This information is summarized below.

Lessons Learned and Best Practices in Independent Research Institutes

✓ There must be a clear focus on competencies with growth opportunities.

Across the U.S., organizations too often try to establish centers of R&D excellence from scratch, using a "field of dreams" approach: if we build it, they will come. In this way, many states and regions have tried but failed to build the next Research Triangle or Route 128 or Silicon Valley. Usually these efforts fail because planners ignored existing strengths or felt they need not take into account industry-driven market opportunities.

Nearly all the bioscience research institutes in the benchmark set were established around some aspects of the evolving "omics" revolution, adapted to greater or lesser extent to local strengths, usually institutional. The primary strengths on which Indiana can build are its deep bioscience industry base, which places Indiana in an extremely competitive position. Battelle's recent analyses for BioCrossroads identify some of the core competencies at the intersection of Indiana industry and university capacity that could form the basis for an Indiana Bioscience Research Institute.

✓ An Institute must be at sufficient scale but also focused.

In the course of our interviews, the leaders of independent bioscience research institutes told us they had learned that unless a new initiative is started at sufficient scale it will not be able to reach the critical mass necessary to move novel research ideas into actual practice.

Scale is necessary but not sufficient. As the head of Sanford-Burnham observed, even the largest independent institute is generally exceeded in headcount by a single research-oriented department at a major academic medical center. Beyond scale, the differences that allow institutes to achieve measurable results where an academic department may not are matters of focus; a commitment to multi-disciplinary collaboration; a culture as interested in translational and clinical work as in basic science; and researchers' adept at connecting the dots from discovery to delivery.

Another distinguishing difference between the two settings is an independent institute's ability to establish core labs (sometimes called "technology platforms") that are completely independent of any faculty member's personal laboratory; equipped with the latest and most-comprehensive technology; and managed by experienced business managers hired from industry to run what amount to full-fledged businesses. These features of independent research labs require sufficient resources at the earliest stages and constant reinvestment to stay on the cutting edge.

✓ Don't underestimate the time frame to get established or the level of funding needed for startup and growth.

Too often there is the temptation either to wait too long in the planning (Stowers took six years to get started) or to begin before sufficient resources are at hand. More recent institutes such as Danforth and TGen secured financial support from multiple parties including government, philanthropy and businesses, often premising the request on projected local economic impacts.

Interviewees advised us that a new institute almost always needs more money during the startup phase than its founders thought it would require, and that it always takes longer than originally thought to reach key early milestones. Sanford-Burnham has prospered in spite of a small endowment; most of the others have started to build endowments that provide some component of the annual operating budget, but only one benchmark — the Stowers Institute — is of sufficient size to live on its endowment.

✓ Major initial funders primarily philanthropic and business.

In almost every case, a key factor driving the formation of an independent research institute was the interest of private foundations and wealthy individuals in making a "naming" gift. Broad, Danforth, Stowers and Sanford-Burnham are all named for major benefactors, and even TGen relied heavily on founding gifts from two regionally significant private foundations (Flinn and Piper). Industry has also contributed to these efforts, as in the case of Monsanto's support for the Danforth Center through its corporate foundation.

Contrary to popular wisdom, government sources are not the primary financial contributor to private research institutes, but government can certainly play an important key catalytic role. Without support from the State of Florida and Orange County, Sanford-Burnham would not have opened an Orlando branch; without the State of Arizona and the City of Phoenix, TGen would not be in downtown Phoenix; and to a lesser degree, State of Missouri financing helped along the Danforth Center in St. Louis. On the other hand, Broad and Stowers received no direct public funding.

✓ An Institute should be established to address opportunities/niches, e.g., tech commercialization, anchor a geographical cluster, etc.

Because success grows from a base of solid acceptance and buy-in, the founders of private research institutes should also take into account what additional contributions a new institute can make to its home community and region, and "tune" the design accordingly so to build on strengths, avoid weaknesses, and create a sense that all parties accept and welcome the new addition to the research landscape.

The Broad Institute has paved new ground in encouraging MIT, Harvard and Harvard's teaching hospitals to work together on larger-scale, cutting-edge initiatives they could not accomplish on their own turfs. And it has helped nurture the collaboration not just among institutions but also among individual scientists and technologists, further cementing the deep research cluster found in Cambridge.

TGen has created a fourth research anchor for Arizona on top of its three research universities, resulting in significant increases in the flow of federal and other funding into the state. The Danforth Center has emerged as an important component of St. Louis' regional efforts to become globally known as a plant-sciences center. These successes are understood and embraced by the respective home communities.

Moreover, while institutes are primarily research enterprises, they also create ancillary economic benefits for operating businesses in allied fields. From Sanford-Burnham's in-house business incubator, to Danforth's adjacent science park, to TGen's revitalization and rebranding of a tired downtown neighborhood, to Sanford-Burnham's "anchoring" of a 600-acre "medical city," many of the benchmarks are justifying the investments that government and philanthropy made in them on economic-development grounds.

✓ World class leadership, multi-disciplinary teams necessary; avoid "endowed" chairs.

Experience in the benchmark set shows that independent institutes are most effective when they excel at cultivating and supporting multi-disciplinary teams composed of investigators who want not just to do research, but also to see their discoveries enter actual practice. Only by pooling skills, interests, and resources can institutes address the most demanding and challenging diseases that attract the best talent and the most interest from industry partners.

Freed from traditional university hierarchies and disciplinary stovepipes, independent institutes can seek out precisely the kind of research talent that thrives on such collaboration. Institute leaders also told us that when industrial or philanthropic support is raised, it should be targeted to teams, rather than simply endowing the lab of a senior investigator. Above all, the institute must make the case for investing in the range of sequencing, imaging, and bioinformatics infrastructure that is necessary to support ambitious, multi-disciplinary team research on the most challenging problems.

✓ **Decide early on whether to build institute's talent base opportunistically or pro-actively.**

Private research institutes have taken varying paths to building their staffs, but in almost every case a key hire is the CEO or President who shapes the directions in which the institute will move. He or she may then decide, given available resources whether to wait to find key hires as they become available or pro-actively seek out, find and recruit such hires to the new institute.

Leaders told us they do not usually make offers targeted at the most-senior-level investigators. Instead, they mostly focus on recruiting junior or mid-career faculty committed to the mission and style of the institute. Sometimes they even hire from within, from the ranks of affiliated postdocs. Still, the basic recruitment packages are critical and must be developed in ways that conserve limited resources of a new fledging organization in its early months and years until it has proven it has staying power for the long term. In this case, all the institutes in the benchmark set have existed at least 10 years.

✓ **Large portion of initial resources of institutes been devoted to "bricks & mortar"; virtual and other approaches should be considered.**

An important lesson learned from leading independent bioscience research institutes is that new buildings can be enormously expensive. Development and construction costs typically consume a major fraction of any initial financial commitments, subtracting resources from what would otherwise be available to support the innovation and discovery work of staff scientists and technicians. If instead a way can be found to reuse older facilities vacated by one of the founding industry or academic partners, this may present a relatively cost-effective way to bootstrap a new research institute in Indiana.

In theory, by using modern communication tools, it should be possible to support coordinated teams of scientists in industry and academic settings, acting as a virtual laboratory. But this is a best practice rarely observed in the field, and except for the earliest days of Sanford-Burnham in La Jolla, all the institutes in the benchmark set their sites on new buildings from the outset, even if they spent a few months in temporary quarters.

✓ Universities should not dominate but serve as collaborators.

It is true that independent research institutes have sometimes met initial resistance from their intended academic partners. But in several instances, notably the Broad Institute and the Danforth Plant Science Center, the new institutes have overcome these challenges by showing that they generate additive opportunities: specifically, more colleagues to work with; more opportunities to secure competitive funding; more-elaborate and better-managed core facilities; spousal-employment opportunities; and even the reputational benefit for the community as a whole. In turn, institutes need certain things that universities alone can provide, including affiliated teaching hospitals as sites for clinical research that turns discoveries into products, treatments, and jobs.

✓ Hallmarks of most institutes have not been collaboration and outreach.

Many of the independent bioscience research institutes reviewed in this study were formed in the late 1990s and early 2000s at a time when the NIH budget was doubling. This provided many funding opportunities for newly hired researchers; consequently, industry partnering was not a significant way they sought financial support. Furthermore, each of the institutes was developed to solve pressing bioscience research questions and issues; except for the Danforth Plant Science Center, none had an initial industry funder.

However, in the current era of stagnant federal funding, nearly all the benchmarks are examining ways to partner with the bioscience industry. Whether in the case of Broad's recent agreements with AstraZeneca or Roche; or Sanford-Burnham's attempts to engage biopharma companies in much the same way a small biotech firm would, these institutes are beginning to view industry as a major partner and funder in the future.

Indiana, being late to the party, can learn from these experiences and become the first institute explicitly created to partner with industry. Given the depth and breadth of the biosciences industry in Indiana, this represents a comparative advantage Indiana should feature and focus in the design and development of its Biosciences Institute.

THE BROAD INSTITUTE (CAMBRIDGE, MA)

Overview

The Broad Institute[1] represents the second generation of independent institutes in Cambridge, MA. It grew directly out of the Whitehead Institute, an Institute affiliated by contract with MIT and founded by Dr. David Baltimore in 1982. The Whitehead Institute's Genome Research Center (founded 1990) became a key resource for the federally funded human genome project. The Center operated under the aggressive leadership of Eric Lander, Ph.D., a mathematician and coding theorist who self-educated in genetics and moved to MIT from a prior appointment at Harvard Business School.

As the genome project concluded and wound down at the turn of the millennium, Dr. Lander began discussions with philanthropists Eli and Edythe Broad about a new, more ambitious institute that could cross disciplinary and institutional boundaries to pursue fundamental changes in human healthcare based on the newly acquired genomic knowledge and automated, high-throughput techniques. The Broad Institute, which involves MIT, Harvard (especially the Institute of Chemistry and Cell Biology) and all Harvard's separately financed teaching hospitals, emerged from these discussions in 2003 and has grown very fast over its first eight years.

