ESTABLISHING A SUCCESSFUL BIOMEDICAL RESEARCH INSTITUTE – THE STORY OF THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH

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ABSTRACT

Biomedical research is enjoying its golden era. It promises improvements to human health in the near future. The field is witnessing a brisk inflow of human and financial capital. In an attempt to capitalize on this growth, biomedical research centers are being established worldwide. There is relatively little literature to explain how biomedical research institutes become successful. This thesis analyzes the founding and growth of the Whitehead Institute for Biomedical Research, a leading not-for-profit biomedical research institute located in Cambridge, Massachusetts, in an attempt to identify its critical success factors.

The Whitehead Institute was founded in 1982 with a generous philanthropic donation. It is affiliated with the Massachusetts Institute of Technology (MIT). The Whitehead Institute has since enjoyed a symbiotic and productive relationship with MIT through their joint teaching, research, and administrative activities. The Whitehead Institute is renowned for its research in a number of biological areas, including the sequencing of the human genome, cancer biology, and developmental biology.

The success of the Whitehead Institute is remarkable because of its relatively small size and short history. Some of the critical success factors of the Whitehead Institute include: quality scientists, Institute endowments, affiliation to a top university, sound scientific decisions, location in a thriving biomedical research hub, and a collegial and family-like culture. These success factors are complementary to one another. In the concluding chapter, the thesis addresses the challenges confronting the Whitehead Institute, and postulates the feasibility of transplanting the 'Whitehead Model' elsewhere.

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DEDICATIONS

This thesis is dedicated to my beloved wife, Florence, my two lovely daughters, Grace and Clara, and my parents, for their understanding and unwavering support during my year in the MIT Sloan Fellows Program.

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Ms Susan Whitehead, Chairperson, Board of Directors
Mr. John Whitehead
Dr. Susan Lindquist, Director
Dr. Gerald Fink, Member
Dr. Robert Weinberg, Member
Dr. Paul Matsudaira, Member
Dr. David Page, Member
Mr. John Pratt, Associate Director
Ms Eve Nichols, Former Director of Public Affairs
Ms. Seema Kumar, Associate Director, Whitehead Institute Center for Genome Research
Ms. Patricia Granahan, Intellectual Property Manager
Mr. Gus Cervini, Project Manager for Institutional Events
Ms. Sandra Luikenhuis, Graduate Student
Mr. Julian Lange, Graduate Student

From Other Institutions:

Dr. Abraham Siegel, Former Dean, MIT Sloan School of Management
Dr. Robert Sauer, Head, MIT Department of Biology
Ms. Lita Nelson, Director, MIT Technology Licensing Office
Ms. Philina Lee, Graduate Student, MIT Department of Biology
Dr. Keith Dionne, VP/GM Technology Business, Millennium Pharmaceuticals, Inc.

Any misinterpretations in this thesis are entirely mine.

Finally, in the course of writing this thesis, I have benefited from the rich resources that are available at the Whitehead Institute and MIT.

Hwai-Loong Kong
Sloan Fellow, April 2002

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INTRODUCTION

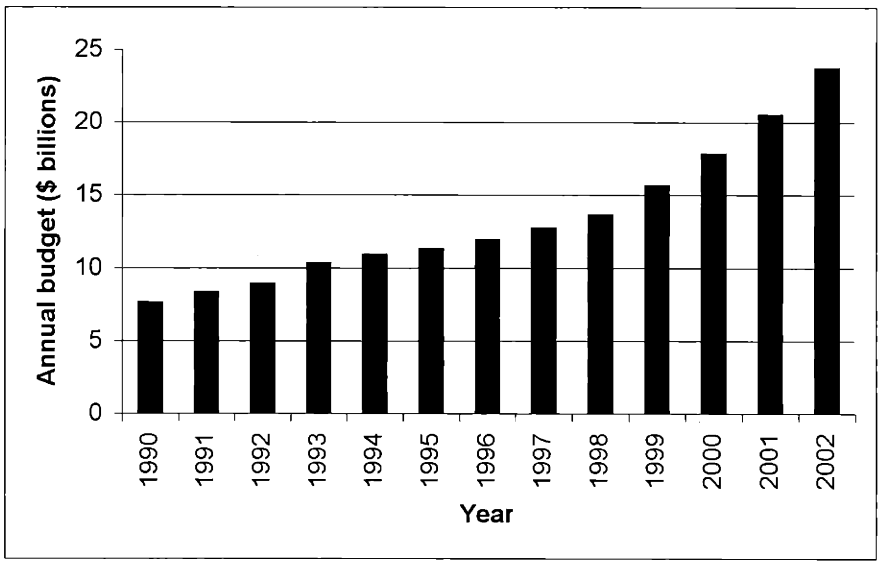
On both its past record and future potential, few would quibble with the pronouncement that the Whitehead Institute for Biomedical Research ('Whitehead Institute' or 'Institute') represents a successful research institute in the world of biology today.

The Whitehead Institute is a not-for-profit biomedical research institute that is affiliated with the Massachusetts Institute of Technology ('MIT'), and situated a stone's throw away from the University. Just 20 years after its founding, the Whitehead Institute is now clearly one of the most successful biomedical research centers in the world.[1] Indeed, examining the performance of the Whitehead Institute over the past 20 years, one would note that its trajectory has been exponential and spectacular. Such success is unusual and leads us to ask several questions: What were the endowments that enabled Whitehead Institute to explode into the biomedical scene in the early '80s? What are the critical elements underpinning the successful growth of this relatively small research institution? What lessons can the Whitehead Institute share with future biomedical research centers?

Why should we care? The most cogent reason is that we are now in a new epoch of unsurpassed opportunities in the field of biomedical science. Biomedical science is a growing industry and a rapidly expanding knowledge space worldwide.[2] The field is

[1] Institute for Scientific Information's (ISI) Science Watch. 1993:4:1.
[2] Ernst & Young. *Focus on Fundamentals: The Biotechnology Report*. Fifteenth Annual Review, 2001.

enjoying a robust growth of human capital and financial support. According to the United States (US) National Science Foundation (NSF) figures, between 1997 and 2000, US universities and colleges saw a 34.2% increase in total research and development (R&D) expenditures in biological science (from US$4.18 billion to US$5.61 billion), and the corresponding rise in R&D expenditure in medical science was 30.2% (from US$6.91 billion to US$9.00 billion).[3] Most universities and colleges in the US derive their predominant funding from federal sources. Indeed, the US National Institute of Health (NIH) budget has been increasing by 8.4% per year from 1990-1999, and by 14% per year between 1999-2001 (Figure 1.1).



Source: NIH website – http://www.nih.gov/

Figure 1.1 – Trend of NIH Annual Budget 1990-2002

[3] National Science Foundation website: http://www.nsf.gov

The 2002 budget stood at a staggering US$23 billion.[4] This represented a third of the National Gross National Product (GDP) of Ireland, and a quarter of the GDP of Singapore.[5]

The The output of biomedical research worldwide over the past decade has been spectacular, including the rapid sequencing of the human genome, the maturation of certain novel therapeutics such as monoclonal antibodies, and the advent of reproductive and therapeutic cloning. These breakthroughs in biological research raise the prospect that human health will be further improved, and that biological research will be an increasingly important industry. Other than satisfying their intellectual curiosity, most investors – including the governments – are expecting an eventual payoff. Historical evidence does suggest that the biomedical industry, such as the pharmaceutical sector, is a lucrative business. There are justifiable enthusiasm to believe that the biomedical industry overall will continue to thrive, so long as sicknesses and death continue to inflict humans. The net result of these recent developments in the biomedical space is a palpable sense of excitement and heightened expectation in the scientific, business, and lay communities. The Whitehead Institute was born in such an era.

Commensurate with these scientific advances, different governments worldwide have been increasing their biomedical investments over the past decade. Countries such as United Kingdom, Canada, Italy, China, Japan, Singapore, Taiwan, and a number of others, have announced a series of impressive efforts aimed at jump-starting their biomedical capabilities. A clear manifestation of these efforts is the establishment of a

[4] National Institute of Health website: http://www.nih.gov
[5] CIA Fact File website: http://www.cia.gov

number of biomedical research institutes in many parts of the world.[6] In the light of this rapid expansion of the global biomedical efforts, and specifically in the context of the establishment of new biomedical research centers worldwide, the success story of the Whitehead Institute becomes both relevant and instructive.

This thesis focuses on understanding the fundamental reasons for the successful establishment and subsequent growth of the Whitehead Institute. Specifically, the thesis explores the possible contributory role of human capital, financial resources, scientific strategy, relationship between Whitehead Institute and MIT, strategic geographical location, and organizational design and culture.

It is interesting to note the relative paucity of published literature on the establishment of biomedical research institutions. To illustrate this point, there is no published academic literature to document the establishment and growth of the Whitehead Institute. A major impetus for writing this thesis is therefore to provide a structured analysis of a successful biomedical research institute, with the hope that the lessons learned from this research will help the establishment of similar research centers in the future.

This thesis is an in-depth case study of a single institution. The content and views presented here have been developed from a variety of literature sources supplemented with interviews of a number of individuals from both inside and outside the Whitehead

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[6] Birmingham K. "British government backs biomedical research strength". *Nature Medicine* 1998;4:1345;
Friesen HG. "The Medical Research Council of Canada: Integrating research to Canada's health care system". *Nature Medicine* 1998;4:1353;
Bordignon C. "The challenge of private biomedical research funding in Italy". *Nature Medicine* 1999;5:135-137; and
Birmingham K. "Singapore pushes biomedical research". *Nature Medicine* 2001;7:1168-1170.

Institute. The literature cited is multi-faceted, representing diverse sources from the life science, social science, and biomedical industry literature, as well as institutional archives and governmental statistics. The interpretation and final conclusions drawn are those of the author, and any omissions and misrepresentations are entirely unintentional.

This thesis is organized as follows: Chapter 1 has provided the backdrop of a thriving global biomedical research environment, and the rationale for undertaking this study. Chapter 2 provides a historical account of the founding of the Whitehead Institute, and takes stock of the accomplishments and current status of the Institute. Chapter 3 probes the importance of the various assets that are at the disposal of the Whitehead Institute. Chapter 4 analyzes the scientific strategies that the Whitehead Institute has adopted over the years. Chapter 5 studies the organizational design and context of the Institute. Chapter 6 delves into the organizational culture and the defining practices that are so characteristic of this Institute. Chapter 7 examines how the various critical success factors interact with one another complementarily, and predicts the future challenges that the Whitehead Institute might confront. Chapter 7 also examines the feasibility of another biomedical research institute adopting the 'Whitehead Model'.

How was the Whitehead Institute created? What has it accomplished in its twenty-year history? Chapter 2 tells the story.

Chapter 2

HISTORY AND CURRENT STATUS OF THE WHITEHEAD INSTITUTE

> "Since I had earned the money from advances in medicine, I wanted to create a premiere biomedical research institution with the resources necessary to produce the finest research possible, all the while sheltering it from outside forces that might compromise its research efforts."
>
> Mr. Edwin Whitehead, 1992[7]

2.1 Founding of the Whitehead Institute

The late Mr. Edwin C. (Jack) Whitehead had envisioned a research facility that would exist outside the boundaries of a traditional academic institution and yet, through a teaching relationship with a leading research university, offer all of the intellectual, collegial, and scientific benefits of the university. He believed that such an institution would give outstanding young investigators broad freedom to pursue new ideas, encourage novel collaborations among established investigators, and accelerate the pace of scientific discovery. To this end, the Whitehead Institute has succeeded beyond all expectations.

In 1939, Mr. Edwin Whitehead and his father launched Technicon Corp, a modest company at the beginning. It later became a leading maker of automated clinical

[7] *The Boston Globe*. Feb 4, 1992.

laboratory testing equipment. In 1969, Mr. Edwin Whitehead owned 100% of the Technicon and went public by selling approximately 5% of the company, or 1 million shares at $42 a share. At that point, Mr. Whitehead decided to make long-range plans concerning his growing estate.[8] Eventually, Technicon Corp was sold to Revlon Inc. in a stock and cash exchange exceeding $400 million.

Given his interest and involvement in biomedical R&D, Mr. Whitehead decided in 1971 that he would build a not-for-profit biomedical research institute. The ideal setting, he believed, would be a small, self-governing research center at, but not of, a leading research university. He further believed that the smallness of the institute would encourage collaborations, thereby allowing new ideas to come to fruition more rapidly.

The search for a suitable location to host the institute proved to be more complicated and protracted than Mr. Whitehead had anticipated. He commented years later: "It's easier to make $100 million than to give it away."[9] Mr. Whitehead was insistent that the institute be financially independent. He vehemently opposed the notion that any university owns the institute, for fear that the institute would be subject to the bureaucratic constraints that he felt was typical of universities. His model of the relatively independent institute was considered unconventional then. Several universities, including Harvard, Duke, and Stanford, were initially interested in the offer.[10] However, no deal was made, as the universities were generally uncomfortable with building a new institute that they could not directly control. The Duke University was the most forthcoming.[11] It

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[8] Based on a speech delivered by Mr. Edwin Whitehead to the annual meeting of the Association of Independent Research Institutes, Buffalo, NY, October 1988. Reproduced in *SRA Journal*, Winter 1988:13-18.

[9] *The Times*. Feb 10, 1992

[10] Brown C. "The institute where some of biotech's best brains storm." *Business Week*. July 11, 1988:98.

[11] Mr. John Whitehead, personal communication, April 19, 2002.

offered 25 acres of land attractively situated on its campus, and even offered free administrative support. Duke's intention at that time was to complement its leading clinical and teaching programs with a strong research component.

With the strong interest from the Duke University in place, a search for the founding director of the institute took place. In 1980, it was brought to Mr. Whitehead's attention that Nobel Prize-winning biologist Dr. David Baltimore – a visionary and brilliant opinion-leader in biology – might champion this project. The Whitehead offer was almost irresistible – Mr. Whitehead would offer $35 million upfront for a new building and equipment, and an additional endowment of $100 million to the tune of $5 million per year in guaranteed income.[12] At that time, this was the largest bequest ever made to American science. Dr. Baltimore was also reassured that accepting this offer would not compromise his own laboratory research.

Dr. Baltimore accepted the project as a consultant in 1980, and started formulating plans. Dr. Baltimore was a natural choice for engineering the birth of the Whitehead Institute. Prior to 1980, he had an unusual career of having worked in a relatively large number of premiere biomedical laboratories in the country, including MIT, the Rockefeller University, Cold Spring Harbor Laboratory, Jackson Lab, Salk Institute for Biological Studies, Mount Sinai Hospital, and the Albert Einstein College of Medicine.[13] Dr. Baltimore drew on this rich experience as he formulated the plans for the new institute. Indeed, he played a major role in the final choice of the affiliating university. Dr. Baltimore had laid down a number of conditions that must be fulfilled in

---

[12] History of the Whitehead Institute, on website: http://www.wi.mit.edu/who/who_history_narrative.html

[13] Crotty S. *Ahead of the curve: David Baltimore's life in science*. Berkeley, Calif: University of California Press, 2001.

the selection of the partnering university.[14] First, he felt that the only way he could build a world-class research institute was if it were dedicated to basic biomedical research. Second, he felt that the institution had to be part of a thriving, research-intensive, urban setting. Third, he was insistent that the new institute needed to be affiliated with a major research university. Duke University did not meet these criteria, notwithstanding its enthusiasm and support for the project. The final choice was between the Rockefeller University and MIT. Dr. Baltimore had worked in both. The costs to build and operate in the New York City, where the Rockefeller University is located, were prohibitive. MIT then became the obvious choice. To Dr. Baltimore, MIT was a good choice, as he viewed MIT as a university that was highly committed to research and had done it well.

The debate of whether to host the new institute carried on at MIT for more than 6 months. A vocal minority of the faculty petitioned and spoke out against the affiliation. The administration of MIT did not take a public position until the end of the debate. There were concerns about the loyalty of the institute, the quality of its scientists, and the potential commercial slant to its activities. MIT Physics Professor Michael S. Feld put it plainly: "In 50 years, I could imagine MIT surrounded by a ring of satellite institutions, if the practice of joint ventures spreads to other departments."[15] There was also concern by some MIT faculty members that this endeavor really masked a vehicle to make a profit for Mr. Whitehead himself. To this concern, Mr. Whitehead later remarked: "A commitment to give away $100 million is a poor start to making profits."[16] Both Mr. Whitehead and Dr. Baltimore assured the public and MIT that the institute would be non-

[14] Mr. John Whitehead, personal communication, April 19, 2002.
[15] "An Offer MIT Can't Refuse?" *McGraw-Hill's Biotechnology Newswatch.* Oct 19, 1981.
[16] Edwin Whitehead, based on a speech delivered to the annual meeting of the Association of Independent Research Institutes, Buffalo, NY, October 1988. Reproduced in *SRA Journal*, Winter 1988:13-18.

commercial in nature, and that no company would have preferred treatment in the licensing of any future Whitehead Institute patent rights. Between 1980 and 1981, Dr. Baltimore worked closely with MIT Provost Jerome Weisner and Biology Chair Gene Brown to convince MIT professors that the Whitehead Institute would be an asset rather than a threat or liability. The MIT faculty demanded compromises, such as insisting on a policy that all faculty appointments at Whitehead Institute were to be made jointly between the Whitehead Institute and MIT, so that MIT could control the quality of the Whitehead researchers. Further, it was made clear that all members of Whitehead Institute would participate in teaching and university activities, to the same degree as full-fledged MIT professors did. Mr. Whitehead and Dr. Baltimore accepted both concessions. Dr. Abraham Siegel, longtime Dean of MIT's Sloan School of Management also smoothed the negotiations with the Whitehead family in 1981, making the case to MIT that the Whitehead children should remain involved, and making the case to Whitehead that MIT should have seats on the Institute's Board.[17]

As Dr. Robert Weinberg, Whitehead Institute Member, later recounted: "And sooner or later, all of these (controversies surrounding the true intent of the founder) gradually melted away, because it became apparent that there was no nefarious scheme....And there was no grand master conspiracy to launch the Whitehead as a way of undoing the rest of MIT."[18] Part of the comfort that MIT faculty eventually gained was derived from the identification of Dr. David Baltimore as the founding Director, and his choice of the other founding Members. Much of the uncertainty concerning the quality of

[17] Ibid.
[18] Interview with Dr. Robert Weinberg, Whitehead Oral History Archive, 2001.

the new institute dissipated with that.[19] Finally, on November 18, 1981, MIT faculty voted to create the Whitehead Institute for Biomedical Research. A formal agreement was approved by the MIT Corporation. It recognized the Whitehead Institute as a financially independent research institute affiliated with MIT through its teaching activities. The Whitehead Institute would accept MIT graduate students for research and training in laboratories, and MIT would, in turn, consider all Whitehead Members and Associate Members for appointment to faculty level positions at MIT. Between 1982 and 1984, when the $35 million, 130,000-square-foot new building was being constructed, the Whitehead Institute quickly developed from an extension of MIT. Mr. Whitehead's wholehearted participation in the founding and subsequent expansion of the Institute was central to its rapid growth. Mr. Whitehead was known for his high energy and unwavering support for the Institute. The advantage of having a hands-on philanthropist behind the project should not be underestimated.

2.2 Growth of the Whitehead Institute

Dr. Baltimore's initial strategy was to attract a founding cadre of eminent biologists to jump-start the research at the new Whitehead Institute. Four other eminent scientists were recruited, two of whom were faculty members of the MIT Department of Biology.

The 5 founding Members were joined by Mr. John Pratt, the Institute's Associate Director. The initial plan was to grow the number of Members (Members are tenured

[19] Interview with Mr. John Pratt, Whitehead Oral History Archive, 2001.

staff at the Whitehead Institute) to 13 during its first 8 years, with a full complement of 20 faculty-level positions (Members and Associate Members) as the final goal.

When the Whitehead Institute moved from its temporary quarters at MIT to the new Whitehead building at 9 Cambridge Center, Cambridge, Massachusetts, in the summer of 1984, signs of good health of the Institute were already evident. The founding Members continued to be very productive in their research. From that point on, the Institute actively recruited and nurtured young talented scientists as Whitehead Fellows. It also had no difficulty attracting graduate students and postdoctoral scientists to support the various research activities at the Institute, including human genetics, cancer, heart disease, AIDS, immunology, and developmental biology. In the '80s, scientific papers from the Whitehead laboratories appeared with increasing frequency in the world's leading biomedical research journals. In 1990, Dr. Gerald Fink, then 49-year-old, succeeded Dr. David Baltimore as the Director of the Institute, inheriting a thriving research institute with 20 laboratories, $15 million annual budget, and 535 scientists on staff.

On February 2, 1992, Mr. Edwin Whitehead died of a heart attack, at the age of 72 years. With his demise, his legacy lived on through his children. From the start, Ms. Susan Whitehead, Mr. Peter Whitehead, and Mr. John Whitehead (the 3 children of Jack Whitehead) contributed their time and energy to the various Whitehead programs. When Mr. Edwin Whitehead died, the children's involvement increased significantly.[20] Such continuity of support from the second generation of the founder's family makes the Whitehead Institute rather unique amongst the biomedical research institutes in the

[20] History of the Whitehead Institute, on its website: www.wi.mit.edu/who/who_history_narrative.html

country. Ms. Susan Whitehead was named the Vice Chairperson of the Board of Directors in 1993, before she was appointed the Acting Chairperson of the Board in 1998. In 1999, she was elected Chairperson, furthering her father's vision for the Institute.

The Institute met its expansion goal in 1996 when a new research wing was opened. This wing increased research space by more than 45%, and provided an opportunity to expand the popular Whitehead Fellows Program. To accommodate the growing efforts in genomic research, the Whitehead Institute leased space at One Kendall Square, and developed a 36,000-square-feet facility at 320 Charles Street in Cambridge, Massachusetts.

In October 2001, acclaimed molecular geneticist Dr. Susan L. Lindquist from the University of Chicago succeeded Dr. Gerald Fink as the Director of the Institute. By this time, the Whitehead Institute had a $115 million annual budget, 750 staff (including 14 Faculty Members and 8 Whitehead Fellows), and ownership to numerous groundbreaking discoveries and patents. At the turn of the century, the Whitehead Institute represented an intellectual powerhouse in the epoch of the new biology.

2.3. Achievements of the Whitehead Institute 1982-2002

There are, unfortunately, no absolute measures to assess the success of a research institute. However, there are a number of surrogate measures that are commonly used to reflect the accomplishments of these research facilities. To evaluate the accomplishments of the Whitehead Institute, I have appropriated 6 measures. Each has its strengths and weaknesses, but, taken together, they paint a picture of remarkable achievements:

2.3.1 Scientific publications and citation index

2.3.2 NIH grant awards

2.3.3 Major scientific accomplishments

2.3.4 Awards and recognition given to individual scientists

2.3.5 Teaching excellence

2.3.6 Community outreach programs

2.3.1 Scientific Publications and Citation Index

The primary mission of the Whitehead Institute is to advance knowledge in biology. As such, it is logical to look at the scientific output of the Institute as one of the measures of its success. The most quantifiable parameters of scientific output are scientific publications and their citation index (impact factor). In 1993, just slightly more than one decade after its founding, the Whitehead Institute was ranked 3rd in the US in terms of the impact of its published papers (Table 2.1).[21]

Rank	Institution	Papers	Citations	Citations/Paper
1.	Salk Institute	403	16,752	41.57
2.	Cold Spring Harbor Laboratory	359	14,641	40.78
3.	**Whitehead Institute**	**392**	**15,543**	**39.65**
4.	Genentech	225	7,452	33.12
5.	Chiron	200	6,566	32.83
6.	Inst. Chimie Biologique, Strasbourg	261	8,315	31.86
7.	Fred Hutchinson Cancer Center	413	11,177	27.06
8.	MIT	1,060	27,296	25.75
9.	Princeton University	369	8,841	23.96
10.	MRC Lab Molecular Biology, UK	430	10,193	23.70

Source: Table reproduced from *Science Watch* 1993;4:1.

