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Amoeba Innovation: The Alternative to Ventures

Introduction

In view of the problems facing independent ventures in Japan, might not the best hope for Japanese industry to remain at the forefront of innovation rest with its large, established companies, or else spin-offs from such companies? In contrast to the USA, where new companies often pioneer successive generations of technologies and compete successfully with large incumbents, in Japan large established companies often remain dominant in their industries even when technologies evolve substantially. This cross-national difference has been documented in the case of personal computers, integrated circuits, photolithography, hard disk drives, and other technologies.[1] At least until recently, the scarcity of independent high technology ventures has implied that Japan has no choice but to rely on its established companies for innovation in new fields of technology.

There are many examples of established newcomers succeeding spectacularly when they moved into new fields related to areas in which they already had expertise. Examples include Toyota's move from weaving machines into automobiles and Honda's from motorcycles into automobiles. NEC built on its expertise in computing and image recognition to develop an automated fingerprint identification system that became the choice of police departments in both Japan and the USA.[2] Sharp developed an early LCD calculator which was a commercial failure, but then went on to make breakthroughs in large active matrix LCD displays and became the world's largest manufacturer of LCDs. It incorporated LCD technology into its core television manufacturing business to become the leading manufacturer of large LCD screen televisions.[3] Canon's expertise in photo-optics helped it to become a leading manufacturer of photocopiers and second generation mask aligners and steppers for manufacturing IC chips.[4]

This process of successful technical diversification has been described by others.[5] It is beyond the scope of this chapter even to summarize the possible reasons for the historical success of Japanese companies relative to established

US counterparts except to mention the following advantages attributed to Japanese companies: Among the advantages over which there seems to be little debate are close communication with customers, close communication within work units and resulting close attention to detail and quality, and a high level of tacit knowledge shared by company employees as a result of lifetime employment and frequent rotations within the company.[6] Reasons that have been debated, or that may have been applicable only when Japanese companies were in a catch-up phase, include: controlled competition mediated either directly by the government or large government controlled corporations such as NTT,[7] a policy of weak protection for IP that encouraged sharing of new technologies especially those originating abroad, a close follower strategy involving rapidly refining or improving technologies that others had pioneered,[8] access to long-term funding from main banks, and a de-emphasis on vertical integration as a means of corporate management and reliance instead on alliances between semi-independent companies.

This latter reason refers not only to the system of manufacturing keiretsu, under which a number of companies are linked to a large manufacturing company. It also refers to diversification by forming spin-offs that the parent companies support by various means and over which the parents maintain partial ownership and control.

Hereinafter, I refer to these as *tethered spin-offs*. I refer to established companies that have moved into new field of technologies that are significantly different from their current core businesses as *established newcomers*.

Compared to independent venture companies, established newcomers and tethered spin-offs often have greater access to complementary assets such as skilled researchers and managers, financing, manufacturing facilities and networks of suppliers and customers. Established companies may also have greater access to complementary technologies, including in-house expertise[9] and technologies of other companies that have been obtained as a result of in-licensing, collaborative research, or other means.[10] In addition, established companies do not face the appropriability problems that small independent ventures often face. If intellectual property rights or first-to-market advantages[11] are weak, innovative ventures run the risk that their hard won technical developments will be quickly copied by rivals. By providing complementary assets, a large company can provide innovators the resources they need to develop new technologies shielded from the awareness of rivals. They can also provide manufacturing facilities and distribution and customer networks that help to maintain a first-to-market advantage.[12] In view of the difficulties Japanese ventures still face in recruiting skilled researchers and managers and in establishing networks of customers and collaborators, and considering also the access of the large, diversified, high-technology Japanese manufacturers to a range of complementary technologies, it might seem natural to expect that established companies will remain the engines of innovation in most new fields of technology in Japan.

Yet at least in the case of biomedical technologies,[13] established newcomers and tethered spin-offs generally are not particularly successful. The case of nonbiomedical technologies is less clear. Nevertheless there is also evidence that, when established companies enter nonbiomedical fields that are far from their core businesses their innovative competitiveness also diminishes.

PART I: ESTABLISHED NEWCOMERS

Established Newcomers in Biomedicine

A Tale of Two Breweries

Kirin and *Suntory* are two of Japan's most respected makers of alcoholic beverages. Kirin was incorporated in 1907, Suntory in 1921. With the establishment of the Suntory Institute for Biomedical Research in 1979 and Kirin's Pharmaceutical Division in 1982, both companies entered pharmaceutical R&D just when the potential of biotechnology was beginning to be apparent and revenues from the sale of alcohol and other beverages were flat. These were not steps into completely alien territory. By emphasizing the development of drugs based on antibodies and naturally occurring proteins that could be mass produced by commonly used microorganisms utilizing new recombinant DNA techniques,[14] these companies could build on their expertise in fermentation. This expertise could be used both to manipulate microorganisms during early stage drug discovery and later to scale up manufacturing to commercial levels. Both were driven to enter the nascent biotechnology field by CEOs with strong personalities and executive powers who perceived the potential of the new science and thought that it would be an avenue to expand their companies' business and visibility. At the time, both companies had positive balance sheets and abundant cash, Japanese companies being under little pressure to return profit to shareholders.[15]

Both companies recruited young scientists as well as some experienced team leaders for their new pharmaceutical operations. The ratio of researchers with Ph.D.s may have been somewhat higher than for mainstream pharmaceutical corporations.[16] However, although they recruited some young researchers from leading Japanese universities, they felt they were not able to recruit enough good scientists and luring good people away from established pharmaceutical companies was nearly impossible.[17] Both companies had close ties with university researchers in Japan and overseas.[18] Both laboratories were well equipped, researchers seemed competent and enthusiastic, and some volunteered that they had considerable freedom to pursue their own drug discovery projects.[19]

Suntory's first and most successful drug was pilsicainide. Launched in 1991 to treat fibrillation and other arrythmias of the upper chamber of the heart, it is synthetic version of a compound naturally secreted by the kidneys. It is a small molecule, not a typical biotechnology therapeutic. In 2001, Suntory earned about US$90 million in sales of pilsicainide—far from *blockbuster* status. Its next best selling drugs were the combined penicillin–cephalosporin antibiotic, Farom® and recombinant carperitide to treat heart failure.[20] All of these drugs have been marketed only in Japan.

In 2000, the Biomedical Research Institute was incorporated as Suntory Biomedical Research, Ltd. (SBR). At the end of 2002, Daiichi Pharmaceuticals bought two-thirds of SBR's stock. Conversations with industry insiders suggest that the reasons Suntory divested its pharmaceutical business relate to the death of the chairman who had championed the pharmaceuticals division,[21] a general retrenchment from several areas remote from Suntory's core business, a realization that substantial investments would be needed to make the pharmaceutical operations competitive, and a difference in corporate culture between the individualistic and free-thinking pharmaceutical researchers and the traditionally minded employees in the rest of the company. Daiichi reportedly pledged that it would keep the Suntory researcher teams intact in the near term, and it continues to operate SBR under the name Daiichi Suntory Pharma Co., Ltd. Clearly, however, control has passed to Daiichi.

In the case of Kirin's Pharmaceutical Division, one strategic decision overshadowed all others in its early years, its 1984 partnership with Amgen under which Kirin helped to bankroll Amgen's development of bioengineered erythropoietin (EPO) and granulocyte colony stimulating factor (G-CSF).[22] In return, Kirin received the right to market these drugs in Asia and comarket EPO in Europe through a joint venture with Amgen. This partnership has paid off financially. EPO and G-CSF are the world's two best-selling biotechnology drugs,[23] and they account for the bulk of Amgen's and almost all of Kirin's pharmaceutical revenue.[24] As of the end of 2003, all of the drugs Kirin was marketing originated in outside laboratories.[25]

Research on EPO and G-CSF was left primarily to Amgen. Although Kirin received licenses to Amgen's technology, to this day it appears that Kirin is not competing with Amgen in drugs that are similar to EPO or G-CSF. For Kirin, the future of its pharmaceutical operations lies with a technology to genetically engineer mice or other animals to produce purely human polyclonal antibodies that can be used as drugs to treat cancer, infectious diseases, and autoimmune diseases.[26]

The point of this comparison is not to pinpoint various corporate strategies that made the difference between failure in Suntory's case and the prospect of continuing success in Kirin's. Luck probably played as great a role as corporate management. What does seem clear, however, is that despite being able to ramp up pharmaceutical operations quickly and to build on their fermentation expertise, the road for both these new entrants was perilous.

Ajinomoto was founded in 1908 by a professor of physical science at the University of Tokyo who had isolated glutamic acid from the broth of cooked seaweed (konbu) and identified it as the source of the savory taste in traditional Japanese dishes made with konbu. He formed the company to manufacture and market glutamic acid as a flavor enhancer. Ajinomoto has grown into a diversified food products company with its core technology centered on the production and utilization of amino acids. In the 1980s, it began to use genetic engineering to produce proteins. Its pharmaceutical R&D also dates from this time, with its genetic engineering of *Escherichia coli* to produce purified interleukin 2 and 6. However, it has ceased development of interleukins, probably because of competition from US biotechnology companies,[27] and is now focusing on the discovery of small molecule drugs using genomic and proteomic technologies. Pharmaceuticals account for only about 8 percent of Ajinomoto's total net sales—a higher percentage than for Kirin.[28]

Ajinomoto can claim at least one partial success. Its researchers were among the first to make a new type of drug to treat adult onset diabetes, a drug that acts quickly to stimulate secretion of insulin by the pancreas and decrease the damaging surges in blood glucose levels that occur during mealtime.[29] Lacking a sales force, Ajinomoto licensed marketing rights outside of Japan to Norvatis, which markets the drug under the brand name Starlix®.[30] FDA-approved Starlix® for use in the USA at the end of 2000. Ajinomoto's other main drug in 2004 was Actonel® for osteoporosis, which is in-licensed from Procter and Gamble.[31]

A new experimental small molecule drug originating in Ajinomoto's laboratories is AVE-8062, the leading drug in a new class of compounds that disrupt both existing and newly developing blood vessels in tumors. Ajinomoto licensed worldwide rights to the drug to Aventis in 2001. As of 2006, early stage clinical trials were still in progress.

In 2000 only about 5 percent of Ajinomoto's researchers had doctoral degrees. It has long-standing relationships with US universities, including MIT, to which it regularly sends researchers. It also has collaborations with German, French, and Dutch universities. All told, it sends about fifteen researchers annually to overseas universities for training and about the same number to Japanese universities. These numbers are high in comparison to the largest Japanese pharmaceutical companies and indicate a considerable commitment of human resources. Ajinomoto provides research support to many Japanese university laboratories.

