

Patent analysis of genetic engineering research in Japan, Korea and Taiwan

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The aim of this study is to reveal the research growth, the distribution of research productivity and impact of genetic engineering research in Japan, Korea and Taiwan by taking patent bibliometrics approach. This study uses quantitative methods adopt from bibliometrics to analyze the patents granted to Japan, Korea and Taiwan by United States Patent and Trademark Office (USPTO) from 1991 to 2002. In addition to patent and citation count, Bradford's Law is applied to identify core assignees in genetic engineering. Patent coupling approach is taken to further analyze the patents granted to the core assignees to enclose the correlations among the core assignees.

13,055 genetic engineering patents were granted during the period of 1991 to 2002. Japan, Korea and Taiwan own 841 patents and Japan owns most of them. 270 assignees shared 841 patents and 16 core assignees are identified by the Bradford's Law. 18,490 patents were cited by the 13,055 patents and 1,146 out of the 18,490 cited patents were granted to Japan, Korea and Taiwan. The results show Japan performs best in productivity and research impact among three countries. The core assignees are also Japan based institutions and four technical clusters are identified by patent coupling.

Introduction

The genetic resources become the “green gold” of the biotech century for the possible academic and commercial developments. The researchers from both public and

Received June 28, 2006

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0138–9130/US \$ 20.00

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private sectors flood into this field and start to seek the protection for the new “inventions”, and the information relates to the invention usually will not appear in other types of publications rather than patents before the patents are granted since novelty is one of the requirements for obtaining patents (WALKER, 1995). Due to the requirement of novelty, patents become valuable and unique resources for technical information.

North American and European countries have been the influential countries in genetic engineering research, and U.S. is the leading country among those countries (LO, 2004). However, the development of genetic engineering research among Asia countries should not be underestimated. The aim of this study is to investigate genetic engineering research done in Japan, Korea and Taiwan by taking patent bibliometrics approach. Besides the productivity and impact, the study also reveals the correlation of genetic engineering research among the priority institutions from these three countries. Japan, Korea and Taiwan are three leading countries in Asia in genetic engineering research based on the results from previous study. This study uses quantitative methods to analyze the genetic engineering patents with emphasis on the patents owned by Japan, Korea and Taiwan. The author examines 13,055 USPTO patents that relate to genetic engineering issued from 1991 to 2002 to give an overall view of the development of genetic engineering and the ones granted to Japan, Korea and Taiwan are studied in details. Besides revealing the distribution of the productivity and the impact of the genetic engineering research, the core assignees of these three countries are identified by applying the Bradford’s Law and patent coupling is used to reveal the correlation among the core assignees.

Literature review

Patent bibliometrics approach is taken in this study. The research adopts the methods from bibliometrics to analyze the patent information. The idea of using bibliometrics methods for analyzing patent information could be dated back to 1940s when Arthur H. Seidel proposed producing a citation index of the patent literatures in the *Journal of the Patent Office Society* and Harry C. Hart endorsed the idea in a later issue. (GARFIELD, 1979) Although the idea was brought up at that time, nothing was done of their suggestions. It was till 1964 when the first citation index to the patent literatures was published. Although the idea of building citation index for patent information was mentioned in 1940s, neither patent citation nor other bibliometrics methods was broadly applied for patent literature analysis until last decade. Several studies were done to bring the attention to the patent analysis over the past several decades and those studies found that only 10% to 20% of the patent information appeared in the journal articles, depend the various subject areas, and missing links occurred when analyses only done for journal articles (ALLEN & OPPENHEIM, 1979;

DEMIDOWICZ & OPPENHEIM, 1981; EISENSCHITZ et al., 1986; EISENSCHITZ et al., 1989; WALKER, 1995). The results demonstrated the necessity of further investigating the patent information.