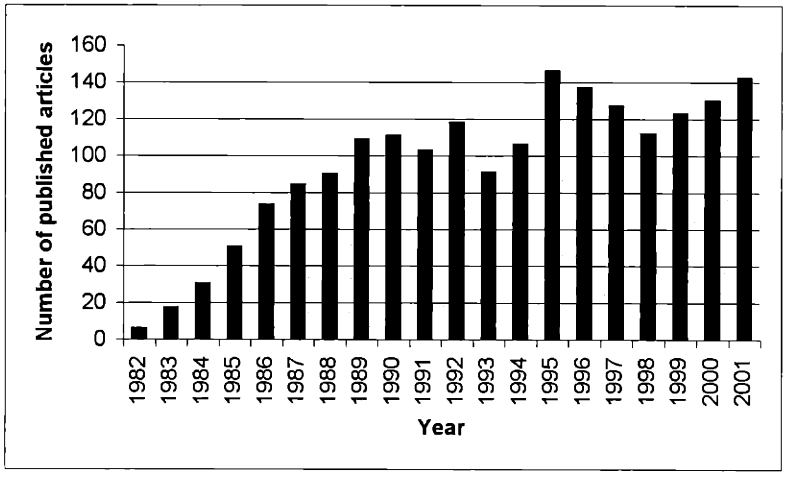
Table 2.1 – Citation Indices of the top biomedical research institutes (Molecular Biology and Genetics), 1988-1992

[21] "US institutions, individuals dominate worldwide genetics research". *The Scientist* 1993;7:14.

In this analysis performed by the Institute of Scientific Information (ISI), covering the period 1988-1992, Whitehead Institute produced a total of 392 papers, which were cited 15,543 times, for an average number of citations per paper of 39.65. On this basis, the Salk Institute was ranked first, and the Cold Spring Harbor Laboratory second.

Of relevance in interpreting such data is the consideration of the relative sizes of the institutions. For example, Whitehead Institute has 14 faculty members presently, compared to MIT Department of Biology with 51 faculty members (excluding Whitehead faculty), Salk Institute with 58 faculty members, and the Cold Spring Harbor Laboratory with 55 faculty members.[22]

Between 1982 and 2002 February, 1925 scientific papers were published by scientists working at the Whitehead Institute.[23] The growth rate of scientific papers from the Whitehead Institute since its inception has been spectacular. Figure 2.1 depicts the annual number of published papers from the Institute between 1982 and 2001:



Source: ISI Web of Science

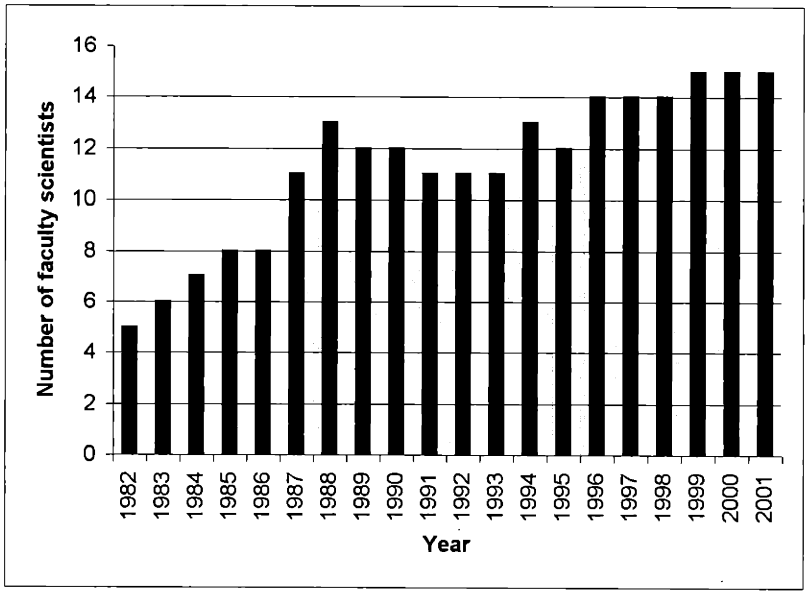
Figure 2.1 Number of published papers from Whitehead, 1982-2001

[22] Websites of Salk Institute and Cold Spring Harbor Laboratory, supplemented by communications with public affairs departments of these 2 institutions.

[23] ISI Web of Science website: http://wos.isiglobalnet2.com/

In 1984, just 2 years after its official establishment, and the year in which the Whitehead Institute moved out of its temporary premise in MIT into its new building in 9 Cambridge Center, the Institute published a total of 30 papers. At that time, the Institute had 5 faculty members. In 2001, the Institute published a total of 142 papers, from a base of 14 faculty members and 8 Fellows. Each of these 22 scientists runs an independent laboratory.

The corresponding number of faculty members in the Whitehead Institute from 1982-2001 is shown in Table 2.2. This number has stabilized between 14 and 15 since 1996.



Source: Whitehead Institute Annual Reports

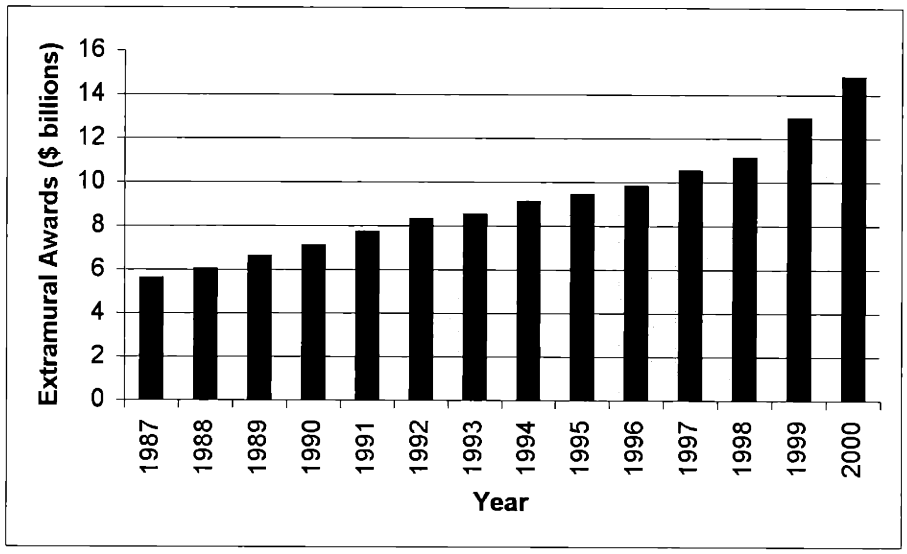
Figure 2.2 Number of faculty members in Whitehead, 1982-2001

The quality of scientific papers is an important consideration too. A significant proportion of the research papers from the Whitehead Institute is published in the top-rank biomedical journals such as *Nature*, *Cell*, and *Science*. Between 1982 and 2001, the

proportion of Whitehead's papers published in 3 prestigious journals was 23.6%.[24] This is remarkable, given the relatively short history of the Whitehead Institute and its relatively small size. The Salk Institute for Biological Studies, in comparison, published 9.3% of its 6,366 papers in these 3 journals over the same period.[25]

2.3.2 National Institute of Health (NIH) Grants Award

NIH is the largest provider of funding for biomedical research in the US, accounting for more than 80% of the federal biomedical funding. More than 83% of the NIH budget is used to support grants and contracts through its Extramural Research Program.[26] NIH funding has been steadily expanding over the past decade (Figure 2.3):



Source: NIH website – http://www.nih.gov/

Figure 2.3 – Trend of NIH Extramural Awards 1987-2000

[24] Compiled from ISI Web of Science on-line database.
[25] Compiled from ISI Web of Science on-line database.
[26] NIH website: http://www.nih.gov

NIH extramural funding is competitive, as the applications are subject to a stringent peer review process. Hence, the ability to attract NIH grants is widely regarded as an indication of the quality of the applicants and their sponsoring institutions.

The Whitehead Institute, despite its small size, has been remarkably successful in attracting NIH grants. In terms of all the US institutions (2,570 in total, including the universities), Whitehead Institute was ranked 54th in terms of NIH funding.[27] Amongst the non-profit research institutions, Whitehead Institute's ranking was even higher (Table 2.2). In 2000, it was ranked 3rd, representing a total award of $81.39 million.

Rank	Non-Profit Research Institutions	City/ State	No. of grants	Total Amounts ($ 1000)
1	Fred Hutchinson Cancer Center	Seattle	184	142,370
2	Scripps Clinic & Research Foundation	San Diego	232	69,925
3	**Whitehead Institute**	**Cambridge**	**35**	**81,389**
4	Sloan-Kettering Inst. for Cancer Research	New York	157	66,276
5	Westat, Inc.	Rockville	2	46,014
6	Salk Institute for Biological Studies	San Diego	82	42,517
7	Cleveland Clinic Foundation	Cleveland	127	39,060
8	Jackson Laboratory	Bar Harbor	74	38,639
9	Research Triangle Institute	N. Carolina	24	31,108
10	Burnham Institute	San Diego	67	29,898
11	Fox Chase Cancer Center	Philadelphia	54	27,491
12	Cold Spring Harbor Laboratory	New York	50	24,271

Source: NIH – http://silk.nih.gov/public/cbz2zoz.@www.tot.resi.dsncc

Table 2.2 – NIH awards to non-profit research institutes, 2000

[27] NIH Extramural Awards website: http://silk.nih.gov/public/cbz2zoz.@www.all.inst.fy2000.dsncc

2.3.3 Major Scientific Accomplishments

"Genetics – the study of individual genes – was quintessentially a child of the 20th century. But in the 21st century, we are moving beyond the study of individual genes to global views of all genes simultaneously – the field of genomics"

Dr. Eric Lander, Director of Whitehead's Center for Genome Research

The biggest and most visible scientific project undertaken by the Whitehead Institute is its sequencing effort in the Human Genome Project (HGP). HGP is an international consortium established in the 1980s to fully sequence the human genome (Appendix A). In March 2000, HGP announced that it had sequenced and deposited into public databases 2 billion of the 3 billion DNA base pairs that constitute the human blueprint. **Whitehead Institute's Center for Genome Research (WICGR)** was a major participant in this effort.

WICGR was officially established in 1993, with a 3-year $6 million grant from the Human Genome Research Institute of NIH. It was designated as one of the initial 4 Human Genome Centers. In 1996, WICGR was funded as one of the NIH human genome sequencing pilot projects. It pioneered the development of large-scale automation, informatics, and organization for sequencing. By 1999, the Center was selected as NIH's flagship sequencing center. When the initial sequence was published in *Nature* in Feb 2001,[28] the Center was the largest contributor to the sequences, providing one-third of the unique base pairs sequenced. WICGR is now the largest DNA sequencing center in the

[28] International Human Genome Sequencing Consortium. Lander ES, Patrinos A, Morgan JJ. *Nature* 2001;409:860-921

world with a current production capacity of 30 million DNA sequences per year, churning out from 125 capillary-based sequencing machines 24 hours a day, 7 days a week, and manned by more than 300 full time staff.

The Genome Center's model is based on large-scale interdisciplinary teamwork, integrating the expertise from biochemistry, microbiology, engineering, and informatics. The sequencing of the human genome represented quite a departure from the traditional biology. Traditional biology is experimental and hypothesis-driven. The proposed sequencing approach, on the other hand, called for large-scale, genome-wide, non-discriminatory, automated decoding of the human genomic DNA blueprint; there were no hypotheses to be tested, and the output would be milestone-driven sequence products rather than discrete pieces of new knowledge *per se*. Despite this untraditional endeavor and the large investment that it entailed, the Whitehead Institute decided to proceed with it. This is the signature of a premiere research institute: namely, the willingness and ability to identify and then decisively support promising new research areas. WICGR's leadership in HGP has assured a healthy stream of federal funding to the Whitehead Institute, and enhanced the reputation of the Institute and the Genome Center.

In addition to Whitehead Institute's major participation in HGP, a large number of **other scientific accomplishments** from the various Institute laboratories similarly command an impressive international leadership. The laboratory of Dr. Gerald Fink focuses on how external signals alter gene expression in 2 organisms: baker's yeast, *Saccharomyces cerevisiae*, and the plant, *Arabidopsis thaliana*. Fink was the first to show that DNA could be taken up by yeast, leading to its stable transformation.[29] He has

[29] Hinnen A, Hicks JB, Fink GR. "Transformation of yeast." *Proc Natl Acad Sci U S A* 1978;75:1929-1933.

identified and cloned genes that regulate the synthesis of amino acids, and discovered a way to make baker's yeast mimic the invasive growth patterns of *Candida albicans* and other disease-producing fungi.[30] This latter finding has generated an important new foundation for anti-fungal therapy.

Dr. Robert Weinberg's laboratory pioneered the research on the well-known retinoblastoma (RB) gene in the '80s.[31] In 1999, the laboratory transformed, for the first time, normal human cells into cancer cells by introducing a set of 3 genes through a process known as 'ectopic expression' – telomerase catalytic subunit (hTERT), the simian virus 40 large-T oncoprotein, and an oncogenic allele of H-ras.[32] Once produced in this way, the transformed cell has the capacity to multiply uncontrollably. This landmark discovery has provided biologists the fundamental building blocks to understand cancer cell transformation. In 1997, Dr. Weinberg was awarded the prestigious National Medal of Science Award, the nation's highest scientific honor.

Dr. Rudolf Jaenisch is an international authority in cloning biology. Cloning by nuclear transfer is, unfortunately, an inefficient process in which most clones die before birth; survivors often display growth abnormalities. The Jaenisch Laboratory found that variation in imprinted gene expression was observed in most cloned mice. Interestingly, many of the animals survived to adulthood despite widespread gene dysregulation, indicating that mammalian development may be rather tolerant to epigenetic aberrations of the genome. These data imply that even apparently normal cloned animals may have

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[30] Gimeno CJ, Ljungdahl PO, Styles CA, et al. "Unipolar cell divisions in the yeast *S. cerevisiae* lead to filamentous growth: regulation by starvation and RAS." *Cell* 1992;68:1077-1090

[31] Friend SH, Bernards R, Rogelj S, et al. "A human DNA segment with properties of the gene that predisposes to retinoblastoma and osteosarcoma." *Nature* 1986;323:643-646.

[32] Hahn WC, Counter CM, Lundberg AS, et al. "Creation of human tumor cells with defined genetic elements." *Nature* 1999;400:464-8.

subtle abnormalities in gene expression.[33] Such findings have shed crucial insights into the exploding field of cloning. Dr. Jaenisch was the recipient of the inaugural Genetics Prize of the Peter Gruber Foundation in 2001, the first-ever international genetics prize, in recognition of his pioneering work in transgenic science.

Dr. David Page's laboratory is a world authority on the genetics of reproductive biology. The Page Laboratory cloned the entire Y chromosome in 1992.[34] It also showed how the mammalian X and Y chromosomes evolved from an autosomal pair. The Page Laboratory theorized that perhaps 300 million years ago, our reptile ancestors had no sex chromosomes, having evolved from an autosome. Today's X chromosome maintains the genetic content of the ancient autosome, while the Y chromosome seems to have lost its ancestral markings. The Y chromosome has lost many of the genes it once shared with the X chromosome. Dr. Page's studies have helped advance the understanding of the history of human populations, the origins of genetic diseases, and male infertility.

Dr. Paul Matsudaira's laboratory focuses on the interface between biology and physics/engineering. Specifically, it studies the mechanics of the 'molecular engine' within cells. Just as springs and ratchets can store or release energy and rectify motion in physical systems, the Matsudaira Laboratory has shown that their cellular analogs can perform similar functions in biological systems as well.[35] Dr. Matsudaira is now studying biological complexity using miniaturized ultra-fast bioanalytical devices.

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[33] Humpherys D, Eggan K, Akutsu H, et al. "Epigenetic instability in ES cells and cloned mice." *Science* 2001;293:95-97.

[34] Foote S, Vollrath D, Hilton A, Page DC. "The human Y chromosome: overlapping DNA clones spanning the euchromatic region." *Science* 1992;58:60-66; and Vollrath D, Foote S, Hilton A, et al. "The human Y chromosome: a 43-interval map based on naturally occurring deletions." *Science* 1992;258:52-59.

[35] Mahadevan L, Matsudaira P. "Motility powered by supramolecular springs and ratchets." *Science* 2000;288(5463):95-100.

There are many more landmark discoveries that have emerged from the various Whitehead laboratories. One conclusion is clear: the scientific output from the Whitehead Institute is diverse, often groundbreaking, and frequently shapes the directions of many branches of biological research. A list of the research areas, and the relevant experts in the Whitehead Institute, is provided in Appendix B.

2.3.4 Awards and recognition given to individual scientists

Table 2.3 shows some of the most prestigious awards and distinguished memberships of current Whitehead Institute Faculty:

	Award / Recognition	Recipient	Current Status in WI
1.	National Medal of Science	Dr. Robert Weinberg	Member
2.	National Academy of Science	Dr. Susan Lindquist	Director
3.	National Academy of Science	Dr. Gerald Fink	Member
4.	National Academy of Science	Dr. Eric Lander	Member
5.	National Academy of Science	Dr. Harvey Lodish	Member
6.	National Academy of Science	Dr. Robert Weinberg	Member
7.	American Academy of Arts & Sciences	Dr. Susan Lindquist	Director
8.	American Academy of Arts & Sciences	Dr. Gerald Fink	Member
9.	American Academy of Arts & Sciences	Dr. Rudolf Jaenisch	Member
10.	American Academy of Arts & Sciences	Dr. Eric Lander	Member
11.	American Academy of Arts & Sciences	Dr. Harvey Lodish	Member
12.	American Academy of Arts & Sciences	Dr. Robert Weinberg	Member
13.	Institute of Medicine	Dr. Gerald Fink	Member
14.	Institute of Medicine	Dr. Eric Lander	Member
15.	Institute of Medicine	Dr. Robert Weinberg	Member
16.	Howard Hugh Med. Inst. Investigator	Dr. David Page	Member

Table 2.3 – Selected personal achievements of current Whitehead Faculty

Dr. Gerald Fink and Dr. Eric Lander are also on the Institute of Scientific Information's 'Highly Cited Researchers' list.[36] In addition, a number of former Members, Whitehead Fellows, and postdoctoral fellows have also achieved outstanding personal accolades, such as the Howard Huge Medical Institute Investigator award. This is yet another evidence to support the notion that the Whitehead Institute, together with MIT, have been a fertile ground for training the future leaders in science and medicine.

2.3.5 Teaching Excellence

Teaching is viewed as an important mission at the Whitehead Institute. MIT and Whitehead Institute together have attracted outstanding biology students. As Mr. John Pratt, Associate Director of Whitehead Institute noted: "Students vote with their feet – they select their mentors."[37] Good teachers attract good students and vice versa. A recent survey of academics by the *US News* magazine showed that MIT/Whitehead Institute had competitive PhD programs (Table 2.4):[38]

Field of Study	MIT's Ranking
Biological Sciences	3rd
Biochemistry / Molecular	2nd
Cell Biology / Developmental	7th
Genetics	6th
Neurosciences	5th (joint)

Source: http://www.usnews.com/usnews/edu/beyond/bcphd.htm

Table 2.4 – *US News* Survey of PhD programs in the US, 1999

[36] ISI HighlyCited.com™ website: http://isihighlycited.com. Jan 15, 2002.
[37] Interview with Mr. John Pratt, Associate Director of Whitehead Institute, Jan 31, 2002
[38] *US News* website: www.usnews.com/usnews/edu/beyond/bcphd.htm

For ranking purposes, Whitehead Institute's teaching excellence is in part reflected by MIT's performance. The teaching accomplishments of Whitehead Institute cannot be easily distinguished from those of the MIT Department of Biology. The faculty members of the units share the same teaching load. Students registered with MIT Department of Biology rotate freely between the 2 units.

According to estimation by Dr. Robert Sauer, Head of MIT Department of Biology, approximately 600 candidates apply for places in the MIT Biology graduate program each year. From that pool, around 120 will be short-listed and invited to visit the Department. Of these, approximately 90 candidates will be selected after interviews and departmental review. Finally, about 45 graduate students will be admitted to the program, giving an admission rate of around 7.5% - a testimony of the highly competitive nature of the biology graduate program at MIT.[39]

2.3.6 Community Outreach

The Whitehead Institute is active in its community outreach efforts. Appendix C shows the various programs. Whitehead Institute seeks partnership with schools, science museum, the press, and the American Society of Law, Medicine and Ethics (ASLME) in a concerted effort to educate the lay and scientific communities. In particular, the well-known Whitehead Symposia have always enjoyed outstanding turnouts. Other programs have also received encouraging public endorsements. Another biomedical institution that is particularly active in educating the general community is the Cold Spring Harbor Laboratory.

[39] Interview with Dr. Robert Sauer, Head of MIT Biology Department, Jan 25, 2002.

2.4 Chapter Summary

The Whitehead Institute is celebrating its twentieth-year anniversary in 2002. It was founded in 1982 with a significant philanthropic contribution. Its conceptualization and early establishment represented a joint effort of the founder and the founding director, who shared the same vision. The Whitehead Institute made a major strategic decision to form close alliance with MIT – a decision that proves to be important to the success of the Whitehead Institute. In addition to attracting 5 'star scientists' as founding members, the Whitehead Institute invested in talented young scientists by creating the Whitehead Fellows Program. The Whitehead faculty scientists, together with the Whitehead Fellows, constitute a cadre of accomplished scientists whose research accomplishments have driven the Institute to its scientific preeminence today. While there are no perfect measures to evaluate the success of a biomedical research institute, the various accomplishments of the Whitehead Institute collectively paint the portrait of a highly successful research powerhouse. Chapters 3 to 6 that follow will analyze the Whitehead Institute in greater detail, seeking to unravel the secrets of its success.

Chapter 3

HUMAN, FINANCIAL, AND PHYSICAL CAPITAL

> "Although science is nourished by interaction, ultimately great science is a product of individual imagination....It is hard to overemphasize the rarity of truly imaginative thinking. There are many scientists who are superb and insightful critics, who have remarkable memories, who easily grasp new ideas and integrate them into their thinking. But there are few who see even one step ahead into the unknown."
>
> Dr. David Baltimore, 1984[40]

3.1 Primacy of the Individual

While acknowledging the importance of physical infrastructure, automation, and financial resources to R&D, it is clear that the primary engine of scientific innovation is human capital. Biology is one of the more human capital-intensive sciences.

The Whitehead Institute believes in an uncompromising standard of excellence in people. This credo is translated into practice, as the rest of this chapter will reveal.

3.2 Founding Members

Mr. Edwin Whitehead's choice of **Dr. David Baltimore** as the founding Director was a crucial decision that underpinned the early success of the Whitehead Institute. Dr. Baltimore won the Nobel Prize in 1975 for the discovery of the reverse transcriptase, at

[40] *Whitehead Institute Director's Annual Report* 1983/1984:3.

the age of 37-year-old. He has been described as someone with "patience, creativity, a meticulous lab manner, and a mind that was stuck in overdrive"[41] When he was approached by Mr. Edwin Whitehead to lead the new institute, he was 42-year-old, a Professor of Biology at MIT, a Member of the National Academy of Science, the American Academy of Arts and Sciences, and the American Association for the Advancement of Science. He was also prolific in his scientific publications. Such was the caliber and stature of the first Member of the Whitehead Institute. Dr. Baltimore's renown and the reputation of MIT were crucial in attracting the other 4 founding Members to the Institute.

Dr. Gerald R. Fink was a Professor of Biochemistry at the Cornell University when Dr. Baltimore recruited him. He was also a Member of the National Academy of Science when he joined the Whitehead Institute. Dr. Fink is a world leader in yeast genetics.

Dr. Rudolf Jaenisch, a native of Wolfelsgrund, Germany and a former post-doctoral scientist at the Max-Planck-Institute, joined the Whitehead Institute in 1984. He was Head of the Department of Tumor Virology at the eHeinrich-Pette-Institute at the University of Hamburg when he left to join the Whitehead Institute. Dr. Jaenisch is one of the pioneers of transgenic science.