These close relations with universities may have paid off. The basic active compound of Starlix® was coinvented with Keio University researchers.[32] Among all the Japan-origin drugs approved by the US FDA from 1998 to 2002, only Starlix® had university researchers listed as inventors on the underlying patents. Along with the university input to Kirin's new antibody technology, this suggests that established newcomers are making use of collaborations with universities to develop innovative products in a way that established incumbents usually do not.[33]

Takara Shuzo was incorporated in 1925 and is best known as a sake brewer. In 1986, a Japanese biochemist who had been a research director at Centocor in the USA joined Takara and began to build its biotechnology operations. Beginning with manufacturing of various enzymes, reagents and test kits for genetic engineering laboratories; these operations expanded to include genome and protein analysis using technologies in-licensed from abroad; then large scale genome sequencing to discover links between genes and diseases and sensitivity to drugs in Asian populations; then gene-therapy using technologies in-licensed from abroad. In 2005, Talara Bio's revenue was mainly from the sale of protein synthesis systems and services based largely upon overseas technologies, supplemented by sales of health food products.[34] Although the company's biomedical operations do involve research at the forefront of science, available information suggests that most of its business activities are based on standard or in-licensed technologies.[35]

Since 1993 Takara Shuzo has been organizing its biomedical operations into tethered spin-offs: Takara Biotechnology in Dalien, China (1993) to produce genetic engineering reagents and to process samples collected in China for genetic analysis; Dragon Genomics near Nagoya (2000) as the gene sequencing center; and Takara Bio near Kyoto (2002) as the main R&D center. Unable to sustain the burgeoning biomedical research budget,[36] Takara Shuzo arranged for Takara Bio to have an IPO on Mothers at the end of 2004. This strategy may have paid off as the market capitalization of Takara Bio three months after the IPO was about US$1.5 billion, higher than for any other new life science company. As of mid-2006, market capitalization was still over US$1 billion.

Japan Tobacco (JT) was incorporated in 1985 as a wholly owned government corporation, continuing the government's monopoly over the sale of domestically produced tobacco products. Beginning in 1994, the government began to sell some of its shares in JT, but as of 2004 it still owned 50 percent of the company. As part of JT's diversification, it established a pharmaceutical research center in 1993 and bought Torii Pharmaceutical Company in 1998 to be the main marketer for its drugs. Currently marketed pharmaceuticals consist of drugs developed by Torii prior to the merger and drugs in-licensed from overseas. The ratio of pharmaceutical R&D expenditures to sales has been very high,[37] indicating a substantial investment of overall corporate revenue, mostly from the sale of cigarettes in Japan and overseas.[38] For its pharmaceutical division, losses as a percentage of sales have also been high.[39] Although total revenue has continued to increase, JT has scaled back its pharmaceutical R&D. In 2002 it had ten in-house origin drugs in early clinical trials, but by 2005, it had pared this number to six.[40] Some of the bioventures I interviewed said that they had recently hired researchers from JT.

However, one of these drugs is among the first in a promising new class that increases high density lipoprotein and thereby reduces the risk of heart disease in persons with high cholesterol.[41] Late in 2004, JT licensed worldwide rights to this drug to Roche, although it retained marketing rights in Japan and Korea.

Several *chemical and foodstuffs companies* have discovered drugs that have subsequently been developed by major Japanese pharmaceutical companies. They play a similar role in relation to the major companies as US biotechnologies play vis-à-vis multinational pharmaceutical companies, although they are the source of a much smaller proportion of the pharmaceutical companies' pipelines than are the US biotechnology companies. However, the drugs discovered by chemical and foodstuffs companies generally are not groundbreaking drugs. Rather they are variations on classes of drugs that have been pioneered by other companies.[42] The pharmaceutical operations of the chemical and foodstuffs companies are generally small. They receive modest funding from the parent, and they employ small numbers of researchers. Other than Ajinomoto, I know of no cases where R&D in such companies has been ramped up, either by generous funding from the parent or by substantial revenues from successful products, to sustain pharmaceutical R&D on a scale that can produce a continuing sequence of drug candidates entering clinical trials.

Asahi Glass produces purified recombinant (genetically engineered) proteins for bioventures and some major pharmaceutical companies to meet their research needs and also for pilot-scale (precommercial) production. Asahi's system uses a yeast isolated from east African beer to synthesize proteins.

However, this basic system was developed in the early 1990s, largely by scientists in the New York State Department of Health, and it appears that other companies are using this system for similar purposes.[43]

Hitachi, Toshiba, Canon, NEC, and Fujitsu all have entered the field of biochips and bioinformatics. *Toshiba* patented and in 2005 was nearing the end of prototype testing of a new type of DNA chip that relies on electrochemical signals rather than fluorescence to detect binding of unknown gene sequences to known strands of DNA.[44] Toshiba claims the system is quicker and more accurate than the 'industry standard' Affymetrix chips, and more suitable for large-scale use in molecular diagnostic laboratories. However, it holds fewer DNA probes than conventional chips and therefore one chip can detect fewer types of DNA or fewer types of mutations. Nevertheless, it might be useful in clinical settings where patient samples are being tested for a limited number of genetic mutations or genetic variations.

Canon, drawing on its expertise in ink jet printers, is developing a new way to make DNA chips by spraying DNA solution onto glass slides. The new chips will be used to diagnose cancer (or cancer susceptibility) and infectious diseases.[45]

Hitachi's activities related to DNA chips are described in one of the case studies in Chapter 4. But Hitachi's involvement in the biological aspects of life science[46] goes far beyond DNA chips.

The development of gene sequencing machines is an intriguing side story to the race to sequence the human genome between the public international consortium[47] and the private sequencing effort of Celera and its lead scientist and CEO, Craig Venter.[48]

Applied Biosystems Incorporated (ABI) was founded by venture capitalists in 1981 to commercialize DNA sequencing technology largely pioneered by Dr Hunkapillar and his research team at Caltech.[49] Among this team's key inventions were methods to attach fluorescent dyes to each of the four nucleic acids that make up DNA sequences, thus enabling their identification when exposed to laser light. By 1987 ABI had a sequencer on the market, although its speed was too slow to meet the original goal of sequencing the human genome by 2005. In 1993 ABI was bought by the mainline scientific instrument company, Perkin Elmer (PE), which soon began to reorient its entire business toward the life sciences.[50]

However, by the mid-1990s ABI had competition. A team at UC Berkeley had also developed sequencing technologies that became the basis for founding another venture company, Molecular Dynamics. In order to gain access to marketing resources and appropriate dye technology, Molecular Dynamics entered into a strategic alliance with Amersham, which had obtained access to ABI's fluorescent labeling technology through a series of technology swaps with ABI.[51] By 1997 the MegaBace sequencer being developed by Molecular Dynamics–Amersham was faster than any ABI machine.

Meanwhile in 1981, approximately three years before the idea of sequencing the human genome began to crystallize in the minds of US scientists, the Japanese Science and Technology Agency (STA) had launched a project to involve various companies, universities, and GRIs in the development of automated DNA sequencing technologies. This project and a follow-on project from 1984–7 were brainchildren of Akiyoshi Wada, professor of physics at the University of Tokyo. Although Seiko Instruments was originally designated as the lead developer of an automated sequencing system under the first of the Dr Wada–STA projects, Hitachi was to make the greatest contribution to genome sequencing technology. As a participant in the second of these projects, Hitachi began development of its own DNA sequencer. A team headed by Dr Hideki Kambara (a former student of Dr Wada) developed new ways to configure the array of capillaries carrying fluorescently labeled gene sequences and the laser beam that would illuminate these sequences. By 1993 this team had developed the *sheath flow capillary array method* that greatly improved the speed and reading accuracy of the sequences, although Hitachi's complete machines were only in prototype stage.

In order to counter the Molecular Dyamics–Amersham threat, ABI licensed this technology from Hitachi around 1997. This enabled ABI to build its new 3700 model sequencer, which became the workhorse for sequencing of the human genome as well as the genomes of other organisms. This machine and later models allowed ABI to continue to hold over 70 percent of the world market for sequencers. Dr Kambara's team made further improvements, simplifying the sheath flow mechanism and adjusting the optical characteristics of the capillaries to improve laser beam focusing. The result is a more compact, lower maintenance system incorporated in the latest DNA sequences sold by ABI designed particularly for clinical use. Hitachi currently markets only a few gene sequencers annually under its own brand name. But ABI brand sequencers sold since the late 1990s contain key technologies from Hitachi.

However, the relationship between Hitachi and ABI has not been entirely cordial. ABI and Hitachi never agreed on terms under which ABI would license its fluorescent tagging patents to Hitachi. Hitachi scientists maintain that this technology was not necessarily crucial, and Hitachi's in-house-originating technology was sufficiently unique and comprehensive that Hitachi could have manufactured and marketed sequencers on its own and probably survived a patent infringement suit by ABI. However, Hitachi felt it would be at a disadvantage marketing its own brand name sequencers internationally and thus its senior management felt a partnership was necessary. At one time Hitachi and Amersham explored a development partnership.

Ironically, Hitachi ended up partnering with the company that some Hitachi scientists regarded as its arch rival.

This story is relevant for this book because it illustrates two different approaches to innovation in new technical fields: (*a*) the US approach where very early prototypes are made in universities, then developed by newly formed ventures which finally partner with large companies to assist in marketing; and (*b*) the Japanese approach where almost all R&D from conception to final product is done in large established companies.

However, one problem for the Japanese effort was the relatively low level of company and government funding devoted to the project. During the peak years of Hitachi's sequencer development efforts, about twenty to thirty Hitachi researchers were working on this project, about ten of whom were under Dr Kambara developing the sheath flow technology. Hitachi funded all the R&D that led to its sheath flow capillary array breakthrough.[52]

In all probability, Molecular Dynamics and ABI each had larger numbers of researchers working on sequencer development. ABI and Molecular Dyanamics both benefited initially from access to substantial VC funding and later from the support of their large partners, Perkin Elmer and Amersham, respectively. Japanese government funding never compensated for the reluctance of Hitachi executives to devote large resources to the project. Over the seven years duration of the two Dr Wada–STA projects, STA contributed a total of only about US$13 million to the genome sequencing projects.[53] In contrast, the US NIH and DOE each began contributing over US$100 million per year beginning around 1989, while the UK government through the MRC and the Wellcome Trust also contributed significant funding.

