

The Emerging Biomedical Innovation System in Kobe, Japan

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Biotechnology in Japan: Overview

- Market growing at around 7 % per year:
 - 819 billion yen in 2002 (\$ 7.9 billion at current exchange rate)
 - Of which the market for bio-pharmaceutical products is 539 billion yen.
- Major products similar to those in the US
 - EPO is biggest seller (15 % of total market)
 - Followed by monoclonal antibody-based diagnostics (8 %), human growth hormone (7 %), and human insulin (6 %), GCSF (5 %).
- Expected to grow to 25 trillion yen in 2010, or about 17 percent of the size of the US market.

- Sector historically dominated by large drug, food, and chemical companies.
- Explosive growth in number of biotech start-ups since late 1990s:
 - To 334 in 2003, according to the Japan Bioindustry Association:
 - Medical/Health care related: 153
 - Research services: 154
 - 112 in Tokyo; 21 in Osaka, 20 in Kyoto, 9 in Hyogo
 - Employing 6,757 people
 - Generating 105 billion yen (\$ 1 billion) in sales.
 - Half employ less than 10 people.
 - Formed at rate of about 15 per year in 1990s, accelerating to 40-50 per year from 1999 to 2002.

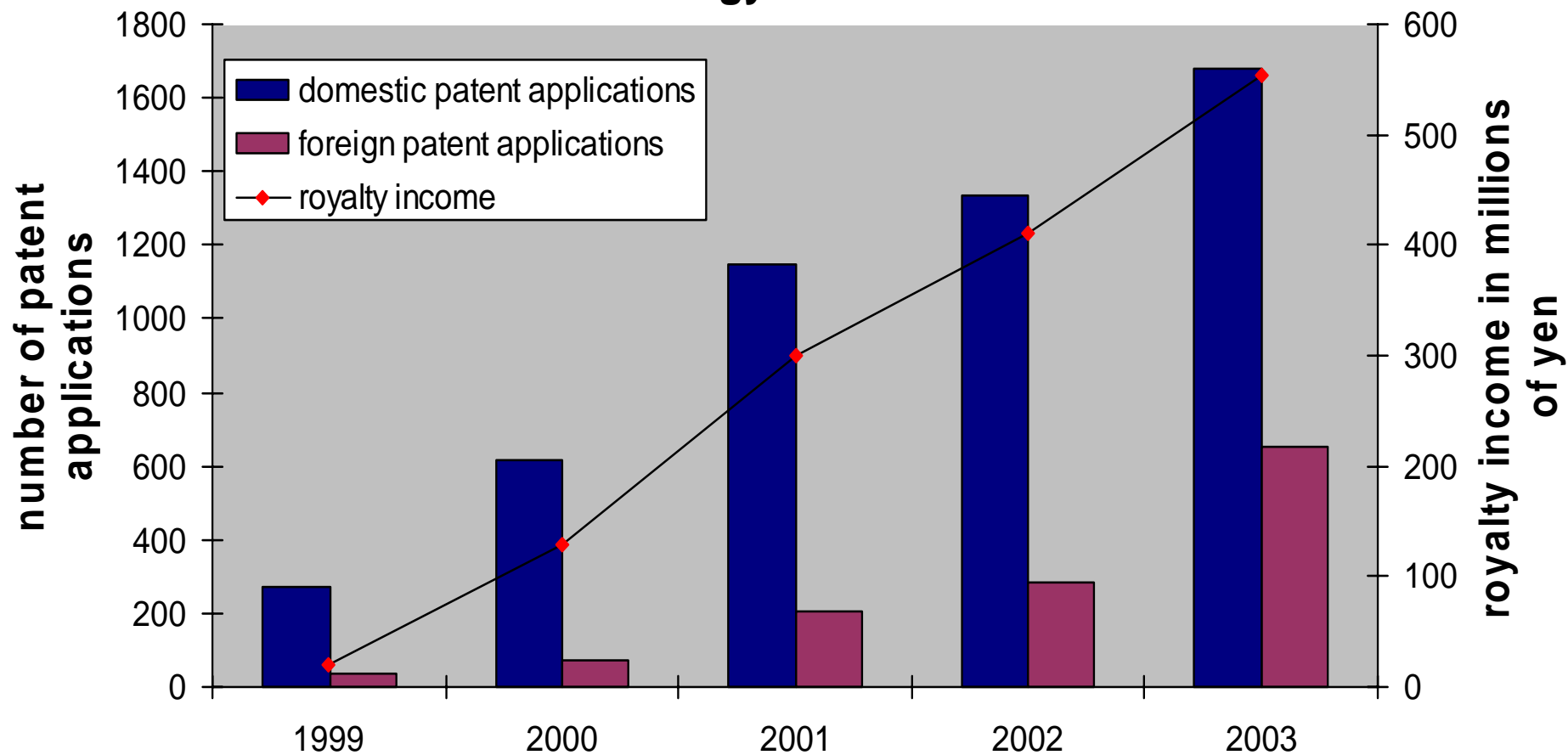
Boom and Bust

- In past 4 years, 12 biotech start-ups (the “bioventure 12”) have gone public against the backdrop of a mini “bio-boom.”
- Mini-boom has turned to mini-bust over the past year: the bio-venture stock index rose from 100 on April 1 to 120 on April 28, then fell to 60 by the end of September. Why?
 - Downward revisions of projected earnings.
 - Correction of sharp initial jump in initial offering price.
- This year expect to see initial Japan listings of three biotech firms established by Japanese nationals in the US.

- Part of the energy has come from major revisions to regulations governing university-industry collaborations and technology transfer.
- National universities became independent corporations on April 1, 2004, giving them effective control over the management of their intellectual property.
- Result is a sharp jump in patenting and licensing activities by universities.

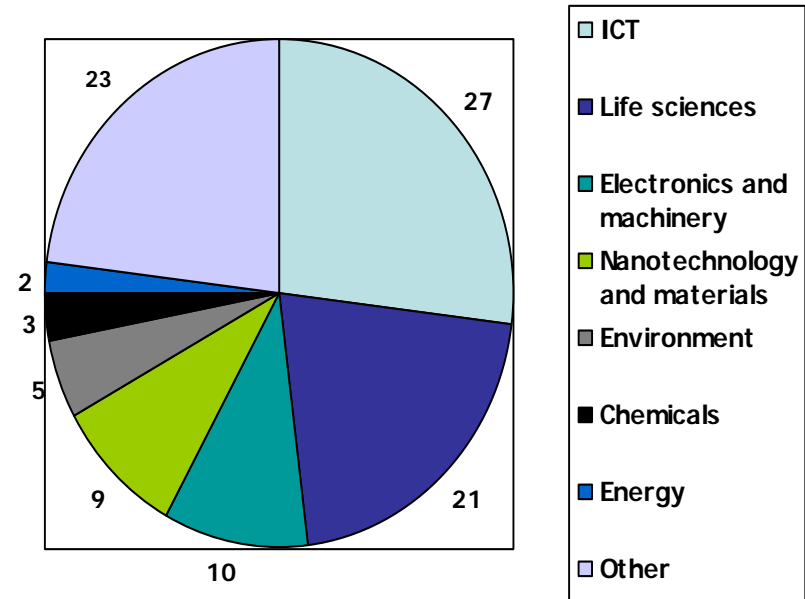
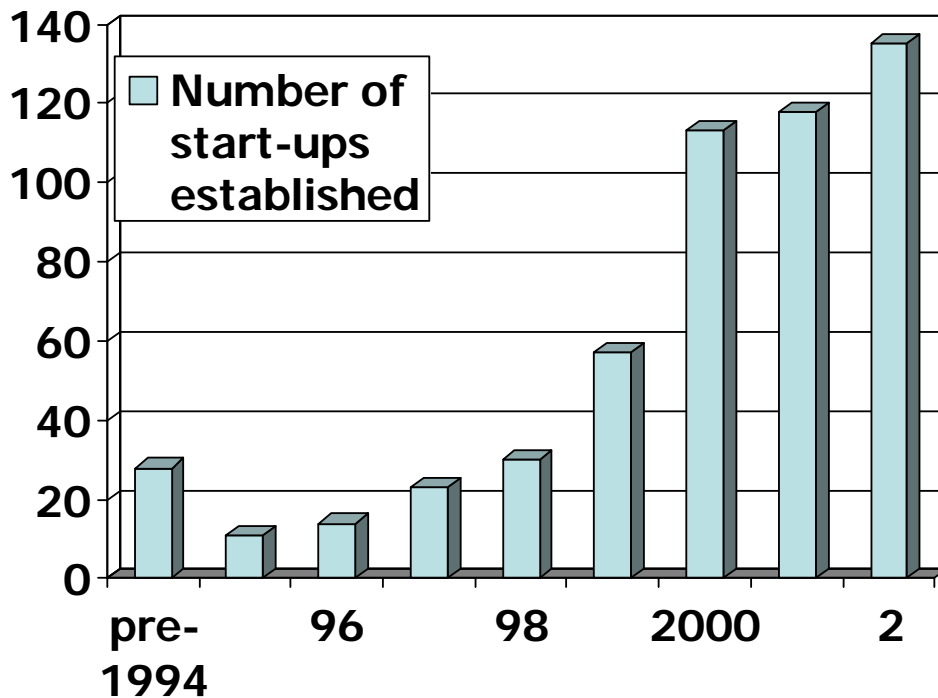
University Technology Transfer Activity