Dr. Harvey F. Lodish was Professor of Biology at MIT when he joined the Whitehead Institute. He was also a visiting scientist in a number of top research centers in the world, including Dana-Farber Cancer Center Institute, Imperial Cancer Research Fund in London, and Children's Hospital Medical Center in Boston. Dr. Lodish is a

[41] Crotty S. *Ahead of the curve: David Baltimore's life in science.* Berkeley, Calif: University of California Press, 2001:12.

leader in the field of membrane biology, and has isolated and cloned a number of proteins that reside on the surface of cells that are responsible for regulating cell growth, glucose transport, and energy metabolism.

Dr. Robert A. Weinberg was Professor of Biology at MIT when he joined the Whitehead Institute. A scientist with numerous awards and scholarships, Dr. Weinberg was also named the 'Scientist of the Year' by the *Discovery Magazine* in 1982. Dr. Weinberg was a pioneer in human oncogenes, tumor suppressor genes, and telomerase, an important enzyme that controls the longevity of cells.

The fact that Dr. Fink and Dr. Jaenisch, non-natives of Massachusetts, left their tenured positions elsewhere to join the Whitehead Institute was a powerful indication of the faith that they had in the new Institute. Indeed, the strategy of importing 'star scientists' to kick-start new research efforts has been used to good effect in a number of different places.[42]

The impact of the initial recruitment effort at the Whitehead Institute was clear. The 5 founding Members were all leading experts in their respective and quite distinctive fields, and were in the prime of the careers when they joined the Institute. Individually, they were able to attract bright young scientists and students to join their laboratories. Collectively, they represented a formidable core of top-notch scientists who anchored the science of the Institute in its formative years. Whitehead Institute made it clear that the subsequent growth of the Institute faculty would depend on the recruitment of young staff.

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[42] *The Straits Times, Singapore*. "He is coming here". Feb 9, 2001. http://straitstimes.asia1.com.sg/mnt/html/webspecial/lifescience/0209_2.html

3.3 Expansion of Membership and Associate Membership

The Whitehead Institute has the following categories of scientific staff:[43]

a) Members (11)

b) Associate Members (3)

c) Whitehead Fellows (8)

d) Post-doctoral scientists (approximately 110)

e) Graduate and undergraduate students

f) Technicians, engineers, database developers, and visiting scientists

The **Members** are tenured Full or Associate Professors at MIT Department of Biology, though a few are also concurrent faculty members of the Engineering Department. Each of the Whitehead Institute Members runs an independent laboratory, supported by a team of post-doctoral scientists, students, and technical staff. A typical laboratory in the Whitehead Institute is manned by 15-25 persons. The Members are nationally and internationally renowned in their respective fields, and many are also members of prestigious scientific organizations (such as the National Academy of Science) and winners of numerous scientific awards for their research excellence. None of the present Members is a Nobel Prize winner. A number of the Members are also noted for their leadership in large-scale scientific projects and educational outreach programs. Dr. Gerald Fink was the former President of the Genetics Society of America. Dr. Eric Lander is the Director of the Whitehead Institute Center for Genome Research. Dr. David Page is the Chair of the Whitehead Task Force on Genetics and Public Policy.

[43] As of March 31, 2002.

Dr. Rudolf Jaenisch has participated in a number of Congressional Hearings as an expert in the field of cloning.

The recent arrival of Dr. Susan Lindquist to the Whitehead Institute is yet another powerful signal to the scientific community that the Whitehead Institute is at the pinnacle of biomedical research. Dr. Lindquist is a world authority on protein research, especially in the realm of heat shock proteins.[44] She has elegantly elucidated how heat shock proteins are regulated post-transcriptionally and how they produce stress tolerance by modulating the activity and aggregation state of other proteins. She is now working on chaperone proteins[45] and prion proteins[46] – 2 important classes of proteins that have shed light on how cells protect themselves against environmental stresses, and how abnormal protein folding can lead to devastating human diseases. Dr. Lindquist left her position as the Professor of Biology in the University of Chicago to join the Whitehead Institute.

The **Associate Members of the Whitehead Institute** are non-tenured, but hold tenure-track appointments in MIT. They run their independent laboratories. With the exception of one, all Associate Members of the Whitehead Institute have been successfully elected to full Membership. This is very high compared to the rest of MIT.

3.4 The Whitehead Fellows

One of the factors behind the meteoric rise of the Whitehead Institute is its ability to support new ideas at the earliest stages of development. A salient feature of this ability is its preparedness to take chances on brilliant young scientists who are eager to extend

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[44] Rutherford SL, Lindquist S. "Hsp90 as a capacitor for morphological evolution." *Nature* 1998;396:336-342

[45] Serio TR, Lindquist SL. "[PSI+], SUP35, and chaperones." *Adv Protein Chem* 2001;57:335-566

[46] Li L, Lindquist S. "Creating a protein-based element of inheritance." *Science*. 2000;287:562-563

the boundaries of their chosen fields. The Whitehead Fellows Program is an integral part of the Institute's mission. Dr. Baltimore first conceived the idea soon after the inception of the Institute. It emerged from the belief that nurturing young scientists during their most creative years will yield a new generation of leaders more rapidly than traditional programs. The career paths of former Fellows, who have blossomed into prominent researchers in their fields, only serves to reinforce this belief.

The objective of the Fellows Program is to provide talented young PhD's and MD's a rare opportunity, namely, to set up their own laboratories, rather than working as traditional postdoctoral scientists, or joining a university faculty somewhere. As junior faculty members in universities, these young scientists would shoulder considerable teaching and departmental obligations, right at the most productive and creative time of their professional lives. The Whitehead Fellows Program provides research support and frees the Fellows of the usual university obligations. It is a highly attractive proposition. Free from financial constraints and teaching responsibilities, the Fellows can concentrate on their research and build thriving scientific programs. These programs are then able to compete for other public grants. The more senior members of the Whitehead faculty often mentor the Fellows informally.

Candidates cannot apply to become Whitehead Fellows; they are recruited by the Institute's Director upon recommendations by the Whitehead faculty, the distinguished Board of Advisory Scientists, and other leaders in the research community. The Whitehead Fellows are carefully handpicked. The criteria for selection include past record, future potential, degree of research independence, interest area, and ability to work together with the rest of the faculty and Fellows. They are known for being bold,

focused, highly motivated, independent, and brilliant.[47] Typically, there are 4-8 Whitehead Fellows at any one time, each running an independent laboratory.

The Program reflects Whitehead Institute's extraordinary commitment towards the promotion of research excellence in individuals, including young individuals. According to Mr. John Pratt, Associate Director who has been with the Institute since its inception gave his account: "Every recruit (scientist), since that time (founding), was someone who was very junior, typically someone who has initiated their independent research career here with us. We never hired an eight hundred pound gorilla from Harvard or some such place to join our midst."[48] The Whitehead Fellows Program calls for an astute judgment on the part of the Whitehead Faculty to identify a few highly selected young scientists who are deemed to have great potential to become leaders in their chosen research fields. Strategically, the Whitehead Fellows Program is a clever one: it allows the Whitehead Institute to go into riskier areas of science, yet without irrevocable or long-term commitment, since the duration of the Whitehead Fellowship usually lasts for a period of 3-5 years. The Whitehead Fellows Program allows the Institute to stay small while having access to a much larger universe of cutting-edge research.

Perhaps the most illustrative success story of the Whitehead Fellows Program is the unusual and meteoric rise of **Dr. Eric Lander**, currently the Director of the Whitehead Institute Center for Genome Research. Dr. Lander's present success and repute belie his most unusual academic background. Dr. Lander earned his doctorate degree in mathematics from Oxford University in 1981. He subsequently obtained his

[47] Ms Susan Whitehead, personal communication, April 17, 2002.
[48] Interview with Mr. John Pratt, Whitehead Oral History Archive, March 2001.

MBA degree from the Harvard Business School. While working as an Assistant Professor of Managerial Economics at the Harvard Business School, he became interested in biology and started working and learning biology in the Whitehead Institute laboratories. Dr. Lander wanted to apply mathematics and computer technology to genetics. When the prospect of his becoming a Whitehead Fellow was being considered by the Whitehead faculty, it was clear that they were dealing with a challenging and most unconventional proposition: to admit a mathematician-cum-business school graduate to the Whitehead Fellows Program, with the tacit understanding that such an individual would soon become a leader in biology. Dr. David Baltimore and his faculty made the decision to elect him as a Whitehead Fellow. Not many departments of biology would have made the same decision. Dr. Lander later became immensely successful in the Whitehead Institute. Other successful products of the Whitehead Fellows Program include Dr. Peter Kim, a highly respected structural biologist who was a former Member of the Institute (currently Executive Vice President of Research and Development at Merck Research Laboratory), and Dr. David Page, current Member of the Institute.

The importance of investing in bright young scientists to the success of any research organization cannot be overemphasized. The ability of a research organization to support and nurture young scientific talents is the most relevant indicator when evaluating the organization's accomplishments.[49] On this basis, the Whitehead Institute has done well.

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[49] Alberts B. "The view from the National Academy of Science." In: Barfield CE and Smith BLR, eds. *The Future of Biomedical Research.* Washington, DC: American Enterprise Institute & The Brookings Institution, 1997:16-20.

3.5 The Students

> "I think one of the important preconceptions, which I believe was a valid one, was that if one wishes to have a research institute that remains successful over an extended period of time, the institute should be affiliated to a high-quality university community. ....Some of the prime engines for scientific success come from the students who train here."
>
> Dr. Robert Weinberg, Whitehead Member, November 2001.[50]

Graduate students, together with Post-Doctoral Fellows, are the main work force in most biomedical research institutes. This section focuses on the role of the graduate students. Whitehead Institute does not admit its own students. Instead, it shares students with the MIT Department of Biology, which formally registers the students. As noted in Section 2.3.5, the quality of graduate students admitted to the MIT Department of Biology has always been high. These students are given an opportunity to rotate through a number of laboratories in the Biology Department, the Cancer Center, and the Whitehead Institute, before they decide on the specific laboratory to continue their graduate research.

Graduate students contribute to the Whitehead Institute in the following ways:

a) Intellectual capital – High-caliber graduate students often become very productive in the laboratories after 3 to 6 months of initiation. They also tend to be more flexible in their choice of research areas, and are somewhat less risk-averse.[51]

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[50] Interview with Dr. Robert Weinberg, Whitehead Member, Nov 20, 2001
[51] Ibid.

b) Vibrant and energetic environment – Graduate students are usually in their twenties. They bring to the laboratories a contagious sense of dynamism and vitality that are important to a creative environment. In Dr. Weinberg's words: "There are many research institutions which are not affiliated with academic centers, and many of them started out strong, but within a decade or 2, they gradually sink into some middling status, because they don't have the continuous inflow of young people to reinvigorate the research."[52]

c) Bridging – All Whitehead faculty members teach at MIT. As a result, the graduate students, and to a lesser degree the undergraduate students bind MIT and the Whitehead Institute together. Because of the students, the 2 organizations work closely together in activities such as teaching, seminars, and sharing of reagents and equipment. In a more subtle way, the students provide a mechanism for the diffusion of scientific knowledge between the 2 organizations, either in the form of joint seminars, or through the rotation of students.

3.6 Administration

A number of supporting functions are critical to the Institute, in order that the scientists are given an optimal environment to further their research. As noted earlier, **Mr. John Pratt** was brought in as the Associate Director of the Institute at its inception. He functions as the chief administrator of the Institute. Scientists and students at the Whitehead Institute have commented that the Institute provides exceptional supporting services to them, including filing of patents, purchase of equipment and reagents, library

[52] Interview with Dr. Robert Weinberg, Whitehead Member, Nov 20, 2001.

services and informational technology. Mr. Pratt is widely regarded as the linchpin of the Whitehead administration. So vital is Mr. Pratt to the smooth running of the Institute that it is often said, in jest, that "if a fire breaks out in Whitehead, the person we should get out first is John Pratt."[53]

The Whitehead Institution also has a well-run Public Affairs Department. Its user-friendly website describes the research that is being done in the different laboratories. It also has a very informative press release collection that captures the major research and policy milestones of the Institute. The Whitehead Institute is well supported by its in-house legal expertise, which works closely with MIT's Technology Licensing Office.

3.7 Financial Capital

External funding is vitally important to biomedical research today, given the escalating research expenditure. Modern biological research often involves the use of sophisticated laboratory equipment, expensive purified reagents, and specialized laboratory animals. The long gestation period before the result becomes apparent only serves to escalate the research expenditure. Industry's competition for scientists also means that research institutions have to offer competitive remunerations. The net effect is a significant financial burden to the research institutes, with no guarantee of return on investment. As a result, all biomedical research units today are heavily dependent on external funding in order to remain competitive.

Mr. Edwin Whitehead's donation 20 years ago was generous at that time. In total, the gift amounted to more than $135 million – representing the largest philanthropic

[53] Interview with Ms Patricia Granahan, Whitehead Institute Intellectual Property Manager, Mar 22, 2002.

contribution to biomedical research, and the second largest gift made by a living person in the history of the US at that time.[54] Even this generous donation would not be enough to sustain the Institute's competitiveness in the long run, given the reality of escalating research costs. The Whitehead Institute recognized the importance of securing a constant stream of donations to its endowment. The challenge was to extend the momentum of the Whitehead philanthropy after the demise of Mr. Whitehead in 1992. To meet this challenge, the Institute established the 'Campaign for Discovery', a $12 million fundraising initiative launched in 1993 that would support the construction of a new research wing ($7 million) and provide enhanced research support for 3 key areas deemed to be fundamental to the future of scientific discovery ($5 million): transgenic science, structural biology, and infectious diseases. Another important goal of this effort was to establish long-term collaborations with individuals, foundations, and corporations who understand the vital role of basic science research in advancing human health. The initial phase of the Campaign was a success, with 200 donors contributing a total of $12,570,637 as of September 1, 1996, including a $1 million donation from Mr. and Mrs. Patrick J. McGovern, well-known publishing moguls.

The annual operating budget of the Whitehead Institute is around $115 million. Like most successful biomedical research laboratories in the US, the Whitehead Institute scientists have been able to attract substantial amount of federal funding, principally from the NIH. In terms of NIH extramural support, Whitehead Institute's ranking amongst the non-profit biomedical research institutions has been rising steadily since its founding,

[54] Whitehead Institute website: www.wi.mit.edu/stw/stw.html

especially in the mid-90s, as shown in Table 3.1. The Whitehead Institute receives significant funding from NIH in support of the Human Genome Project.

Year	Ranking of WI Amongst Non-Profit Research Institutes	Number of Grants	Total Support (in thousand dollars)
2000	3	35	81,389
1999	4	33	58,541
1998	7	33	26,819
1997	8	28	25,058
1996	10	26	21,615
1995	8	26	22,881
1994	12	19	17,847
1993	10	19	15,967
1992	24	22	7,793
1991	22	28	8,789
1990	20	26	9,238
1989	21	26	8,938
1988	20	26	8,226
1987	22	24	6,773
1986	27	17	5,087
1985	27	18	5,392

Source: NIH – http://silk.nih.gov/public/cbz2zoz.@www.tot.resi.dsncc

Table 3.1 – NIH Awards to Whitehead Institute, 1985-2000

The rich coffer at the Whitehead Institute provides a competitive advantage in the following ways:

a) Physical infrastructure, laboratory equipment and reagents. Scientists appreciate a good environment to work in. The Whitehead laboratories are equipped with state-of-the-art scientific instrument, including the sequencing facilities at the Genome Center and the W.M. Keck X-ray Crystallography Facility in the 9 Cambridge Center. The Whitehead buildings were carefully designed to ensure

that they combined a comfortable and practical home for the research efforts with contemporary design.

The scientists in the Institute also enjoy high-quality shared services such as the animal facilities, flow cytometry, imaging facilities, to name a few. Scientists can also easily obtain a wide array of biological reagents from common reagent rooms without incurring an inordinate amount of requisition procedures or delay. Laboratory glassware is cleaned and autoclaved by technicians; culture media and agar gels are prepared in advance by the central store.

This level of luxury is made possible by the relative wealth that the Whitehead Institute enjoys. Rotating students and scientists have observed that Whitehead Institute creates a 'sense of abundance' and comfort amidst highly competitive scientific endeavors.[55] This remarkably high level of ancillary support, it is felt, will allow the researchers to do what they are best at, namely, the creation of new knowledge in biomedical research.

b) Bridging funds and supplementary support. While the Whitehead scientists are fully capable of securing competitive federal funding such as the NIH extramural grants, there is usually a waiting period between application and the actual disbursement of funds. Such a period may be important for the researchers to forge ahead and capitalize on the research momentum, in order to secure leadership in that particular area. The Whitehead Institute funds are used to bridge this period.

[55] Interview with Ms Philina Lee, MIT Biology Department Graduate Student, Feb 28, 2002; and interview with Dr. Meng-Ling Choong, Visiting Scientist at Whitehead, Mar 14, 2002.

The Whitehead Institute also provides funds to help kick start pilot research projects. Such seed funds (typically $250,000 in the first year) are particularly important to the junior faculty members, who are relatively young in their independent research careers. After starting their projects, these faculty members would continue to apply for other sources of funding. The amount of Institute support does not tend to decline as the federal grants come in. Instead, these grants are used to support expansion of the laboratories.

Sometimes the bridging funds were so large that the Institute had to look for alternative sources than its own endowment. For instance, in 1999, as the Genome Center was rushing into the final phase to decode the human genetic blueprint, it needed a large capital outlay to purchase new equipment. The Institute did not have $38 million to support this effort immediately. With the help of the Massachusetts Health and Education Facilities, a state agency, the Institute was able to borrow $38 million from BankBoston Corp, to be repaid in less than 5 years.[56] The Whitehead Institute was confident that NIH would fund this major research effort. The Massachusetts Health and Education Facilities was particularly helpful in this deal, as it offered a 'capital lease' program that allowed institutions to acquire new equipment through a rent-to-own arrangement. This deal illustrated the risk-taking attitude of the Institute, and the flexibility that it is prepared to exercise in order to advance scientific frontiers.

The Whitehead Institute also uses its Institute funds to provide ongoing supplementary support for about 30% of the research projects.

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[56] Griffith T. "Whitehead Institute borrows $38M to buy equipment." *Boston Business Journal.* June 18, 1999.

c) Less tangible benefits. The Institute endowment confers a general sense of psychological well-being and security to the Institute employees. The Institute's financial strength may also be leveraged in recruitment exercises or to counter-offer better remunerations to stave off the potential loss of star scientists or key administrative staff.

3.8 Chapter Summary

This chapter has described the assets that the Whitehead Institute possesses, namely its human capital, financial resources, and physical infrastructure. The principal investigators at the Institute comprise the tenured Members, non-tenured Associate Members, and the Whitehead Fellows. The Whitehead Fellowship has been a successful model in which promising young scientists are given scientific independence, ready funding, and a nurturing environment at the Whitehead Institute. The Fellows bring about new ideas and youthful dynamism to the Institute, and help diversity the research portfolio of the Institute. The Whitehead Institute's financial position has been relatively strong, given the substantial initial endowment in relation to the small size of the faculty. The resultant financial freedom has had a multiplier effect on the quality of the human capital, physical infrastructure, and supporting services at the Institute. The next chapter will examine some of the Whitehead Institute's scientific strategies that leverage the various assets.

Chapter 4

SCIENTIFIC STRATEGIES

> "As an Institute, we must continue to evolve in ways that will allow us to derive the maximum benefits from new technologies. If we are going to lead the charge against human diseases, we must: build bridges to the medical community.....forge new alliances at MIT.....recruit a new generation of biomedical scientists.....seek partnerships with different sectors of industry..."
>
> Dr. Gerald Fink, Past Director of the Whitehead Institute, 2000[57]

The success of the Whitehead Institute is due, in no small part, to deliberate choices in its scientific strategy. The Institute's scientific strategies influence the manner by which the human, financial and physical assets are deployed, which, in turn, determines the Institute output and return on investment.

Questions that have confronted the Institute included: What research areas should the Institute pursue? Who should decide on these choices? How could the Institute avoid internal competition arising from overlap in research areas? Where along the continuum between basic research and clinical research should the Institute be positioned? How could the Institute promote creation and cross-fertilization of scientific ideas? These are the questions that this chapter addresses.

---

[57] Dr. Gerald Fink, commenting in the *Whitehead Institute Annual Report* 1999/2000.

4.1 Research Decisions at the Whitehead Institute – Independence of Faculty

There is sometimes a difference between the organization of research institutes and universities. Dr. David Baltimore wrote in his Director's Report: "Universities allow their faculty members both very great personal independence in their choice of research goals and a major voice in decisions about staffing and curricula. Research institutes often have stronger direction from their administrations. The Whitehead Institute has been founded on the principles of the university: each faculty level scientist is an independent investigator, free to set his or her own directions, and decisions about future directions are made collaboratively among the existing faculty and in close consultation with our colleagues at MIT."[58]

And this philosophy persists today. In the Whitehead Institute, the appropriate strategy should be to assemble an outstanding faculty with the resources necessary to respond quickly to new opportunities for advancement. The prevailing wisdom is that a research institute should not decide what research areas its scientists should or should not pursue. At the Whitehead Institute, the individual principal investigators – comprising the Members, Associate Members, and the Fellows – choose their respective research areas with relatively little direct interference from the Institute administration. Instead, the scientists seek feedback on their research pursuits through their fellow faculty members. This degree of freedom appears to be at odds with the survival imperative that a small research institute is confronted with. For a small institute, one does not have the luxury of size to buffer many failed research projects. Every project counts. The natural tendency is therefore to exercise significant control and interference on research directions. How does

[58] Dr. David Baltimore, in *Whitehead Institute Director's Annual Report* 1983/1984

one balance scientific creativity and freedom with organizational control and oversight? This is a question that confronts a number of research institutes and universities, especially where there are greater constraints on resources, or where there have been a culture of 'top-down' decision-making.

From the series of interviews conducted for this study, the author has concluded that the Institute leadership does exercise an indirect, often subtle, influence over the research directions:

a) The recruitment of the faculty and the Fellows to the Whitehead Institute is an highly deliberate and elaborate process. It is essential that the potential hire is well regarded by the entire Whitehead faculty. There is even a deliberate effort to ensure that the MIT department shares the same view. In addition, the research background and the future research pursuits of the candidate are carefully considered. Great care is taken to ensure that there is little overlap between the newcomer and the existing faculty, unless the scope of the particular research is so broad that partial duplication of expertise and interest is thought to be harmless, and indeed beneficial. Other than this consideration, however, there does seem to be considerable flexibility in accommodating the research interest of the newcomer. This process is distinguishable from the hiring process in many larger research organizations, especially in research universities, where the recruitment effort is often designed to fill vacated positions in specific departments, often in relation to particular teaching needs.

b) In-house peer opinion plays a significant role in shaping the scientific directions of the individual scientists (especially the junior members) and the Institute as a

whole. It is remarkable how closely-knit the Whitehead faculty is. The faculty scientists meet weekly to share their views on specific scientific issues. The 2 different annual retreats give the researchers further opportunities to review the work of each laboratory, and to deliberate over long-term strategic issues. Additionally, there is so much communication between Whitehead faculty members, and between Whitehead investigators and their counterparts in MIT, that cross-fertilization of ideas and subtle auditing of output are built into the system. What is conspicuously absent in this scientific decision-making process is an overbearing influence by the formal leadership of the Institute. Indeed, the Director functions, in this instance, as a facilitator and a senior colleague whose advice is sought and well respected. The central elements behind the success of an in-house, continual peer review process are: open communication, frequent interactions, trust, and collegiality. These themes will be revisited in Chapter 6, where the culture of the organization will be discussed.

c) The third means by which the research directions of investigators are indirectly shaped by the Whitehead Institute is through the availability of the start-up or bridging funds. As noted earlier, the Whitehead Institute provides funds to the investigators in support of particular research projects, prior to their receiving federal support. The Institute also supports about 30% of the research budget. The formal approval process for such Institute support involves the leadership of the Institute, which therefore has significant influence over the final decision.