The Japanese project from the beginning had a strong focus on developing sequencing technology. The US/UK project was more focused on the scientific and medical benefits from sequencing the genome. But ironically the scientifically and medically focused US/UK government funding ultimately provided a greater incentive for the development of sequencer technology than the instrument-focused Japanese project.

Separate from sequencer operations, the Hitachi Life Science Group and other groups within Hitachi offer various genomics and proteomics services that build on Hitachi's experience in gene sequencing and analysis.[54] Hitachi Life Science has been the main provider of data analysis and hardware for two government organized consortia.[55] However, the genomics and proteomics services that Hitachi Life Sciences offers seem duplicative of services available elsewhere in Japan and abroad. Conversations with Japanese researchers suggest that Japanese laboratories sometimes do much of this analysis themselves. Takara Bio offers similar services as do Affymetrix, Gene Logic, Celera, or Roche Diagnostics, to name just a few examples. In other words, although

Hitachi has become a major provider of genomics and proteomics services in Japan, outside its core competence of developing electronic instruments, it has not developed new technologies that have given it a competitive advantage. It does not appear to be playing the same role in innovation that venture companies play in the USA.[56]

Nonbiomedical Cases

Although I am more familiar with biomedical technologies, the following example of a consortium research project in optical communications bears resemblance to the case of DNA sequencers just described. Based on my knowledge of other large scale collaborative projects and conversations with government and business officials, it is probably fairly representative in terms of priority setting, funding, and organization of high-priority government-initiated collaborative R&D projects. As noted in Chapter 7, because these projects are so numerous, they probably constitute one of the main mechanisms by which established companies enter new fields of technology.

This particular project was inspired by the success of US companies such as Cisco Systems and Juniper Networks[57] in creating systems for transmitting large amounts of data efficiently and securely over fiber optic networks. It aims to have each member of a consortium of well-known Japanese companies develop cutting-edge expertise in specific components of broadband optical communication—expertise that can then be integrated into a commercially viable system that each consortium member would contribute to and profit from. Thus, for example, a major electronics company is responsible for R&D in optical switches, a major manufacturer of fiber optic cables for packaging, a major telecommunications company and university researchers for integration, and another major electronics company for cables, splitters, couplers, and tunable lasers.

Japanese government funding averages roughly US$1 million per corporate project participant, each of whom is expected to devote some of its own resources to the project. The corporate participants are expected to develop at least a prototype of the equipment or system assigned to them.[58] However, it is difficult for them to convince higher corporate management to commit the additional resources to refine the prototype and scale up manufacturing for a viable commercial product. Usually much more funding is required for such translational research following development of a prototype. But in this case and others, senior managers of large corporations, whose attention is directed mainly to existing product lines and to customers who each account for hundreds of millions of dollars of annual sales, are reluctant to commit scarce resources to an uncertain technology, the current market for which is only a few million dollars.[59]

No venture companies or other SMEs are taking part in this consortium. Some of these technologies are capital intensive and thus perhaps not suitable for venture companies. However, in some technical fields of optical communications, the acknowledged industry leaders are US venture companies. For example, the consortium member responsible for tunable lasers[60] perceives its main rivals to be Agility,[61] Iolon,[62] and Santur,[63] all of which are new VC backed companies. In 2005 all three companies were manufacturing tunable lasers for commercial sale. All had patent portfolios.[64] As of the end of 2004, Agility had raised over US$200 million in venture financing, Iolon approximately US$85 million, and Santur US$60 million. Any of these amounts is probably greater than the combined investment of the consortium member responsible for tunable lasers and the Japanese government in this technology.

This situation appears analogous to Hitachi's and STA's investment in DNA sequencers compared to that of ABI or Molecular Dynamics and their VC investors and large company partners. By the time large market size became apparent, US ventures already had a substantial development lead.[65]

The ministry promoting the consortium would like to have Japanese SME participants, but no eligible companies could be found. One reason is that private VC funding for new companies in IT and materials fields is difficult to obtain for companies without a revenue stream. But a related reason, discussed in the final chapter, is that the government's policy of cobbling together consortia of large companies and major universities to pursue R&D in new fields of technology leaves few high-growth-potential niches for venture companies or entrepreneurial faculty to exploit. To the extent SMEs are involved at all in high priority, cutting-edge projects, their role is usually limited.[66]

Concluding Observations on Established Newcomers

These cases suggest that when established companies move into new fields of technology that are relatively distant from current areas of expertise, the road is difficult. Although there have been some successes in terms of new products, the newcomers in drug development have not shown a distinct advantage over established Japanese pharmaceutical companies.

Even though they offer the assurance of large reputable corporations, many of the established newcomers have had difficulty recruiting skilled persons for their new operations. Even though, in theory, they had an opportunity to embark on new lines of research unencumbered by prior business goals, often they ended up pursuing lines of R&D that are not new. Some, such as Ajinomoto and Japan Tobacco, did eventually pursue innovative projects, but it took time and they devoted considerable resources to less innovative projects. Often it seems as if the decision to move into a new area was made before specific new projects were clearly conceived. Thus there was a tendency to focus on tried and true technologies that offered the prospect of a relatively quick although modest return.

The case of Hitachi's gene sequencer R&D is different. The project was close to Hitachi's prior core operations, building on experience in engineering and medical instruments. Moreover, from the outset, an experienced scientist in Hitachi had a clear vision of the project, including its importance and the technical challenges that needed to be overcome. The decision of senior management to move into a new field seems to have been matched[67] by the desire of experienced research scientists and their realistic confidence in the company's ability to carry forward the project.

Are the challenges of the established newcomers less if they are entering an uncrowded field? In the 1980s and early 1990s, genetic engineering and the related fields of protein and antibody science were new to most pharmaceutical companies. Kirin, Suntory, and Ajinomoto all initially targeted these biotechnology fields. Nevertheless, they ended up at a disadvantage with respect to US bioventures. Whatever advantages the Japanese established newcomers possessed with respect to access to complementary assets did not compensate for the greater ability of US biotechnology companies to assemble and concentrate resources on promising new fields of drug discovery—and perhaps also to benefit from the in-depth academic knowledge base and plentiful supply of skilled researchers resulting from generous, astutely allocated, NIH funding for basic research.

Is the picture different with respect to nonbiomedical fields? This chapter began with numerous examples of relatively large Japanese automotive and electronics companies outcompeting even larger US or European companies in fields pioneered by the latter. But what about fields that are very new, where successful commercial applications are still few and where the competitors also include venture companies?

Nanotechnology may soon provide another test case. Since commercial applications are still few, all companies are newcomers. Progress is probably most advanced in the US and Japan. Again, the US companies in the forefront of R&D include new as well as established companies, while the Japanese leaders are almost all large established companies. For example, among nineteen companies identified in a 2005 survey as leaders in the electronic application of carbon nanotubes, six are large Japanese companies, five are large US companies, six are US ventures (four of which are university startups), one is a major Korean electronics company, and one is a large spin-off from a large European electronics company.[68] All told, approximately 500 US companies are developing commercial applications of nanoscale technologies compared to about 50 in Japan.[69]

Japanese and US government spending for nanotechnology R&D were both close to US$1 billion in 2004.[70] In the Japanese case, much of this was for collaborative university–industry projects.[71]

PART II: TETHERED SPIN-OFFS AND KEIRETSU

Background: The Case for Spin-Offs as Engines of Innovation

Many of Japan's best known companies, including some of its leading high technology and financial investment companies such as Toyota, Fujitsu, Mitsubishi Electric, Mitsubishi Motors, Nomura Securities, and JAFCO, originated as spin-offs from established parents.[72] The Hitachi group has over 650 companies, most of which are spin-offs. The Matsushita Electric industrial group[73] has over 150 companies, many of which are spin-offs.[74] Spin-offs from established companies may be the most common way that new companies in high technology industries are formed in Japan.[75]

Spin-offs may be initially 100 percent owned by their parents. As time goes on and particularly if the spin-off is successful, the parent's ownership share will likely diminish. Sometimes the spin-off grows to be much larger than the parent and may own more of the parent than vice versa. For example, by 1990 Toyota Motors's sales were twenty times larger than that of its parent, Toyoda Automatic Loom, and it owned 25 percent of its parent, while the parent owned only 4.3 percent of Toyota Motors.

Are tethered spin-offs, that is, spin-offs partially controlled by their parents, likely to succeed better in new technology fields than independent ventures? Can they combine the advantages of independent ventures[76] with the advantages of large established companies?[77] To answer these questions, I first explore reasons established companies form spin-offs and then the degree of control they exercise over their spin-offs, before considering information about actual spin-offs.

Formation of spin-offs can be a means to reduce labor costs[78] or to increase the number of high level management positions for senior employees who might otherwise have to retire at age 60.[79] It can be a means to outsource the manufacturing of component parts, allowing the parent to maintain some control but also increasing incentives to market to outside companies.[80] It can be a step in preparation for obtaining outside investment, or for divestiture.[81] But most importantly from the perspective of spin-offs as engines of innovation, it is a means to let a promising new line of business flourish on its own, to give scope to entrepreneurship among new managers, and to relieve the parent of the burden and complexity of having to manage the operations of the spin-off internally so that both the parent and spin-off can focus on their core competencies.[82] In other words, spin-off formation is a growth and adaptation strategy for Japanese companies where primary value is placed not on a single corporate entity but on a family or loose federation of firms.

Those that emphasize this pro-entrepreneurship rationale for spin-offs, along with the rationales of management efficiency and maintaining focus on core competence, often contrast the Japanese style of growth and diversification through spin-offs with the tendency of large US companies to be more diversified and vertically integrated.[83] They note that vertically integrated, diversified firms often encounter problems related to coordination, inappropriate incentives, and hierarchical control that deadens initiative.[84] Operations that are not internalized have to be managed by arm's-length market transactions.

For example, Dyer (1996) analyzed manufacturer–supplier relations in the automobile industry and showed that coordination and integration, including sharing of information valuable for productivity improvements, between Toyota and Nissan and their partially owned suppliers were better than between GM and Ford and even their internal parts divisions—and substantially better than between Ford and GM and their arm's-length suppliers. Coordination between Toyota and Nissan and their independent suppliers was closer than between GM and Ford and their affiliated suppliers, and of course much closer than between the US automakers and their independent suppliers.[85] Dyer concluded that the Japanese system of production based on close alliances between each of the main automakers and their networks of supplier companies (some partially owned, some independent) resulted in greater overall value chain specialization. This in turn allowed for gains in productivity which could not be matched by their US competitors whose parts suppliers were either internal parts divisions or independent companies whose relationship with the main manufacturer was defined by arm's-length contracts.[86] Others have noted the innovative capabilities of Japanese spin-offs and affiliated suppliers, particularly in the auto industry, and the extent to which main manufacturers rely on their supplier affiliates for important product innovations.[87]

In other words, at least in the automobile industry, there is evidence that a system of manufacturing and innovation based on close long-term coordination between a 'family' of companies led by a main manufacturer[88] can be more effective than a system where manufacturing and innovation occur either within a single, large, hierarchical company or in independent suppliers dealing at arm's length with the main company. So both the genealogy of various leading high technology companies and Dyer's case study of the automobile industry show that spin-off formation in Japan can enhance entrepreneurship, management efficiency, and improvement of core technical competence.