There are 11 core members who have faculty appointments at MIT or Harvard and labs at "the Broad." The core members function as the PIs of the Institute, each leading a laboratory supported by a large team of graduate students, postdoctoral fellows, and scientific staff. There are also 160 associate members (about three dozen classified as "senior") all of whom hold primary appointments at a home department in one of the partner institutions, but participate actively in one of the interdisciplinary teams. The Institute itself has dozens of professional scientific staff, both operating core facilities and managing some of the interdisciplinary programs. There are 950 direct employees, but counting the labs of the associate members, the community considers itself closer to 2,000 in number.

1 For background see http://www.broadinstitute.org.

The Broad Institute defines its overall mission as:

- Assemble a complete picture of the molecular elements of life;
- Define the biological circuits that underlie cellular responses;
- Uncover the molecular basis of inherited diseases;
- Unearth all the mutations that underlie different cancer types;
- Discover the molecular basis of major infectious diseases; and
- Transform the process of therapeutic discovery and development.

The Broad occupies a newly constructed building in the heart of Cambridge, custom-designed to promote interaction and community.

Startup Phase

History and Motivation

The vision shared by Dr. Lander and the Broads was to create an interdisciplinary community organized around key problems rather than departments, supported by large-scale analytic infrastructure that had been developed as part of the genome project. These "platforms" are equipped, staffed and supported at a level of intensity and sophistication that is completely unknown in any academic institution, even MIT.

Dr. Lander's ambition was to leverage these capabilities to allow research teams to work at a scale that could not possibly be supported by one university and one department alone. The Broad actively seeks federal funding, but Dr. Lander also wanted to raise and aggregate enough unrestricted funds that ambitious, risky topics could be pursued at full blast, rather than be constrained by the small pieces that NIH might agree to fund at any one time. Together, these elements comprise the approach that he describes as a "community," rather than an institute.

The Broads, who are from Los Angeles, initially urged a West Coast location, but Dr. Lander's firm conviction was that no West Coast environment, not even the San Francisco Bay region, afforded the compact density of exceptional research talent that would allow him to involve faculty who could simply walk across the street or jump on a quick subway ride to participate in weekly program meetings. He urged and eventually prevailed on a Cambridge location, which seemed to offer these advantages.

Startup Financing

In 2003, the Broads agreed to a founding donation of $100 million over 10 years, and the Institute began as an experimental program managed by MIT on behalf of all the partners. Within 18 months, the Broads had doubled their funding commitment. Then, in 2008 – recognizing five years of success and growth — they pledged an additional $400 million as a perpetual endowment. At that point, the Institute was independently incorporated, and in 2009 MIT transferred $147 million in relevant assets (cash, pledges, plant and equipment) to the new corporation's control.

Initial Leadership

Dr. Lander is himself a core member, as are his chief academic officer/deputy director and chief scientific officer. Among the core members, about half are considered "senior" — that is, they have the rank of full tenured professor in their home academic departments. The remaining, "junior" core members must meet their home department's criteria for tenure track professorships, but are not yet tenured. All the core members represent exceptional figures in biomedical research across a very wide range of disciplines. Included among the initial core members — but separate from the institute administrative staff – were several with executive experience, such as the former provost of Harvard and the former president of Merck's research laboratories.

Current Operations

Research Profile

There are three broad categories of research programs: the central areas of medical and population genetics and genome sequencing; three disease-specific programs; and several thematic "organizations." Each program is guided by intensive questioning of experts and pushing them to identify the findings and results that would significantly change their fields, because these are the topics the Broad desires to support. The following table lists those programs as well as the disciplines represented by the core members, and the platform technology facilities.

(Columns are independent of each other)

Topical programs	Underlying disciplines of the core members	'Platforms' (Core lab facilities)
Medical and population genetics	Genetics and molecular genetics	Genomic sequencing
Genome sequencing and analysis	Endocrinology	Technology development
Cancer	Biological engineering	RNA interference
Chemical biology and novel therapeutics	Oncology	Chemical biology/novel therapeutics
Psychiatric research	Biochemistry	Proteomics
Infectious disease	Cell biology	Biological imaging
Computational biology	Brain and cognitive sciences	Metabolite profiling
Metabolism	Biology and molecular biology	Therapeutics discovery and development
Epigenomics	Microbiology	Genetic analysis
Cell circuits	Stem cell and regenerative biology	
	Computational biology	
	Chemical biology	
	Synthetic biology	

Academic Partner Relationships

The Broad is only the second major effort (other than a joint M.D./Ph.D. program) that Harvard and MIT have ever mounted together. Associate members are offered only three-year terms, and are not entitled to direct salary support, but they are entitled to apply for certain internal awards and to write external grant proposals from either their home institution or the Broad depending on the circumstance, leveraging its capabilities. Some spend as much as two days a week at the Broad, while others come only for weekly program meetings.

Dr. Lander wanted to create a fundamentally different culture that was professionally managed and accountable. At the same time, the Broad is less constrained than a typical industrial lab to look only at opportunities for revenue and profit. It can screen for infectious diseases that don't currently constitute major markets, addressing a spot somewhere between academic and commercial R&D.

When associated faculty walk across the street to Broad, it is said that their mindset changes. The associate members already have their own large and successful labs back at their home institutions, and they do not use Broad to secure more research funding, or to

take another try at a grant they could not secure, but rather to join one of the overarching programs that extends beyond their own discipline. They regularly travel to the Broad to brainstorm about new ways to take on large problems and the latest results on a pre-publication, confidential basis.

While both core and associate members have faculty appointments, resources and responsibilities at their home university or hospital, the Broad pays the salaries for core members (subject to salary-setting by the home institution) while the institutions retain responsibility for the salaries of associate members.

Either category of member may run a new grant either through the Broad or their home department depending on circumstance. Relations between the Broad and both Harvard and MIT sponsored-research offices are good, and arrangements are easy to finalize. The member institutions have satisfied themselves that the Broad brings more money into the entire system of institutions, even if a given grant goes through the Broad.

In cases where a grant or contract requires work to be done both at the Broad and a home institution, subcontracts may be used in either direction, or in the case of very small crossovers, simple re-billing arrangements are made. Broad members may seek salary support from external grants if the granting agency so permits. This does not increment their actual salary but may relieve the salary burden on whichever entity has responsibility for paying them.

Talent Recruitment

Dr. Lander himself handled recruitment of the initial core members, both senior and junior. The Broad started with four core members and grew to 10, all of whom were recruited in conjunction with one of the partner institutions. These in turn fanned out to recruit associate members.

Salaries and recruitment packages for core members are typical of what star faculty would receive at prestigious and wealthy institutions. Staffs who manage the platform areas have substantially stronger management backgrounds than those who would be typical at a university core facility. The sequencing platform is a $30 to $40 million-a-year annual operation and is staffed like a business of that scope.

Subsequent Growth and Sustainability

The operating budget of Broad has grown rapidly from $160 million in 2007 to close to $300 million in 2011. Support has been raised from nearly every institute of the NIH that makes extramural grants, as well as from at least two dozen foundations that have made unrestricted gifts and those that make grants for biomedical or disease-oriented research. In the latter category, the largest, "named" gifts were:

- $150 million over 15 years (announced in two waves) from the Stanley Medical Research Institute to establish a research program in psychiatric diseases. This project grew out of the efforts of Dr. Skolnick (ex-Merck) to connect researchers in the Cambridge area already working on the genetics of various diseases.
- $65 million over three years from the Carlos Slim Foundation, to support a joint program with Mexico's National Institute of Genomic Medicine. This project addresses kidney disease, an area of personal interest to the Slim family and many Mexicans, and involves training Mexican scientists.

The operating budget is derived 60% from federal grants and contracts. Of the 35% classified as philanthropically derived, probably 15 or 20 percentage points are simple gifts, such as the Broads'. The balance may be from foundations but are actually grants-in-aid in support of specific projects, essentially a sponsored-research agreement with a non-profit. Therefore, this figure changes dramatically from year to year rather than being stable and predictable like a giving program.

Future Growth

The Broad expects to be working at its ambitious multi-part mission for many years, but it has not published explicit roadmaps. In making their pledge of $400 million for permanent endowment, the Broads stipulated that the Institute should first finish expending the first $200 million in annual gift commitments. As the endowment collects on the Broads' $400 million pledge, all earnings will be reinvested until after 2014. After that, it appears likely that the share of operating revenue accounted for by gifts will drop, and the share accounted for by endowment earnings will grow, possibly to as much as 25%.

Industry Relations

Existing Industry and Research Partnerships

In 2012, the Broad announced a new agreement with AstraZeneca under which the Institute will use its chemical biology platform to screen a pre-assembled library of 100,000 small-molecule compounds, with the goal of identifying promising treatments for bacterial or viral infections. The outcomes of this work belong to AstraZeneca, but the sponsorship affords AstraZeneca no special access to the ongoing programs, whose teams meet without industrial participation. Broad has not publicly valued the arrangement in dollar terms. Another arrangement was recently disclosed by the Roche Clinical and Translational Research Center.

Emerging Industry and IP Management

A great deal of Broad's output is in the form of data and computer codes that are released into the public domain at least in part. However, enough proprietary intellectual property is generated (about 30 patent filings/year ranging from biological to technological in nature) to require a technology transfer staff of six, which also negotiates any industry-sponsored research agreements.

To date commercialization revenues have been minimal, but there have been about five new companies created that could be attributed to the existence of the Broad. Sometimes these are independent startups created by direct arrangement between Broad members and Boston-area venture capitalists.