Recent Technology Transfer Indicators



Source: Ministry of Education

Trend in Formation of University-Affiliated Start-Ups



Source: National Institute of Science and Technology Policy

Welcome change that may halt the slide in Japan's international competitiveness!

Institute for Management Development (IMD) World Competitiveness Score:
Japan's Rank and Score in 2004

	Japan's Rank	Score	Country Ranked No. 1	No. 1 Country's Score
Business Efficiency	37	47.9	US	86.693
Infrastructure	2	81.943	US	100
Economic Performance	17	58.720	US	90.502
Government Efficiency	37	46.791	Singapore	84.333

60 economies ranked on 323 competitiveness criteria, hard and soft, grouped into the four categories shown in table. See <http://www02.imd.ch/wcy/factors>

Regional Specialization and Clustering in Biotechnology

- As in the US, different regions in Japan are specializing in different market niches.
 - Medical devices: Yamaguchi, Kyoto, Tokushima
 - Agriculture: Wakayama and Hokkaido
 - Food: Hokkaido, Shizuoka, Niigata, Mie
 - Pharmaceuticals: Kobe, Osaka (Saito), Shizuoka, Chiba
- Nikkei Biotech, a publisher, has identified 42 emerging biotechnology clusters. The top five:
 - 1 **Kobe (Hyogo)**
 - 2 Sapporo (Hokkaido)
 - 3 Ibaragi (Osaka)
 - 4 Kurime (Kyushu)
 - 5 Tsu (Mie)

The Kobe Biomedical Cluster

- Serves local population of about 1.5 million.
- Less than 3 hours by bullet train from Tokyo.
- Historically important port city.
- About to be served by new Kobe Airport being built off Port Island.
- Tightly linked to the broader Kinki economy, which includes Kyoto and Osaka.



Comparison with Seattle

- *Like Seattle*, Kobe developed as a major port city with a significant foreign population.
- *Like the Puget Sound Region*, the Kansai region is home to many excellent universities and research institutes:
 - Especially the schools of medicine of Kobe, Osaka, and Kyoto Universities; and the RIKEN Center for Developmental Biology and Tissue Engineering Research Center.
- *Unlike Puget Sound*, the Kansai region is home to several large drug companies, such as Shionogi, Takeda, Eisai, and Fujisawa.
- A major difference between Kobe and Seattle is that the Kobe cluster is taking shape as part of a grand plan: the Kobe Medical Industry Development Project.
 - The project leverages support from the City of Kobe, Hyogo Prefecture, and private sources.
 - The central government also provides support through several regional policy initiatives aimed at revitalizing regional economies and promoting the development of industrial and knowledge clusters.