Control versus Flexibility

But to what extent does parental assistance and control compromise spin-offs' ability to be competitive innovators in new fields of technology?

It is common for parents to provide spin-offs with management support, especially on launch or if the spin-off runs into trouble. A substantial proportion of a parent's managerial effort may be devoted to cooperation with or supporting spin-offs.[89]

In the case of a spin-off that is supplying components or services to its parent, incentives do exist for the spin-off to upgrade its technical capacity, for example from production of components designed by the parent to components it designs on its own. Apportionment of risks and benefits in the supplier–buyer relationship is relatively equal in the case of parents and their subsidiaries.[90] If a spin-off is successful, that is if it generates growing revenue, the parent typically reduces its ownership share over time, often considerably below the 33 percent that constitutes veto power over major corporate decisions.[91] Even spin-offs over which the parent maintains a substantial ownership interest are often able to sell to competitors of the parent, although parents will discourage their selling products that may leak key technologies to the parent's main competitors.[92]

So far the picture is of a relatively benign, if somewhat, paternal relationship where both spin-off and parent usually operate under a mutual-benefit obligation.[93] But in the case of ventures that are developing new technologies requiring large investments in R&D, where substantial sales may be years away, does this system allow for the benefits associated with independent ventures?

First let us consider the seven University of Tokyo, Keio, and AIST startups that are at least one-third owned by another company.[94] Only two of these had annual revenues greater than US$1 million,[95] approximately the same proportion as for all startups from these institutions.[96] In other words, being closely tied to a larger company does not seem to increase the chance of rising above the low average indices of success that characterize the start-ups from these three institutions.

Next let us consider the case of UP Science, which was spun off from Sumitomo Electric Industries (SEI) in 1999 to commercialize the achievements of a biomedical R&D group within SEI related to a class of enzymes linked to cancer and autoimmune and neurological diseases.[97] Backed by Sumitomo Pharmaceuticals and JAFCO, UP Science would continue the development of assay systems to screen candidate compounds to correct or mitigate the effects of the defective enzymes, optimize candidate drugs, and finally take the lead candidates into clinical trials. It would also screen compounds submitted by pharmaceutical companies and possibly enter into joint drug development partnerships with pharmaceutical companies. It aimed for an IPO in 2004 or 2005.

UP Science called itself Japan's first satellite bioventure.[98] It was praised by knowledgeable independent observers of the Japanese biotechnology scene as the harbinger of the future for Japanese ventures. It was to have independence and to be subject to good corporate governance procedures.[99] Yet it would also have the backing of one of Japan's largest electrical equipment and engineering companies and a midsize pharmaceutical company also within the Sumitomo group. JAFCO would provide not only funding but also advice on business development. In other words, it had at its disposal a wide range of complementary assets of the type that constitute the main advantage of incumbent companies over independent ventures. The head of the biomedical research laboratory in SEI was given leave to be the CEO. Recruitment of other skilled personnel would not be a problem. Most would simply transfer to the new company from the parent. They would do so without the fear of the company failing because UP Science had strong backing from large companies.

Fail it did. By mid-2004, UP Science had ceased operations. Of potential interest, it appears that some, perhaps most, of the key staff did not return to SEI and but instead had to find jobs in universities and other companies. In other words, the project was not reconstituted back in the parent, and there was no safety net for the employees.[100] The reasons for UP Science's failure are not completely clear, but evidence suggests that the control exercised by the parent was an important factor. My requests to interview the company in 2001 and 2002 (before I had any idea it was in trouble) were refused. But the reason given for the refusals, that management was busy preparing reports for the parent, is consistent with management being preoccupied with relations with the parent. After it failed, sources familiar with the Japanese biotechnology industry said concerns had arisen about inaccurate reporting of scientific data, and that pressure from the parent to meet development milestones probably were at the root of these reporting irregularities.

Have similar problems arisen between US ventures the private VC funds that have invested in them? Undoubtedly—so perhaps not too much should be made of this case. However, it was launched with some fanfare and it appears to have been well planned. Its failure suggests that the traditional way parents manage relations with tethered spin-offs may not be appropriate for fields of considerable technical uncertainty, where sustained sales revenue is remote and flexibility is necessary to respond to changing risks and opportunities.

There are other tethered bioventure spin-offs or affiliates of large Japanese companies. As a group, they account for a small proportion of bioventure drugs under development and sales of bioventure products and services.[101] Some of these feel their development is constrained by limited funding from their parents and the parents' unwillingness to yield control to outside investors. Investment analysts now tend to be skeptical about tethered spin-offs and express concerns that they lack the independence necessary to adjust their businesses quickly in order to grow and meet the challenge of competitors. In the USA, the situation appears similar with independent bioventures tending to outperform those owned by established firms.[102]

What about tethered spin-offs in nonbiomedical fields? The former director of Sony's computer science laboratory is reported to have said that all sixty spin-offs based on business plans submitted by employees were unsuccessful.[103]

A colleague who has discussed spin-offs with executives in leading Japanese electronics companies notes that spin-offs face unique challenges because of their relationship with the parent corporation. These challenges relate to personnel, organization, strategy, resource availability, and general decision-making. He writes:[104]

> In the late-1990s, at the height of the telecommunications boom, corporations such as Sony and Toyota announced that they would spin out dozens, perhaps a hundred, venture companies. After the dust settled, there were in fact very few viable spin-outs, at least among those pursuing pioneering R&D. A review of the reasons reveals two general problems: (1) lack of consensus throughout management regarding the priority for spinning out companies and (2) unproductive intrusion of the parent corporation into the operation of the venture company which often handicapped substantially the growth of the venture.
>
> The success of venture companies typically stems from their ability to exploit speed and focus. However, spin-off ventures must deal with their parent corporations, which usually adds inefficiency and frustration. I know of spin-outs that are being smothered by the need for their CEOs to spend a great deal of time responding to inquiries and directives from the parents. This takes away large chunks of valuable time from the needed task of running the venture.

Issues that arise include the following:

Personnel. The parent company often wants to dispatch the CEO—who may have no venture business skills—as well as the staff—who may be 'second tier' staff that the corporation's personnel department is desperate to rotate.

Decision making. The parent corporation often wants to participate or control key business decisions of the venture. The parent usually does not know the details of the venture's needs and changing environment it faces. The need to negotiate with the parent usually slows the venture. The venture usually loses if disagreements arise.

Strategic focus and strategic flexibility. Venture businesses have limited staff. Thus management attention and staff time have to be focused on moving forward toward clear targets. At the same time, most ventures change direction as they develop their business lines. So an ability to make quick, well defined strategic adjustments is also essential. Large corporations are not flexible once directions have been established.

Process orientation versus outcome orientation. Large corporate organizations typically emphasize processes. This often becomes ingrained in the habits of workers and managers. Venture businesses focus on outcomes.

Resource availability and financing. It is common for the large corporation to want to control the spending of the venture, requiring time consuming justifications for everyday operating expenses. Typically, spin-offs feel they need more resources than the parent corporations allow. Allowing for outside investment is an important asset for venture businesses.

Strategic partnerships hindered when they go beyond corporate group. While the parent generally agrees that the spin-off can sell products and services widely, strategic partnerships that might involve transfer of core proprietary technologies or joint investments in high priority projects are often restricted to companies within the parent's group. Conversely, companies outside the group may not trust a venture associated with a different corporate group.[105]

Limitations on acting against the interests of companies in the same group. Competition against companies in the same group is discouraged, and thus vigorous growth is often handicapped.[106]

An example was recounted to me of a project by an internationally respected high technology company to establish a spin-off venture in a new field of technology. Although the technical field was new, the company had world leading expertise in related technologies that could be applied to the new field. The complementarities between the company and its outside partners were good in terms of technical experience and other resources. The company assigned a senior manager with good business and technical expertise to head the venture. The researchers were competent, and lines of communication between the various parties seemed good.

However, the head of the spin-off had to spend much time seeking permission from the parent for a wide range of decisions related to the collaboration and in reporting back to the parent. He had to spend almost as much time managing the parent as managing the venture. Particularly time consuming were decisions related to funding by the parent and expenditures by the venture. Another problem was the parent's involvement in personnel decisions, both in recommending/insisting that particular persons from the parent be transferred to the venture even though they are not suited and in questioning the venture head's attempts to obtain persons with skills needed by the venture. Moreover, the venture head had to justify his requests and actions to multiple hierarchical levels within the parent. The delays caused by this internal oversight delayed the entire project and ultimately turned the venture toward more conservative technologies.[107]

The reasons UP Science and the venture described above ran into trouble seem similar to the problems that beset 19 internal ventures initiated by Exxon in the late 1970s and early 1980s. None managed to reach a break-even point or to have an IPO or merger. By 1986 Exxon had terminated and written off all of them.[108] More generally, the points my colleague raised above echo some of the problems besetting US spin-offs, particularly in competing for resources, markets, and the dedication of managers transferred from the parent. So long as the primary motivation for spin-off creation is strategic (to contribute to the growth of the parent and its affiliates), as opposed to financial (to increase revenue and profits), then providing the spin-off greater autonomy increases the potential for conflict with the parent's established business.[109]

The opposite problem can also occur. A former director of international licensing at IBM commented that when large companies form spin-offs, they usually have to hire someone from the outside who understands the particular business to head the spin-off. But if they adopt a hands-off policy, they often end up spending lots of money at the behest of the outside manager. Because monitoring is ineffective, resources are often wasted on projects that should have been terminated or redirected earlier.[110]

As a more promising example, let us consider the New Ventures Group (NVG) that Lucent Technologies established internally in 1997 to form spin-offs to commercialize some of Bell Laboratory's technologies. By December 2001 when Lucent sold most of its interest in NVG, the fund had launched thirty-five ventures. Eight had had IPOs or mergers. Together with the US$100 million that Lucent received from the sale of most of its ownership stake in NVG, these 'liquidation events' gave Lucent a 46 percent gross annual internal rate of return on its investments from 1996 through 2001, a rate that constitutes a financial success. Some of these were internal ventures, where NVG provided almost all the investment. However, a larger number were syndicated investments involving NVG coinvesting with outside VC companies that took the lead in forming the management team and overseeing the businesses.