If any Broad member makes a patentable discovery, all royalty and equity rights are shared between their parent institution and The Broad depending on whose employee made the discovery, where the discovery was made, and with what resources including especially Broad infrastructure and staff. The formula for royalty sharing never varies from a template that was defined in the Institute's organizing agreements. In negotiating these arrangements, the Broad considered it much more important to be able to manage the disposition of jointly owned IP than to receive a large royalty share, and that once this issue was settled, deals have proceeded without friction.

DONALD DANFORTH PLANT SCIENCE CENTER (ST. LOUIS, MO)

Overview

The Donald Danforth Plant Science Center[2] is an independent nonprofit research institute with ambitions for impact on hunger, health, and sustainability. It was founded through local philanthropic and corporate support as part of a regional economic-development initiative, and its mission embodies both global and local goals. The Danforth Center occupies a modern, custom-built structure on 40 acres across the road from the corporate and R&D headquarters of Monsanto in suburban St. Louis County. Its plans include development of additional acreage on the site as a three-building research park, separate and distinct from a larger research-park initiative six miles east, in midtown St. Louis, adjacent to the region's medical district.

The Center has grown steadily since its founding in 1998 to annual operating revenues of about $25 million. As of this year, its endowment stands close to $200 million thanks to substantial additional contributions received from the Danforth Foundation as it liquidated over the last decade (see below). The Danforth Center is organized around the laboratories of principal investigators (currently 20), supported by about 200 additional staff, including visiting scholars, postdoctoral and graduate students, and both technical and non-technical support staff.

The Center's mission, which has evolved over time, is now encompassed in three broad goals:

- Feed the hungry and improve human health;
- Preserve and renew our environment; and
- Enhance the St. Louis region as a world center for plant sciences.

The Center's current president is James Carrington, Ph.D., a bioinformatician who studies RNA mechanisms, and the board chair is William H. Danforth, M.D., retired chancellor of Washington University in St. Louis and founding donor through his family's foundation.

2 For background see http://www.danforthcenter.org.

Startup Phase

History and Motivation

The Danforth Center was established by the Danforth Foundation, an independent foundation capitalized by stock in the Ralston Purina Company (merged long afterward into Nestlé, in 2001). Donald Danforth was the son of the company founder, long-time chairman of the company, creator of the Danforth Foundation, and a passionate advocate for ending global hunger. At the time of the Center's establishment, the Danforth Foundation board was chaired by Donald's son and the founder's grandson, former Washington University Chancellor William Danforth, and vice-chaired by another son, former United States Senator John Danforth.

The idea for the Center emerged in the late 1990s in discussions among civic leadership, the Danforth Foundation, and executive leadership of the locally based Monsanto Company, which was enduring a turbulent decade. The company's troubles[3] were seen as threatening the future of one of St. Louis' leading corporate citizens and therefore the region's entire economic destiny. As a consequence of these discussions, the Danforth Foundation re-oriented its grant-making away from a national program of education reform toward one of regional economic revival.

The Danforth Foundation underwrote a 10-year regional economic strategy, focused on exploiting the region's comparative advantages in the plant and life sciences. As part of this strategy, the Foundation funded staff for a Coalition for Plant and Life Sciences, and began making major gifts for strategically targeted R&D capacity to various biomedical and plant-science departments in Washington University, and a founding commitment to the Danforth Center. The endowments of the Danforth Foundation and Washington University also collaborated with the members of the McDonnell family (inheritors of the McDonnell aircraft fortune) to make investments in venture-capital limited partnerships and source early-stage deals in plant and life sciences.

As part of this wave of activities, the Danforth Center was envisioned as a connector among several regional sources of plant-science leadership: Washington University, the Missouri Botanical Garden, the University of Missouri at Columbia, and Monsanto. It was intended to strengthen Monsanto's connection to the region and to increase the community's understanding of the potential around plant and life sciences. The Danforth Foundation endorsed all these goals but wished also to honor the commitment of Donald Danforth to application of new knowledge to alleviation of global hunger through crop improvement.

3 Monsanto was well into a transition from a traditional pesticide manufacturer into a biotech giant, when some of its earliest genetically modified crops ran into political opposition, depressing the stock price and making Monsanto vulnerable to a merger engineered by the then-independent Pharmacia-Upjohn, which was interested mainly in Monsanto's G.D. Searle subsidiary, and ran Monsanto's operations from Chicago. Eventually, the agbiotech operations were spun back out into a new company named Monsanto. Control returned to St. Louis, where the main agbiotech assets had remained all along.

In order to achieve those goals, the Center was positioned somewhere between the basic mission of an academic institution and the applied motivations of private enterprise. Its goal was always to convert research findings into actual change in agricultural practice, partnering with farmers and institutions worldwide.

Startup Financing

The Monsanto board and its philanthropic partners set a go/no target of $100 million in firm commitments that they would need in order to launch the Center, although they ultimately succeeded in raising more. The final set of commitments achieved by 1998 included:

- $60 million from the Danforth Foundation;
- $25 million in tax credits from the State of Missouri (this is typically the way this state funds such public-purpose projects);
- 40 acres of Monsanto-owned land, valued at $11.4 million; and
- $50 million in grants from the Monsanto Fund, a corporate foundation, and agreement to fund $30 million in research in future years.

These funds financed the design and construction of a 170,000 square-foot facility (carried on the audited financial statements at $72.4 million before accumulated depreciation); fit-out of laboratory, core services, and greenhouse/growth chamber equipment (which had reached $12.6 million in total as of 2010); establishment of an initial endowment; and early recruitment and operations.

Initial Leadership

The Center's founders quickly identified as their founding leader Dr. Roger Beachy, a plant scientist known for his work on virus-resistant tobacco and other crops. Dr. Beachy had at one time been on the faculty of Washington University, and so was known to Dr. Danforth. He was recruited in 1999 from what was then his position with the Scripps Institute in La Jolla, CA, and was given wide latitude to set the initial research directions and recruitment targets for development of the Center.

Simultaneous with Dr. Beachy's recruitment, Sam Fiorello joined the Danforth Center as CEO, transferring from the executive ranks of the Monsanto Company, and has been there ever since. In 2009, Dr. Beachy left to assume leadership of the USDA's newly created National Institute of Food and Agriculture, and was replaced by Dr. Carrington. Dr. Beachy completed his public service in Washington in 2011 but continues to serve the Danforth Center as vice chair of its board.

Current Operations

Research Profile

Dr. Beachy's earliest commitments were to (1) basic research in biotic and abiotic stresses in plants and (2) applied research that attempts to take findings in model systems and apply them in the field, especially internationally. These latter tasks would not typically be recognized as important in a university environment, or worthy of direct corporate investment. Dr. Beachy focused his efforts on recruiting PIs whose work seemed to align with these broad interests, and who shared his commitment to a culture of open collaboration with university, industry and non-governmental organizations internationally. Eventually the research program has settled into several broad buckets, supported by a set of underlying academic disciplines and core laboratory services:

(Columns are independent of each other)

Topical programs (short list)	Underlying disciplines	Core lab facilities
Biofuels	Plant biology & genetics	Proteomics
Biofortification	Cell & root biology	Mass spectrometry
Disease resistance	Biochemistry	Integrated microscopy
Pesticide/fertilizer reduction	Chemistry	X-ray crystallography
Biosafety/regulation	Phytochemistry	Plant tissue culture/transformation
Enabling technologies	Computational/structural biology	
Translational plant science	Plant immunology	
	Plant physiology	
	Plant pathology	

Academic Partner Relationships

Originally a broad set of institutions with strong agricultural programs including several out of state universities (e.g., Illinois and Purdue) were given board seats, but the strongest interaction has always been with the local academic partners. Most Center PIs have joint faculty appointments (full academic rank but non-salaried) at Washington University or the University of Missouri at Columbia, which allows them to take graduate students into their laboratories. This has proved a key factor in successful recruitment.

Bench-to-bench interaction continues to occur between the Center and academic institutions nationwide, but Purdue has withdrawn from formal affiliation with the

governance of the Center. In projects involving specialized field trials, especially internationally, it is not uncommon for the Center to subcontract funds to institutions that are not involved in its governance at all.

Talent Recruitment

Center staff includes a mixture of full (4), associate (8) and assistant (8) members, at different levels in their careers. As part of standard recruitment packages, the Center pays the initial salary of new investigators and asks them over time to finance about one-third of that salary through direct charges to external grants and contracts. Any additional funds in the package can be used in any way the PI wishes, from equipment acquisition to set aside as a rainy-day fund.

There is no tenure. Assistant members are offered three-year contracts and associate and full members five years at a time. Incumbents are judged on a range of measures including their performance at attracting grants and contracts, their skills at collaboration and technology management, etc. Some PIs have moved on to other positions at the end of their terms.

Subsequent Growth and Sustainability

Since the initial founding, the Center has looked for operating growth and stability to major, multiyear grant awards, both from the federal government (NSF, USDA, NIH and Department of Energy) and from private philanthropies like the Howard Buffet Foundation, the Monsanto Fund, and the Bill and Melinda Gates Foundation, all of which have strongly backed field trials in Africa of biofortified and virus-resistant cassava strains. There is also an active annual giving program aimed at wealthy individuals and generally modest corporate giving.

To date, 90% of the Center's endowment has come from local sources. In 2003, the Danforth Foundation announced that it would wind down its affairs, expending all remaining assets on the plant and life science initiatives it had already started. In 2011, the Foundation made a liquidating distribution of nearly $75 million to the Danforth Center, bringing its total current endowment to nearly $165 million.

In 2007, the Taylor family, owners of St. Louis-based Enterprise Rent-A-Car, made a $35 million gift to endow an Institute for Renewable Fuels within the Center. This financed the recruitment of Dr. Thomas Brutnell from Cornell's Boyce Thompson Institute and led to major research awards from the U.S. DOE.

The $24 million operating budget is derived 60% from either federal or industrial grants or contracts, and about one-third from philanthropic gifts, with the small balance from endowment earnings.