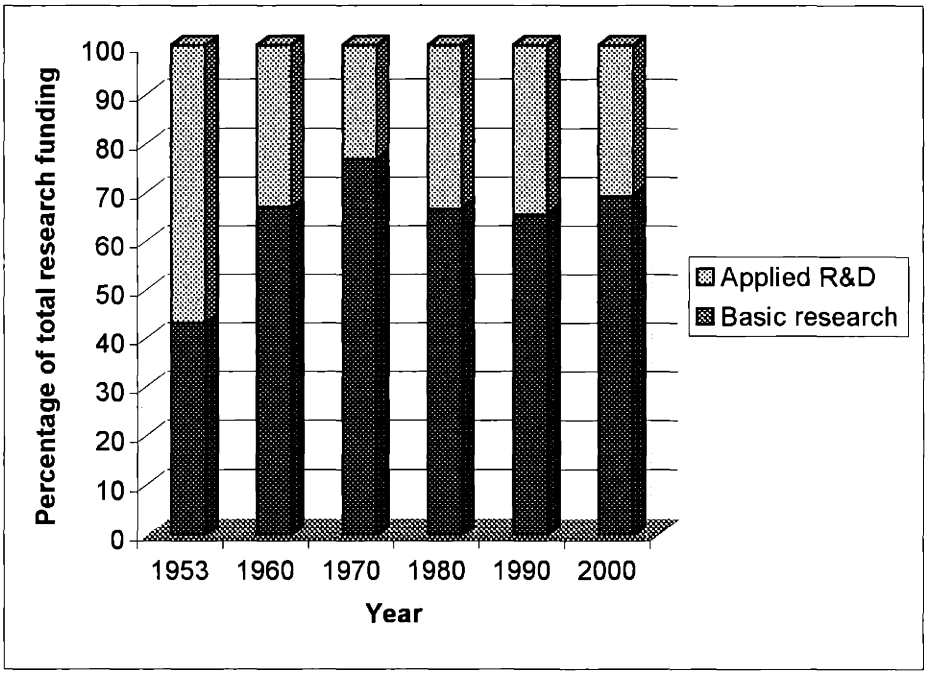
The net result of these 3 measures is a combination of a high degree of scientific freedom with some institutional oversight, which is often more indirect than direct. The process is one of influence rather than control – a 'soft' rather than a 'hard' approach. Such 'bottom-up' research approach provides scientific diversity, which in turn offers ample opportunities for significant scientific breakthroughs.

4.2 Basic *versus* Applied Research

Should a biomedical research institute concentrate on 'basic' research as opposed to 'applied' research? Is this differentiation relevant nowadays? This section addresses these questions. The question of whether a biomedical research institute should focus primarily on 'upstream', basic research *versus* the more applied, clinically-relevant, 'downstream' research has received much attention over the past few decades. Dr. Arthur Kornberg, Nobel Laureate and Professor Emeritus of Biochemistry at the Stanford University School of Medicine argued for the relative importance of basic research. He wrote: "It may seem unreasonable and impractical, call it counterintuitive, even to scientists, to solve an urgent problem, such as a disease, by pursuing apparently unrelated questions in basic biology or chemistry. Yet, the pursuit of curiosity about the basic facts of nature has proved throughout the history of medical science to be the most practical, the most cost-effective route to successful drugs and devices. Investigations that seemed totally irrelevant to any practical objective have yielded most of the major discoveries of

medicine..."[59] Dr. Kornberg is hostile to the notion of a strategic plan for biomedical research. In contrast, NIH has adopted a more disease-focused approach.

Over the past 50 years in the US, there has been a general emphasis on basic research vis-à-vis applied research and development, as reflected by funding expenditure. Figure 4.1 shows this trend in terms of funding to the entire field of science and engineering.



Source: National Science Foundation/Division of Science Resources Statistics, 2000

Figure 4.1 – R&D expenditure at universities and colleges, FY 1953-2000

The question of upstream *versus* downstream research does not seem to have an easy answer. Upon closer examination, however, one cannot help but realize the futility of this dichotomous argument nowadays. It is now quite clear that biomedical research

[59] Arthur Kornberg. "Support for basic biomedical reeaerch: How scientific breakthroughs occur." In: Barfield CE and Smith BLR, eds. *The Future of Biomedical Research.* Washington, DC: American Enterprise Institute & The Brookings Institution, 1997:39.

increasingly represents a continuum that spans from the seemingly irrelevant or impractical basic interrogations of natural phenomena, to the narrowly focused practical applications in the biotechnology industry and the clinics. Indeed both forms of research can, and do, exist at the same time in the same project. Scientists who are working on a basic question may stumble upon some findings that serendipitously become immediately applicable to practical issues. For instance, studies of *Drosophila sp.* (the fruit fly) and *C. elegans* (the worms) have yielded invaluable insights into homologous human processes and human diseases. Conversely, downstream or applied research has provided interesting leads and posed challenging questions that bring basic research back to the drawing board. For instance, the pursuit of *in vitro* fertilization and other assisted reproduction techniques in the clinics have spawned interest in stem cell research. The relentless pursuit of doctors to understand why tumors tend to spread explosively after their surgical extirpation has resulted in the birth of tumor angiogenesis research. More generally then, basic and applied research more properly represent 2 inter-dependent expressions of our efforts to understand human health and diseases, and to improve existing treatment options. Downstream applications provide the context in which to frame the relevant research questions, while upstream basic research provides the tools and the methodologies to gain the necessary fundamental insights into practical problems.

What is the state of the 'basic *versus* applied' debate at the Whitehead Institute? Dr. David Baltimore made the following remark after his discovery of the reverse transcriptase: "When I discovered the reverse transcriptase, there wasn't much more to be said. There it was, but that wasn't going to help cancer.....My life is dedicated to

increasing knowledge. We need no more justification for scientific research than that."[60] In reality, the distinction between these two arbitrary research polarities is blur at the Whitehead Institute. A survey of the Whitehead Institute's research profile yields a variegated, yet balanced, landscape (Annex B). While a number of Whitehead laboratories may be working on seemingly 'basic' research questions, such as the signaling pathways in fungi or the study of cytoskeletal motors using horseshoe crabs' sperms, there are foreseeable practical applications to these important research efforts. Indeed, the Whitehead Institute itself does not make a distinction between 'basic research' and 'applied research'. Perhaps it is fair to say that most biomedical research projects are both basic and applied; any separation between the two is largely temporal, or even semantic. The Whitehead Institute embraces such duality of biomedical research.

To obtain further insights into the increasing irrelevance of the differentiation between basic and applied science, one can look at the background of the Whitehead researchers. From the graduate students to the faculty, there are researchers who have come from a 'basic science' background, and others who have come from a 'medical background'. Of course, there are also the MDs/PhDs amongst the researchers.

At the Institute level, there is a concerted effort to bring together laboratory research and clinical applications. Dr. Fink wrote in his Director's Report in 2000: "...we need to partner with more academic physicians and clinical departments. Physicians are the most skilled observers of human biology and disease. In addition, they have access to the medical histories of large populations of patients; such information is vital to the identification of disease genes and to the determination of the interaction between our

[60] Crotty S. *Ahead of the curve: David Baltimore's life in science*. Berkeley, CA: University of California Press, 2001:81.

genes and the environment."[61] Whitehead Institute is deliberately bridging the gap between the 'front-end' and 'back-end' of biomedicine.

In modern biomedicine, not only is the differentiation between basic and applied research blurring, even the different types of basic research are beginning to blend into one another. For example, there increasingly more researchers in Whitehead Institute whose formal training did not even include biology, but physical sciences, computing, and mathematics. Biological questions today are increasingly more complex, calling for a rich and creative mix of laboratory, clinical, and computational expertise. Whitehead Institute's philosophy of choosing the right people in the first instance, relatively free of training or other background biases, allows it to absorb a diverse group of people with vastly different expertise. Such diversity will prove to be an increasingly powerful competitive advantage in the era of the new biology.

4.3 Multidisciplinary Research

The new biology today demands the co-participation of different disciplines of science and engineering. Increasingly, we see the creation of 'double-barrel' words in the biological parlance, such as bio-engineering, bio-imaging, bio-informatics, bio-computing, and bio-ethics. This trend is more than just of lexicographic concern; indeed, it signifies the amalgamation of scientific fields that have different origins and methodologies. This development is widely felt to be the new force that will bring about the next wave of changes in biology.

[61] Dr. Gerald Fink, in *Whitehead Institute Annual Report* 1999/2000.

Whitehead Institute has seen this trend coming. The Genome Center, for instance, is a prototypical hybrid research center that possesses a mixture of expertise, including biology, mathematics, and informational science. Also, the Whitehead Institute has significant collaborations with the engineers and physical scientists at MIT. It should be pointed out that the lack of rigid departmentalization in the Whitehead Institute allows it to mold itself quickly into a form that can bond synergistically with disparate research disciplines.

Multidisciplinary research is potentially a powerful approach through which 'disruptive technologies' in biomedical research might be created.

4.4 Chapter Summary

Resources are finite, even for a relatively well-endowed biomedical research institute such as the Whitehead Institute. The scientific philosophies and strategies that the Institute adopts significantly influence the chances of its success. Insofar as the choice of research directions, the Whitehead Institute believes that its scientists know best. Each of the 22 principal investigators is given a significant degree of scientific freedom, although peer input is readily available and sought. The Institute generally does not make the distinction between basic and applied research. Indeed, the boundary between these 2 domains is increasingly blur and irrelevant worldwide. The Whitehead Institute endorses the belief that the future of biology depends heavily upon multidisciplinary collaborations between seemingly disparate branches of science. The establishment of the Whitehead Institute Center for Genome Research, which combines biology with mathematics and informational science, is a concrete manifestation of this belief.

Thus far, we have identified the various assets that the Whitehead Institute possesses (Chapter 3), and explored the manner in which the Institute deploys these assets through its scientific strategies (Chapter 4). The next chapter examines the organizational design and context in which the Whitehead Institute performs its research.

Chapter 5

ORGANIZATIONAL DESIGN AND CONTEXT

This chapter looks at the Whitehead Institute as an organization embedded in the Greater Boston Area in general, and on the MIT campus in particular. The relationship between these 3 entities is schematically represented in Figure 5.1:

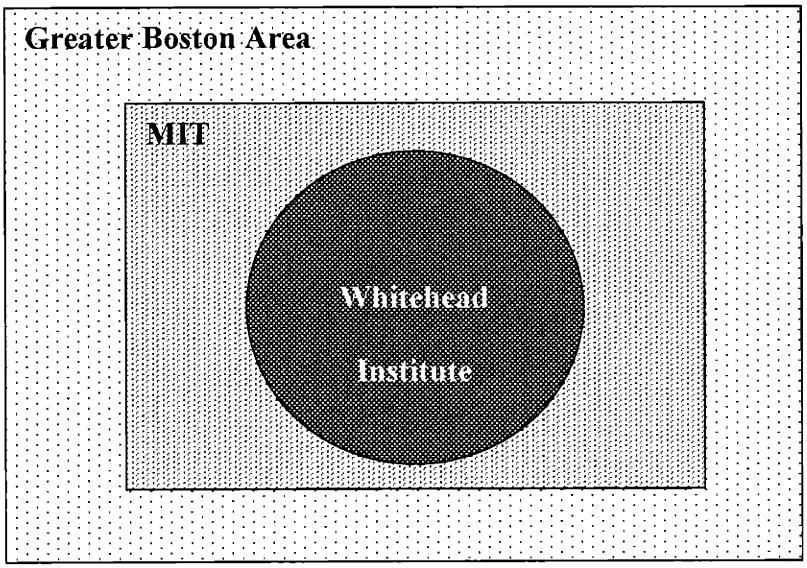


Figure 5.1 – Whitehead Institute is embedded in MIT and the Greater Boston Area

This chapter asks the questions: What is the optimal size of a biomedical research institute? How should the research organization be designed internally? What is the optimal relationship between a research institute and a university? What is the influence of geographical factors on the research institute's competitive advantage?

5.1 Relative Small Size is an Advantage

The size of an organization has a primary strategic relevance, although this is not always recognized as such. Often, a larger organization is thought of as being more productive and successful. This is particularly the case in the corporate world. In the setting of R&D organizations, there is also a tendency to equate size with ability. The thesis of this section is to argue that a relatively small size may offer significant advantages in the setting of a creative and learning environment.

In the corporate setting, the issue of organizational size has been studied quite extensively. Francis Fukuyama, a Senior Social Scientist at the RAND Corporation, wrote that "the purpose of large corporations is to exploit economies of scale in sectors that are capital-intensive, involve complex manufacturing processes, or require extensive distribution networks. Small companies, on the other hand tend to be better at organizing more labor-intensive activities and cluster in sectors demanding flexibility, innovativeness, and speed in decision-making."[62] This analysis may be extended to the setting of not-for-profit organizations as well. To the extent that a top-notch biomedical research institute needs to be flexible, adaptable, innovative, and quick to enter promising emerging areas, Fukuyama's analysis would suggest that a relatively small size might indeed be more appropriate. How does this apply to the Whitehead Institute? Moreover, how do the 2 distinct moieties of the Whitehead Institute – the labor-intensive, more traditional moiety in 9 Cambridge Center, and the highly automated, high-throughput

[62] Fukuyama F. "Social capital and the global economy." *Foreign Affairs* 1995;74:89.

Genome Center – fit in the size equation? These questions are of major strategic importance to the Whitehead Institute.

As noted earlier, the Whitehead Institute has a small faculty – 14 members in all. If one includes the 8 Whitehead Fellows, the total would be 22. This is considerably smaller than many elite university biology departments and biomedical research institutes (Table 5.1).

Institute	Founding Year	Total Staff Number	Number of Faculty Members
Whitehead Institute	1982	751	14*
Salk Institute for Biological Studies	1960	≈900	58
Scripps Research Institute	1961**	≈2800	276
Cold Spring Harbor Laboratory	1890	925	55
Fred Hutchinson Cancer Research Center	1975	≈2400	215

*22, including the Whitehead Fellows
**Scripps Metabolic Clinic was established in 1924, and Scripps Clinic and Research Foundation was established in 1955.
Source: Respective institutions' websites

Table 5.1 – Relative sizes of selected non-profit biomedical research institutes

To a research organization, is small size an advantage or a handicap? On one hand, a larger outfit allows a broader diversity of research areas and personnel. It also tends to increase the overall research output and total number of grants awarded on an institutional basis, though not necessarily productivity. On the other hand, a smaller outfit promotes greater personal contact amongst the faculty members, which, in the case of the Whitehead Institute, has become an important feature of its culture. The smallness also engenders a positive pressure on the individual laboratories to be more inter-dependent on one another in order to create greater synergy. A smaller outfit, however, also means

that the research institute has to exercise greater caution when deciding its research directions.

The small size of the Whitehead Institute was a conscious decision by the founding pioneers, based on the belief that the ponderous bureaucratic machineries of the large universities would slow down operations and reduce efficiency. What are the specific reasons that encourage, or compel, the Whitehead Institute to remain small, 20 years after its founding?

a) Physical space limitation. This is perhaps the most obvious reason. There is a genuine space constraint to any major expansion of the Whitehead Institute. As it stands today, the Institute, including the Genome Center, occupies 4 different sites within a half-mile radius. The new Bioimaging Center is being established in a 5th building. Real estate in Cambridge, Massachusetts is expensive. At the same time, the Whitehead Institute is not prepared to scatter its units more widely than they are today.

b) Impact of organizational size on the decision-making process. The small size of the Institute and the belief that the laboratories must be co-located help keep the organizational structure relatively flat. As noted in Section 4.1, each principal investigator at the Whitehead Institute is free to set his or her own research direction. There is no distinct 'senior management level' *per se* above the faculty. The 14 Members and Associate Members essentially form a self-governing 'scientific council' within the Institute itself, although it is not formally recognized as such. Decisions pertaining to the Institute are taken collaboratively amongst these 14 men and women, all of whom are highly regarded scientists.

Whitehead scientists describe their business meetings as resembling gatherings between siblings within a family. The Director's role is to facilitate the discussions, and to provide his or her own expert opinions as a senior colleague. The final decision reflects a consensus view of the faculty, though not necessarily a unanimous one. For instance, during the recruitment process, if there were a few members of the faculty who are uncomfortable with the candidate, that recruitment would not be pursued further. In order to manage such a consensus-driven organization effectively, Whitehead Institute believes that the size of the decision-making group (i.e. the faculty in this case) should remain relatively small. Through a process of trial and error, the Whitehead Institute has decided that 15-20 faculty scientists would be a comfortable number.

c) Organizational culture, structure and size. Overall, the small size of the Whitehead Institute allows it to engender a high degree of collegiality that is borne out of personal regard for one another. The faculty scientists know their peers wll, personally. This level of familiarity extends to the scientists' families too. The resultant organizational culture is characterized by mutual respect, trust, and professionalism, embedded in a tight network of personal friendships. This level of intimacy cannot be created if the faculty size was much larger.

Organizational culture, structure and size interact with one another. There are 2 basic patterns or organizational structures.[63] One is vertical, characterized by a hierarchical or pyramidal layering of authority; communication is often unilateral and limited in scope and frequency. The vertical structure is appropriate

[63] Sapienza AM. *Managing Scientists: Leadership Strategies in Research and Development*. New York: Wiley-Liss, 1995.

under stable operating conditions and in work processes for which rules and established procedures exist. The vertical structure emphasizes efficiency, and is compatible with a large organizational size. The other structure is a lateral one, characterized by peer-to-peer relationships and other horizontal networks; communication is often more spontaneous and active. The lateral structure is more appropriate under unpredictable conditions and in work processes for which few rules or established procedures exist. The lateral structure emphasizes creative expression and tolerates ambiguity and unconventional behaviors.

Organizations with a lateral structure tend to have a relatively small size, since one can only communicate openly and informally with a limited number of people. R&D work favors a lateral structure. With this normative description in mind, the relationship between organizational structure, culture and size can be depicted as follows (Figure 5.2):

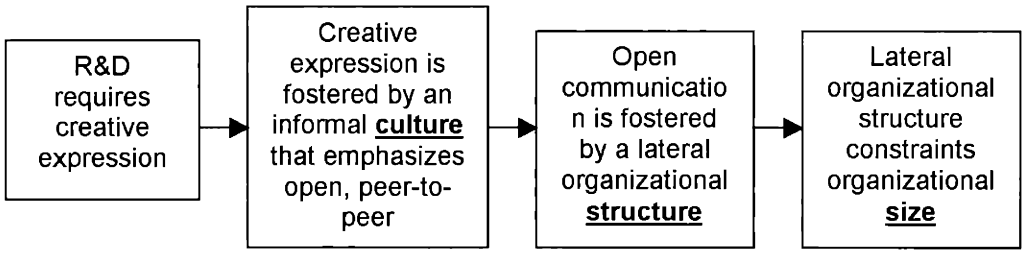


Figure 5.2 – Relationship between organizational culture, structure and size in an R&D organization

d) Relative sizes of the Whitehead Institute and MIT. MIT is a relatively small university by the US standard, with slightly more than 10,000 students. As noted

in Chapter 2, when Mr. Edwin Whitehead and Dr. David Baltimore founded the Whitehead Institute, there was a deliberate attempt to reassure MIT that the Whitehead Institute would not be a threat to the existing MIT Department of Biology. The intricate balance between the Whitehead Institute and MIT, especially its Biology Department, might be threatened if the former were to grow much larger. As such, the limit on the size of the Whitehead Institute is political as much as strategic.

The small size of the Whitehead Institute has its disadvantages too. Most important of all is the shortage of human resource to pursue certain new research areas that appear to be promising.

Overall, however, the author is of the opinion that the benefits of a relatively small biomedical research institute outweigh the costs. Indeed, the Whitehead Institute conjures up the image of a lancet – small, pointed, and draws blood easily. There is an important lesson here for future research institutes.

5.2 Lateral Organizational Structure – Lack of Formal Departmentalization

Most university faculties and schools are divided into large departments, which in turn are composed of smaller divisions. A number of large research institutes are similarly organized into specialized departments, each with a number of principal investigators. This is often borne out of necessity, rather than organizational preference *per se*. It is nearly impossible to efficiently manage a research organization with several

thousand employees, including several hundred investigators, without some form of departmentalization.

The relatively small size of the Whitehead Institute permits a flat or lateral organization without an absolute need to erect boundaries between groups of scientists. Indeed, the 14 faculty scientists and the 8 Whitehead Fellows pursue such diverse areas of biomedical research that it does not make any sense to aggregate them into artificial groups. Also, the Whitehead Institute also tries to minimize any distinction amongst the principal investigators. For instance, it does not distinguish between the founding Members and other Members.[64]

The lack of departmentalization in the Whitehead Institute has several effects, which can be summarized as follows:

a) Most large universities are organized into different schools and department, such as the Department of Engineering, Department of Biology, Department of Chemistry, Department of Computing, Department of Mathematics, and so on. Such departmentalization has a tendency to engender 'isolationism' and 'turf protection' issues. The risk of 'silos mentality' is minimized in the Whitehead Institute. The lack of formal departmentalization in the Whitehead Institute encourages open and frequent communications between scientists, and promotes cross-fertilization of research ideas. Formal collaborations are not uncommon in the Whitehead Institute. For example, Dr. Rudolf Jaenisch, a Whitehead Member, and Dr. George Daley, a Whitehead Fellow, collaborated and published a joint research that entailed the tandem application of 2 distinct technologies, namely,

[64] Interview with Dr. Paul Matsudaira, Jan 8, 2002.

ex vivo gene transfer and therapeutic cloning.[65] The gene transfer experiments were carried out largely in Dr. Daley's laboratory, while the Jaenisch Laboratory performed the cloning experiments. Such collaborations provide opportunities to create synergy between Whitehead laboratories with distinct but complementary expertise.

b) The lack of departmentalization allows the individual laboratories to be flexible and nimble. They are quick to respond to emerging research trends through a continual process of re-positioning.

5.3 Whitehead Institute's Affiliation with MIT

> "The bare bones of our institutional organization are, simply stated, that the Whitehead Institute for Biomedical Research is an independent basic research institute located near and affiliated with the Massachusetts Institute of Technology.....He (Mr. Edwin Whitehead) insisted on its independence from other entities because he believed that small, internally-directed research units can make special contributions – that they create a climate for research different from that in a large university. But he also understood that small units may not function optimally in isolation and believed that affiliation with an existing center was necessary."
>
> Dr. David Baltimore, 1983[66]

[65] Rideout W.M III, Hochedlinger K., Kyba M. Daley G., and Jaenisch, R. "Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy." *Cell.* Published online March 8, 2002.
[66] Dr. David Baltimore, in *Whitehead Institute Director's Annual Report* 1983/4.

The Whitehead Institute and MIT enjoy a strong and thriving symbiotic relationship with each other. While the logic of this alliance now seems obvious, it was, as noted, not always so obvious in the late '70s and '80s, when Mr. Edwin Whitehead proposed the new institute. The university wanted to maintain significant control over the operation of the research institute so that the university's reputation would not be tarnished by any act that would be unbecoming of an esteemed institution of tertiary education.

As detailed in Chapter 2, a deal was eventually made which permitted a win-win outcome. Under this affiliation, the MIT Corporation recognized the Whitehead Institute as a financially independent research institution affiliated with MIT through its teaching activities: the Whitehead Institute would accept MIT graduate students for research and training in its laboratories and MIT would, in turn, consider all Whitehead faculty for appointment to faculty level positions at MIT.[67] To facilitate this cross-appointment, searches for Whitehead Institute faculty would be carried out jointly with MIT. To ensure parity between the faculties of both sides, Whitehead Institute faculty scientists would enjoy comparable compensations and benefits as their counterparts in MIT.[68]

The intellectual property arrangement between the Whitehead Institute and MIT has worked efficiently. The former owns all inventions and other intellectual properties that originate from its faculty scientists. Whitehead Institute files its own patents, but engages the services of MIT's Technology Licensing Office (TLO) for the purpose of

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[67] Whitehead Institute website, "A history of the Whitehead Institute". http://www.wi.mit.edu/who/who_history_narrative.html

[68] Interview with Dr. Paul Matsudaira, Whitehead Institute Member, Jan 8, 2002.

commercialization of its inventions.[69] Typically, 15% of the revenue stream goes to TLO as licensing fees; one-third of the remaining 85% (less other expenses such as patent filing fees) goes to the inventor, and the rest goes to the Whitehead Institute.[70]

The affiliation between the Whitehead Institute and MIT has been a productive one. Whitehead Institute gains access to a rich pool of talented students at MIT as well as a number of administrative services that MIT provides. In return, MIT benefits through sharing of teaching load with the 14 Whitehead faculty members. MIT students enjoy an expanded research opportunity. Additionally, both organizations benefit from having a greater number of outstanding colleagues with whom their scientists can interact. Finally, both organizations share the limelight that each one brings to the joint partnership. The Whitehead Institute-MIT relationship has been so productive that it is now inconceivable that this relationship should be jeopardized in any way.[71]

It is important to appreciate how this relationship, so disproportionate in size and history of its 2 elements, can thrive without any major distortion of power and influence. Four factors, in the author's opinion, have helped maintained this equilibrium:

a) Whitehead Institute's founding Director, Dr. David Baltimore, and 2 other initial founding Members (Dr. Harvey Lodish and Dr. Robert Weinberg), came to the Whitehead Institute from the MIT Department of Biology. Therefore, strong personal ties and understanding helped link the 2 organizations.

b) There is apparently considerable mutual respect for the scientists in both camps. Both organizations can boast of renowned scientists in their midst.