Background to Kobe's Biomedical Research Cluster

- Born of crisis! Kobe's great earthquake of January 1995.
 - Killed more than 6,000 people and lopped 7 trillion yen (\$68 billion) off the economy.
 - By end of 2003, the economy had recovered only 80 percent of pre-earthquake output.
- And of a perceived need for reform of the health care system:
 - Everyone covered under a comprehensive health insurance system.
 - But rapidly aging population and increase in chronic illness pushing up costs rapidly.
 - Leading to the need for government to hold down or lower drug prices.
 - Resulting in sharp drop in numbers of drugs in Phase 2 and 3 trials.
 - Diminishing the international competitiveness of domestic drug firms.
 - Exacerbated by the introduction of new GCP (Good Clinical Practice) system in April 1998.

- The result was a proposal to lift the economy through investment in a future-oriented medical industry complex that would
 - Create the infrastructure of a next-generation medical system.
 - Raise the level of medical services and improve the welfare of Kobe's citizens.
 - Develop a cluster of new medical-related firms while using new medical technologies to raise the performance of existing enterprises.
 - Be located on Port Island Phase II, the land of which was owned by the city of Kobe.
- Based on planning studies, the city determined that over two decades, the project would create 18,000 new jobs in Kobe alone, and 23,000 in the entire Kansai region.

- In October 1998, the “Kobe Medical Industry Development Project” study group was established.
 - Chaired by Dr. Hiro Imura, former president of Kyoto University, at the time the president of Kobe City General Hospital.
- Issued report in March 1999, and decision made to go forward in August.
 - This is amazingly fast by Japanese standards!
 - No doubt in part a testimony to Dr. Imura’s determination, vision, and power of persuasion.

- Factors influencing the decision to move on the proposal:
 - Establishment of WHO Kobe Center
 - Expectation that the economic effects of the project would extend throughout Kansai.
 - Excitement over progress in sequencing the human genome and prospects for regenerative medicine.
- The Foundation for Biomedical Research and Innovation was established in March 2000 to manage the project.
- The RIKEN Center for Developmental Biology opened at the site April 2002, followed by...
- The Kobe International Business Center in June...
- The Translational Research Informatics Center in March 2003...
- The Institute of Biomedical Research and Innovation fully opened in April 2003.

Plugging into the Kansai Network

- The regional Kobe project quickly became part of broader regional and national projects.
 - Designated, along with Osaka’s life science project, by national government as a special metropolitan redevelopment project.
 - Designated by the Ministry of Education as a “Knowledge Cluster” under its Knowledge Cluster Initiative.
 - Designated by national government as an “Advanced Medical Industry District”

The Concept

Establish on Port Island Phase II a base for research and development of advanced medical technology, and use the results to foster formation of a cluster of medical-related firms.



- Areas of focus:
 - R&D on medical equipment
 - Support for clinical research of new drugs
 - Clinical application of regenerative medicine
- Partners:
 - Kyoto, Osaka, Kobe Universities, private firms, RIKEN's CDB
- Goals:
 - Revitalize Kobe economy and secure new jobs.
 - Improve welfare of city residents through advanced medical technology.
 - Make international contribution to improve medical care elsewhere.



Port Island Phase II, looking south from Portopia Hotel.
Flanking the Portliner elevated train: Kobe Medical Industry Development Project
Background: New Kobe Airport under construction

Core Facilities

- Institute of Biomedical Research and Innovation:
 - Core facility for bridging basic research and clinical application.
 - Medical treatment and clinical research being carried out:
 - Hematopoietic stem cell transplants (bone marrow transplants, umbilical cord blood transplants).
 - Regeneration of peripheral blood vessels in the lower limbs and blood vessels in the heart.
 - Regeneration of alveolar bone and artificial dental root transplants for use the regeneration of alveolar bone.
 - Medical treatment using PET and CT-Linac
 - Treatment of brain blood vessels.
 - Cancer chemotherapy
 - Clinical trials on drugs and medical equipment.