Future Growth

The Center is reported to be hoping to secure a major gift for international partnerships, and begin a new development campaign to help build a new wing and both endowment and expandable funds to support recruitment of additional PIs. For the first time, the Center expects to reach outside the region for major gifts

Industry Relations

Existing Industry and Research Partnerships

Danforth Center management views its job as building relationships with key individuals on corporate research teams, so that they visit the Center often and exchange information with Center PIs about goals, priorities, and current activities. Then, when a proposal is submitted for a research contract, it builds on clear understanding of each party's interests and capabilities.

Typically senior Center management will reach out to the target company's senior R&D executives, and invite them for a visit where they receive presentations by all 20 PI labs. The Center follows up to ask how best to push the interaction down to the level of bench-to-bench collaboration so that corporate scientists can link up with Center PIs. Then, senior management at the Center monitors the relationship in order to encourage progress but stays out of detailed management of the research projects. Such arrangements now exist with Bayer, Dow AgroSciences, BASF, Syngenta and other major companies. Companies represented on the Center's board like Monsanto enjoy no advantages over other corporate partners. The Center has until now not tried to raise substantial endowment funds from agricultural companies, preferring to develop research contracts and partnerships as a priority, and to develop an identity distinct from its roots in Monsanto.

In partnership with the research-park developer Wexford, the Center is developing unused acreage from the original Monsanto donation into a Bio-Research & Development Growth Park (spelled BRDG-Park and pronounced BRIDGE Park) that will ultimately comprise three buildings totaling 450,000 square feet.[4] The Center very much desires large agricultural companies based elsewhere to take space in the park, so they can use the Center's core facilities and develop relationships. At present, three of Building One's 17 tenants have such close connections.

4 See http://brdg-park.com. According to the Danforth Center's financial statements, a long-term ground lease issued to a Wexford affiliate generates $1.158 per rental square foot, yielding $127,000 a year on Building One, which is not a very significant component of the Center's operating budget.

Emerging Industry and IP Management

The Danforth Center has been an active player in the Coalition for Plant and Life Sciences, and supports the regional agenda to develop startup companies around knowledge generated in local institutions. Building One houses Nidus Partners, created originally as a plant-science incubator that was staffed and paid for by Monsanto, but now operating as a privately owned virtual accelerator[5]. The Center also sponsors an annual Ag Innovation Showcase, which serves as a "pitch event" for agbiotech ventures and venture capitalists nationwide and showcases the St. Louis region.

The Center asserts ownership to discoveries made under federal research sponsorship, but emphasizes an open-door policy on collaboration. The Danforth Center presently contracts its IP management to the Global Patent Group, a group of private-sector patent practitioners who are based in the BRDG-Park.

The Center has available limited discretionary funds, which in a university context might be called a "gap fund," to help PIs define fundable projects that will translate findings into field trials, but does not maintain any capacity for equity investment. Instead, it leverages the capability of BioGenerator,[6] a nonprofit accelerator, an important component of the region's plant and life science strategy and equipped with funds to make pre-seed and seed-stage equity investments. BioGenerator maintains its own incubator facility in Midtown St. Louis, and was a key factor in the region's success at obtaining a regional innovation cluster award from the federal government's multi-agency i6 Challenge program.[7]

Three years ago the Center announced the formation of the spin-off Agrius BioForms LLC, a joint venture with GeoSynFuels in which the Center holds a 49% interest, with the mission of commercializing certain biofuels research supported by USDA. On current financial statements, no value is assigned to the JV.

5 See http://niduspartners.com.

6 See http://www.biogenerator.org/index.shtml.

7 See http://www.eda.gov/challenges/i6/ and http://www.biogenerator.org/i6/index.shtml.

HOWARD HUGHES MEDICAL INSTITUTE INVESTIGATORS PROGRAM (DISTRIBUTED)

Overview

The Howard Hughes Medical Institute (HHMI) was formed in 1953 and after a tumultuous early history, now expends nearly $900 million annually for biomedical research; only the federal government spends more in this arena.

The HHMI Investigator program is HHMI's flagship and is a distributed or virtual institute, rather than site based. HHMI selects accomplished or highly promising faculty members at universities nationwide and designates them as HHMI Investigators. They remain in place on various university campuses but become HHMI employees, fully supported for five years at a time, and relieved of any obligation to seek grant support while they pursue their research visions. Universities embrace the program for reasons of prestige and financial incentives provided by HHMI as part of the appointments.

HHMI expends more than $500 million annually for the HHMI Investigators program. The program attempts to identify and nurture leaders in biomedical research. Currently there are more than 340 designated HHMI Investigators, including 14 Nobel laureates and 161 members of the National Academy of Sciences. At one time, investigators were selected only from nominations made by invited universities, but today faculty who believe they meet the criteria may apply directly. Historically, HHMI's Investigators are selected from those with research interests in the areas of genetics, immunology, cell biology, neuroscience, structural biology, and computational biology.

The design of this program allows HHMI to fund "people not projects" and allows investigators to focus on science, not grantsmanship. However, HHMI also permits its investigators to seek competitive research grant support for research staff remaining on university payroll; enabling the faculty to phase back into conventional university positions should their HHMI Investigator status not be renewed after its five year term. Such outside funds may also enable activity that the HHMI itself will not support. HHMI Investigators have usually focused on basic research; however, in recent years HHMI has expressed increasing interest in translational and patient-oriented work.

Several recent studies have ranked HHMI among the best research organizations in the world (along with Whitehead Institute). A recent review of performance by MIT and NBES found that HHMI Investigators more often widened the scope of their research or explored unknown territory than was the case for a comparable group receiving NIH funding during

the same period. This study concluded that the HHMI funding strategy is driving scientific creativity and excellence by the nature of HHMI's incentives to explore novel lines of inquiry.

Startup Phase

History and Motivation

Howard Hughes wrote into his will in 1925 his desire to set up an institution to support biomedical research, but it was not until 1951 that six physician-scientists were appointed as Howard Hughes Medical Research Fellows, all paid personally by Hughes. The HHMI was incorporated in 1953 (with initial offices in Florida). Hughes deeded to HHMI his entire interest in Hughes Aircraft and served as the Institute's sole trustee, although there did exist an advisory committee. From the outset, this arrangement was regarded with suspicion by federal tax authorities. Though the Institute characterized itself as a "medical research organization" (a less restrictive classification than that of private foundation), it conducted only a few million dollars a year in research, and the Treasury apparently saw the arrangement as an attempt to make all of Hughes Aircraft's earnings tax-exempt while maintaining Mr. Hughes' lifestyle.

Startup Financing

A long-running legal battle between the Institute and the IRS escalated with Mr. Hughes' death intestate in 1976. As the various claims on the state were identified and dealt with, in 1984 a Delaware court ordered the HHMI spun off under the control of an independent, blue-ribbon board of trustees, which promptly moved headquarters to Bethesda, MD and ramped up the spending rate.

In 1985 the trustees sold all HHMI's shares of Hughes Aircraft to General Motors, instantaneously creating a multi-billion dollar endowment. Electing to retain the claim to "MRO" status, the new board insisted that HHMI Investigators, wherever they were physically located, all be HHMI employees – thus emphasizing the "people not projects" mantra and turning a necessity into a virtue.

In 1987 the trustees reached a final settlement with the Treasury Department that required them to expend at least 3.5% of endowment assets annually (less than the 5% required of private foundations) in some combination of direct employment and extramural grants. Today, the $870 million operating budget remains supported almost entirely by endowment earnings.

Current Operations

Research Profile

As noted there are no pre-defined research topics or "centers" among the pool of HHMI Investigators, nor any centralized core facilities except at Janelia Farm (see below).

Academic Partner Relationships

Appointment of each HHMI Investigator is for a five year renewable term, with no requirement for annual reporting. The Investigator remains at his or her home campus and retains a faculty position but becomes an employee of HHMI, supported by a regional office rather than by campus staff, and deriving all salary and benefits from HHMI itself. Each Investigator leads a team of up to 25 postdocs, grad students and technicians — some of whom go on the HHMI staff roster, while others remain on university payroll. HHMI Investigators must spend at least 75% of their time on biomedical research and may spend up to 25% on teaching, consulting and administrative duties.

To facilitate interaction with the institutional partners, HHMI enters into a collaboration agreement with the host university, paying rent on laboratory space and supporting major renovations or equipment purchases. Costs per Investigator are reported at approximately $1 million annually or $5 million over the five year term. Postdocs are covered no more than six years in total (in cases of a renewal), and doctoral students have to be financed from non-HHMI sources.

Talent Recruitment

The application process for HHMI Investigators is designed to capture rising stars; it is not a young scientist program. Applicants must have a Ph.D. or M.D.; hold a tenured or tenure-track position at the assistant professor or higher level; have more than five but no more than 15 years' experience since appointment at the assistant professor level; and, be the PI on one or more active national peer-reviewed research awards of at least three years duration.

Investigator designations are made through rigorous national competitions. In 2008, HHMI scrapped the process in which HHMI Investigators were "nominated" by their home institutions. Instead, individuals may now apply directly. From time to time, on no formal schedule, HHMI now announces open competitions for researchers from universities, medical schools and other research institutions to apply to become Investigators. In some competitions, HHMI may focus on a specific research area or investigator career stage. The most recent competition ended in 2012, under which HHMI will select another 30 Investigators in 2013 at an estimated total additional investment of $200 million.

Applicants are evaluated by review committees of distinguished scientists (usually current and past members of the Institute's Medical Advisory and Scientific Review Boards and HHMI's scientific staff). Criteria for selection of investigators include:

- They identify and pursue significant biological questions in a rigorous and deep manner;
- They push their chosen research field into new areas of inquiry, being consistently at its forefront;
- They develop new tools and methods that enable creative experimental approaches to biological questions, bringing to bear, when necessary, concepts or techniques from other disciplines;
- They forge links between basic biology and medicine; and
- They demonstrate great promise of future original and innovative contributions.