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[69] Electronic mail correspondence with Ms. Lita Nelson, Director of MIT's TLO, Jan 4, 2002.
[70] Interview with Mr. John Pratt, Associate Director of Whitehead Institute, Jan 31, 2002.
[71] Uniform sentiment from all interviewees who were asked the question: "Do you think Whitehead Institute or MIT would consider becoming totally independent in the future?"

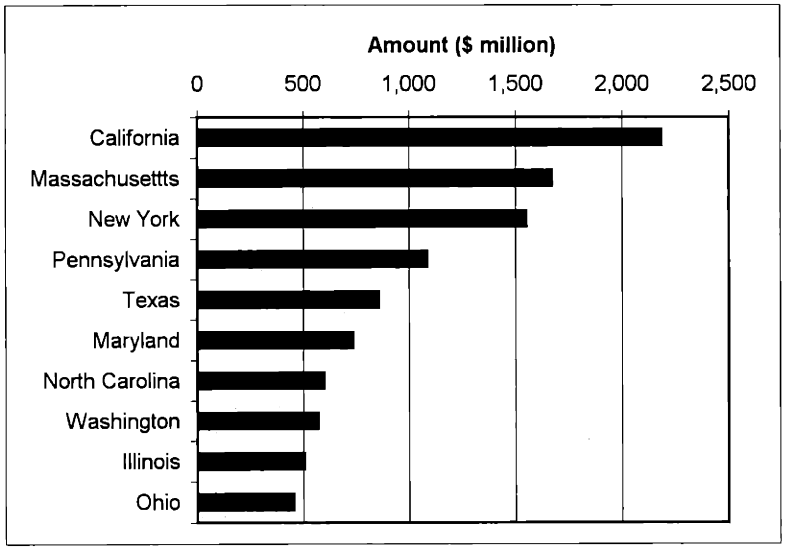
c) The Whitehead Institute is located across the street from the MIT Department of Biology and the MIT Cancer Center. This physical proximity is a critically important factor that binds the 2 parties together.

d) Whitehead Institute enjoys a high level of financial independence from MIT. This protects its autonomy.

5.4 Advantages of Being in the Greater Boston Area

A major contributory factor to the success of the Whitehead Institute is its strategic location in the midst of the Greater Boston Area, a bustling biomedical hub.

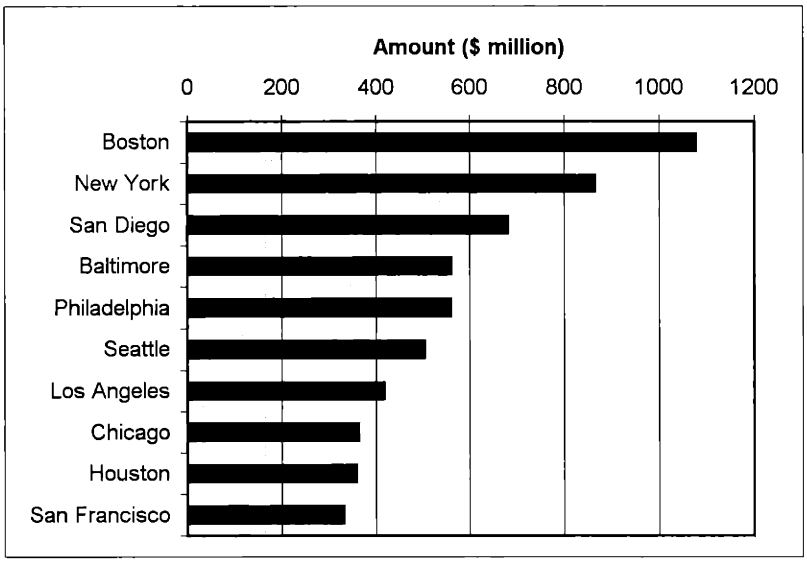
In 2001, Massachusetts had the second largest amount of NIH extramural funding, totaling $1.674 billion (Figure 5.3):



Source: The Boston Globe, Feb 18, 2002

Figure 5.3 – Top 10 States with the most NIH extramural funding, 2001

Within Massachusetts, Boston City was the biggest recipient of NIH funding in 2000, with a total of $1.078 billion (Figure 5.4). The City of Cambridge was ranked 15th, with $216 million.



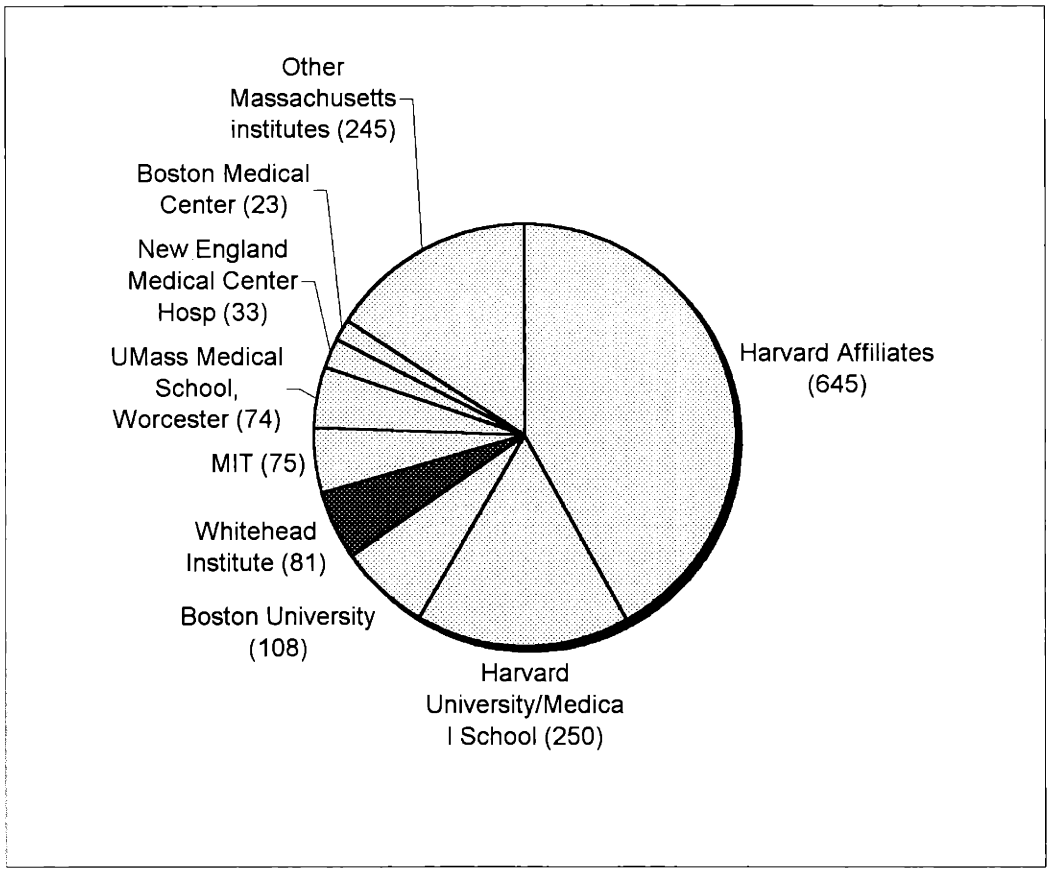
Source: The Boston Globe, Feb 18, 2002

Figure 5.4 – Top 10 Cities with the most NIH extramural funding, 2000

Within Massachusetts, Harvard University, including its Medical School and its affiliates, captures the greatest amount of funding. The Whitehead Institute, despite its relatively small size, had a significant share of the funding (Figure 5.5).

The federal funding that has been injected into the Greater Boston Area has become one of the region's prime economic engines. The $1.6 billion NIH grant awarded to Massachusetts is estimated to pay the equivalent of about 10,000 researcher salaries. This money has a multiplier effect in that the researchers and the scientific projects supported by this large sum of money in turn create high-quality scientific output that attracts further funding. Interestingly, the Greater Boston Area's biomedical research has

done so well that politicians from states that get relatively paltry amounts from NIH have begun to complain.[72]



Source: Boston Globe, Feb 18, 2002

Figure 5.5 – NIH funding in MA Institutions, 2000 (Numbers in chart refer to funding amounts in $ million)

The unique attributes of the Greater Boston Area that promote the development of biomedical enterprises, both private and public, are briefly summarized here.

a) High concentration of outstanding universities and research centers in the area, including MIT, Harvard University, Tufts University, and Boston University.

[72] *The Boston Globe*. Feb 18, 2002.

These institutes of higher learning provide the rich intellectual capital that drives the creative engine in the area. Being in the area also increases access to state-of-the-art equipment and reagents. Some observers have predicted that well-known centers in MIT, such as its Engineering School and the Artificial Intelligence Laboratory, represent important resources to biomedical research in the region, since the research will rely more heavily on computation and engineering in the future.[73]

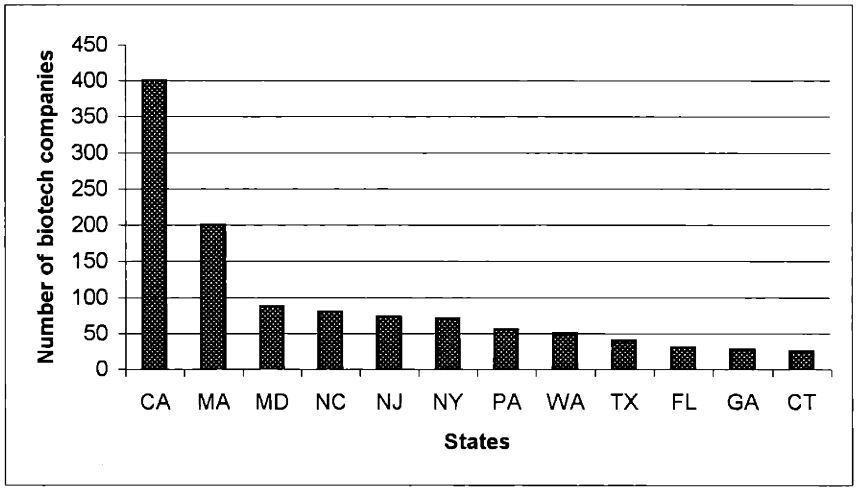
b) Presence of 3 medical schools and 8 major affiliated teaching hospitals, including the well-known Massachusetts General Hospital and the Brigham and Women's Hospital. The Massachusetts General Hospital was recently ranked 3rd, and the Brigham and Women's Hospital 11th, in the 'America's Best Hospitals' ranking conducted by *US News*.[74] Biomedical research institutes benefit from close collaborative relationships with these major teaching units. The hospitals provide clinical materials for bench research and human subjects for clinical trials. In addition, their doctors provide a downstream (clinically-relevant) perspective that may shape the direction of biomedical research.

c) The thriving biotechnology and pharmaceutical industry in the Greater Boston Area adds vibrancy to the region. There is a perception that Massachusetts' biotechnology industry is thriving, whereas the electronic and informational sectors are not faring as well. 'Bio' has replaced 'E' as the hot prefix, reports the

[73] Interview with Dr. Keith Dionne, VP/GM Technology Business, Millennium Pharmaceuticals, Inc. Jan 24, 2002.

[74] Usnews.com website Jan 2002: www.usnews.com/usnews/nycu/health/hosptl/honorroll.htm

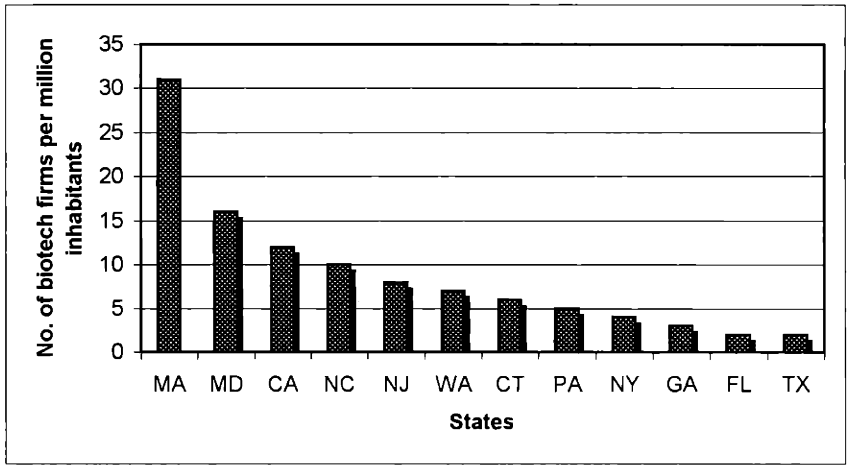
Boston Globe.[75] Massachusetts has the second highest number of biotechnology companies in the US (Figure 5.6).



Source: Focus on Fundamentals – The Biotechnology Report, Ernst & Young 2001

Figure 5.6 – Top 12 biotechnology States in United States

When adjusted for the sizes of the different states, as reflected by their residential populations, Massachusetts has the highest number of biotechnology firms per million inhabitants, as shown in Figure 5.7:



Source: Focus on Fundamentals – The Biotechnology Report, Ernst & Young 2001

Figure 5.7 – Number of biotech firms relative to population for top 12 States

[75] Kirsner S. "Biotech's now the big thing in Mass". *The Boston Globe*, April 22, 2002.

Major biotechnology companies such as Millennium, Biogen, and Genzyme, as well as smaller biotechnology companies have mushroomed in the area over the past 10 years. More recently, even giant pharmaceutical companies have begun to increase their presence in this area, including Merck, Pfizer, and Amgen. It is notable that these companies have decided to set up their businesses in the Greater Boston Area despite the high cost of living expenses in the region. Millennium, for example, would not move out of its present Cambridge campus (only 200 yards from MIT) to another location just a few miles away.[76]

These firms seek to be physically close to, and collaborate with, top academic research institutes such as MIT and the Whitehead Institute. To these firms, collaborations with renowned academic centers augment the capacity of businesses to solve complex problems.[77] Interestingly, studies have shown that academic research collaborations might enhance firms' sales, R&D productivity, and patenting activity.[78] Conversely, academic research institutes also benefit from the presence of these companies, for they inject a sense of corporate dynamism and additional funding, and make available proprietary equipment and methodologies. Furthermore, interactions with downstream-oriented corporate scientists deepen academic scientists' appreciation of the industry. The net result is a mutually reinforcing relationship between the academia and the industry. In fact, research has shown that the rate of entry of biomedical firms into a region is

[76] Interview with Dr. Keith Dionne, VP/GM Technology Business, Millennium Pharmaceuticals, Inc. Jan 24, 2002.

[77] Burnham JB. "Evaluating industry/university research linkages." *Research-Technology Management* 1997;40:52-55.

[78] Cockburn I and Henderson R. "Public-private interaction and the productivity of pharmaceutical research." *NBER Working Paper* 6018, April 1997.

significantly increased by higher numbers of actively publishing stars, top-quality universities, federally supported bioscience researchers, and average wages.[79]

There are at least 5 conventional ways by which the academia forms relationship with the industry, namely:[80]

- Research relationships
- Consulting relationships
- Patenting or licensing relationships
- Equity relationships
- Training relationships

The interactions between the Whitehead Institute and the blossoming biotechnology industry in the Greater Boston Area are further discussed in Appendix D.

d) The high concentration of venture capitalists in the Greater Boston Area, and the relative abundance of risk capital promote entrepreneurial activities in the region. Venture capital represents an important source of funding in any high-technology industry. For a number of years, the US has enjoyed an active venture capital market. More than 70%, or $97 billion, of world private equity and venture capital investment was in the US in 1999. About a third of that was invested in high-technology firms. The New England area is the third strongest biotechnology financing belt in the United States, after Northern California and the Pacific Northwest. New England raised a total of $4.5 billion for biotechnology between

[79] Zucker LG, Darby MR, Armstrong JS. "Commercializing knowledge: university science, knowledge capture, and firm performance in biotechnology." *NBER Working Paper* 8499. Oct 2001.
[80] Blumenthal D. "Growing pains for new academic/industry relationships." *Health Affairs* 1994:13:176.

July 2000 and June 2001.[81] Venture capital plays a significant role in heating up the biotechnology enterprise in the Great Boston Area.

e) Geography and network effects play an important but indirect role in stimulating the biomedical environment in the Greater Boston Area. Boston City and the City of Cambridge are geographically compact; many parts of these 2 cities are within walking distances, or are well-linked by the public transport system. This high density of buildings and people create a vibrant hub where it is easy to meet people who share the same interests. Indeed, when Whitehead Institute or MIT organized biomedical symposia, it was not uncommon to see people from different sectors of the biomedical world, including scientists, students, venture capitalists, large corporate representatives, and entrepreneurs. The end result is a dynamic network of people and information that is shared and reinforced whenever there is a biomedical symposium or workshop.

Whitehead Institute finds itself deeply embedded in this vibrant and inter-connected academic and business network of the Greater Boston Area. The area represents a rich mixture of quality biomedical science, first-class talents, blossoming biotechnology industry, and an entrepreneurial exuberance. The richness and uniqueness of this environment may be hard to reproduce elsewhere.

[81] Ernst & Young. *Focus on Fundamentals: The Biotechnology Report*. 2001

5.5 Chapter Summary

This chapter has explained why the Whitehead Institute has made the conscious decision to remain relatively small, in comparison to many other established biomedical research centers and university biology departments. The small size permits a consensus-driven decision-making process and promotes collegiality amongst its workers. The latter appears to be an important factor in fostering research collaborations. Additionally, the small size also enables the Institute to be highly responsive to changing trends in research, and remain nimble in its administration.

The Whitehead Institute and the MIT Department of Biology have benefited from their symbiotic relationship. The former gets access to talented students, while the latter gains by having additional faculty to share the teaching load. Both parties gain by having a greater critical mass of top-notch biologists on the campus. The Whitehead-MIT relationship is strengthened by a high level of mutual respect and cooperation.

The Whitehead Institute and the MIT Department of Biology are embedded in the Greater Boston Area, which is now enjoying a biotechnology boom. The relatively high concentration of universities and academic medical centers, coupled with a growing venture capital industry, have attracted an increasing number of biotechnology firms to this region. There is a thriving relationship between biomedical research centers and biotechnology firms in this region. The Whitehead Institute is a good example.

The next chapter delves into the culture of the Whitehead Institute, and relates some of the Institute's strategies and actions to its cultural values and assumptions.

Chapter 6

ORGANIZATIONAL CULTURE AND DEFINING PRACTICES

> "There is great camaraderie..... Usually you would think in a group like this, there would be a lot of prima donnas, but in fact we get along with one another..... There is a conscious attempt to bring in people who are not only of high scientific quality, but who would make good colleagues."
>
> Dr. Robert Weinberg, Whitehead Member, November 2001[82]

What is organizational culture and what is its relevance to a biomedical research institute? The theses of this chapter are two-fold: first, organizational culture is highly relevant to the study of biomedical research institutes; second, the Whitehead Institute exhibits at least 2 distinct subcultures. This pattern may exist in other academic research centers as well.

6.1 Organizational Culture: A Brief Introduction

Organizational culture is an enormous research field within social science. A comprehensive study of organizational culture in general, and Whitehead Institute's organizational culture in particular is beyond the scope of this chapter. Instead, this

[82] Interview with Dr. Robert Weinberg, Whitehead Member, Nov 20, 2001

chapter attempts to provide a framework for understanding organizational culture and then use the framework to appreciate the cultural elements of the Whitehead Institute.

Organizational culture may be defined as the system of shared actions, values, and beliefs that develops within an organization and guides the behavior of its members.[83] The elements that define organizational culture – including values, beliefs, norms, symbols, language, rites and rituals, and myths – are shared and accepted by organizational members. An organization is said to have a strong culture when most members accept a set of interrelated assumptions that forms an internally consistent cultural system that endures over time.[84]

What is the role of the organizational culture? Culture guides the way the members of an organization deal with the outside world (external adaptation), and the way the members create a collective identity and find ways of working and living together (internal integration). Organizational culture is a predictor of employee satisfaction and competitive performance.

Given that 'culture' is an intrinsically abstract concept, how does one analyze an organizational culture? One way to do so is depicted in Figure 6.1.[85] The different dimensions of organizational culture may be envisioned as layers. The most superficial level of the culture can be thought of as the observable culture or artifacts of the organization. The artifacts are palpable and vivid, but their true meanings are difficult to decipher. The next level calls for the elicitation of the espoused values. These values are often expressed as official philosophy, mission statement, and the various justifications

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[83] Schein E. "Organizational Culture." *American Psychologist* 1990;45:109-119.
[84] Schein E. Coming to a New Awareness of Organizational Culture. *Sloan Management Review* Winter 1984: 4.
[85] Adapted from: Schein EH. *Strategic Pragmatism.* Cambridge, Masschusetts: The MIT Press. 1996:160.

that members use to justify their behavior. Espoused values can provide a powerful motivational mechanism for members of the culture. However, one will often note inconsistencies between the espoused values and the overt artifacts. To resolve such inconsistencies it is necessary to go to the deepest level of analysis, which comprises the shared tacit assumptions. These common assumptions are the real drivers of behavior – the underlying essence of the organizational culture.

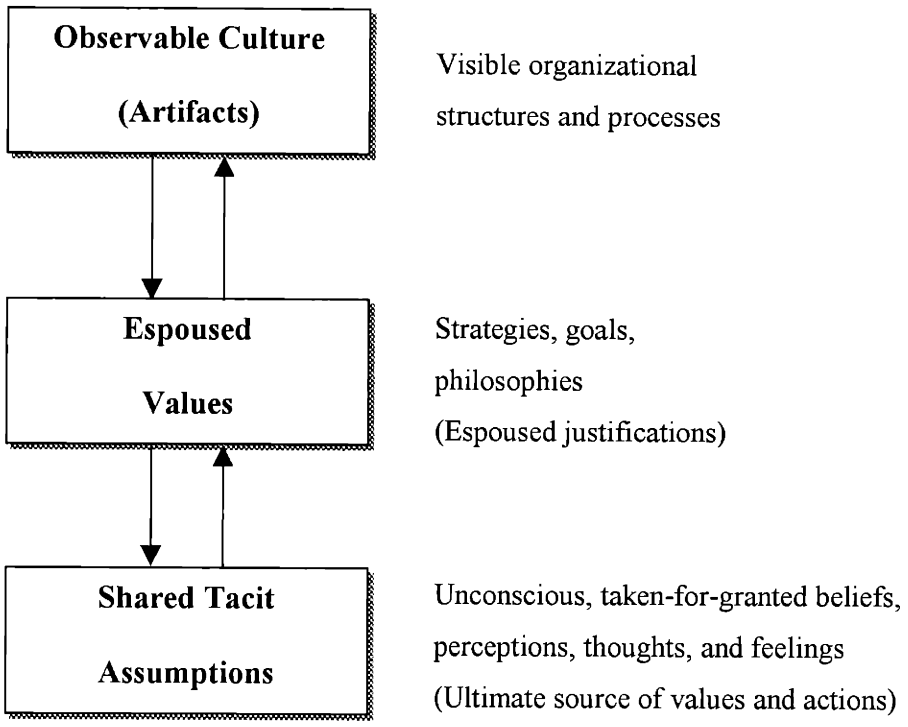

Figure 6.1 – Three levels of organizational culture analysis

The following section examines the organizational culture of the Whitehead Institute using this 3-level framework. At appropriate points in this section, certain cultural themes will be deliberately discussed in relation to phenomena and strategies that

characterize the Whitehead Institute. Indeed, an organization's actions and planning often have a deeply-embedded cultural undertone.