The program was probably also a success in terms of business and technology development. Chesbrough attributes the success to NVGs by combining the benefits of traditional private VC investment (including insulating the ventures from having decisions reviewed, delayed, and possibly overturned by Lucent executives)[111] with benefits associated with internal corporate investments.[112]

Nevertheless, when the downturn in the IT industry struck in 2000 and Lucent's year-on revenues fell over 26 percent from 2000 to 2001, Lucent had to divest all but its core business activities in order to survive. It sold all but 20 percent of its interest in NVG and its portfolio companies to a group led by Coller Capital, which specialized in secondary equity investments. The NVG team, renamed New Venture Partners, became the general partner of the fund and now manages the portfolio for the new investors.

Does Japan provide a better environment for a corporate spin-off program modeled on Lucent's?[113] On the positive side, large Japanese manufacturing companies have not yet faced the life or death situation that Lucent faced in 2001, so they have not been forced to shed noncore businesses. Furthermore, these large companies are less constrained by short-term earnings targets. Because of the uncertain and lumpy nature of revenue from venture businesses, Lucent may not have been able to build revenues from venture investments into such targets, which were nevertheless key to maintaining the support of investors and creditors.

But on the negative side, Lucent's experience suggests that a successful corporate spin-off program requires either a long-term commitment to building and maintaining a professional in-house venture business team or a willingness to let outside VC companies manage the spin-off process and the resulting portfolio companies. To my knowledge, very few Japanese manufacturing companies have taken either of these steps. More fundamentally, the underlying objective of spinning off companies is usually diversification and growth of the parent and its affiliates, rather than financial returns.[114] For this reason, there appears to be a strong tendency for parents to maintain control over spin-offs, particularly those requiring support from the parents, rather than to give them the autonomy to maximize growth and thus financial returns to the parents.

There are exceptions. Fujitsu seems to have the reputation not only of creating many spin-offs, but also giving them considerable autonomy—regarding them more as sources of profits and perhaps part of a voluntary commonwealth than as part of a mutual support alliance dominated by the core manufacturer.[115] One of the nonbiomedical venture case studies in Chapter 4 concerns a Fujitsu spin-off. Information from this venture, as well as a few other Fujitsu spin-offs, tends to be consistent with this reputation. However, I know of no other large manufacturing company that has adopted this approach to spin-offs. The other nonbiomedical spin-off profiled in Chapter 4, Chip Detect, also has autonomy (at least for the time being), but only after a less-than-cordial separation from its parent made possible by unique circumstances enabling it to garner outside support.

It may seem that some of the recent high profile spin-offs of major operating divisions from large electronics companies are also exceptions. But on closer examination, at least some of these have been plagued by interference from the parents. Elpida was formed in 1999 as a joint venture between Hitachi and NEC to absorb the loss making DRAM operations of both those companies. In the fiscal year ending March 2005, it registered its first operating profit and sales growth, although its share of the global DRAM market was only about 5 percent. However, when its current CEO, Yukio Sakamoto, took over in 2002, the company was in crisis. Morale among engineers was low due to downsizing and also because work teams combined employees from both parents who often did not communicate well with each other. Hitachi and NEC bickered about issues such as where to site the new manufacturing plant, from which parent to source purchases, and who should fill executive positions. Sakamoto had to demand that NEC and Hitachi cede him investment authority. He forced an end to the practice of appointing executives alternately from the parents.[116] Sakamoto was not affiliated with either parent, having previously headed the Japan operations of UMC.[117] His leadership helped to turn Elpida around and reduce interference from the parents. He was aided in 2003 by investments from about thirty outside companies, including Intel.[118] Intel's influence as a major investor was important in helping Hitachi and NEC to tone down their squabbling and to give the company real autonomy. Following a late 2004 IPO on the Tokyo Stock Exchange, Hitachi and NEC each held about 24 percent of Elpida's stock and Intel held about 6 percent.

Even mergers between members of the same group can be problematic and time consuming, as was the case of the 1994 merger of Mitsubishi Kasei and Mitsubishi Petrochemical.[119]

Fanuc, the robotics spin-off from Fujitsu which now is one of the world's largest manufacturers of computer controllers for machine tools, is sometimes cited as a successful spin-off in a new field of technology.[120] However, at the time of Fanuc's founding in 1972, it had approximately 300 employees and its first year operating revenue was approximately US$20 million.[121] Six years after founding, those revenues began to increase dramatically. In other words, when it was spun off, Fujitsu's robotics division already was fairly large, and it had sales revenue which, although not particularly large, had the potential to realize substantial increases within a relatively short period.[122] This size and access to revenue may have given it a degree of independence that spin-offs aiming to develop more early stage technologies with more distant market prospects lack.

The above examples do not prove that tethered spin-offs are less effective than independent ventures as sources of innovation. But they do suggest that across a wide range of industries, tethered spin-offs face obstacles to becoming successful pioneers of new technologies, and perhaps the most significant of these relate to control by the parents.

Conclusion

This chapter has endeavored to provide representative case studies of established companies attempting to innovate in new fields of technology that are removed from their core expertise. These cases suggest that these attempts usually do not lead to internationally competitive operations. Some of the reasons may be unique to Japan, for example, the prevalence of lifetime employment that prevents established newcomers from hiring experienced researchers and managers, and the deference paid to the welfare of a corporate family that may prevent established newcomers and spin-offs from competing vigorously. However, other reasons are not unique to Japan.[123] Thus, in other countries as well, established newcomers and tethered spin-offs may face similar difficulties.

Chapter 7 considers the evidence (and also the circumstances) under which independent ventures can, in many industries, be superior innovators in new fields of technology. It also examines the remaining possible strategies for established Japanese companies to become innovation leaders in new fields.

NOTES

1. See overviews of this issue in Chesbrough (1999) and Rtischev and Cole (2003). Chesbrough (1999) has documented this phenomenon with respect to hard disk drives (HDD). Henderson (1996) and Henderson and Clark (1990) have documented it with respect to photolithography and IC chipmaking technologies, and Fransman (1995) with respect to manufacturers of mainframe computers entering into the manufacture of PCs.
2. This latter example is described in Fransman (1995). Another reason NEC developed a better system than its main rival, Rockwell International's Printrak

system, was because it worked closely with retired Tokyo police officials to determine the most important aspects of fingerprint identification, aspects that the police officials themselves sometimes had not consciously conceptualized (e.g. the importance of ridge counts in differentiating between sets of fingerprints, particularly when prints had been degraded).

3. See Johnstone (1999) and Jim Frederick, 'A Sharper Focus', *Time Magazine*, May 9, 2005, 36–37.
4. See Suzuki and Kodama (2004), which analyzes the subject classification of Canon's patents over time pertaining to cameras, copiers, and semiconductor manufacturing equipment. This analysis shows the flow of technology from cameras into copiers and also into mask aligners and steppers (see also Henderson, 1996).
5. See, e.g. Friedman (1988), Henderson and Clark (1990), Henderson (1996), Kodama (1991), Aoki and Dore (1994, 1992), Odagiri and Goto Odagiri (1993), Fransman (1995, 1998), Nonaka and Tekeuchi (1995), Goto and Odagiri (1997), and Johnstone (1999).
6. See Chapter 7.
7. Fransman (1995).
8. e.g. Canon with respect to lithography (Henderson and Clark 1990, Henderson 1996), and Hitachi with respect to hard disk drives (Christensen 1993).
9. Sometimes formally protected as intellectual property, sometimes simply uncodified, tacit knowledge.
10. See Chesbrough (1999) for a discussion of access to *complementary assets*.
11. Also known as first mover advantages, i.e. the ability to maintain market share by being first to produce and market a new product.
12. The flip side of this argument, that strong IP protection enables innovators to organize their efforts in independent ventures and to obtain the complementary assets they need (sometimes even more so than they could if restricted by a large corporate bureaucracy), while maintaining entrepreneurial drive, flexibility, and responsiveness to customers, is discussed in Chapter 7.
13. Biomedicine is the one field where I have a fairly comprehensive picture of the main Japanese innovators, and where I feel can make comparisons between Japanese and overseas companies.
14. As opposed to small molecules usually made by synthetic chemical processes.
15. To date, Suntory remains a privately held company. Kirin's stock has been publicly traded on the Tokyo Stock Exchange (First section) since 1949.
16. One of Kirin's main laboratories, the Central Laboratory for Key Technology, was home to thirty-seven researchers, eighteen of whom (just under half) had Ph.D.s. Within this laboratory, the protein engineering group (which would have been considered to be working on cutting edge technologies) consisted of two scientists with doctoral degrees and three with master degrees (Protein Engineering in Japan 1992). In comparison, about 20–30% of researchers

in the large mainstream pharmaceutical companies have doctoral degrees (Kneller 2003).

17. It is interesting to compare the 1992 observations of the Protein Engineering study team with discussions with one of the senior scientists in one of these companies in 2004. What was not apparent to the foreign observers in 1992 was that the new companies were having recruitment problems and often had to rely on researchers from their brewery divisions.
18. A professor at the University of Tokyo provided Suntory researchers with the amino acid sequence of a bacterial protein that catalyzes the breakdown of penicillin. Using this information and information about the structure of a similar bacterial enzyme, beta-lactamase, Suntory researchers were able to design a combined penicillin–cephalosporin antibiotic, Farom®, that overcame bacterial resistance and has been marketed in Japan since 1997. This professor and another professor at the Kyoto University would create mutations at specific points in the DNA sequence of the gene coding for this resistance protein. The resulting changes in protein structure and function would give Suntory researchers clues as to good drug targets. Suntory was one of the founding members of the Protein Engineering Research Institute (PERI), a consortium of companies and academic researchers organized by MITI to pursue protein research. Suntory also had collaborative research agreements with Rockefeller University and the University of California at Irvine.