HHMI expects not only productive results but wants Investigators to have "spectacular" results. Renewal is based on peer review focused on the creativity and originality of the Investigator and their plans for the future. About 15% of HHMI Investigators are not renewed at some point. If an Investigator is not renewed, there is a phase out plan for HHMI funding withdrawal over a period of several years.

Subsequent Growth and Sustainability

Except at times when difficult financial markets affect the endowment returns, HHMI's main challenge has not been sustainability. HHMI's endowment now fluctuates around $16 billion, and in FY 2011 HHMI expended a total of $835 million on biomedical research, of which about $500 million (the 3.5% minimum) went to the Investigators program and the balance to other programs.

The HHMI Investigator program is primarily a virtual extramural institute, with Investigators and collaborators spread across 70 universities, medical centers and research institutes in the U.S. However, at the turn of the millennium, the HHMI decided to build and finance its own intramural research program, centered on a new $500 million campus (Janelia Farm) it designed and built in Ashburn, VA, close to Dulles Airport and separated from the current HHMI headquarters in Bethesda, MD.

Janelia Farm opened in 2006 and will eventually employ 50 interdisciplinary teams with twice as many visiting scientists. The two broad themes at Janelia Farm are neuronal circuits and imaging technologies. Janelia Farms hires two kinds of lead investigators on five year renewable appointments: fellows, with labs of up to two additional members, and group leaders, who are more analogous to HHMI Investigators and may lead labs with up to six additional members. No extramural grants are sought, and lab heads have no formal teaching duties or major administrative responsibilities.

Besides the Investigator program HHMI has also added additional programs including international scholars; early-career support for biomedical scientists both domestically and internationally; a $75 million collaboration on plant sciences with the Gordon and Betty Moore Foundation (15 investigators); a collaboration on tuberculosis and HIV with University of KwaZulu-Natal in South Africa; and $50 million in education grants to small colleges and universities. HHMI has also begun a four-year, $10 million/year pilot program to support eight teams of HHMI Investigators and other non-HHMI faculty on collaborative research.

Industry Relations

Existing Industry and Research Partnerships

HHMI's position on industry support to its Investigators is traditional. HHMI says that interaction between industry and academe can promote innovation and faster development of products that ease suffering and save lives, "but it must not come at the expense of academic vitality and integrity." HHMI wants a balance between interaction with industry and "minimizing potential distractions and conflicts of interest."

Except for unrestricted gifts in appropriate circumstances, company funding is not permitted in HHMI laboratories. Collaboration with for-profit firms is welcomed if they are driven by "scientific considerations." Industry funding is neither sufficient nor desired: there must be direct scientific contributions by industry to the collaboration. Critically, HHMI does not permit sponsored research by one of its Investigators with a firm that would result in giving industry rights to any HHMI intellectual property.

Emerging Industry and IP Management

HHMI Investigators are allowed to consult for companies including those they found, but must pass conflict-of-interest screening and — once there is an established market value for a spinoff — may not consult with a startup in which they own more than 5%. If there is no consulting involved, the Investigator may own any amount of a startup company.

IP generated by an HHMI Investigator is assigned to the host institution, which makes decisions regarding patenting, licensing and commercialization of inventions. However, HHMI "strongly encourages" the receipt of cash-only consideration in licenses of IP because of the potential conflict of interest that might arise by holding equity in a startup company coming out of the Investigator's research.

SANFORD-BURNHAM MEDICAL RESEARCH INSTITUTE (LA JOLLA, CA, AND ORLANDO, FL)

Overview

Sanford-Burnham Medical Research Institute,[8] founded in 1976 as the La Jolla Cancer Foundation, has gone through several name changes, the most recent of which honors a $50 million pledge in 2010 by South Dakota financial entrepreneur-turned-research-patron Denny Sanford. While its headquarters remain in the Torrey Pines Mesa, a northern suburb of San Diego, the Institute has also steadily expanded its physical footprint, first to Santa Barbara and most recently at the Lake Nona "Medical City" development in Orlando, FL.

Research now encompasses broad "centers":

- Cancer;
- Neuroscience, aging and stem cell;
- Infectious and inflammatory disease;
- Diabetes and obesity; and
- Children's health (a dual-site program in collaboration with Sanford Health of Sioux Falls, S.D.).

Startup Phase

History and Motivation

The La Jolla Cancer Foundation was established in 1976 by Dr. William Fishman and his wife, Lillian. Dr. Fishman was at that time a distinguished cancer researcher who was approaching mandatory retirement age at Tufts University in Boston. He had come to California for a scientific congress at a time when a vibrant bioscience ecosystem was beginning to emerge in San Diego and decided to start his own cancer research program, joining the new and rapidly growing research community defined by the Scripps Clinic and Institute, the Salk Institute, and UCSD itself.

8 See http://www.sanfordburnham.org.

Startup Financing

Initially, the Foundation existed only on paper, but was bootstrapped through transfer of NIH grants to the new entity. It did not start with any kind of endowment and existed in rented space that had previously been occupied by Scripps. In 1996, the Foundation was renamed The Burnham Institute in honor of a $10 million gift from local businessman Malin Burnham. One of the five "centers" (the one in neuroscience) is also named for a donor, California real-estate developer Del Webb, and one of the core facilities (in high-through put screening) is named for Conrad Prebys. Despite this, the overall endowment remains modest, approximately $20 million. Sanford's gifts came in two waves, starting in 2006. The 2010 gift is payable over time and is not targeted at endowment but at current research activities.

Initial Leadership

Dr. Fishman was the initial scientific leader and president of the Cancer Foundation, and the current president is only the second after him.

Current Operations

Research Profile

Sanford-Burnham is organized into two "pillars": discovery-oriented research and technology infrastructure.

As at an academic institution, within the discovery-research pillar, the faculty laboratory is the fundamental unit of organization. Collections of six to eight laboratories working on related or complementary themes are organized into "programs," of which there are now about 15. Each program has a director, who is responsible for making sure the constituent faculty labs are meeting, sharing data, and figuring out how to work collaboratively on science and grant applications. Then, at the highest level of aggregation, between two and four programs are grouped under one of the five "centers" listed above. Each of the centers also has a director.

Within the infrastructure pillar, "core facilities" or "shared resources" are the fundamental unit of organization. These are managed by dedicated staff that do not have faculty appointments and typically come from backgrounds in pharma or biotech companies. There are 33 such facilities, spanning aspects of the "omics," small-molecule drug discovery, assay development, screening, chemical informatics, medicinal chemistry, pharmacokinetics, animal vivarium, etc. The core facilities are aggregated in turn into "technology centers," such as a Center for Drug Discovery that includes cores for assay development, high-throughput screening, chemical-library management, etc. Each center reports to a vice president and comes equipped with ample "project-management capability to make sure the parts work together."

Centers	Programs	Technology Centers	Shared Resources
Cancer	Tumor microenvironment	Chemical genomics (8 primary cores)	Animal resources (6 services)
	Tumor development	Stem cells (7 cores)	Cell analysis & histopathology (6 services)
	Signal transduction	Translational research	Structural biology (4 services)
	Apoptosis & cell death		Genomics (5 services)
Neuroscience, aging and stem cell	Degenerative disease		Proteomics & metabolomics (3 services)
	Development and aging		Bioinformatics (3 services)
	Stem cells and regenerative biology		Chemical biology & drug discovery (9 services)
Diabetes and obesity	Metabolic signaling and disease		
	Cardiovascular pathology		
Infectious and inflammatory disease	Infectious diseases		
	Inflammatory diseases		
	Bioinformatics and systems biology		
Children's health	Genetic disease		
	Muscle development and regeneration		
	RNA biology		

Academic Partner Relationships

Structurally Sanford-Burnham is completely independent of its academic partners. Relationships with UCSD and other institutions are largely informal and bottom up, reflective of a highly collaborative community that has emerged in San Diego over the last 40 years. Many Sanford-Burnham faculties have taken adjunct appointments at UCSD, often teaching once a year, hosting a graduate student, etc. At the bench level, it is extremely common for scientists from the several academic and research institutions to write papers together and to submit and win grants together, with one party serving as the prime contractor and the other as a subcontractor. Similar arrangements are developing at the Lake Nona campus.

Talent Recruitment

Sanford-Burnham recruits across the board, a combination of people with academic and business backgrounds. For faculty hires, the formal startup package is three years, though it is more generous in Florida than in California, because the funding from the State of Florida was specifically targeted for recruitment. For an entry-level assistant professor, the package includes their salary, two or three FTEs of laboratory professionals, and equipment. If the recruit is not self-funding by grants after three years, there is no guarantee of continued support by policy, though in practice a fourth year is now granted. After that point, if the investigator is not successful at self-supporting, they are released.

At the senior level, recruits are expected to cover up to the NIH "cap" on salary support, and the Institute provides everything after that, so in practice Sanford-Burnham covers about half the salary, while the balance is grant-supported. These hires usually bring several grants with them, and the Institute provides mainly capital equipment, some supplemental bridge funding, and — most importantly — commitment to hire others in allied areas that can be grouped into "programs." These arrangements are highly variable.

Generally Sanford-Burnham will not hire away from the other La Jolla institutions, unless someone has been offered an opportunity elsewhere, their host institution does not have the resources to compete, and there is a consensus on the importance of keeping them in town. The institutions may also team up to make husband/wife hires that make each individual recruitment easier because both know the spouse will also have a local job at an appropriate level.

In Florida, in order to successfully recruit, Sanford-Burnham emphasizes that it is operating as an integrated institution, building on a 36-year heritage of success and an established brand: there is collaboration between the two campuses, and the technology facilities are complementary and not duplicative wherever possible. Samples and data are moving constantly between the two sites, and there is ubiquitous videoconferencing.