- Bioethics deliberation council established Sept 2001
- Ethics guidelines released April 2004
- Conducting three major R&D projects on medical devices with a study group consisting of 74 companies, mostly members of the Kobe Machinery and Metal Firms Association, along with 11 medical device companies.
- Provide clinical trials support and training for local hospitals.
- Maintain human cell processing center, used jointly by
 - Kirin Brewery (medical treatment for leukemia using hematopoietic stem cells)
 - Olympus Corporation (bone regeneration)
 - Terumo Corporation (myocardium regeneration)
 - Osteo Genesis (regeneration of alveolar bone)

- RIKEN Center for Developmental Biology:
 - Japan's first center of excellence in regenerative medicine.
 - Director: Dr. Masatoshi Takeichi (Visiting Professor, Kyoto University Graduate School)
 - 7 core program directors, including Dr. Takeichi.
 - 243 researchers in 30 research groups.
 - Major research areas include cell differentiation and embryology, research on stem cells of planarian and drosophilae, birth mechanism of cloned mouse, and study of spinal vertebrae of zebra fish and mouse.

- Translational Research and Informatics Center:
 - Aims are to support translational research activities of Ministry of Education, provide data management support for clinical trials, and distribute information on cancer research reported monthly by the US National Cancer Institute.
 - Has wet lab and dry lab space.

- **The Biomedical Accelerator:**
 - Incubation facility with 11,000 sq meters of floor space.
 - Designed to foster cross-university and cross-disciplinary collaboration that will open up new opportunities for new bio-business creation.
 - Has cell processing center, animal laboratory, radio isotope facility.
- **Kobe International Business Center**
 - Offers warehouse, assembly, and manufacturing space; R&D laboratory space, and office space.
 - Will include a business incubation facility and center to support clinical trials.
 - Managed by Kobe City Urban Development Corporation