    Kirin collaborated on government sponsored projects with several Japanese universities and GRIs. It was also one of the founding members of the PERI consortium. It still has an important collaborative relationship with the La Jolla Institute for Allergy and Immunology dating from 1988. It regularly sends its researchers there and also to the University of Oregon. It also has collaborated in genetic engineering with Konstantz University (Protein Engineering in Japan 1992).
19. Protein Engineering in Japan (1992). However senior scientists did voice frustration that young scientists, whom the company had sent to PERI and perhaps to other academic institutions, became enamored with basic research, and on their return experienced difficulty readjusting to applied corporate research. Also, as noted above, they were in fact concerned about the quality of the researchers they were able to recruit.
20. 2001 sales about US$50 million and US$40 million, respectively. Farom® is described in note 18 above.
21. He was succeeded by his son, a graduate of an American business school.
22. EPO is a naturally occurring hormone that prompts the body to increase red cell production. It is used to treat anemia resulting from chronic renal failure (e.g. in dialysis patients) and cancer radiation and chemotherapy. G-CSF stimulates the production of white cells and is used in the treatment of neutropenia and some malignancies and also in bone marrow transplantation. Amgen scientists cloned the genes coding for these two naturally occurring substances [US patents 4,703,008 (EPO) and 4,810,643 (G-CSF)]. The patent record suggests this was a competitive field with several US biotechnology companies

and several Japanese pharmaceutical companies pursuing drug discovery research related to these two compounds in the early 1980s.

23. Edwards, Murray and Yu (2003).
24. Most of Kirin's pharmaceutical revenue has come from domestic sales (55.3 of 57.5 billion yen in 2003). Of its domestic sales, 96% came from sales of EPO and G-CSF.
25. Aside from EPO and G-CSF originating from Amgen, its other two marketed products, Rocalcitrol® to treat hyperparathyroidism and Phosblock® to treat hyperphosphatemia, are in-licensed from Roche and Genzyme, respectively.
26. By virtue of being fully human, these antibodies are less likely to generate adverse immune reactions than many currently marketed antibody drugs that are either pure mouse antibodies or antibodies that are partly mouse and partly human. By virtue of being polyclonal rather than monoclonal, they are not directed against a single molecular structure (antigen) on a tumor cell or an invading infectious particle, but rather an array of such antigens. The basic technique for transferring complete human genes coding for completely human antibodies into mice was invented by a Japanese professor of medicine in a university distant from Japan's major urban centers. As in the case of many US biotechnology companies, Kirin is building its future pipeline on discoveries made in universities.
27. Interleukin 2 (IL-2) is used to stimulate the immune system of patients with cancer and some infectious diseases. Interleukin 6 is used to stimulate the production of immune cells following bone marrow transplantation or chemotherapy. Ajinomoto holds several US patents covering the gene for IL-2 and methods for producing IL-2 using genetically engineered cells. However, in 2000 company officials said Ajinomoto is no longer developing IL-2 or IL-6. To my knowledge, most IL-2 sold commercially in Japan is manufactured either by Chiron, which has FDA approval to market the drug in the US under the tradename Proleukin®, or Shionogi under license from Biogen.
28. Ajinomoto's 2003 net sales were about 1 trillion yen (just under US$10 billion), while Kirin's were 1.2 trillion yen. Kirin's pharmaceutical sales accounted for 5% of the company's net sales.
29. Antidiabetic drugs in this class are known as meglitinides. Ajinomoto's drug was second in its class after Novo Nordsk's repaglinide approved by the US FDA in 1997.
30. However, worldwide sales (US$96 million in drug 2002 about half the level of Novo Nordsk's drug), did not meet expectations at least in the first years after launch.
31. Procter & Gamble (P&G) holds the basic patent covering this drug. Aventis comarkets Actonel with P&G outside Japan. In Japan, Takeda also markets this drug under the brand name Benet®.

    Ajinomoto's pharmaceutical products also include oral amino acid supplements for patients with liver disease (Livact®) and other medical nutritional supplements.
32. See US Patent No. 4,816,484.

33. See Kneller (2003) and Chapter 2.
34. Takara Bio's total revenue for the fiscal year ending March 2006 was 16 billion yen or about US$140 million, 85% from biotechnology systems and services and 12% from health food products (Accounting summary [kessan tanshin], May 2005, available at www.takara-bio.co.jp/news/pdfs/05051302.pdf.)
35. Takara Bio in-licensed genome and protein analysis technologies from Affymetrix, Lynx Therapeutics and other overseas biotechnology companies. It has been testing gene therapy technologies in-licensed from an Italian biotechnology company and Indiana University to treat leukemia, solid tumors and HIV/AIDS. It has been conducting clinical trials with the gene for vascular endothelial growth factor (VEGF) to produce new blood vessels in legs disabled by circulatory problems—an effort that closely parallels that of Gene Angiogenesis (Chapter 4). Most Variants of VEGF, the genes coding for it, and even therapeutic methods were discovered by researchers in the US and Europe, and related patents are held by US and European universities and companies. Among the key technologies underlying its current genetic engineering/protein synthesis core business, mRNA interferase was invented by New Jersey Medical and Dental University researchers, and the cold-shock expression vector system was jointly invented by researchers at the same university and Takara Bio. (Various public sources including www.takara-bio.co.jp and the USPTO patent data base.)
36. Hayakawa (2003). In 2002, biotech R&D accounted for 3.1 billion yen (∼US$28 million) compared with 500 million yen (∼US$4.5 million) related to brewing. Beginning in 2004, Takara Bio was planning to increase R&D expenditures to almost US$50 million annually.
37. About 56% in 2002.
38. Since 1999 when JT purchased the international tobacco operations of RJR Nabisco, JT has marketed Camel, Salem, and Winston cigarettes outside the US. Non-US sales of these brands substantially exceed US sales. In 2003, tobacco accounted for over 81% of JT's net sales, food products 12%, and pharmaceuticals 5%.
39. About 20% in 2002.
40. For the fiscal year ending March 2004, pharmaceutical R&D expenditures were down by 34% compared to their peak of 35 billion yen (about US$330 million) in the fiscal year ending March 2002.
41. This new class of drugs is known as cholesteryl ester transfer protein (CETP) inhibitors. Pfizer is also developing a drug in this class.
42. One exception is sorivudine, discovered by scientists at Yamasa, a soya sauce maker and a new type of treatment for shingles and some types of herpes rash. Unfortunately, when given to patients receiving 5-fluorouracil (5FU), a common chemotherapy for cancer, it sometimes resulted in 5FU rising to toxic levels. Therefore it is no longer marketed as a systemic medication although it is now being developed as a topical medicine.

None of the Japanese drugs approved between 1998 and 2003 on a high priority basis by the US FDA originated in small foodstuffs or chemical companies, although one, the anticancer drug oxaliplatin, originated in a metals company.

43. The yeast is *Schizosaccharomyces* pombe. See Frederick D. Ziegler, Trent R. Gemmill, and Robert B. Trimble (1994). 'Glycoprotein Synthesis in Yeast', *Journal of Biological Chemistry* 269 (no. 17, April 29): 12527–5; and Michael A. Romanos, Carol A. Scorer, and Jeffrey J. Clare (1992). 'Foreign Gene Expression in Yeast: A Review', *Yeast* 8: 423–88. See also http://www.stratagene.com/Newsletter/vol10_2/p72-74.htm
44. Toshiba is cooperating with universities, such as Osaka University and Tokyo Women's Medical University, on development of this system.
45. 'Canon to enter pharmaceutical business, focus on DNA chip'. *Nihon Keizai Shimbun*, March, 29, 2005.
46. As opposed to diagnostic and therapeutic machines of which it has long been a leading developer and manufacturer—e.g. MRI and CT scanners, ultrasound machines, automated biochemical analyzers, and electron beam accelerators for radiation therapy.
47. Funded primarily by US NIH, US DOE, UK Medical Research Council (MRC), and the Wellcome Trust.
48. The following account is based on the following sources: Kambara and Takahashi (1993), Kishi (2004), Pollack (2000), Takeda Foundation (2001), Yoshikawa (1987), various materials from Hitachi, various Japanese and US government memoranda and reports, and interviews with industry officials and scientists.
49. Hunkapillar's team was working under the direction of Lloyd Smith and Leroy Hood, two well-known geneticists.
50. Later in 1998, PE and ABI were to bankroll the formation of Celera as ABI's sister company and Celera's entry into the genome sequencing race.
51. Amersham was to buy out Molecular Dynamics in 1999.
52. According to Hitachi scientists, no government funds were used, at least for the sheath flow R&D.
53. 'Concensus elusive on Japan's genome plans, 1998'. *Science* 243, March 31, 1998: 1656–7.
54. e.g. gene sequencing, functional genomics (predicting protein function from information about the genes that code for the proteins), protein structure determination, drug target identification, and prediction of adverse reactions to drugs.
55. One initiated around 2001 was intended to allow pharmaceutical companies to match their data on various proteins with the data on gene sequences held by a METI-affiliated research company, Helix, to help the pharmaceutical companies decide which of the proteins might be useful drugs or drug targets ('Firms to set up genome laboratory', *Asahi Shimbun*, May 5–6, 2001).

Another project initiated in 2004 involved Riken, Hitachi Life Science, the University of Tokyo, the National Center for Genomics Research, and fifteen companies in research to elucidate the genetic basis of various diseases and to construct a related database that would initially be open only to the consortium members and paying companies. (Riken, GSC shutai no genomu netto 9 gatsu shidou, bousai na bunshikan saiyou o DB ka [Beginning Sept. 2004 Riken's Genome Science Center to lead research into genome networks and construction of data base on multiple molecular interactions] (*Kagaku Kougyou Nippou* [Chemical Engineering News], Aug. 23, 2004).

56. This assessment is based on published reports in the general and trade-oriented press, but it is generally confirmed by discussions with biomedical researchers. It is possible, of course, that some members of the Hitachi group have made life science breakthroughs unrelated to relatively large-scale instruments that are not yet apparent. In 2002 Hitachi Life Science was planning to increase its number of employees to approximately 120 (Nikkei Shimbun Sept. 10, 2002, 8). It declined to release sales data.
57. Founded, respectively, by Stanford researchers in 1984, and by a researcher from Xerox PARC's Computer Science Laboratory in 1996.
58. In some projects of this nature, companies dispatch their researchers to the participating university laboratory where they may work alongside researchers from other companies involved in the project. In other cases, most of the R&D occurs in the corporate laboratories, and the university laboratory plays more of a coordinating and synthesizing role, perhaps hosting regular meetings where all the corporate and university researchers can discuss progress.
59. This echoes Christensen's (1993) observations how existing product lines and customers confined the perceived technology development options of large US manufacturers of computer hard disks, even though venture companies later developed small drives that captured most of the market from the large companies (see next Chapter 7).
60. Tunable lasers help to distribute the load of broadband Internet communication (e.g. enabling just in time capacity) and also allow optical communication infrastructure companies such as Lucent and Nortel to handle long and short distance communications in the same system.
61. Founded in 1998 by researchers at the University of California at Santa Barbara.
62. Spun off from Seagate in 2000.
63. Santur was founded in 2000 by researchers and managers from SDL and who were soon joined by key personnel from Nortel/Xros. SDL was a manufacturer of semiconductor diode lasers for fiber optic data transmission. It was formed in 1983 as a joint venture between Xerox and Spectra Physics, but it was bought out by a competitior, JDS Uniphase for US$41 million in 2000, the same year that some of its staff left to form Santur.