Subsequent Growth and Sustainability

In 2007, following Florida's high-profile incentives provided to Scripps Research Institute to open "Scripps Florida" in West Palm Beach, FL, the Burnham Institute also let it be known that it was recruitable. After entertaining offers from several Florida communities, Burnham leadership chose Orlando, where it could discern the outlines of an emerging ecosystem not unlike Torrey Pines in the rapidly developing "medical city" being created by Tavistock Realty on 600 acres of its Lake Nona mega-development. The package was generally estimated to be worth at least $300 million in total, including parallel investments in infrastructure at the Lake Nona site, and was seen by management as enabling more rapid growth in research activity than would be possible at the home site or under any other circumstances. The general outline of financing for Burnham at Lake Nona was as follows:

- $155 million in cash from the State of Florida Innovation Fund;
- $70 million in cash from the City of Orlando and Orange County combined, about evenly divided;
- $12 million in cash and land from Tavistock, the developer of Lake Nona;
- A new fire station, road work and infrastructure from the county and associated financing districts, and loans from Tavistock for rapid construction of middle and high schools;
- A donation of human tissue valued at $30 million from Orlando Regional Healthcare and Florida Hospital;
- Exhibit space at Epcot for 10 years valued at $11 million;
- Community commitment to raise another $15 million philanthropically for Burnham; and
- Miscellaneous employee incentives.

The cash support from the state and localities was targeted at providing operating capital for build out of 30-35 faculty labs and supporting infrastructure. The specific focus of the Florida site is on diabetes, obesity and metabolic diseases. Other medical institutions at Lake Nona that will comprise the emerging community include: Nemours Children's Hospital, a VA Medical Center, the UCF College of Medicine and its School of Biomedical Sciences, the M.D. Anderson Orlando Cancer Research Institute, and a University of Florida branch.

The overall $161 million operating budget for the combined sites is derived 82% from federal grants and contracts, about 11% from industry projects and the balance from philanthropic gifts or endowment earnings (small).

Future Growth

Startup of Lake Nona was modeled on experience in La Jolla, but now that growth in NIH grant funding has stalled, the Institute is re-doing its 10-year plan for expenditure of the residual state incentive funds, so that the new campus can end up fiscally viable. Leadership also expects to have to diversify beyond NIH and has ongoing efforts with other agencies such as DOD and NASA, with healthcare systems, and with pharma companies (see below). It also expects to make a major push for philanthropic funding and development for the first time of a significant endowment.

Industry Relations

Sanford-Burnham exemplifies a rapidly changing environment for industry partnerships. At one time in the not too distant past, the main path to partnership with industry was via support of an individual faculty laboratory, sometimes spinning out venture-backed companies that went public or survived until some big pharma company acquired them. More recently, large companies have developed interest in partnering earlier in the process, at the bench level. At the same time, the Institute developed capabilities in drug discovery and protein therapeutics that meant that work on site need not stop with target discovery/validation, but can also advance to prototype therapeutics, animal model validation, and so on. Therefore the interests of industry and the capabilities of the Institute are converging.

The preferred relationship is now to have large-scale, Institute-wide "thematic partnerships" with a company based on its interests, managed by a steering committee that nominates candidates. The sponsoring company has a "first right" to pursue these topics, and if they pass on the opportunity, it can be shopped to other sponsors. Existing partnerships include with J&J on inflammation and neuroscience; with Takeda on obesity, though at the earlier stage of target and biomarker discovery; and with Cellgene, as a fee-for-service target-screening activity. The Institute also is a partner in the Pfizer Center for Therapeutic Innovation based in San Diego.

To build these partnerships, the Institute has had to add business-development capability, moving away from traditional university tech-transfer staffing and adding seasoned people from industry with knowledge of how to negotiate deals similar to what a biotech company would obtain from big pharma. Their emphasis is on outreach, conversation-starting, getting academic and industrial scientists together, and then intensive project management. Individual faculty are still welcome to generate their own industry support, and to create startup or spinoff companies (which can be housed in a small in-house incubator), but this is not where Institute funding growth is projected to increase substantially compared to the broad thematic partnerships.

STOWERS INSTITUTE FOR MEDICAL RESEARCH (KANSAS CITY, MO)

Overview

The Stowers Institute for Medical Research[9] (Stowers) is an independent basic research institute, functioning primarily at the national and global level, although it is situated in Kansas City. Structured as a nonprofit medical research organization, its mission is to improve human health by studying the fundamental processes of life. Stowers seeks to be recognized as a member of the elite group of institutions that drive cutting-edge life sciences research through both the discoveries they make and the future leaders they train.

The focus of Stowers is on outstanding science, enabled by an interdisciplinary culture of collegiality and state-of-the-art core lab facilities and support staff. From its inception, the Stowers Institute set out to create a "best of its kind" institution within 25 years. The founders wanted the Institute to become known as the most innovative and effective medical research institution in the world. Stowers' leadership understood that recruitment would play a critical role in reaching this goal and worked to match this commitment with appropriate funding. Today Stowers is the nation's second-largest medical research organization after the Howard Hughes Medical Institute and has endowments totaling $2 billion or so.

The Stowers Institute does not work directly with industry, which has access only through BioMed Valley, a wholly owned technology-transfer and commercialization company.

Startup Phase

History and Motivation

Jim Stowers, a physician by training, made his fortune as the founding entrepreneur of the American Century mutual fund companies. Both cancer survivors, Jim and his wife, Victoria, a registered nurse, wanted to "give back" something more valuable than money to advance medical research. The idea of creating an independent basic research institution came to the couple in 1994, and they started Stowers Institute with a personal contribution of $50 million, followed by subsequent contributions of more than $1 billion in cash and shares of American Century.

9 See http://www.stowers.org.

The financial commitment was soon turned toward the purchase of a 10-acre site in Kansas City, MO and construction of a 600,000 square foot research campus. It took six years to conceptualize and develop the plan for the Institute. Doors officially opened for the Institute in November 2000. Located on the former campus of Menorah Medical Center, this location is directly across the street from the University of Missouri-Kansas City (UMKC), which is not itself a research-intensive institution. The site is also remote from the University of Kansas Medical Center (KUMC), the main academic medical center, on the Kansas side of the border.

An additional 280,000 square-foot complex was added in 2009 to accommodate additional support functions and storage facilities, but this building is located at a South Kansas City location. This site is apparently near where a biotech office park is planned by one of the Stowers' sons, and also close to the offices of the Institute's captive commercialization company, BioMed Valley Discoveries.

Startup Financing

In 1998, J.P. Morgan (now J.P. Morgan Chase) purchased 45% percent of American Century, allowing the Institute to accumulate the cash assets to begin operation with a sizeable endowment that today amounts to nearly $2 billion.

Initial Leadership

There are several legal entities involved with Stowers: the Stowers Institute itself; Stowers Resource Management[10] (which manages the endowment); Stowers Real Estate Holding Corporation (a title-holding company); and BioMed Valley Discoveries. The founders sit on both the Institute and Resource Management board, and the latter also includes regional health and business leaders, though not the local universities or public agencies.

Dr. William Neaves served as Stowers' president and chief executive officer until 2010. Initially tapped by Jim Stowers with the charge of recruiting the best talent, he played a critical role in influencing the early structure and governance of Stowers. Partnering with a scientific director, Robb Krumlauf, Dr. Neaves applied "rigorous good citizenship standards to any potential recruit. We called it our anti-prima donna screen." Neaves sought to mirror the qualities of the Howard Hughes Medical Institute (HHMI), which he referred to as the "gold-standard of basic research," whereby all work would be evaluated according to rigorous scientific standards.

10 Stowers Resource Management Inc. is a supporting organization and public charity. It is the legal entity that manages the endowment, provides corporate governance and core administration functions.

Current Operations

Research Profile

Over time, Stowers has grown from a few narrowly focused research platforms to now hosting 22 independent research programs and three technology development programs, involving 150 ongoing projects. An early goal was set by Stowers leadership to ensure that the Institute housed at least 50 independent research programs led by highly ranked experts. Stowers currently has 550 researchers, support personnel[11] and 22 independent research programs and more than a dozen technology development platforms (bioinformatics, proteomics, imaging) and core laboratories. It hosts 180 undergraduates, pre-doctoral research fellows and postdoc residents from over 30 countries.

While Stowers began with a focus on cancer alone, this changed during the formative years to a broader focus on mechanisms of disease. The research programs at the Stowers Institute focus on basic biomedical research in model organisms as a way to understand how cells function and to decipher what goes wrong when they malfunction. Stowers' investigators analyze how genes and proteins control virtually all biological processes; from cell division to cell differentiation; from processing smells to storing fat; from generating memories to regenerating missing body parts. All research within Stowers falls into six loosely defined scientific platforms aimed at accomplishing their basic research focused mission.

(Columns are independent of each other)

Program areas

- Chromatin and regulation of gene expression
- Chromosome structure and cell division
- Computational biology, modeling and technology
- Developmental genetics and cell biology
- Developmental neuroscience
- Stem cells and regeneration

Underlying disciplines

- Anatomy and cell biology
- Molecular and integrative physiology
- Biochemistry & molecular biology
- Pathology and laboratory medicine
- Chemistry

Core lab facilities

- Computational biology
- Cytometry
- Electron microscopy
- Histology
- Imaging
- Laboratory animal services
- Media preparation & tissue culture
- Microscopy
- Molecular biology
- Proteomics
- Reptile and aquatics
- Screening

11 This is broken down roughly as 425 staff, including 22 PIs, 64 scientists in core support, 80 post doc researchers and fellows, 45 graduate students, 82 technicians, and 4 research advisors (microarrays, imaging, modeling, mathematics).