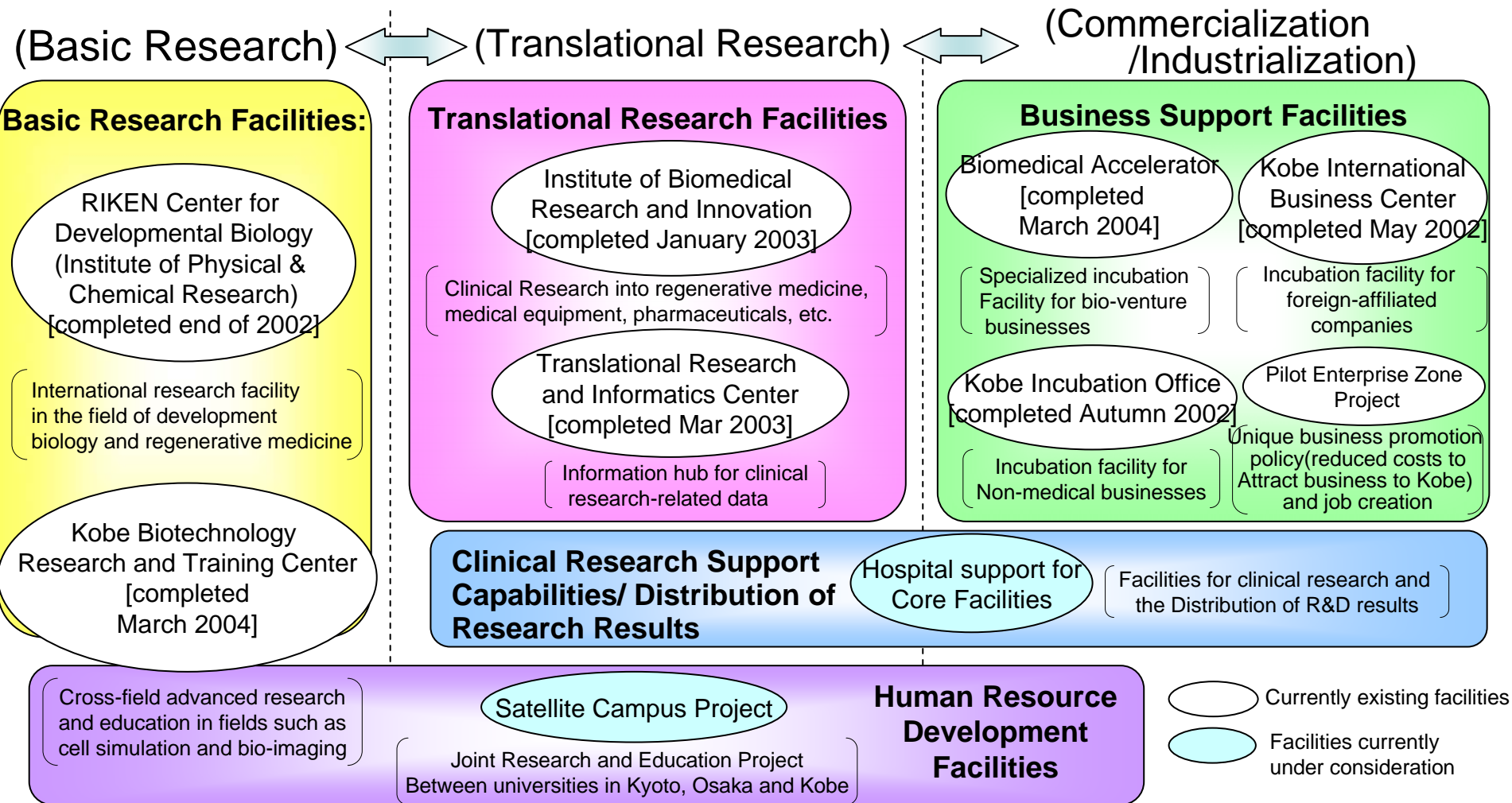
Support Available to Foreign Firms

- Assistance with developing incubation facilities.
- Introduction to venture capital funds.
- Subsidy for feasibility study.
- Subsidies for office rent, construction cost, and interest.
- Tax reduction and exemptions.
- Low-cost space in Kobe International Business Center.

Financial Support

- Kobe city provides incentives for companies to establish operations in designated enterprise zones, including rent subsidies, reduced taxes on fixed assets, and various lease payment systems.
- Kobe Biomedical Fund: Established by Sumitomo Mitsui Financial Group to support venture businesses related to biotechnology and medicine. Three funds, totaling 6.3 billion yen, have been set up to date.

Putting it all Together: Future Plans for Core Facilities



Source: Mr. Takeshi Yamamoto, Director of the Kobe Trade and Information Office in Seattle.