64. As of May 2005, Agility had eighteen issued US patents and ten published pending patents, Iolon twenty-one issued patents and two published pending patents, and Santur seven issued patents and one published pending patent.
65. This is not, however, to say the position of the US ventures is secure. In 2004, reports were circulating that Agility was in trouble, although in early 2005 it was still releasing new products. See Agility's February 28, 2005 press release available at www.agility.com. See also the August 6, 2004 report, Iolon's Alright, available at www.lightreading.com
66. See the discussion of consortia research in ch. 7 and the example of Phoenix Wireless in Chapter 4.
67. Perhaps, in this case, overmatched.
68. See the summary of carbon nanotube electronics under NanoMarkets. Market Report: Semiconductors/Electronics (May 4, 2005) available at www.nanomarkets.net. The companies identified in this summary are:

    Large Japanese: Fujitsu, Hitachi, Mitsubishi, NEC, Noritake and NTT
    Large US: DuPont, General Electric, IBM, Intel and Motorola/Freescale
    US ventures with founding date and university affiliation (if university source of core founding technology): Eikos (1996), Molecular Nanosystems (2001, Stanford), Nanomix (∼2001, U California at Berkeley), Nano-Proprietary (1989), Nantero (∼2000, Harvard), and Xintek/Applied Nanotech (2000, U North Carolina)
    Large Korean: Samsung
    Large European: Infineon, the 1999 spin-off of Siemens's semiconductor operations

69. See NanoInvestorNews.com. Nanotech Company Distribution (Nov. 15, 2004) available at www.nanoinvestornews.com under Facts and Figures.
70. Regarding government budgets, the Tokyo Office of the NSF estimates that Japanese government support for nanotechnology R&D amounted to 94.6 billion yen in 2003 and 93.5 billion yen in 2004. (See Report Memorandum 05-02, Japanese Government Budgets for Nanotechnology JFY, 2005 available at www.nsftokyo.org.) Nano Investor News estimated that in 2003 US, Japanese, and EU government spending for nanotechnology R&D amounted to 800, 780, and US$660 million, respectively (available at www.nanoinvestornews.com under Nanotechnology Facts and Figures). Since nanotechnology encompasses many fields including biology, materials, and electronics, estimates may vary according to the definition of *nanotechnology*.
71. See Chapter 7.
72. Toyota Motors was spun off from Toyoda Automatic Loom in 1937, two years after the latter began to produce trucks for the army. Toyoda Automatic Loom was itself a spin-off from Toyoda Boshoku, established in 1895 by Sakichi Toyoda who invented high quality automatic looms.

Fujitsu was spun off from Fuji Electric in 1935 in order to concentrate on automatic exchange equipment and telephone sets. Fuji Electric was established in 1923 as an electrical machinery joint venture between Furukawa Electric and Siemens. Furukawa Electric was spun off in 1883 from Furukawa Co., a copper mining company, in order to concentrate on wire making. Fujitsu itself spun off a high technology robotics subsidiary, Fanuc in 1972.

Mitsubishi Electric was spun off in 1931 from Mitsubishi Shipbuilding (now Mitsubishi Heavy Industries) so that the former could pursue its own growth and be more independent with respect to manufacturing equipment, components, administrative resources, engineers, and sales. Mitsubishi Heavy Industries also spun off its automobile division in 1970 to form Mitsubishi Motors.

Nomura Securities was spun off by Osaka Nomura Bank in 1925. Managers of the bank thought it was necessary to separate the capital of the banking and securities operations as the securities industry grew, and thus formed a separate securities company that could expand into this growth area. In 1926 the parent bank then changed its name to Nomura Bank and then in 1948 to Daiwa Bank (no connection with Daiwa Securities, Nomura Securities's largest competitor). In 2003 Daiwa Bank merged with Asahi Bank to become Resona Bank. But Resona, beset by financial troubles in 2003, is a less prominent in the banking industry than its child, Nomura Securities, is in the securities industry.

JAFCO was established in 1974 with the backing of Nomura Securities and other financial institutions such as Nippon Life Insurance and Sanwa Bank, and it has remained Japan's largest VC company in terms of invested capital.

Sources: Ito (1995) and Ito and Rose (1994). Also Odagiri and Goto (1993) with respect to the entrepreneurship of Sakichi Toyoda, and various corporate histories with respect to Nomura and JAFCO.

73. Matsushita sells under brands such as Panasonic, National, Technics, and Quasar. The Matsushita group includes Japan Victor Corporation, which originated the VHS standard and which is majority owned by Matsushita.
74. The notion of *Hitachi* or *Matsushita group* brings up the complicated issue of terminology. These membership totals are from Ito (1995), whose definition of *group* probably means companies affiliated by familial (spin-off) relationships or companies in which one of the main members has acquired a significant ownership interest, usually by acquisition or joint venture.

    As used by Odagiri, however, the notion of *keiretsu* (literally *related linkage* or simply *linked companies*) focuses on supplier–assembler relations within a particular industry. So under this definition, keiretsu would include a dominant manufacturing firm, its related spin-offs and acquired subsidiaries, and companies linked by long-standing subcontracting relationships (*shita-uke* and more independent subcontractors). In other words, it could be narrower than the notion of corporate group (because it is limited to a particular industry or even a particular line of manufacturing) or broader (because it includes companies linked only by subcontracting relationships).

Another definition of *keiretsu*, which Odagiri (1992) calls *kinyu-keiretsu* (financially linked companies), refers to a group consisting of a bank and the companies for which it is the main supplier of funds. Prior to the consolidation of Japanese banks around 2002, the most influential kinyu-keiretsu were those organized around the most influential banks, Mitsubishi (Tokyo-Mitsubishi after its merger with the Bank of Tokyo), Mitsui (now merged with Sumitomo to form Sumitomo-Mitsui), Sumitomo (merged with Mitsui), Fuji (Yasuda before World War II, now merged with First Industrial Bank and Industrial Bank of Japan to form Mizuho), Sanwa (now part of UFJ which merged in 2005 with Tokyo Mitsubishi to form Mitsubishi-UFJ), and First Industrial Bank (Daiichi Kangyo, now part of Mizuho). Gerlach (1992), Odagiri (1992), and Gilson and Roe (1993) provide helpful descriptions of these kinyu-keiretsu. Odagiri emphasizes the independence of the kinyu-keiretsu members, noting that rates of cross shareholdings and shareholdings exclusive to group members are not particularly high—which should be even more so today as banks and companies have sold many of their cross held shares. He concludes the main benefits they offer to their members are information exchange, some degree of mutual insurance, and reduction of the risk of hostile take over.

75. See Odagiri (1992), Ito (1995), Dyer (1996), and Gerlach (1992), all of which describe the role of spin-offs in the Japanese economy. None of these estimate the proportion of new, technology-oriented companies accounted for by spin-offs. But according to Ito, 17.5% of the companies listed on the Tokyo Stock Exchange were spin-offs, in contrast to only 20 (1.3%) of the companies listed on the New York Stock Exchange (17 of which were established as the result of antitrust actions).
76. e.g. entrepreneurship, motivated staff, flexibility, and access to private capital.
77. Especially access to supply and distribution networks, manufacturing resources, funding, and other complementary assets.
78. Until very recently, and still within many organizations, wages within a company have been primarily seniority based. Transferring workers into a start-up allows them to be paid according to different salary scales and also to have different retirement benefits (Odagiri 1992). Also Chesbrough (1999), quoting from T. Tatsura and S. Adachi (interview at the Tokyo office of FDK, a Fujitsu spin-off), Tokyo, March 19, 1998).
79. Ito (1995) and Odagiri (1992). Ito notes that in order for spin-offs to provide greater employment opportunities, the spun-out operations need to grow faster in the spin-offs than they would have if they had remained within the parent.
80. Odagiri (1992) describes examples of spin-offs from NEC to manufacture relatively low technology components. Chesbrough (1999) describes examples of

spin-offs from Hitachi, Fujitsu, NEC, Toshiba, and Matsushita, some of which engaged in sophisticated development of disk drives (HDD). For example, NFL, a joint venture formed by Hitachi and Fujitsu, was the first Japanese company to reverse engineer the IBM 3340 and 3350 disk HDDs and to develop 8″ and 5.25″ HDDs. Other spin-offs or partially owned subsidiaries also manufactured HDD; NEI for NEC; Fuji Electric (Fujitsu's parent) for Fujitsu; and JVC, KME, MKE, and MCI for Matsushita. Other spin-offs developed HDD testing equipment (e.g. Hitachi DECO), manufactured HDD heads (e.g. Hitachi Metal and FDK from Fujitsu), or provided maintenance for such heads (e.g. Hitachi Electric Service).

81. Suntory's spinning off its pharmaceutical operations just before their sale to Daiichi may be an example of preparation for divestiture, while the spinning off of Takara Bio from Takara Shuzo and UP Science from Sumitomo Electronics (see below) may be examples of preparation for raising outside funds.
82. Some of the HDD spin-offs mentioned in note 80 above are probably examples of high technology spin-offs formed to give the new companies greater operational flexibility than they would have had as branches within their parents.
83. Ito (1995) and Dyer (1996). See Odagiri (1992) for evidence that the proportion of diversified firms is smaller in Japan than the US.
84. In economists' terms, specialized assets are vital to the productivity of any firm. Centralized management of a variety of specialized assets can create economies of scope. Sometimes, however, these economies of scope are not achieved and the transaction costs associated with management, e.g. difficulties in coordination, bureaucracy, loss of individual initiative, shirking, low morale, etc., outweigh the benefits from accumulation and central management of specialized assets. (Ito 1995, Dyer 1996).
85. Interestingly, these unaffiliated Japanese suppliers relied to a lesser extent than either the American affiliated or unaffiliated suppliers on one auto manufacturer for their sales (19% of sales to one manufacturer for the Japanese independent suppliers, on average, vs. 34% for both the US affiliated and independent suppliers). So the greater cooperation among the Japanese firms was not due to the Japanese suppliers being more beholden to the main manufacturer than their American counterparts.
86. Of some interest, the same advantages that Dyer attributes to Japanese manufacturing families compared to US integrated companies, particularly the disincentives to innovation faced by internal suppliers, could also be attributed to independent ventures with respect to manufacturing groups. In other words, taking Dyer's analysis at face value and extending it to its logical conclusion, the ideal supplier–manufacturer relationship would be independent small companies as suppliers, provided they could communicate effectively with the manufacturer. The subsequent discussion in the text deals with some of the problems that arise when a main manufacturer tries to exert too much control over spin-offs and other subsidiaries.
87. See e.g. Asanuma (1992), Odagiri (1992), and Nishiguchi and Ikeda (1996) with respect to the automobile industry. See also Friedman (1988) and

Whittaker (1994) with respect to innovation in machine tools and other fields of manufacturing.