Academic Partner Relationships

Stowers maintains some relationships with regional academic institutions and hospital centers for clinical trials. Most senior scientists in the Institute do have adjunct appointments, primarily at the University of Kansas Medical School (KUMC), across the state line in Kansas. In the early years of the Stowers Institute, senior staff tended to have adjunct appointments at UMKC, a much weaker player in biosciences research historically. KU Cancer Center did have Stowers as a partner in its recent application to NIH/NCI and both just received an award to become the 67th NCI-designated cancer center in the U.S. Graduate students at KUMC come to Stowers for training. However, a Stowers investigator is not expected to teach or provide time other than to his or her work and obligation to the Institute. Other institutions, including KU and UMKC, have their students doing dissertation research in Stowers labs.

Talent Recruitment

The Institute's Scientific Advisory Board (SAB) played a critical role in recruiting talent. SAB members receive a per diem reimbursement for their time, which includes an annual meeting and occasional consultations throughout the year. No outside consultants were hired to assist in the creation of the Institute; rather the SAB played this role initially and continues to do so today. Two of the six members are also current Howard Hughes Medical Institute Investigators.

Rather than launching with a single recognized and celebrated leader, the Institute's first hires were two assistant investigators who were postdocs, followed by a Scientific Director, and only then two senior investigators. Stowers took "baby steps" and matured carefully into its current state. Even now, Stowers does not recruit senior faculty who are used to running independent labs. Stowers' explicit strategy is to nurture and support young and mid-career scientists who go on to become world leaders either at Stowers or elsewhere, accruing prestige and reputation to Stowers in the process. This focus is at an earlier career stage than the Howard Hughes Medical Institute's Investigator program. Stowers seeks recruits who have the personality traits of a team player, and avoid "prima donnas or standalone rock stars."

Stowers investigators are surrounded with technological expertise (e.g., histology, imaging, microscopy, proteomics, high throughput screening, mass spectrometry) to assure they do not have to learn the newest technology, but rather have state-of-the-art support ready at hand to accelerate research. Stowers has an independent peer panel review the work of each investigator every five to seven years. The one key question that is posed is: how has this scientist contributed new knowledge and helped us think differently? If there is clear progress against this single goal, the investigator remains. If there is not, the investigator is supported over the next 18 months to two years in an effort to secure a new position elsewhere.

Subsequent Growth and Sustainability

Stowers operates on the assumption that its endowed reserve will sustain its current and future operations. The theory underlying the Institute is if researchers are free from the pressures of securing their own funding and are allowed to focus all their talent and energy on scientific research, their productivity and creativity will soar. While some Stowers investigators bring with them or secure new federal funding (including funding from NIH, disease advocacy groups, and others), they are not placed in a position where they have to chase funding from external sources. Rather, they are expected to excel in their science, as measured by awards (including selection as HHMI Investigators or election to the National Academies of Science) and publications (700 to date since founding).

The $2 billion endowment[12] of Stowers has generated over $900 million to date in earnings expended on research operations. The expected distribution is about $70 million a year, or more in a year with good investment performance. Although Stowers did issue a bond to build their facility, endowment earnings provide a strong cushion to support investment, hiring and ongoing expenditures. One-third of their budget is dedicated to technology-center staffing, equipment and running the facility.

Future Growth

In 2012 the Institute started its own graduate school, offering a doctoral program in biology that will enable students to obtain the Ph.D. within five years of enrollment, with a strong focus on integrative approaches.

In the last decade, Stowers stated it would totally fill all existing space by 2008, but it is not clear if this has happened. Stowers quietly purchased an additional 100 acres of land (near where the Stowers family bio/office park is proposed to be located) and indicated plans to add 600,000 additional square feet of research space each decade at a cost of $300 million for the next phase alone. However, since the Missouri Legislature and Governor have not been able to release fully the tobacco settlement funds that had been promised for biomedical research, these plans have apparently been put on hold.

12 Stowers points out that this endowment is twice as large as the combined endowments of all the medical research institutions in San Diego, including Salk, Scripps, Burnham, and Ludwig.

Industry Relations

Existing Industry and Research Partnerships

Within the region, there are more than 200 biotech companies, 20 academic institutions offering various educational options, and numerous medical centers and health systems. During the early years of Stowers' growth, the Kansas City region began to emphasize this cluster of bioscience institutions, companies, and startups as an economic-development strategy. Modest support was available to Stowers through investments channeled by the Kansas City Area Life Sciences Institute (KCALSI), a regional funding collaborative, and the Kansas Bioscience Authority (KBA). However, Stowers is not currently significantly involved in these activities, perhaps due to its global view of its own mission and its dominant focus on basic research.

The only outside groups permitted to use the Stowers facilities are not for profit organizations with a scientific mission. Use by commercial entities is restricted, and the preferred way for industry to access Stowers research is through BioMed Valley Discoveries, a captive company dedicated to commercializing discoveries that emanate from the Stowers labs or elsewhere. BioMed Valley was announced in 2004 as a "bench to bedside" translational organization, aimed at addressing unmet medical needs rather than necessarily achieving commercial return. It is designed to finance and manage projects too early or risky or small for industry. It focuses on diagnostics and development of new therapies in cancer and both inflammatory and infectious diseases. It supports three kinds of projects: (1) research to answer clinical hypotheses; (2) collaborations with a network of partners on proof of concept studies in the $5-15 million range; and (3) taking therapeutics into the marketplace directly or by outsourcing.

Three of the organization's staff initially were to focus on commercializing research coming out of the Stowers Institute; but the organization also planned to look across the life sciences industry and around the world for opportunities as well. As of 2012, it has some of the features of a seed-stage venture capital investment company focused on the life sciences. Initially BioMed Valley was to raise external capital as well, and as of early 2012, the organization claimed it had raised in excess of $120 million.

Emerging Industry and IP Management

Stowers' investigators assign all intellectual property (IP) to the Institute and receive 50% of any commercialization revenues. All IP is marketed by BioMed Valley Discoveries, acting as the Institute's technology transfer agent. Initially BioMed Valley was conceived as exclusive agent for KUMC and UMKC as well, in exchange for endowment contributions to be made by Stowers to the universities. However, the IRS opposed this plan, and instead Stowers made $2 million awards to each university for endowed chairs in the life sciences without reference to IP rights. Both schools continue to have their own technology transfer and commercialization vehicles.

TRANSLATIONAL GENOMICS RESEARCH INSTITUTE (TGEN) (PHOENIX, AZ)

Overview

The Translational Genomics Research Institute (TGen)[13] is an independent nonprofit research institute created to develop diagnostics and therapies for patients with serious diseases through personalized molecular therapies. The center's founding visionary and current president is Jeffrey Trent, Ph.D., the former director of the NIH Human Genome Institute. TGen received substantial state, local and philanthropic support in part because it was conceived as an economic-development platform for the region. Its six story building now anchors the Phoenix Biomedical Campus,[14] a 15-acre, city-owned site on the edge of the civic and entertainment district. This campus also houses a Phoenix branch campus of the University of Arizona (UA) Medical School; the first-ever downtown presence of Arizona State University (ASU); the Arizona Bioscience Collaborative, intended to link various units of the UA, ASU, and the region's larger hospitals and health chains; a magnet bioscience school; NAU's occupational therapy programs; and commercial space for business incubation.

TGen was founded in 2002 and opened its facility in 2005. Since then, annual operating revenues have climbed to about $57 million as of the latest financial statements. It has a small endowment ($6 million) and a separate fund-raising arm discussed further below. The center is organized around teams led by principal investigators, currently 16 at the professor level, 16 associate professors, 15 assistant professors, and 22 adjuncts whose primary appointments are at collaborating institutions in Arizona and nationwide. Total personnel currently employed at TGen stands at nearly 300 including scientific staff and technical and non-technical support staff.

The center's research division is organized around several principal disease groups:

- Cancer;
- Neurological disorders; and
- Diabetes and other metabolic diseases.

13 For background see http://tgen.org.

14 See http://phoenix.gov/econdev/reinvest/focus/index.html.

TGen maintains a satellite TGen Clinical Research Services unit at Scottsdale Health, in partnership with the latter's Clinical Research Institute, and a biopathogen research satellite in a rented building near Northern Arizona University in Flagstaff. The latter fulfills its commitment to the Arizona Board of Regents to collaborate with all three research universities in the state. It has also launched a new program in canine health, and just this year terminated a three-year experiment merging with the Van Andel Research Institute of Grand Rapids, MI. Overall, it plays a key role bridging between Phoenix, the state's largest city and home to many large hospital systems, and Tucson, the location of the state's only university with a medical school.

Startup Phase

History and Motivation

TGen had its origins in the experience of a Phoenix attorney and power broker who lost his wife to an aggressive cancer. In the course of taking her for treatment to Tucson, where the state's only medical school and most advanced clinical trials were situated, he concluded that Phoenix needed better biomedical capabilities of its own, and he was introduced by the UA faculty to Dr. Trent, a Phoenix native who had done his doctoral work at UA.

Dr. Trent let it be known that he was willing to be recruited back to Arizona if he could be provided with resources to pursue his vision for a nonprofit cancer tissue bank (a pre-existing entity that became the International Genomics Consortium (IGC), a tenant and service provider to TGen) and an institute oriented to translational medicine (what eventually became TGen). Dr. Trent became the centerpiece of a competition among several regions, which served to engage political and civic support in Arizona.

These discussions took place at the same time as the Flinn Foundation of Phoenix was transitioning its programs from modest support for medical education, the arts, and equitable access to healthcare into the holder of the state's strategy for bioscience-based economic development. Flinn was originally a family foundation established by an area physician but had lately passed into the hands of a non-family board and professional management, and was looking for the opportunity to place a large imprint on the state.

The same year, Flinn commissioned on behalf of a still-relatively passive state government a comprehensive bioscience "roadmap" that identified three broad platforms on which the state's economic development could be built: bioengineering, cancer research, and neurosciences. The state's voters had already agreed to dedicate a share of sales-tax revenues to biomedical research (Prop. 301 of 2001). In the year after release of the Roadmap the Legislature also committed $440 million to new university research facilities, the first time in a generation that such statewide investments had been made.