6.2 Observable Artifacts:

Most organizations display a wide array of observable artifacts, including stories and sagas, rites and rituals, and symbols.

The **founding story** is alive in the Whitehead Institute (see Chapter 2). The visionary and courageous attributes of Mr. Whitehead and Dr. Baltimore are often emphasized in the story. The founding story has been so embellished that it has become a **saga**, which is a heroic account of accomplishments. Founding stories, and particularly sagas, are important because they are used to tell new members the real mission of the organization. Interestingly, literature suggests that rarely is the founding story totally accurate, and it often glosses over some of the more negative aspects of the founders.[86]

Rites are standardized and recurring activities that are used at specific times to influence the behaviors and understanding of organizational members; **rituals** are systems of rites. Perhaps one of the most celebrated rites at the Whitehead Institute is the annual Vail Retreat that the Whitehead faculty attends. This is a week-long skiing holiday that involves the families of the faculty as well as the Whitehead family. The purpose of this retreat is to strengthen the personal bonds between the faculty members. As Ms Susan Whitehead, Chairperson of the Whitehead Institute's Board of Directors, once remarked on the culture of the Institute: "(There is) a lot of community-building. We have a lot of stars, and stars can get temperamental if they don't know each other, (and)

[86] John R Schermerhorn Jr, James G Hunt, Richard N Osborn. *Organizational Behavior*, 6th Edition, New York: John Wiley & Sons, 1997:265-288.

each others' families very well."[87] This retreat appears to hold special significance to the Whitehead faculty. There are 3 salient reasons to account for this. First, the faculty members spend a number of evenings during the retreat discussing the long-term strategic direction of the Institute. Second, faculty members spend a good deal of time socializing with one another during the retreat. Third, faculty families socialize extensively with one another as well. The presence of the families allows the peers to see more, and different, facets of their colleagues; this tends to engender greater mutual understanding and trust. The retreat reinforces the 'family culture' of the Whitehead Institute, at least to the faculty and the Whitehead family.

Scientists of the Whitehead Institute, including the graduate students and the postdoctoral scientists, participate in the annual Whitehead Institute scientific retreat. At this larger event, every Whitehead laboratory puts up scientific posters and gives presentations. There are also ample opportunities for socialization. The Institute pays the expenses. The event reinforces the message that people matter to the Institute; it also represents a ritual to celebrate the diverse biomedical research that the Institute carries out. The notion of 'family' is less emphasized here.

Another rite that is celebrated at the Whitehead Institute is the monthly Beer Hour. This is a pan-institute social drinking event that is usually held on a particular Friday afternoon each month. It is usually lively, and involves a large segment of the Institute, regardless of job description or seniority. It has apparently helped to create a sense of belonging and collegiality amongst the Whitehead employees.

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[87] Warsh D. A bicoastal good deed. *The Boston Globe*. Mar 5, 2000.

A **Cultural symbol** is any object, act, or event that serves to transmit cultural meaning. Like many other research laboratories, the dress code at the Whitehead Institute is casual. In the summer, scientists are seen working in their laboratories wearing crew-neck T-shirts and jeans. They even give scientific presentations dressed in a similar attire. The relaxed dress code symbolizes freedom, openness, and a priority that is given to science rather than formalities, and suggests membership in the larger MIT community where such attire is de rigueur.

The building was designed to achieve maximum human contacts. Faculty offices are not buried within the laboratories, but are situated at both ends of the laboratory corridors, clustered with other offices. This arrangement gives the faculty members the opportunity to step out of their laboratories and talk to their peers. In other research institutions, it is not uncommon to find laboratories that are organized in silos – the principal investigators work in close proximity to their own laboratory staff, but interact relatively little with people from other laboratories.

Organizational culture often specifies when various types of actions are appropriate and where individual members stand in the social system. These **cultural rules and roles** are part of the normative controls of the organization and emerge from its daily routines. One of the salient cultural rules in the Whitehead Institute is the high level of cooperation and sharing that exists amongst its workers, regardless of their work capacities. Reagents are freely shared between laboratories in the Whitehead Institute, and even with the MIT Department of Biology and Cancer Center. Expert technical help is freely available. There are several reasons to explain this high level of cooperation in the Whitehead Institute. First, the senior members of the Institute have set the cultural

norm through their own display of collegiality. Second, the relative abundance of resources in the Institute permits such behavior. Third, there appears to be a tacit understanding that mutual assistance is a pragmatic behavior to adopt. When asked why the busy scientists in the laboratories are willing to put aside their work to help others, a visiting scientist said with some candor: "They never know when they'll need help from you in future."[88]

The cultural role in the Whitehead Institute deserves some comment. Despite the different levels of experience and seniority that exist amongst the researchers in the Institute – ranging from students to senior scientists – there appears to be a high level of mutual respect. The younger colleagues are well respected. It is common in the Whitehead Institute to address the senior scientists on a first-name basis.[89]

6.3 Espoused Values:

Shared common values help tie the organization to the broader values of the society, and may provide a distinctive source of competitive advantage. Many organizations today have a broad, fairly common, system of shared values: many have pledged to be good corporate citizens, non-discriminatory, and merit-based. Beyond that, however, unique shared values can provide a strong organizational identity, enhance collective commitment, provide a stable social system, and reduce the need for formal and bureaucratic controls. This section examines the espoused values of the Whitehead

[88] Interview with Dr. Meng-Ling Choong, Visiting Scientist at Whitehead, Mar 14, 2002.
[89] Interview with Ms Sandra Luikenhuis, Whitehead Graduate Student, Mar 11, 2002; and interview with Dr. Meng-Ling Choong, Visiting Scientist at Whitehead, Mar 14, 2002.

Institute, and matches these with some of the observable actions that the Institute has undertaken.

Mission. The mission of the Whitehead Institute is to pursue excellence in biomedical science. Implicit in this mission is that human health will eventually improve by the general advancement in biomedical knowledge. The Institute matches its action with its mission. Whenever the Institute is confronted with a decision, it often asks itself if the decision that it takes will help advance the science in the Institute; if it does, a positive decision will be taken.[90] This single-minded quest for biomedical knowledge is an important defining attribute of a successful research institution. The relative financial freedom that the Whitehead Institute enjoys allows it to strive towards its holistic goals of creating knowledge, while minimizing distraction by physical, fiscal, or bureaucratic limitations.

The Whitehead Institute, especially in the past decade, has said it must make a more visible contribution to the society at large. Dr. David Page puts it well: "Whitehead Institute sees itself as having a place in the world that goes beyond the simple published production of its laboratories.... We try to convey to our trainees that it is important that scientists talk not just to one another, but for a scientist to be a real scientific leader, you've got to be prepared in some way to communicate to the rest of the world what science is about, and why science is important, because we are utterly dependent for our continued existence on the rest of the world."[91] To this end, the Whitehead Institute is proud of its not-for-profit community outreach programs that reach out to various segments of the local community (Section 2.3.6, and Appendix C).

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[90] Interview with Dr. Susan Lindquist, Whitehead Director, Feb 1, 2002
[91] Interview with Dr. David Page, Whitehead Member, Feb 8, 2002.

This value system of pursuing knowledge and contributing to society appears to be widely shared by the senior scientists and senior management of the Whitehead Institute. However, interviews with the graduate students have revealed a different picture. It came to light that students and postdoctoral scientists are motivated by their desire to produce excellent scientific data that lead to publications in the top biomedical journals and, in so doing, strengthen their resume. These junior researchers view the Whitehead Institute as a temporary training ground and a well-endowed facility that gives them the best chance of succeeding in their own careers. They do not seem to express the same value and aspiration that the Institute itself espouses. The motive of the graduate students and postdoctoral scientists is almost entirely a pursuit of self-interest.

One can therefore see that the Whitehead Institute really has 2 sets of value systems: on one hand, the Institute and its permanent (more senior) members espouse a set of values that are apparently more holistic and noble; on the other hand, the junior scientific workforce of the Institute espouses more self-interested aspirations. Such dichotomy is probably not unique to the Whitehead Institute.

Does the co-existence of these 2 seemingly disparate missions pose a problem or conflict? The author holds the view that this discrepancy is nearly inevitable, given the design of the research organization and the shape that research careers take in biology. The 2 may even be complementary. The self-interested aspiration of the junior researchers leads to hard work and quality science, which in turn helps the Whitehead Institute. The motivation at the individual level is thus aligned with the Institutional mission. We have therefore a situation in which all are striving to produce the same result, yet the underlying value systems that motivate the 2 are distinctly different. This

situation, however, may not hold if there is a change in the aspirations in either party. This could arise, for example, if the Institute decides to be more application-oriented or commercialization-oriented, at the expense of producing knowledge for knowledge sake.

Collegiality and Collaborations. Whitehead Institute prides itself on its friendly and collaborative environment. Dr. Harold Varmus once commented that the environment at Whitehead Institute was one in which serious work is done in a playful, joyful, manner.[92] When asked why she had decided to join the Whitehead Institute, Dr. Susan Lindquist replied that she was attracted by the quality of its science, the entrepreneurial spirit, but most of all, the collegiality of its scientists.[93] Even the senior scientists at the Whitehead Institute are friendly and unassuming. This is a remarkable observation, for there is a common assumption that highly successful scientists are not usually modest or self-effacing. In the words of Peter Medawar, winner of the 1960 Nobel Prize in Medicine: "Humility is not a state of mind conducive to the advancement of learning."[94] The Whitehead Institute has demonstrated the limitation of this pronouncement.

6.4 **Underlying Assumptions:**

One can think of 'shared assumptions' as 'shared mental models' that the members of an organization use to structure their reality. Such assumptions do not reveal themselves easily, precisely because they are tacit and taken for granted. Many of the organizational assumptions are unproven, and often are beliefs that are accepted

[92] Dr. Harold Varmus's keynote address at the dedication ceremony of the new wing at the Whitehead Institute, 1996. Bahcall OG. Whitehead Institute dedicates new research wing. *The Tech.* 1996;116.
[93] Interview with Dr. Susan Lindquist, Whitehead Director, Feb 1, 2002.
[94] Medawar P. *The Art of the Soluble.* London: Methuen, 1967:110.

uncritically. The cultural paradigm of the Whitehead Institute is schematically represented in Figure 6.2. The different elements in this paradigm exist at various degrees of explicitness.

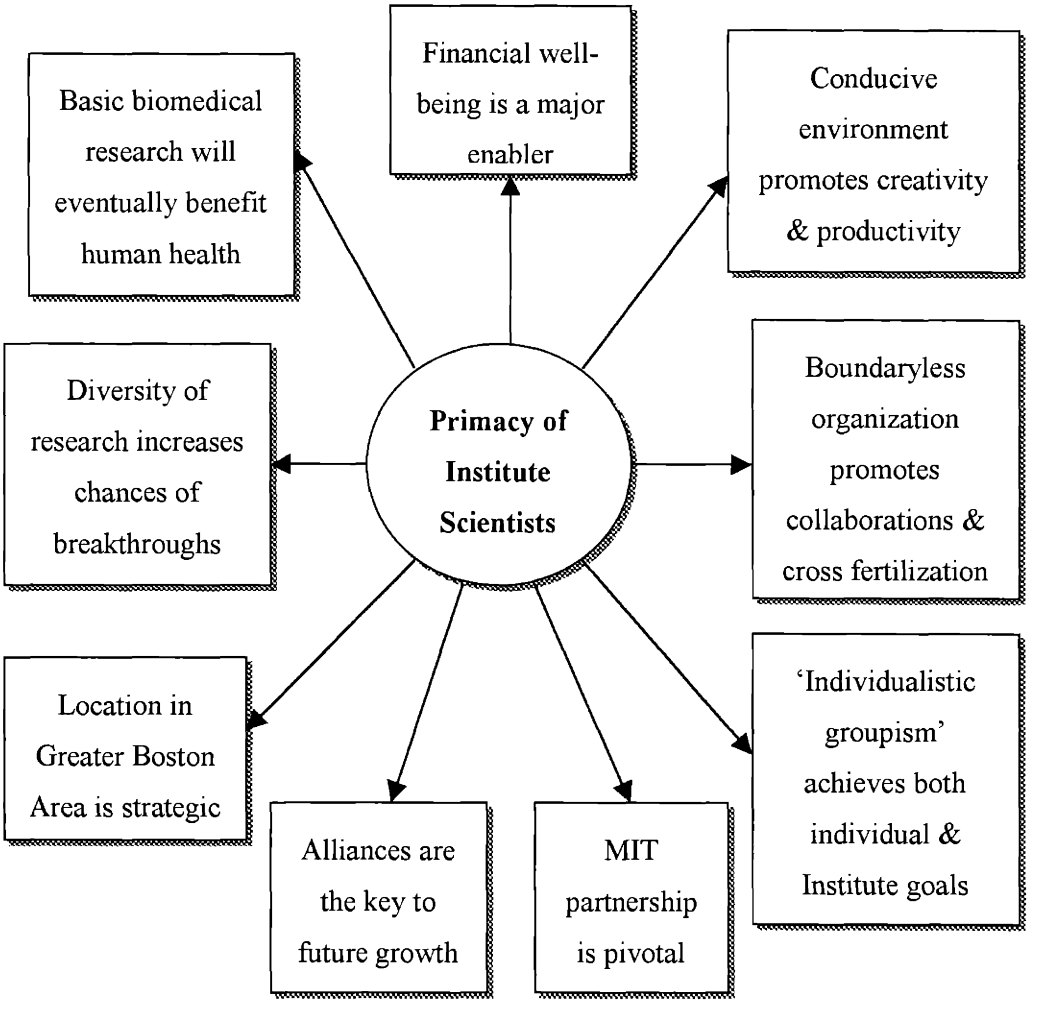


Figure 6.2 – Cultural paradigm (shared assumptions) of Whitehead Institute

- Primacy of Institute scientists. Whitehead Institute believes that brilliant scientists are the main ingredients that will assure its future success. The corollary is that the standing of the Institute will inevitably fall if the caliber of its scientists cannot be

maintained over time. Further, the Institute is convinced that its recruitment effort should target the young and talented scientists, rather than established stars, as noted earlier. In the recruitment process, there is a conscious attempt to avoid overlap in research areas, so that the existing scientists do not feel threatened. Interestingly, there is an unstated policy that postdoctoral scientists are not promoted to faculty positions. This is to avoid the situation whereby the postdoctoral scientists-turn-faculty members develop laboratories in the Institute that overlap significantly with the research areas of their former mentors.

- Conducive environment promotes creativity and productivity. This assumption is difficult to validate objectively, but is pervasive in the Institute.
- Boundaryless organization promotes collaborations and cross-fertilization of ideas. The Whitehead Institute tries to realize this assumption through architectural and organizational design.
- 'Individualistic groupism' achieves both individual and Institute goals. The pursuit of science, to many researchers, is an individualistic experience. Implicit in the process of discovery is the reality that one researcher must be first. Yet, despite the highly individualistic pursuit, there is nevertheless a high level of commitment to teamwork in Whitehead Institute. The scientists collaborate in research because joint efforts often bring about benefits to the individuals in the group, either as co-authors in publications, or in the form of accumulation of social capital that can be leveraged in the future.
- MIT partnership is pivotal to the success of the Whitehead Institute. This assumption is widely shared by the Whitehead Institute and MIT alike. There are now concerted

efforts to broaden the linkages between the Whitehead Institute and MIT beyond the Department of Biology, as noted earlier.

- Alliances are the key to future growth. The obviousness of this strategy arises from the realizations that Whitehead Institute is a relatively small institute, and that biology today is so sub-specialized that it is nearly impossible for the Institute to possess all the expertise. The assumption here is that synergistic alliances will overcome the size handicap and broaden diversity.
- Location in the Greater Boston Area confers a major advantage. This assumption has led the Whitehead Institute to its policy of expanding around the main campus at 9 Cambridge Center, rather than choosing larger and even cheaper real estate elsewhere. As noted earlier, this policy places significant constraint on future expansion of the Institution.
- Diversity of research increases the chances of breakthrough. Given the unpredictability of biomedical research, having a diverse research portfolio, if that can be achieved without undue costs, is an advantage. Diversity can be achieved in a number of ways, including: support of young talented scientists in pursuit of relatively unmapped research areas (such as the Whitehead Fellows Program); formation of alliances with academic or industrial partners with complementary expertise; direct technology transfer through formal agreements; indirect technology transfer through recruitment of scientists; and formation of collaborative relationships with overseas partners. The latter approach may expose the Institute to different research mindsets and methodologies, new sources of funding, different patient profile, and possibly different governmental and regulatory forces.

- Basic biomedical research will eventually benefit human health, but the relationship between the 2 is more of a chance event than an engineered one. The Whitehead Institute was founded with a broad assumption that the prudent approach towards basic research is to be broad-based and non-utilitarian. However, the opportunities and pressures from the health care-related industry and philanthropic fund-raising may force the Institute to take a more pragmatic stance, at least in rhetoric.

6.5 Chapter Summary

This chapter has described how the tacit assumptions of the Whitehead Institute influence its mission and philosophies, and how the shared values in turn materialize in the form of observable cultural artifacts. The central assumption of the Whitehead Institute is that its human capital is its most valuable asset – it is the primary engine that drives the Institute. The author shares this belief. Many of the Institute's designs and policies are predicated on this pivotal mental model.

The final chapter summarizes the critical success factors of the Whitehead Institute, and postulates how these various elements interact complementarily with one another.

Chapter 7

CONCLUSIONS – COMPLEMENTARITY AND FUTURE CHALLENGES

7.1 Complementarity and the Positive Reinforcing Loops

Chapters 3 through 6 have described some of the critical factors that have contributed to the success of the Whitehead Institute. It would be erroneous to presume that any of these factors on its own would be sufficient to assure success. Instead, a careful examination of these factors suggests that they are mutually interacting and reinforcing. The inter-dependence of these factors constitutes what can be described as a complementarity effect.[95]

Figure 7.1 depicts the complementary relationships between the key elements that are central to the success of the Whitehead Institute. Note the presence of a number of reinforcing or positive feedback loops in these relationships. Four salient ones will be discussed in turn. Pivotal to these loops is the primacy of the top-notch scientists.

[95] Barua A and Whinston AB. "Decision support for managing organizational design dynamics". *Decision Support Systems.* 1998;22:45-58.

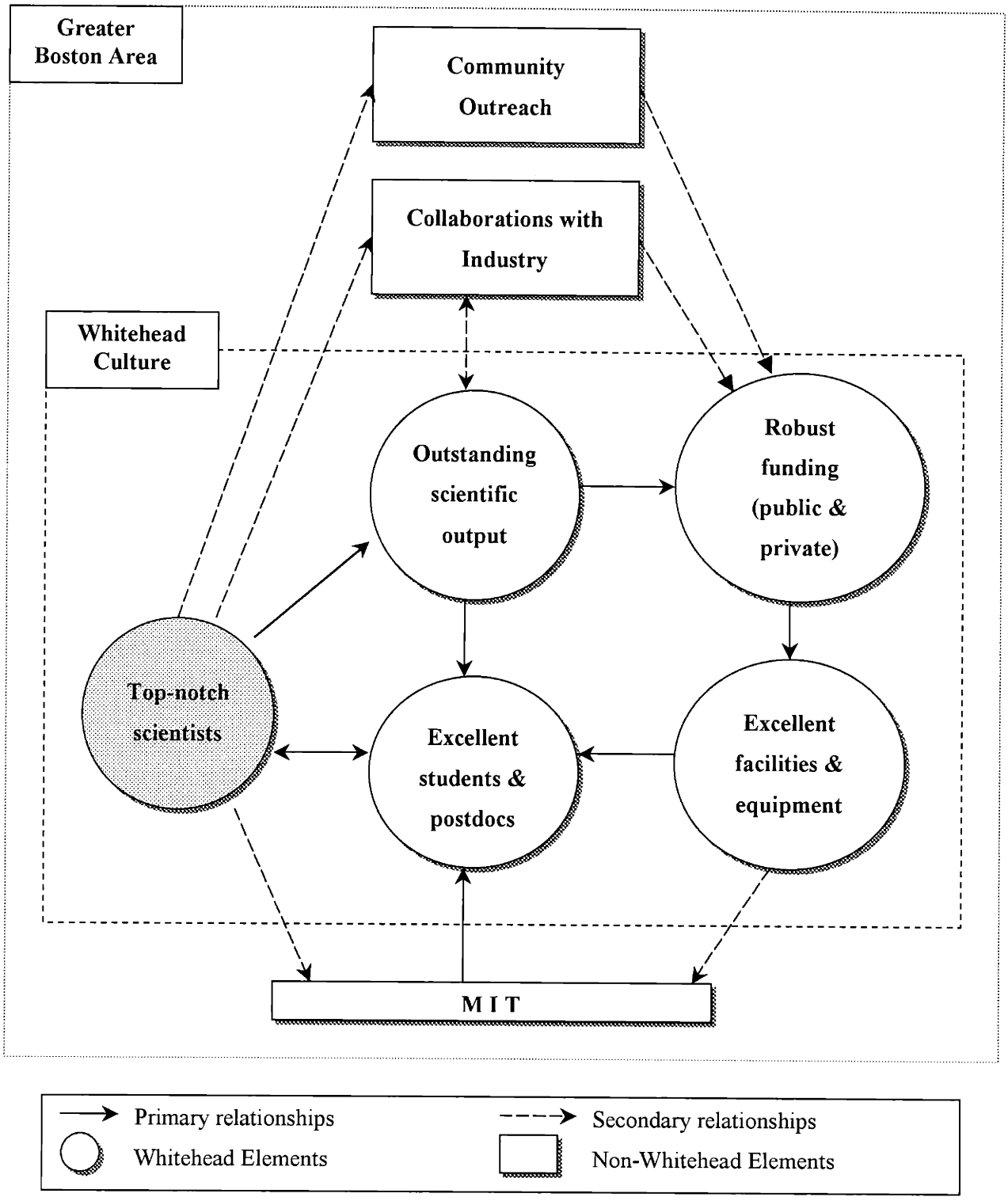


Figure 7.1 – Complementarity between Whitehead Institute's success factors

7.1.1 Loop 1: Scientists-Students Loop

The first loop is the 'top-notch scientists → outstanding scientific output → good students and postdoctoral scientists → top-notch scientists producing great science' loop. Top-notch faculty constitutes the center of gravity in the Whitehead Institute – their scientific output is what the Institute is known for. The quality science from the Whitehead laboratories, in turn, serves as a magnet to draw in talented graduate students and postdoctoral scientists. These young researchers represent the main workforce in the Whitehead laboratories. Collectively, top students also attract top scientists to the Institute, thereby setting up a reciprocal relationship. The scientists-output-students triad is one of the most dynamic and visible loops in this complementarity network.

How does MIT come into this picture? The graduate students provide the primary linkage between MIT and the Whitehead Institute. They are the 'glue' that cements the relationship between the 2 institutions. The critical role of the scientists-students relationship to the success of the Whitehead Institute explains why it is so important for the Whitehead Institute to be closely affiliated to a top research university like MIT. Indeed, an inability to attract top students would severely dampen the scientific vigor of the Whitehead Institute.

7.1.2 Loop 2: Role of Funding and Facilities

This loop is an expanded version of Loop 1, whereby the availability of robust funding as well as excellent facilities and equipment positively reinforces the scientists-output-students loop. The outstanding scientific output from the Whitehead laboratories

brings critical acclaim to the individual laboratories and the Institute as a whole. Such a reputation and track record, in turn, provide the principal investigators and the Institute the necessary scientific credential to attract more research funds, both federal and private donations.