88. Odagiri (1992) and Hikino, Harada, Tokuhisa and Yoshida (1998) use the term *manufacturing keiretsu* to refer to such families or groups of firms centered around a dominant manufacturer. See also n. 74.
89. Overall about 17% of parent companies' management staff is on loan to spin-offs—including about 12% of director level executives. Overall, about 7% of total employees are on loan to spin-offs (Odagiri 1992 citing 1989 Ministry of Labor statistics). (Some of these may be to non-spin-off affiliates.)
90. Odagiri (1992).
91. Ito (1995).
92. Among the 171 companies in Toyota's supplier association in 1985, Toyota owned at least 20% of the stock of only 36 of these companies (21%), indicating that the glue that holds together Toyota's family is probably not shareholding but simply long-term involvement in Toyota's production process. (One of these is Nippon Denso, a 1949 spin-off from Toyota which is now the largest producer of electronic automobile components in Japan, and which was 30% owned by Toyota in 1990.) Even among these 36 firms, 16 (44%, including Nippon Denso) were members of the supplier association of another automobile manufacturer. *But only two of these were members of Nissan's supplier associations.* In other words, membership in one manufacturing *family*, even to the extent of being a spin-off, often does not preclude membership in that of a competitor. Nevertheless, there are limits to the freedom of family members to diversify their markets, and it seems that Toyota would not tolerate suppliers working with an arch-rival if there were danger of technology leakage. Also other main manufacturers may typically exert more control over their spin-offs and other partner companies (Odagiri 1992).
93. Although as the economic slump that began around 1990 grew longer and as large manufacturers began to outsource more of their operations to China and other Asian countries, the limits of these mutual obligations have often been reached, and many subsidiaries have had to diversify their customer and technology base. It is not clear the extent to which spin-offs receive preferential treatment compared to independent subcontractors (*shita-uke* companies) in hard economic circumstances.
94. CMD Research (Keio U, 47% owned by Simplex), InternetNode (Keio U, 50% owned by Yokogawa Electric), EcoPower (Keio U, 82% owned by Ebara), GenoFunction (AIST, 95% owned by Hisamitsu Pharmaceuticals), Summit GlycoResearch (UT, >33% owned by Sumitomo Pharmaceuticals), Fluidwave Technologies (UT, >33% owned by Pentax), StarLabo (UT, 40% owned by Sumitomo Electric). Probably most of these university-related spin-offs arose by the 'parent' backing formation of a new company based on discoveries from UT, Keio, or AIST. See the analysis of the startup from these three institutions in Chapter 4, Appendix 2.
95. GenoFunction and EcoPower.

96. See Chapter 4, Appendix 2 Table 4A2.4.
97. These enzymes are involved in the intracellular decomposition of proteins, and dysfunctions of these enzymes are linked to various diseases.
98. Sumitomo Electric News Release, Nov. 2, 1999, announcing the formation of UP Science.
99. JAFCO and Sumitomo Pharma would have substantial minority shareholdings and be represented on the board of directors.
100. The fact that the employees ended up without a bridge back seems somewhat unusual for Japanese spin-offs. It suggests that one of SEI's main motives in forming the company was cost savings, i.e. it wanted to shed its biomedical research division, and SEI's willingness to support UP Science through rough business periods may have been limited.
101. Two have had IPOs Takura Bio and DNA Chip. However, of 13 Japanese bioventures identified at the end of 2006 by an organization that follows the biotech sector closely as having drugs in (or about to start) formal clinical trials, only one Takura Bio, is a tethered spin-off (Tsujimoto, Kenji, 2006. 'Sector view and introduction', presentation at the 13th Nomura Bio Conference (Tokyo, Nov, 20). This spin-off's therapy in human trials is based upon technology in-licensed from abroad. (I happen to know of two other tethered spin-offs that together have three drugs in (or about to start) formal clinical trials. Both of these companies have the same, mid-size pharmaceutical parent. Two of the drugs are licensed from the parent. The third was discovered in a university.) Among the other tethered bioventures with which I am familiar, two had annual revenues over US$1 million in 2005—mostly from contract research.
102. Zahra (1996) surveyed US biotechs in the early 1990s and found that those started by independent entrepreneurs and those owned by established companies had introduced similar numbers of new products, but the independent biotechs had more pioneering products and higher sales.
103. These sixty were competitively selected from among the employee business plans, and financed by an internal fund to start new ventures based on such business plans (Rtischev and Cole 2003).
104. From a 2005 communication.
105. Conversations I have had with venture companies substantiate this, although most of these conversations have been with independent ventures assessing the conditions of tethered spin-offs. It is not so much that there is an absolute prohibition against strategic alliances with outside group companies, but rather that such alliances need special approval from the parent and important decisions related to the alliance require frequent back and forth communication with the parent.

    Lincoln and Gerlach (2004) tabulated reports between 1992 and 1997 from the *Nikkei Shimbun* and similar newspapers about alliances involving 128 large publicly traded Japanese which they classified as belonging either to one of ten vertical networks (Hitachi, Toshiba, NEC, Fujitsu, Sony, Matsushita, Oki, Kobe Heavy Industry, Sumitomo Electric, and Yasukawa Electric) or to none of these networks. They found that the likelihood of R&D alliances between firms in different networks was not different from the likelihood of alliances between firms in the same network. However, considering the sources of these reports, these alliances probably dealt with mature or downstream technologies. Moreover, the analysis does not consider what was at stake for the parent in the alliance and how it turned out. The case described below of Elpida, the joint venture spin-off of Hitachi's and NEC's DRAM operations, is an example of a strategic alliance with a strong R&D component between two large companies from different families. However, it involved protracted negotiations between NEC and Hitachi.

106. This constraint on growth is also suggested by Odagiri (1992: 196, Chapter 7), who notes that when the markets a new firm wishes to enter are already served by other members of the same group, entry is often discouraged because it is likely to create intragroup competition, which will threaten the group's harmony and cohesion. See also Hikino et al. (1998: 117) who describe the same process of inhibited competition among chemical companies that are members of the same bank keiretsu.
107. These observations echo descriptions of the Japanese chemical industry, where construction and operation of large petrochemical complexes required the participation of many companies, usually from the same manufacturing or bank keiretsu. Hikino et al. (1998) observe, 'The complexity of the ownership, transactional and operational ties among firms forming a petrochemical complex became a significant structural rigidity. [D]ownsizing often meant the liquidation of those enterprises, a strategy that their management (and some of their parent companies) vigorously opposed.'
108. Chesbrough (2000), summarizing the first-hand account of Hollister Sykes in 'The Anatomy of a Corporate Venturing Program: Factors Influencing Success,' *Journal of Business Venturing* 1 (1986): 275–93.
109. Chesbrough (2000) summarizing studies by Eric von Hippel, Norman Fast, Kenneth Rind, R. Siegel, E. Siegel, and I. MacMillan.
110. Discussion with Robert Myers, Fairfield Resources International and Adjunct Professor, Columbia School of Business, Nov. 3, 2004.
111. Other such benefits including hiring outsiders as CEOs and financing in staged milestone-dependent increments (Chesbrough 2000, Chesbrough and Socolof 2000).
112. These include flexibility regarding life of fund (no end-of-fund drive for liquidity), ability to rejoin company, the associated retention of group learning, and the potential for large-scale funding for capital intensive businesses.
113. The following builds on the analysis in Chesbrough and Socolof (2003).
114. Ito (1995) makes this point most clearly, but it also appears to be the consensus among other observers of Japanese industry.
115. See Takahiro Shibuya (2003), 'Fujitsu fosters spin-off system'. *Nikkei Weekly*, November 24, 2003, 37. In contrast, Mr Yuji Mizuno, senior staff writer of the *Nihon Keizai Shimbun*, considered Hitachi's plan to launch more spin-offs 'hardly different from organizational reforms of a smaller scale,

where authority is delegated to departments or sections'. Mr Mizuno added:

> Concerned about keeping various operations within the group, Japanese companies tend to transfer assets from one company to another, thereby failing to improve business efficiency. . . . If Japanese companies want to be truly accountable to shareholders, giving up their stake in spinoffs is worth considering. . . . In contrast [to US corporations such as ATT and Hewlett Packard], Japanese companies resist spinning off some [independent] businesses, citing the importance of maintaining synergy. But the practice of expanding a corporate group at the expense of business efficiency does not really benefit shareholders regardless of what it does for synergy. ('Time is ripe for spinoffs in true sense'. *Nikkei Weekly*, October 15, 2001, 9).

116. See the following three articles on Elpida in the *Nikkei Weekly*: Shuhei Yamada, 'Sole DRAM maker sets the bar high', Nov. 24, 2003: 12; Hiroyuki Shioda, 'DRAM maker Elpida ready for big time', June 20, 2004: 30; and 'Elpida goes solo with daring scheme', Nov. 22, 2004: 3. I am also grateful to Professor Yoshitaka Okada of Sophia University for information related to Epilda, some of which will be contained in his forthcoming book, *Struggles for Survival: Institutional and Organizational Changes in Japan's High-Tech Industries* (Springer-Verlag). Any misrepresentation of Professor Okada's perspective is my responsibility.
117. UMC is a Taiwanese chip foundry.
118. These 2003 outside investments totaled about US$1.6 billion, of which Intel contributed US$110 million.
119. Hikino et al. (1998: 118).
120. Ito (1995).
121. Six billion yen, 1 US$ being equivalent to about 300 yen in 1972.
122. Early revenue and employment data at www.fanuc.co.jp/ja/profile/ir/index.htm
123. e.g. the inability of large corporate bureaucracies to anticipate market demand and to allocate adequate resources in a timely manner to R&D projects in new fields, and excessive control over spin-offs. Moreover, lifetime employment may be prevalent in other countries including those of Continental Europe and Korea.

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