The Flinn Foundation and TGen's early champions set a $90 million go/no target for fund-raising and ultimately exceeded it (see below under startup financing). The catalyst of the TGen recruitment also enabled the state to broker the first-ever agreement between UA and ASU to bring elements of the UA Medical School to Phoenix, where the larger number of patients and hospital beds resided. ASU continued to build its life-science capacity (expressed now in a Biodesign Institute) but was convinced to forego a costly political fight for its own medical school (Note: in later years ASU pulled out of UA Medical School-Phoenix and has since joined with the Mayo Clinic to expand its healthcare operation in Scottsdale into a proposed branch of the Mayo Medical School in Arizona).

A number of TGen's PI laboratories are difficult to distinguish from those in a university or academic medical center, several are structured as "research services" (core facilities), and TGen as a whole embraces applied, translational and clinical research as fundamental to its mission.

Startup Financing

Although there was no large endowment available to begin the effort, Flinn was an early champion and brought along with it another important area foundation with which it had already collaborated on healthcare issues, the Virginia Piper Charitable Trust. Elements of the financing package included:

- $46 million in construction and tenant-improvement costs contributed by the City of Phoenix, which built the structure, owns it, and leases it to TGen and its co-tenants (which include IGC, an NIH laboratory, and clinical operations of a local hospital system). Phoenix offered TGen and IGC a five-year abatement in order to give them breathing room until they could begin building revenue, but the city will recapture all its costs over the 30-year term of the lease;
- $30 million from the State of Arizona, through matching commitments to faculty lines by the three universities operated by the Arizona Board of Regents and cash research grant commitments from what was then called the Arizona Disease Control Commission, a public-health research institution since renamed the Arizona Biomedical Research Commission.[15] The latter entity expends funds from the state's lottery, and has directed considerable support to TGen and its TGen North biopathogen program in Flagstaff;
- $15 million from the Flinn Foundation, structured as initial operating support over a declining five year schedule;[16]

15 See http://azdhs.gov/biomedical/.

16 The Flinn Foundation and the Piper Trust later gave TGen an additional $45 million in conjunction with recruitment of Dr. Lee Hartwell from the Fred Hutchinson Cancer Research Center to ASU for work on personalized medicine. See http://www.flinn.org/news/918.

- $5 million from the Virginia Piper Charitable Trust, which co-funded the clinical-translational facility at Scottsdale Health;
- $5 million from the Salt River-Pima-Maricopa Indian Community; and
- Miscellaneous smaller contributions and pledges.

As noted above, the City of Phoenix financed up front TGen's building, enabling the center to launch on a capital-light strategy, reserving scarce capital for equipment acquisition and PI recruitment and bridging. TGen occupies floors 4-6 of the 173,000 square-foot building, also known as the Phoenix Bioscience Center. The IGC occupies the third floor; the second floor is rented to a laboratory of the NIH National Institute of Diabetes and Digestive and Kidney Diseases. St. Joseph's, a regional hospital chain, rents part of the first floor.

Initial Leadership

As noted, TGen was driven by its founding director, Dr. Jeffrey Trent, a genomic scientist. TGen's chief physician and the chief scientist of the clinical trials program at Scottsdale Health is Daniel Von Hoff, M.D. The IGC, originally envisioned as the commercialization partner to TGen, went its own way with its own board and leadership.

Current Operations

Research Profile

From the outset, TGen has pursued the root genetic causes of complex, multi-factorial diseases deemed to hold the most promise for applications of personalized medicine. The commitment to develop understanding, diagnostics, and therapies for three broad classes of disease has not wavered since establishment of TGen. However, the specific set of "divisions," "programs," and "units" has varied somewhat as recruitment unfolded and both research and clinical leaders were identified.

The research agenda was also affected by the three year alliance with the Van Andel Research Institute. For example, TGen eagerly embraced the idea of a Van Andel investigator to establish a new program in canine genetics and diseases, since highly bred dog populations are comparatively easy to test for genomics-derived "targets" for conditions that parallel human diseases.

The table below lays out the main topical programs, the disciplines represented by the full and associate professors, and the facilities that might be called TGen's core laboratories.

(Columns are independent of each other)

Topical programs (short list)	Underlying disciplines	Core lab facilities
Cancer and cell biology	Genetics and molecular genetics and population genetics	Bio4D (software for specimen management)
Proteomics	Clinical medicine	Genome technology core
Clinical translational (at Scottsdale, focusing on pancreatic cancer, rare cancer, & developmental therapeutics)	Cancer biology	Computational bioscience
Computational biology	Computational biology	DNA microarray technology
Diabetes, cardiovascular & metabolic diseases	Cellular and molecular biology	Pharmacodynamics and pharmacokinetic lab (at Scottsdale)
Genetic basis of human disease	Structural biology	
Integrated cancer genomics	Endocrine surgery	
Pathogen genomics (TGen North)	Computer science	
Canine health and performance	Hematology-oncology	
	Microbiology	
	Biology (and theoretical biology)	
	Medicine	
	Psychiatry	
	Applied physics	
	Neurogenetics/neurogenomics	
	Biochemistry	
	Analytical chemistry	

Academic Partner Relationships

In addition to the separate class of adjuncts, a significant number of full faculties at TGen also have academic appointments at one of three cooperating universities. These are not automatic, but depend on the collaborative relationships each basic or clinical investigator desires. University appointments are usually nonsalaried and without teaching duties, but on occasion full-time university faculty serve as the prime grantee or contractor and subcontract work to TGen. It is common for funds to flow in either direction.

Talent Recruitment

TGen has found that the field of personalized medicine is so new that it can be difficult to make senior recruitments, and the last one was completed several years ago. Instead, TGen often hires from the ranks of postdoctoral students engaged by its PIs who also hold university faculty appointments, and then promotes them up the chain of seniority.

TGen attempts to give each recruit between three and five years of "runway" to develop a sponsored program.

Subsequent Growth and Sustainability

Because its endowment earnings are limited, TGen relies heavily on grants and contracts (federal, state and industrial) and annual or special philanthropic gifts. As of 2008, TGen ranked 118th on the National Science Foundation's list of federal obligations to nonprofit institutions, garnering just under $10 million in support, all apparently from the NIH. Since then the figure has risen but no full public disclosure is available. One example of a significant federal grant is $7.5 million from NIH for a Southwest Comprehensive Center for Drug Discovery and Development, in collaboration with the University of Arizona.

In consideration of the state's role in the startup financing package, and the continuing support of the Arizona Board of Regents, the TGen governing board includes the presidents of all three research universities in the state. TGen appreciates their support, but concluded early in its history that to avoid conflicts of interest it would also need a Translational Genomics Research Institute Foundation, a separate public charity with its own board, with staff overseen by TGen officers. This foundation maintains no significant endowment, and pays out in TGen's favor an amount approximately equal to what it has raised in each year, which appears to fluctuate substantially.

In 2009, in an attempt to grow, TGen combined with the Van Andel Research Institute (VARI) of Michigan, itself one of three inter-related institutes, all endowed by the family that started Amway, and all situated in Grand Rapids, remote from any of Michigan's major academic medical centers. Van Andel wanted to complement its basic research capability with the translational and clinical end of the spectrum, and TGen believed it would be able to raise external funding more easily by being partnered with Van Andel investigators.

The mechanism of combination was not a statutory merger, but a contractual arrangement under which TGen's bylaws were restated to make it a "member" nonprofit, of which VARI was the sole member. Dr. Trent served as director of both institutes, but the experiment was not successful. Eventually the arrangement was dissolved amicably and in 2012 TGen was returned to its former organization non-member, self-perpetuating board structure.

As a revenue-generating program, TGen has also leveraged its core services in sequencing into a revenue generating Collaborative Sequencing Center that serves outside clients, both academic and industrial. Revenue from this operation does not seem to be material to TGen's financial status.

The $57 million operating budget is derived in approximately equal proportion from federal grants and contracts, industry grants and contracts, and philanthropic gifts.

Future growth

TGen's planning assumption is that federal funding will become progressively harder to come by, and that the breakdown will shift to 20% federal, and 40% each industrial contracts and philanthropic gifts. Consequently, TGen will be seeking to hire investigators who are less dependent on grant funding and more "entrepreneurial" and able to establish contract relationships with the biopharma industry.

Industry Relations

Existing Industry and Research Partnerships

TGen recognizes three broad classes of industry partners: the hospitals and healthcare systems and physician groups with which it is partnered on clinical trials; the manufacturers of sequencing equipment and other instrumentation deployed in the core labs (e.g., Agilent and Affymatrix); and biopharma companies or contract research organizations that want to mine TGen's genomic data in search of drug-development targets suitable for further validation.

Clinical contracts are handled by one of TGen's partners, whether at Scottsdale, Banner, Mayo or Maricopa Health. Pre-clinical work and compound development are handled through TGen Drug Development (TD2), a wholly owned subsidiary which is located in Scottsdale and capitalized in part with a $3 million loan from the municipality. TD2 is set up as a single-member LLC. Currently TD2 is carried on TGen's tax returns as a "disregarded entity" whose financial results (including industrial contract revenue) are consolidated with those of TGen.

Emerging Industry and IP Management

TGen prides itself on managing "accelerators" that parallel each of its research divisions. In practice, these are managed through another disregarded entity, TGen Accelerator Management LLC, which also serves as the technology transfer, licensing, and commercialization agent for TGen. The TGen COO wears a second hat as president of the Accelerator, and spends most of her time on finding the right structure for commercialization, whether straight licensing or startup.

This unit has produced about 10 spin-outs, some of which it has exited from. For example, Molecular Profiling Inc., the first spinoff catalyzed by both TGen and IGC, was subsequently acquired for $40 million by Caris Diagnostics of Garland, TX, though it maintains operations elsewhere in the Phoenix area. TGen has no direct funds available to capitalize startups and must rely on the local ecosystem and investors who may avail themselves of various tax credits and incentives now in place.

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