A robust funding allows the Institute to purchase state-of-the-art scientific equipment, and to provide excellent ancillary support services at the Institute. The excellent physical and service infrastructure at the Whitehead Institute permits the scientists to concentrate on their primary scientific pursuit without undue delay or distraction. Such luxury in research helps attract graduate students and postdoctoral scientists as well. While Loop 1 represents the core strength of the Whitehead Institute, there is little doubt that Loop 2 provides the financial boost that further strengths the core.

7.1.3 Loop 3: Collaboration with the Industry

The mutual benefits to be gained through the relationship between the Whitehead Institute and the biopharmaceutical industry have been explored in Chapter 5. To summarize, biotechnology and pharmaceutical companies gain through collaborations with renowned scientists who have the inclination, freedom and technical expertise to interrogate basic scientific questions that may ultimately impact on the companies' long-term R&D strategies. Conversely, the Whitehead Institute benefits by having access to additional research funds and specialized research technologies and equipment, as well as opportunity to interact with corporate scientists who are generally more focused on creating products that have practical applications and market relevance. This 'industry loop' provides additional resources to energize Loops 1 and 2.

7.1.4 Loop 4: Community Outreach Programs, Public Image and Funding

By reaching out to the different communities in the Greater Boston Area, the Whitehead Institute consolidates its reputation as a good corporate citizen in this vibrant and thriving milieu. The Outreach Program focuses on education that is targeted at the various segments of the community, ranging from Supreme Court Judges to high school students to professional scientists within and outside the region. This is a strategic move, since a good reputation helps the Institute to secure a leadership position in the community, and which, in turn, helps in the private donation process.

A number of new research areas in biology are fraught with ethical minefields. Cloning, stem cell research, genetic screening, and genetic therapy are some examples. Whitehead Institute is involved in all these areas. In order to ensure that the scientific research of the Institute is accepted, and even embraced, by the community at large, it is important that such research is sufficiently understood by the general public and special interest groups. The Outreach Program is a good vehicle to achieve this goal. Therefore, in a number of ways, the Community Outreach Program plays an important 'enabler' role.

7.1.5 Interactions Between Different Loops

Figure 7.1 shows that a number of the loops are inter-dependent. The net result is synergy, where the value of the whole network is greater than the sum of the individual loops. For example, financial prowess enhances talent recruitment; successful collaborations with the industry inject additional funds to the Institute, which in turn helps strengthen the research capabilities. However, such mutually inter-dependent

networks also have their drawbacks. If one or several elements in the network were to breakdown, there is a danger of a precipitous collapse of the system. For instance, if the Whitehead Institute ceases to attract or retain top-notch scientists amongst its faculty, the quality of science would deteriorate over time; this would cause a fall in the intake of good students, which in turn adversely affects the scientific output of the laboratories. The Whitehead Institute has to constantly look out for specific challenges that may threaten the integrity of this reinforcing network. This is the subject of the next section.

7.2 Future Challenges and Transplantability of the Whitehead Model

While there is little dispute that the Whitehead Institute has done well since its founding 2 decades ago, it is pertinent to ask the following questions:

- Can the Whitehead Institute sustain its high level of performance going forward?
- Can the Whitehead model be replicated elsewhere, either in the US or internationally?

There has been some concern that the Whitehead Institute's leadership position in biomedical research can be maintained into the future. There are at least 2 sets of issues that have led to this caution. First, some observers have noted that there appears to be a nearly inevitable cyclical trend that afflicts most research institutes. A number of biomedical research institutes that once enjoyed preeminent positions in the middle of the last century have since weakened considerably. Examples would include the Rockefeller University in New York, and the Max Plank Institute in Germany. The reasons behind this cyclical trend are not totally clear. Plausible reasons include a diminishing talent pool, funding constraints, or leadership issues. Whether such ill-understood cyclical fate would befall the Whitehead Institute is largely conjectural.

The second set of concern involves challenges that are more specific to the Whitehead Institute, and will therefore receive greater attention in this section. A number of these challenges to the Whitehead Institute are individually discussed in the following sections.

As noted in Chapter 1, a number of biomedical research institutes are being established in the US and elsewhere. This thesis has identified some factors that underlie Whitehead's success. To what extent could other institutes, especially fledgling ones, utilize this insight to enhance their chances of success?

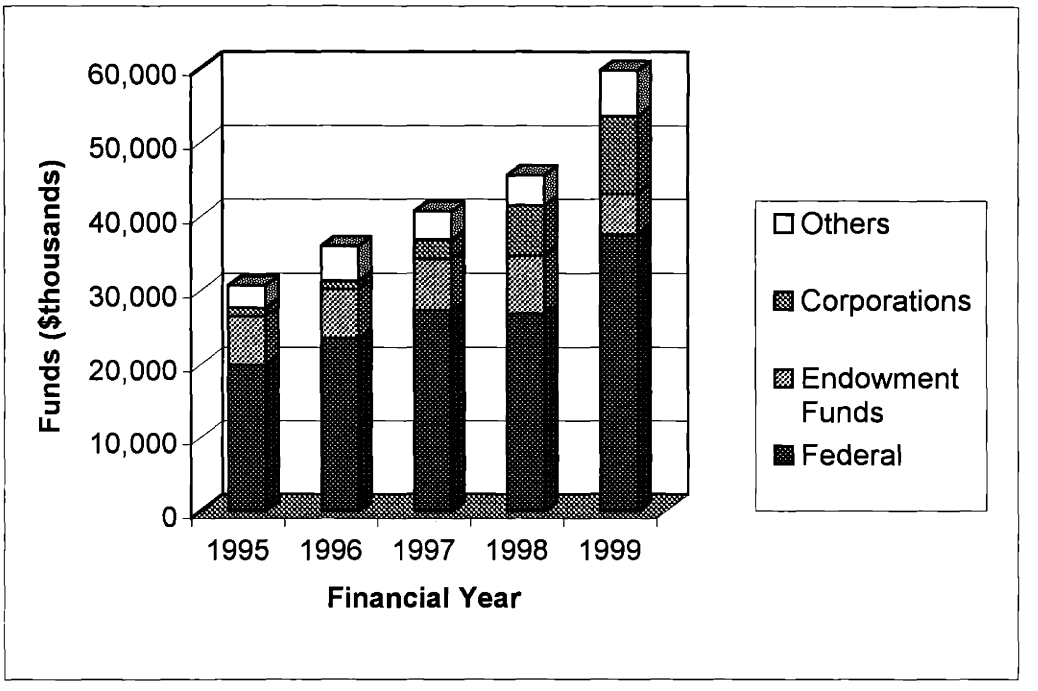
In the remainder of this chapter, specific features of the 'Whitehead model' will be revisited, and discussed in the context of the 2 questions raised at the beginning of this section.

7.2.1 Funding

- Future Challenges to Whitehead.

The Whitehead Institute has an annual operating budget of around $115 million; more than half of the fund comes from competitive research grants awarded by the federal government (Figure 7.2).[96] Philanthropic contributions to the total research budget are considerably smaller. The latest published financial summary (up to FY 1999) is shown in Appendix E.

[96] Whitehead Institute Funding Sources. www.wi.mit.edu/who/who_funding.html



Source: Whitehead Institute for Biomedical Research Annual Report, 1999/2000

Figure 7.2 – Sources of operating funds at the Whitehead Institute

Figure 7.2 shows that the Whitehead Institute, like most other biomedical research institutes, is heavily dependent on federal sources of funding, especially the NIH. In 1999, 62.8% of the funds came from federal sources; NIH alone contributed to 55.2% of the total operating funds. In the foreseeable future, federal sources of funds will continue to represent the lifeline to the Institute. In this regard, the Whitehead Institute should continue to aggressively compete for federal grants. Besides the regular individual grants, the Institute should also explore emerging research areas that can attract large federal research awards. The Genome Center has won large NIH grants for its work in HGP. It remains to be seen if the Whitehead Institute could repeat this feat a different research area.

NIH funding in the US has been increasing over the past decade, as noted earlier (Figure 1.1). Notably, 63% of the increase in total federal R&D spending in the US between FY 1996-2000 went to the NIH, from $12.1 billion (inflated-adjusted 2000 dollars) in FY 1996 to $17.1 billion in FY 2000.[97] This should augur well the research institutes. However, this federal largesse may not necessarily persist. Wide fluctuations of federal budget year-by-year cannot be ruled out. The National Science Foundation (NSF), for instance, was budgeted for an increase of nearly 20% in FY 2001. But the Republican-dominated House of Representatives agreed to just a 4% rise. The lesson to be learned here is that plurality of funding is prudent for any research institute, in order to hedge against sudden fluctuations in federal funding.

The biopharmaceutical industry is a potentially lucrative source of funding. In 1979, the federal government provided 69% of the biomedical R&D funding in the US, and the industry provided 29%. By 1994, the federal government provided 37%, and industry, 52%.[98] The challenge and opportunity for the Whitehead Institute is to find mutually interested research areas with biotechnology and pharmaceutical companies, and to seek co-funding from these companies. An important consideration for the Whitehead Institute in such collaborations is to stay on the scientific course that it has charted for itself, without being sidetracked as a result of such partnerships.

Philanthropy is a potential source of funding. In 1930, private, not-for-profit support of medical research equaled federal support. This has since dwindled. By 1940, private funding represented only 27% of the total; and by 1980, it was less than 4%, and

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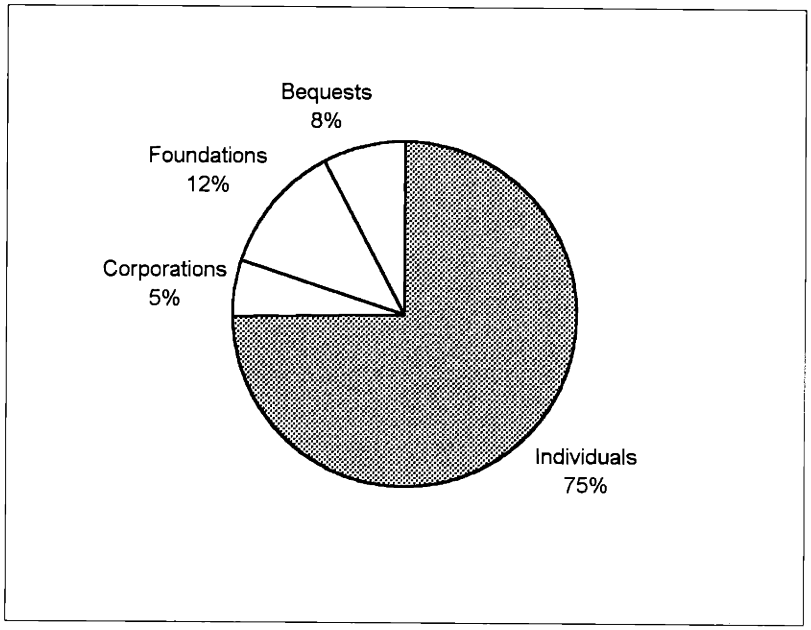
[97] Hart DM and Branscomb LM. Research, Innovation and Politics. *Nature* 2000;407:561-2.

[98] Purnell W. Choppin. "The View from the Howard Hughes Medical Institute." In: Barfield CE and Smith BLR, eds. *The Future of Biomedical Research.* Washington, DC: American Enterprise Institute & The Brookings Institution, 1997:16-20.

has remained around this level ever since.[99] Despite its small contribution today, philanthropic support of biomedical research plays a relevant role, mainly because it can be more speedily and flexibly disbursed than federal or state funds. The Whitehead Institute has efficiently used its relative financial freedom to help the researchers go into emerging areas quickly. Campaigning for philanthropic donation should be an ongoing effort.

It is pertinent to understand who the potential donors might be. By far, the most active source of donation in the US has been individuals, rather than corporations or foundations, as Figure 7.3 shows.



Source: American Association for Fund-Raising Counsel (AAFRC), Trust for Philanthropy, Giving USA, 2001. http://www.aafrc.org/

Figure 7.3 – Donors of Philanthropic Giving, 2000

[99] Purnell W. Choppin. "The View from the Howard Hughes Medical Institute." In: Barfield CE and Smith BLR, eds. *The Future of Biomedical Research.* Washington, DC: American Enterprise Institute & The Brookings Institution, 1997:16-20.

Unfortunately, the New England region is not particularly known for its philanthropic efforts. According to National Center for Charitable Statistics (NCCS), the State of Massachusetts was ranked 12th in terms of average charitable contribution in 1999. When adjusted for average income, Massachusetts' average charitable contribution was rated in the lowest state quartile.[100]

Although the Whitehead Institute is primarily engaged in basic science research, it is understandable that donations might be more forthcoming if the research could be linked to a foreseeable prospect of improving the human health. Notably, in 2000, only 9% of the recipients of philanthropic giving in the US were pursuing health or health-related endeavors.[101] It is conceivable that this slice of the pie may be increased further. Additionally, campaigning through specific disease activist groups, such as the AIDS lobbyists and breast cancer foundations, may be another feasible approach.

- Transplantability

Mr. Edwin Whitehead's donation to the Institute in the early '80s was the largest philanthropic contribution to biomedical research in the US at that time. It gave the Institute a good head start. To establish a new biomedical research institute in the US, it is unlikely that the funds will come from the government. Like the McGovern Institute for Brain Research at MIT, the establishment funds are more likely to come from philanthropic donations or university endowments. Unfortunately, large endowments such as the Whitehead or McGovern donations do not come by easily.[102] Outside the US,

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[100] http://nccs.urban.org/stgive99_p2.pdf

[101] American Association for Fund-Raising Counsel (AAFRC), Trust for Philanthropy, Giving USA, 2001. http://www.aafrc.org/

[102] Mr. and Mrs Patrick J. McGovern donated $350 million in 2000 to establish the McGovern Institute for Brain Research at MIT.

the situation may be rather different. For instance, in Singapore, the government is providing total funding to establish a number of new biomedical research institutes.[103] In other parts of the world where both philanthropic donations and government funding are not forthcoming, the ability to establish an internationally competitive biomedical research institute is significantly thwarted. This is particularly true in this era of modern biological research where heavy capital investment in sophisticated equipment has become the norm rather than the exception.

7.2.2 Scientific talent.

- Future Challenges to Whitehead

Given that the most pivotal element of the Whitehead Institute is its human capital, it is pertinent to ask whether the Whitehead Institute is successful in renewing its talent pool. For the purpose of this analysis, the current Whitehead faculty can be divided into 3 arbitrary generations, based on when they first joined the faculty; this is also an indirect indication of their relative seniority. The Founding Members are those who joined the Institute at its inception in 1982; the 'Second Generation Members' are those who joined the Institute between 1982 and 1990; and the 'Third Generation Members' are those who joined the Institute after 1990. On this basis, one can attempt to quantify the relative scientific output of the different generation of Whitehead scientists, so as to a get an approximate sense of their scientific productivities.

Using such an approach, one must of course be mindful that the 3 generations differ in seniority. Another pitfall in this method is that there are no perfect indicators of

[103] Cyranoski D. "Building a biopolis". *Nature* 2001; 412:370 – 371.

scientific output. The author recognizes that measuring the number of papers published *per se* does not reflect the actual contribution to science, since quality is not factored in. Nevertheless, for the purpose of this analysis, the number of publications is chosen as an imprecise surrogate measure of scientific production. With these caveats in mind, the relative output levels of the Whitehead faculty scientists in the year 2000 are shown in Table 7.1:

Generation	No. of scientists	% of total faculty size	No. of published papers	% of total contribution
First (Founding)	4	26.7%	47	36.4%
Second	6	40.0%	65	50.4%
Third	5	33.3%	17	13.2%

Source: ISI Web of Science

Table 7.1 – Publications from different generations of Whitehead scientists in 2000

Note that the founding cohort, comprising the 4 members, produced disproportionately more than what their cohort size would predict; this is a reflection of their rich research experience. Within the Second Generation cohort, Dr. Eric Lander alone produced 30 papers in 2000, representing almost half of the output from this cohort; this coincided with the maturation of the research at the Genome Center. The Third Generation scientists produced fewer papers than their more senior colleagues, reflecting their relatively young scientific careers. It is important to emphasize that the difference in the number of publications across the 3 generations is very much a direct reflection of their seniorities. The purpose of this snapshot view of published papers in the year 2000 is simply to provide a baseline, against which other time periods can be

compared. The resultant temporal trend does give one a sense of the scientific productivity over time.

Figure 7.2, for example, illustrates the number of published papers across the 3 generations in 1995. Of note is the finding that the Third Generation scientists more than doubled their cohort contribution when one compares the output in 1995 with that in 2000, presumably reflecting their growing research experience. If this trend persists, it augurs well for the Institute.

Generation	% of total contribution in 1995	% of total contribution in 2000
First (Founding)	46.0%	36.4%
Second	49.0%	50.4%
Third	5.0%	13.2%

Source: ISI Web of Science

Table 7.2 – Publications from different generations of scientists in 1995 and 2000

The structure of the Whitehead Institute is designed such that there is little overlap between the different Institute laboratories. This might create instability when principal investigators leave the Institute. When Dr. Peter Kim, former Whitehead Member and a well-known structural biologist, left the Institute to join the Merck Research Laboratory, there was an immediate weakening of the structural biology research in the Whitehead Institute. It would take several months or even longer to replace such expertise at the Institute. Thus, the flat structure of the Whitehead Institute exposes it to significant volatility in research core competencies whenever there is movement of key research personnel.

Whitehead Institute's location in the midst of a thriving biotechnology industry hub will always pose a threat that its scientists may leave to join a company. In major research areas, such as structural biology, genomics, developmental biology and cancer biology, it may be prudent for the Institute to allow some degree of research overlap. The Institute must also continue to attract talented young scientists to keep the pipeline robust and vibrant. Finally, the Institute's endowment may be leveraged to counteract any 'brain drain' to the industry or other academic research units.

- Transplantability

How difficult is it to build up sufficient human capital in a new research institute? Can the Whitehead's experience of recruiting 5 top scientists as founding members be readily repeated elsewhere? Why would a star scientist leave his or her current position to join a new research institute?

It is probably useful to first state the obvious: human capital is a mobile asset. Places that provide an internationally competitive research environment stand a good chance to attract star scientists. This is happening in the US and elsewhere. For example, in 2001, Singapore was able to attract Dr. Edison Liu, a well-known breast cancer researcher and former director of the US National Cancer Institute's (NCI) Division of Clinical Sciences, to Singapore to lead its nascent Genome Institute of Singapore. The decision for a star scientist to leave his or her present position to join another organization often involves a complex set of motivations and trade-offs. The motivations may involve: financial remuneration, career development opportunities, research autonomy, access to unique research equipment or technologies, and even personal considerations such as living environment and children's education. For Dr. Liu, the

opportunity to have a major impact on a nation's research was a large part of the attraction. He told *Nature Medicine*: "This is the first time that Asia is relatively free of imperialism, famine and genocide. Since the 1400s the world GDP shifted from East to West and now it's shifting back somewhat, so it's good to be part of this unusual time in history when Asia is reemerging."[104] Importantly, such foreign scientists sometimes transplant an entire research team to the hosting organizations or countries.

China and Taiwan are the other Asian countries that are actively recruiting star scientists to help build their respective national biomedical enterprises. They are particularly targeting overseas Chinese scientists, especially those in the US.

In order for a research organization, or even a nation, to succeed in such recruitment efforts, it is important to achieve a critical mass of quality scientists in the target location as quickly as possible. Perhaps contrary to popular beliefs, scientific research is very much a social process. Scientists work better when they are in an environment that is teeming with quality scientists and bright students, in addition to good physical facilities. In the present climate of multidisciplinary research, the need to network with other scientists is even more keenly felt. Recruitment of scientists therefore involves managing the entire research environment, both physical and social.

7.2.3 Affiliation to Top University and Location Factors

- Future Challenges to Whitehead

Whitehead Institute can leverage its affiliation with MIT even more. MIT is renowned for its science and engineering R&D capabilities. Presently, the Whitehead

[104] Birmingham K. "Singapore pushes biomedical research." *Nature Medicine* 2001;7:1169-1170.

Institute is collaborating mainly with MIT's Department of Biology, and to a lesser extent, the Department of Engineering. Given the evolution of modern biological research towards bioengineering, bioinformatics, and biophysics, MIT's broad array of expertise in engineering and the physical sciences presents a unique opportunity to the Whitehead Institute to form synergistic collaborations. Such relationships will give both the Whitehead Institute and MIT a leadership position in these emerging areas.

The existing Whitehead-MIT Biology relationship can serve as a useful model as the Institute forms new relationships with other MIT departments. The Whitehead Institute can also consider leading the formation of a multidisciplinary R&D consortium on the MIT campus that involves a number of different departments in MIT. Bioimaging, a promising research area, would be an ideal platform to explore such an idea, given that it involves biology, engineering, physics and informatics.

Another challenge that the Whitehead Institute faces, and one that will be more acutely felt in the near future, is space constraint. As noted earlier, Whitehead Institute's location in Cambridge, Massachusetts is a competitive advantage, from the point of view of its exposure to scientific talent, academic competition, financial capital, and biotechnology industry. The Institute has made a concerted effort not to displace itself from its current location. This presents a challenge to the Institute as it considers future expansion. The fact that the 'industrialized biology' of tomorrow is likely to require more physical space than conventional biology (including space with special features such as vibration-free rooms to house special bioimaging equipment) will impose an even greater physical space constraint on the growing Institute.

- Transplantability

The Whitehead Institute's location in relation to MIT and the Greater Boston Area is probably the most difficult feature to be replicated elsewhere. The creation of the thriving Greater Boston Area is as much by chance as by design. Few areas in the US have been able to recreate such an exciting and competitive environment. Outside the US, a number of countries are trying to reproduce such a competitive environment that will foster biomedical R&D and enterprises. An example of such an effort is Singapore's vision of the Biopolis, which will be ready for occupancy in 2003.[105] The Biopolis is designed as a multiplex of buildings that will house state-of-the-art biomedical laboratories, teaching facilities, offices, and incubator space for start-up companies. It is situated adjacent to a tertiary education belt that comprises the universities and polytechnics. All the major biomedical research institutes in the nation will be relocated to the Biopolis. In addition, it will be supported by other ancillary activities to create a 'live, work, learn, and play' environment. Whether such an engineered effort is able to recapitulate some of the exciting biomedical activities that one sees in the Greater Boston Area remains to be seen.

7.2.4 First Mover Advantage into Promising Research Areas

- Future Challenges to Whitehead

The ability of the Whitehead Institute to maintain its leadership position in biomedical research depends significantly on the ability of its faculty and administration to discern emerging trends in biomedical research, and to harness enough momentum and

[105] Cyranoski D. Building a biopolis. *Nature* 2001; 412:370 – 371.

resources to engage that area strategically and decisively. The success of the Genome Center illustrated the wisdom of such a strategy. Biomedical research is becoming more globalized and competitive. Besides the US, Europe and Asia are also marshalling national resources in an attempt to jump onto the biomedical bandwagon. In this environment, the Whitehead Institute must constantly scan the research landscape for emerging and promising trends, and map the global arena for potentially synergistic partnerships or competition.

The Whitehead scientists should fully leverage its diverse in-house scientific expertise to create new research fields and 'disruptive technologies'. Exploiting research diversity is an increasingly important strategy in the future. We are now witnessing the growing influence of physics, mathematics and engineering on biology.[106]

The Whitehead Institute is intensifying its multidisciplinary research effort. It recently approved a major project in bioimaging. The Institute realizes the growing importance of imaging in biological research. The project also capitalizes on the wealth of engineering and physical science expertise on the MIT campus, a strategic move that was discussed earlier. The process behind the establishment of the MIT/Whitehead Institute Bioimaging Center is similar to that of the Genome Center. Dr. Paul Matsudaira, a faculty member from the Whitehead Institute, first proposed the concept, and has convinced the Institute to pursue this area. He is now the founding director of this project. The Center will be located in a refurbished building close to the present Whitehead Institute, and international collaborations are being sought. If the field of bioimaging

[106] Editorial. "The changing face of biomedical research." *Nature Medicine* 2000;6:113.

develops fully in the near future, Whitehead Institute's early participation in this should confer a substantial competitive advantage.