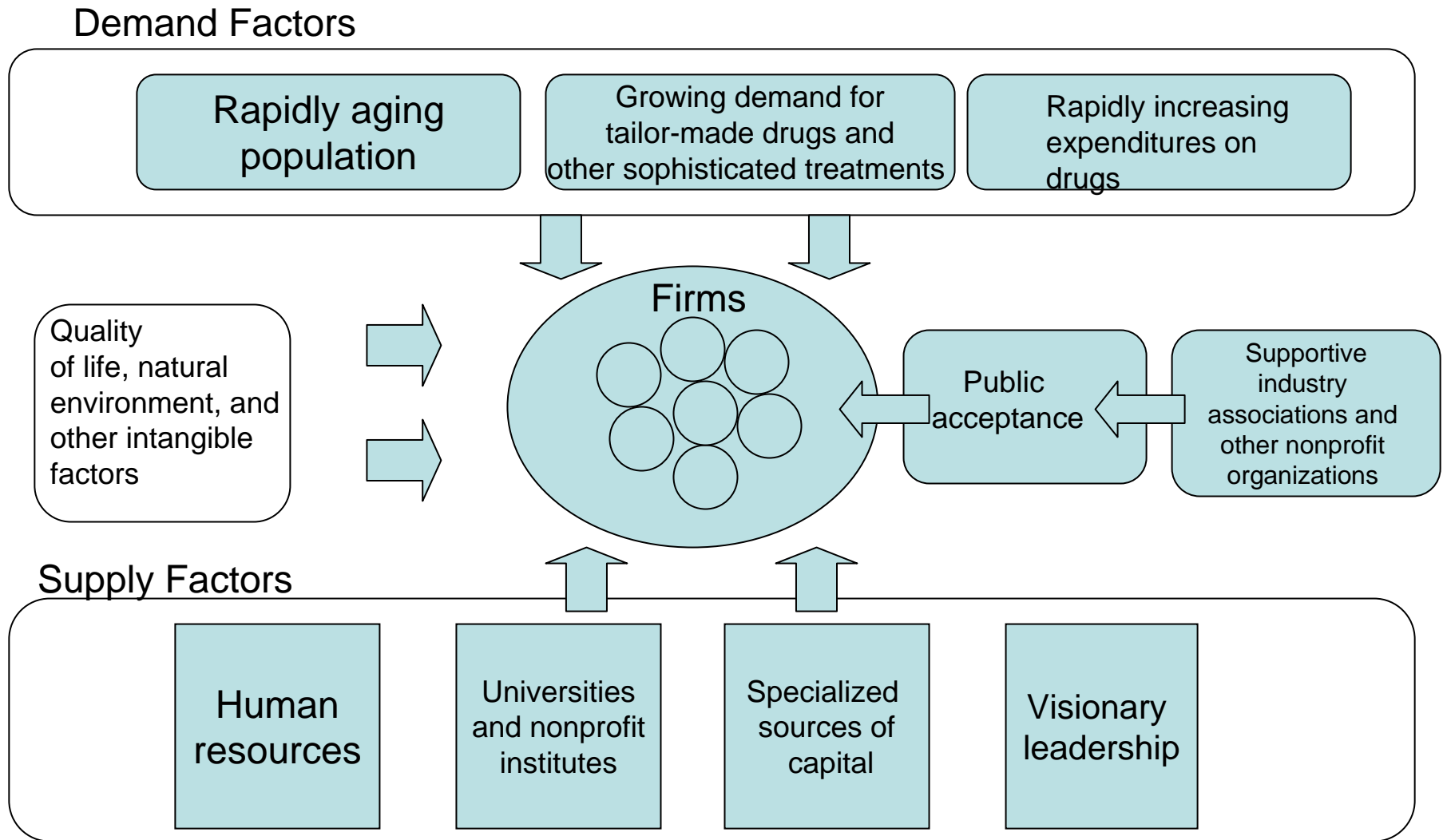
Accomplishments

- The Kobe project has attracted 73 foreign and domestic firms to locate on Port Island Phase II.
- It has involved dozens of local SMEs, mostly metal and machinery companies, in research projects related to medical devices.
 - 28 medical equipment projects have been completed; 18 are in development.
- Major projects are underway in the clinical application of stem cell and tissue engineering:
 - leukemia treatment using cultivated umbilical cord blood.
 - Regeneration of skin, cartilage and bone.
 - Regeneration of nerve cells, pancreas cells, and blood vessels.

Conclusions

- Kobe is well positioned to remain one of the major biotechnology clusters in Japan.
- Favoring Kobe is its mix of large and small firms, proximity to the historical center of the pharmaceutical industry in Osaka, and proximity to many excellent universities and research institutes.
- Also favoring Kobe is the crisis mentality that followed the 1995 earthquake. This probably forced the region's leaders to be more radical and creative in their thinking about how to revitalize the economy.

Factors Driving Cluster Development in Biotechnology



Supportive public policies, especially supports for academic R&D, protection of IP, smooth regulatory processes, and a strong framework for technology transfer

- The Kobe Medical Industry Development Project is striking in its ambition and philosophy. In developing the biomedical cluster, it correctly acknowledges the importance of..
 - Translational research as a means of bridging basic research with clinical application.
 - Locating complementary institutions in close proximity to each other.
 - The region's older SMEs, which have been invited to participate in the project's research.

- The project has already succeeded in attracting more than 70 companies.
- On the other hand, when governments take the initiative, there is always the chance that firms will be responding not to the market but to the opportunity to receive public assistance.
- So a big question: Will the Kobe cluster be self-sustaining once the public support has ended?

Acknowledgements and Sources

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- Thanks also to Mr. Takeshi Yamamoto at the Kobe Trade and Information Office in Seattle for providing helpful information and contacts, and to the National Institute of Science and Technology Policy in the Ministry of Education for research support and introductions.
- I also consulted the following resources in preparing this presentation:
 - *Nikkei Baio Nenkan* 2003
 - *Nikkei Baiobijinesu*, various issues, especially the December 2004 issue on regional biotechnology clusters in Japan.
 - Steven W. Collins, *The Race to Commercialize Biotechnology* (London: Routledge Press, 2004)
 - Various brochures and pamphlets produced by the City of Kobe