- Transplantability

The ability of a biomedical research institute to rapidly and correctly enter a new biomedical research area is contingent on having the following elements: quality scientists who are at the cutting-edge of research, adequate financial support, an environment that encourages prudent risk-taking, and an enlightened leadership and administration. In addition, the proximity to regions where there are exciting R&D activities also helps the research institute to have a good feel of the evolving scientific trends. The US is probably the most productive country in biomedical R&D today. For research institutes outside the US, it behooves them to 'keep their ears close to the ground', so that they are current with new research ideas that are evolving in the leading centers. More challenging, however, is the will and ability to make the investment, seemingly risky, in order to move from a follower position to one of international leadership.

7.3 International Opportunities

There are significant assets in biomedical research in the international scene. The Whitehead Institute could consider exploiting these opportunities. Specifically, the Institute could consider establishing formal international partnerships. There are already a number of research niches in biology in which non-US countries have a growing presence and expertise. For example, the current restriction on the use of embryonic stem

cells for research in the US is not found in a number of other countries such as the United Kingdom, Israel, and Singapore. This situation presents a unique opportunity for collaboration at the individual and institutional level. In the case of stem cell research, the extent of the collaboration clearly depends on the precise restrictions that the US government will impose on this form of research; this is an evolving issue. Another research area in which there is much international expertise is the study of certain infectious diseases that are less commonly encountered in the US. Malaria, dengue fever, and tuberculosis are prime examples.

In theses strategic areas, the Whitehead Institute can gain substantially by forming collaborations that complement its own expertise, bypass policy hurdles, or overcome access deficiencies that exist in the US. Another reason for collaborating with international partners is the availability of new sources of funding. A number of countries, such as Singapore, Taiwan, Italy, and Ireland, are mobilizing significant national resources to build up their respective biomedical infrastructures, as pointed out earlier. What these countries need are human capital and certain technological platforms. What they do have, in general, are significant amount of funds to support their research. The Whitehead Institute can look to international partnerships in which the Whitehead Institute offers knowledge and technologies while the overseas partners contribute financial resources. A win-win outcome is conceivable.

7.4 Chapter Summary

The same factors that make the Whitehead Institute successful are facing significant challenges in the future. Research expenditure is rapidly rising. The founding members of the Whitehead faculty are into their late '50s. A number of new research areas in biology require expertise that is beyond what the Whitehead Institute and the MIT Department of Biology can offer. The ability to maintain a leadership position in biomedical research calls for significant risk-taking and heavy investment in emerging areas of research. These challenges are also new opportunities to the Whitehead Institute. The Institute is showing signs that it is capitalizing on these opportunities. The aggressive recruitment of bright young talents as Whitehead Fellows, the initiative to invest heavily in bioimaging, and the increasing collaborations with non-Biology departments of MIT are good signs. The Whitehead Institute may not have fully exploited international opportunities for research collaborations and joint funding. This presents unique opportunities that the US may not be able to offer to the same extent. Overall, the future of the Whitehead Institute is bright, notwithstanding a number of significant challenges ahead.

EPILOGUE

"I believe we have achieved an institution which is endowed with absolute dedication to excellence; is novel in its relationship to a university, and is unparalleled in its facilities. Its choice of program is perfectly timed to take advantage of all that is new in biology."

Mr. Edwin Whitehead, 1984[107]

The late Edwin C. Whitehead, entrepreneur, philanthropist, and founder of the Whitehead Institute, said these words in the year that the Whitehead Institute moved into its present building. Even today, this description of the Whitehead Institute still holds true. The Institute had a difficult birth. Mr. Edwin Whitehead spent eleven futile years, from 1971 to 1982, trying to find a surrogate mother for his brainchild. Under the expert care and visionary direction of Mr. Edwin Whitehead and Dr. David Baltimore, the Institute was finally delivered in 1982, amidst considerable skepticism of its viability or its future proclivities.

During its childhood between 1982 and 1990, under the Directorship of Dr. Baltimore, the Institute grew up spectacularly, leaving an indelible impression in the world of biological research. In the 'teenage' phase, between 1992 and 2002, the Institute grew from strength to strength under the directorship of Dr. Gerald Fink. It embarked on adventurous but promising projects, and courting alliances from the academia and industry within and outside the country. The Institute is now mature and it is looking far

[107] Mr. Edwin Whitehead in: *Whitehead Institute Director's Annual Report* 1983/4.

down the road to see what might lie ahead. At the same time, it finds itself poised at the threshold of an unknown, but extremely promising journey of biological discoveries and biomedical interventions.

What does the future hold for the Institute? What path should the Institute take? What philosophy and culture should the Institute embrace as it confronts the rapidly changing, and increasingly intermingling, academic and commercial worlds? In the face of rapid automation and invasion by almost all branches of science, what identity should this premiere biomedical research institute hold? These, and many other questions confront the Institute and its new Director, Dr. Susan Lindquist. The challenge to maintain the leadership position of the Whitehead Institute is a major one – one that is fraught with known challenges, such as the increasing complexity of science and the scarcity of top-notch talent, as well as unknown pitfalls, such as capricious changes in federal funding and unexpected societal backlash directed at the research its scientists pursue. Despite these challenges, however, Whitehead Institute can find solace that the philosophy on which it was founded and the team of renowned scientists upon whose shoulders the Institute has rested for the past twenty years, will help ensure that the Institute makes the wisest decisions in its next exciting voyage.

Appendix A

Human Genome Project & Whitehead Institute Center for Genome Research

1. The Human Genome

- The human genome (the full set of genes in each human cell) comprises approximately 3 billion DNA base pairs that are functionally organized into approximately 30,000 genes. The 4 universal types of DNA are denoted by the letters A, T, C, and G (representing adenosine, thymidine, cytosine, and guanine).
- The human genome sequence is likened to the periodic table. Knowledge of these sequences is already ushering in a new era of biology, which allows scientists and doctors to understand evolution, human variations, and human diseases in greater detail. More importantly, this knowledge may offer newer methods of diagnostics and therapies.
- An important by-product of human sequencing effort is the birth of newer generations of automations and robotics, as well as the birth of a new and important field – bioinformatics, which involves the study of biological processes and phenomena through the use of mathematical algorithms and high-capacity computing.

2. The Human Genome Project (HGP)

- The idea of fully sequencing the human genome was first mooted in the mid-'80s, and received a mixed review initially regarding its technical feasibility, methodology, and intellectual appeal. After much debate in the scientific community, the Project was finally launched. In the '90s, the advent of newer automation methods, coupled with the intense competition offered by Celera Inc, accelerated the pace of the HGP, culminating in the completion of the first draft of the human genome sequences ahead of schedule.
- The international Human Genome Sequencing Consortium includes scientists at 20 institutions located in France, Germany, Japan, China, Great Britain and the US. The full list of participating centers is shown in the table below; the top 5 centers contributed 82% of the sequences at the time of the first draft.

	Institution	City / State / Country
1.	Whitehead Institute for Biomedical Research, Center for Genome Research	Cambridge, MA, USA
2.	The Sanger Centre, The Wellcome Trust Genome Campus	Hinxton, Cambridgeshire, United Kingdom
3.	Washington University Genome Sequencing Center	St. Louis, MO, USA
4.	US DOE Joint Genome Institute	Walnut Creek, CA, USA
5.	Baylor College of Medicine Human Genome Sequencing Center, Department of Molecular and Human Genetics	Houston, TX, USA
6.	RIKEN Genomic Sciences Center	Yokohama-city, Japan
7.	Genoscope and CNRS UMR-8030	Evry Cedex, France
8.	GTC Sequencing Center, Genome Therapeutics Corporation	Waltham, MA, USA
9.	Department of Genome Analysis, Institute of Molecular Biotechnology	Jena, Germany
10.	Beijing Genomics Institute/Human Genome Center, Institute of Genetics, Chinese Academy of Sciences	Beijing, China

11.	Multimegabase Sequencing Center; The Institute for Systems Biology	Seattle, WA
12.	Stanford Genome Technology Center	Stanford, CA, USA
13.	Stanford Human Genome Center and Department of Genetics, Stanford University School of Medicine	Stanford, CA, USA
14.	University Washington Genome Center	Seattle, WA, USA
15.	Department of Molecular Biology, Keio University School of Medicine	Tokyo, Japan
16.	University of Texas Southwestern Medical Center at Dallas	Dallas, TX, USA
17.	University of Oklahoma's Advanced Center for Genome Technology, Dept. of Chemistry and Biochemistry, University of Oklahoma	Norman, OK, USA
18.	Max Planck Institute for Molecular Genetics, Berlin	Germany, USA
19.	Cold Spring Harbor Laboratory, Lita Annenberg Hazen Genome Center	Cold Spring Harbor, NY, USA
20.	GBF - German Research Centre for Biotechnology	Braunschweig, Germany

Table - Institutions of International Human Genome Sequencing Consortium

- The project is funded by grants from government agencies and public charities in the various countries. These include the National Human Genome Research Institute at NIH, the Wellcome Trust in the United Kingdom, and the US Department of Energy, as well as agencies in Japan, France, Germany, and China.
- The Human Genome Project has a budget of $3 billion. However, this figure refers to the total projected funding over a 15-year period (1990-2005) for a wide range of scientific activities related to genomics. The total cost for Phase One ("working draft") was $300 million worldwide, half of which came from the NIH in US.

- On June 26 2000, the Consortium announced that it had collected roughly 90% of the letters of the text for the "Book of Life." This was widely regarded as a major breakthrough in modern biological endeavors, as well as a triumph in international collaboration. The draft was published in *Nature* in February 2001.[108]
- There are small sequence gaps still remaining to be filled, but scientists are already getting a good sense of what the genome landscape looks like and the surprising stories it has to tell.
- Though a definitive count of human genes must await further experimental and computational analysis, scientists now estimate that humans have some 30,000-35,000 genes in their genomes. This new estimate indicates that humans have only about twice as many genes as the worm or the fly.
- In a companion volume to the 'Book of Life', scientists have also created a catalogue of 1.4 million single-letter differences, or single nucleotide polymorphisms (SNPs), and specified their exact location in the human genome. This SNP map, the word's largest publicly available catalogue of SNPs, promises to revolutionize disease mapping and the tracing of human history, as well as providing the basis for the design of personalized medicine.
- The sequence information from the Consortium has been immediately and freely released to the world, with no restrictions on its use or redistribution. The information is scanned daily by scientists in academia and industry, as well as by

[108] International Human Genome Sequencing Consortium. Lander ES, Patrinos A, Morgan JJ. *Nature* 2001;409:860-921

commercial database companies, providing key information services to biotechnologists.

- The Consortium's ultimate goal is to produce a completely 'finished' sequence– with no gaps and 99.99 percent accuracy. Although the near-finished version is adequate for most biomedical research, the HGP has made a commitment to filling all gaps and resolving all ambiguities in the sequence by 2003.
- Other organisms that have been sequenced, or are being sequenced, include: *Haemophilus influenzae* (bacterium), *Saccharomyces cerevisiae* (yeast), *Caenorhabditis elegans* (round worm), *Arabidopsis thaliana* (mustard plant), *Drosophilia melanogaster* (fruit fly), and *Mus musculus* (mouse). Comparing genomes across species will provide researchers key tools for understanding the essential elements that evolution has designated as important to survival. Comparative genomics will also offer scientists insights into important regions in the sequence that perform regulatory functions.

3. Contribution of Whitehead Institute Center for Genome Research (WICGR) to Genomics Research[109]

Genetic maps:

- Produced the first genetic map of the human chromosomes, in collaboration with researchers at Collaborative Research Inc.
- Produced the first large-scale collection of human single-nucleotide polymorphisms (SNPs)

[109] *Whitehead Institute's Discovery Magazine. July 2000:7.*

- Produced the first broadly-applicable genetic map of the mouse genome
- Produced the first SNP map of the mouse genome
- Produced the first genetic map of the rat genome

Physical maps and genome sequences:

- Produced the first physical map of the human genome
- Produced the first dense gene map of the human genome
- Produced the first physical map of the mouse genome
- Produced 1.1 billion bases of human genome sequence for the 'working draft'
- Developed ultra-high throughput automated system for DNA purification and sequencing.

4. Future of WICGR

The Genome Center has succeeded beyond expectations. As the Genome Center ponders over its future, it finds itself confronting the inevitable question of whether it is best off being spun out as a separate Institute.[110] There are at least 3 main reasons in support of this strategy:

a) The Genome Center is felt by some to be too large to remain as an element within the Institute. The Genome Center, as noted, employs more than 300 employees, just under half of the total number of Whitehead Institute employees. As one staff member at Whitehead Institute noted: "We don't know everyone anymore – there

[110] Szechenyi CA. "Whitehead Genome Center shopping for new organizational model; split from Institute not implausible." *GenomeWeb*, Jan 4, 2002. www.genomeweb.com

are just so many people around here these days."[111] Others have begun to note that the atmosphere in the Institute is not as cozy as it used to be in the past.

b) The Genome Center's approach to biology is quite different from the more traditional, experimental approaches that typify the rest of the Whitehead Institute. The Genome Center is heavily dependent on high throughput, automation, and high-end computing. In such pursuits, a large size is an advantage. In contrast, the 9 Cambridge Center portion of the Whitehead Institute relies more on a small-team approach to study a narrowly defined biological question and to do so in great depth. Here, an intimate, fluid team of scientists will achieve its objective better than a stable, large organization. The underlying organizational framework of the Genome Center is inspired by lessons learned from industrial organization. In this regard, the workflow and philosophy of the Genome Center is quite different from the rest of the Whitehead Institute. While this difference between machine-intensive *versus* human labor-intensive approaches does not *per se* warrant the separation of the Genome Center from the rest of the Institute, there is continued discussion about the Genome Center going independent.

c) The Genome Center is a rapidly growing subunit within a relatively small research institute. Diversion of resources and distraction are almost inevitable. As the Genome Center continues to expand, it is imposing an increasing strain on the space and the supporting infrastructure of the Whitehead Institute. In fact, the Genome Center is already situated several hundred yards from the main

[111] Interview with Mr. Gus Cervini, Whitehead Project Manager, Mar 12, 2002

Whitehead building due to its growing space requirement. The Genome Center has its own administrative, technical and other ancillary support. Whitehead Institute is increasingly feeling the strain of holding the mammoth Center under its wings.

On the other hand, the Genome Center has generated considerable public attention to the Center and the Institute as a whole. Insofar as philanthropic donation depends on good publicity, having the high-profile Genome Center in the same organizational is a distinct advantage. In addition, the Genome Center has also attracted much federal funding, collaboration, and goodwill for both the Genome Center and the Whitehead Institute.

Another potential downside of separating the Genome Center from the Institute lies in the setting of precedence for other growing units in the Institute. Whether such precedence is desirable or not depends on the prevailing philosophy of the organization.

Whitehead Institute is cognizant of the belief that WICGR's efforts in 'industrializing biology', through automation and high-throughput system management, may become increasingly useful to the rest of the Whitehead Institute in the future. This is understandable, given that biology of tomorrow will become increasingly more informational in nature.

In the final analysis, the likelihood of the Genome Center separating from the Whitehead Institute is high. Both parties will remain truer to their respective missions if they are separated organizationally but remain tightly linked through formal affiliations, historical roots, personal ties, and physical proximity. This resembles closely the way in which MIT and the Whitehead Institute have co-existed with each other over the years.

Appendix B

Whitehead Laboratories By Subjects

Subject	Expert
Agrobiology	Fink
AIDS	Young
Angiognesis	Weinberg
Antibiotic resistance	Fink
Bioengineering	Matsudaira
Bioinformatics	Daly, Fraenkel, Ideker
Biomaterials	Lindquist
BioMEMS chips	Matsudaira
Biotechnology	Lodish
Brain	Chess, Sive
Brain and spinal cord development	Sive
Cancer	Daley, Fraenkel, Lander, Jaenisch, Stockwell, Weinberg
Cancer genetics	Weinberg
Catalytic RNA	Bartel
Cell biology	Lodish
Cell cycle	Orr-Weaver, Weinberg
Cell cycle clock	Weinberg
Cell death	Hacohen, Sabatini
Cell division	Orr-Weaver
Cell signalling	Sabatini, Lodish
Cell-cell signaling	Rebay
Chaperone proteins	Lindquist
Chemical genetics	Stockwell
Cloning	Jaenisch
Combinatorial chemsitry	Stockwell
Computional biology	Daly, Ideker
Cytoskeleton	Matsudaira
Data mining	Lander, Young, Jaenisch
Development	Orr-Weaver, Rebay, Sive
Diabetes	Lodish
DNA arrays	Ideker, Young
DNA methylation	Jaenisch
DNA rearrangement	Chess
DNA replication	Orr-weaver
Drosophila	Rebay
Drosophila genetics	Orr-Weaver
Expression cloning	Sabatini
Eye development	Rebay

Source: http://www.wi.mit.edu/far/far_labsub.html

Frog & Zebrafish genetics	Sive
Fungal infections	Fink
Gene expression	Ideker, Young
Gene mapping	Lander
Genome project	Lander
Genomics	Daley, Daly, Ideker, Page, Stockwell, Young
HIV	Young
Immune system	Hacohen
Infection	Hacohen
Infectious diseases	Fink, Hacohen, Young
Interdisciplinary science	Lindquist
Leukemia	Daley
Male infertility	Page
Molecular evolution	Bartel
MRI	Jasanoff, Matsudaira
Nanotechnology	Lindquist
Neural networks	Jasanoff
Neurobiology	Chess, Sive
Origin of life	Bartel
Plant genetics	Fink
Prions	Lindquist
Protein chemistry	Fraenkel
Protein folding	Lindquist
Rapamycin	Sabatini
Receptors	Lodish
Ribozymes	Bartel
RNA	Bartel
Sensory system	Chess
Sex chromosome evolution	Page
Single neuron imaging	Jasanoff
Small molecule screening	Stockwell
Smell	Chess
SNPs	Lander
Statistical genetics	Daly
Stem cells	Daley, Lodisch, Jaenisch
Structural biology	Fraenkel
Telomerase	Weinberg
Tolerance	Hacohen
Transgenic science	Jaenisch
Transporters	Lodish
Tuberculosis	Young
Vaccine development	Young
Variation	Lander
Vision	Jasanoff, Rebay
Visual biology	Ideker, Matsudaira
X-inactivation	Jaenisch
Y chromosomes	Page
Yeast genetics	Fink

Appendix C

Whitehead Institute's Community Outreach Programs[112]

d) Whitehead Symposium – a 3-day seminar on a major theme selected for its timeliness and broad scientific appeal. In 2000, for example, it organized a symposium entitled: 'Genes and Society: Impact of New Technologies on Law, Medicine, and Policy'. This symposium covered a wide range of topics in genomics and genetics and featured renowned scientists from the academia and the industry.

e) Partnership for Science Education – programs tailored for high school teachers and students.

f) Whitehead Task Force on Genetics and Public Policy – a forum for encouraging broad public discussion about the impact of new genetic technologies on society. The Task Force was established in 1992 and comprises a multidisciplinary membership. It has formed collaboration with the American Society of Law, Medicine and Ethics (ASLME), Boston's Museum of Science, the Federal Judiciary Center, the Massachusetts Medical Society, the Boston Citizens Seminars, and the New York Academy of Sciences. In 1998, in collaboration with ASLME, the Task Force organized the first Whitehead Policy Symposium, 'The Human Genome Project: Science, Law, and Social Change in the 21st Century'. Two other symposia have since been held.

[112] Whitehead Institute website: www.wi.mit.edu/who/who_community.html

g) Whitehead Press Seminar – an annual event to update science and medical reporters on medical or public health topics.

h) Museum of Science Lecture Series – a collaboration with the museum to present leading-edge science to the Boston community.

i) Biology Week – a newsletter that provides calendar listings for meetings and seminars throughout Boston's extensive research community.

Appendix D

Whitehead Institute's Relationships with the Biotechnology Industry

The Whitehead Institute forms the following types of relationship with the industry:

i) Exclusive and non-exclusive licensing agreements. For example, in the year 2000, Genset SA, a genomics company headquartered in France, received an exclusive license to Whitehead's issued US patent entitled 'DNA Encoding a Novel Serum Protein Produced Exclusively in Adipocytes'. The collaboration is established to evaluate the therapeutic potential of Acrp30 gene for obesity and Type II diabetes through a combination of functional cloning technologies developed in Dr. Harvey Lodish's laboratory in the Whitehead Institute and the outstanding genomic resources in Genset. In 2001, Microbia Inc., a Cambridge-based company founded by Dr. Fink's postdoctoral scientists, licensed from the Whitehead Institute the 'Biofilm' technology that is believed to help find ways to slow down or prevent fungal biofilm formation. Dr. Fink sits on the Scientific Advisory Board of Microbia.

ii) Research collaborations. Whitehead Institute has formed a number of research partnerships with biotechnology companies. Biotechnology companies often have a fairly narrow range of research directions that are geared towards the identification of molecules that may be developed into drugs or diagnostic tools. In this sense, they are fairly 'downstream'. They benefit from academic collaborations through an expansion of the scope of their research. Conversely, Whitehead Institute benefits through funding

support and sometimes access to certain equipment or proprietary reagents or methodologies. Additionally, both parties benefit through intellectual exchange on their common interests through different perspectives. In 1997, Whitehead Institute forged a well-publicized strategic alliance with Bristol-Myers Squibb, Affymetrix, and Millennium Pharmaceuticals for the purpose of funding a 5-year research program in functional genomics. The companies will provide funds of about $8 million per year for 5 years and provide Whitehead Genome Center with access to certain Affymetrix and Millennium technologies. Whitehead participants in the program retain the rights to publish their research results promptly. The last arrangement is a critical element in any academic-industry relationship, in that the participation of private partners should not in any way jeopardize the creation and dissemination of scientific knowledge.

At the level of the individual scientists, a number of different relationships have been formed with the industry. More commonly, the scientists (usually the senior ones) serve as consultants to the companies, or collaborate with the companies on research projects. Less commonly, Whitehead Faculty also found companies, using technology platforms that originated from their own research. Dr. Richard Young sits on the Board of StressGen which is developing Dr. Young's intellectual property licensed to StressGen by the Whitehead Institute. Dr. Harvey Lodish is a founder of DYAX, which is not based on Whitehead intellectual property. Dr. Eric Lander was a founder of Millennium, which was not founded on Whitehead intellectual property, and sits on both its Board of Directors and its Scientific Advisory Board.

Appendix E

Financial Summary of the Whitehead Institute

Sources and Uses of Operating Funds

($ thousands)	FY 95	FY 96	FY 97	FY 98	FY 99
SOURCES					
Federal Government					
National Institute of Health	19,205	22,506	25,656	25,337	33,008
National Science Foundation	652	575	576	570	918
Other Fedaral Agencies		420	1,007	878	3,629
Subtotal Federal	19,857	23,501	27,239	26,785	37,555
Corporations	1,139	1,182	2,590	6,824	10,519
Endowment Funds Applied	5,319	6,619	7,023	7,873	5,470
Other Sources	3,006	4,653	3,852	4,073	6,226
TOTAL SOURCES	29,321	35,955	40,704	45,555	59,770
USES					
Research & Education	18,058	22,011	25,543	27,958	39,322
Admin & Research Support	5,978	6,555	7,211	8,423	10,726
Facilities Operations	4,011	4,738	5,357	5,929	5,491
Allocation to Plant Renewal	1,805	2,011	2,548	2,865	3,959
TOTAL USES	29,852	35,315	40,659	45,175	59,498

Net Assets

($ thousands)	FY 95	FY 96	FY 97	FY 98	FY 99
Current Fund Net Assets	(1,337)	1,892	124	54	193
Endowment Fund Net Assets	201,212	229,501	267,127	302,857	332,543
Plant Renewal Fund Net Assets	10,360	14,486	19,719	21,614	25,000
Net Investment in Plant					
Physical Plant Assets*	47,808	56,452	66,334	70,856	76,750
Indebtedness	(19,700)	(29,440)	(40,318)	(44,357)	(46,182)
Net Investment in Plant	28,108	27,012	26,016	26,499	30,568
TOTAL NET ASSETS	238,343	272,891	312,986	351,024	388,304

* *Physical plant assets are reported net of depreciation*

Source: Whitehead Institute for Biomedical Research Annual Report, 1999/2000

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