NARIN (1994) applied the bibliometrics methods including citation analysis to establish the use of patent bibliometrics methods. Since then several studies had been conducted by taking the patent bibliometrics approach. Most of the works used the patent bibliometrics methods mainly deal with three issues, the productivity, impact and correlation. For the productivity, patent counting is the most common method used. By counting the number of patents granted each year, the growth of the research productivity could be drawn. The method was applied to analyze the productivity on countries, assignees, inventors (KARKI, 1997; NARIN, 1994; NARIN, 1995; NARIN et al., 1994; BANEJEE et al., 2000) and technology levels (RAMANI & LOOZE, 2002; LOPEZ-MUNOZ et al., 2003). As for the research impact studies, citation count was used as indicator to present the level of impact (MOED, 2000; ALBERT & PLAZA, 2004). Besides the cited patent count, counting numbers of shared patent citation, Patent Coupling, was applied to establish the technological relationships among countries, assignees, inventor and techniques in very limited studies. To establish relationships among documents various methods have been applied, including direct citing, reference to earlier documents, bibliographic coupling, citing same source documents (KESSLER, 1963), and co-citation, links cited documents through later documents (SMALL, 1973; CAWKELL, 1976; BELLARDO, 1980). Patent Coupling is transferring the bibliographic coupling method originally proposed by Kessler onto patent analysis. The hypothesis is two articles relate to each other if they share the same cited references. The relevance intensifies as the number of shared references increases. Every two-article form a bibliographic coupling pair and the ones with more shared cited references are more relevant to each other. The article-network could be built upon this hypothesis and the correlation could be also tested (WEINBERG, 1974; EGGHE & ROUSSEAU, 1990; GARFIELD, 1998). In this study, patents were reviewed instead of articles to show the correlation among core assignees.

Most patent related studies used patent or citation count to get an overview picture of the research productivity and impact. Few studies utilize further methods to study the patent information in depth. In this study, not only patent and citation counts used, Bradford's Law and Patent Coupling are also used for further analysis.

Data and research methods

The data source used in this study is USPTO Patent database, one of the most exhaustive patent sources. This database contains over 4 millions USPTO patents that were issued from 1976 to the present time. The patents analyzed in this study were selected by the International Patent Classification (IPC) numbers and assignee country

was added to the criteria to identify the patents granted to Japan, Korea and Taiwan. The International Patent Classification is based on an international multi-lateral treaty administered by World Intellectual Property Office (WIPO) and the first edition entered into force in 1975. IPC, in its seventh edition, divides technology into eight sections with approximately 69,000 subdivisions. The patents, which have the principal IPC numbers belong to the following groups and subgroups, are defined as genetic engineering patents. The groups and subgroups include "Mutation or genetic engineering" (C12N 15/00), "Preparation of peptides or proteins" (C12P 21/00, C07H 21/00, C07K 14/00) and "Measuring or testing processes involving nucleic acids" (C12Q 1/68). The U.S. Patent Classification (USPC) numbers were also included in the strategies to guarantee the completeness of the dataset. The USPC numbers relate to the genetic engineering, such as subclasses 435/440 and 435/69.1 were added to search strategies. For setting apart the patents granted to Japan, Korea and Taiwan, the assignee country was used in the strategies. Two fields relate to country in the patent information. One is assignee country and the other one is inventor country. Assignee country was chosen as the search criteria. However there are patents that the patent rights belong to inventors and no assignee information. The inventor country would be used as the criteria in the cases. The country codes response to Japan, Korea and Taiwan are JP, KR and TW. The patents with the countries codes would be screened out for further analysis. One thing needs to be aware of is the country code for Japan was changed from JA to JP. Both JP and JA were used in search strategies.

The notion of patent bibliometrics was borrowed from bibliometrics. "Patent Count" was used for productivity analysis and "Citation Count" was used for impact analysis. As the basis of this study, other bibliometrics theories were applied for productivity analysis besides the patent count in this study. Price's idea on productivity that was originally proposed in the 1963's work and utilized in later study (PRICE, 1965) was applied to show the patent growth of the genetic engineering research. To reveal the distribution of the patents among assignees, Bradford's model (NARIN & MOLL, 1977; GARFIELD, 1980) was used to identify the core assignees that hold a substantial portion of the genetic engineering techniques. Patent being cited by other patents was seen as an indicator of one patent's impact over others. This study used times cited of patents as a measurement of the research impact. The patents that were highly cited were identified as patents had high research impact. The same conception was applied to the analysis on countries and assignees. The highly cited countries and assignees were assumed to have greater research impact on the development of genetic engineering research than others do. It implied that those research entities hold the essential technologies. Besides the citation count, Patent Coupling was used to reveal the correlation among the core assignees. The assumption was that the assignees cited same patents are more technological related than the assignees that did not share same citations. The higher of the number of shared citations presents the higher correlation of the assignees.

Patent Count. Count the numbers of the patents granted to different entities, include countries and assignees, during the period of 1991 to 2002. The entities are ranked based on the numbers of patents granted to.

Citation Count. Count the times cited of the patents owned by different entities, include countries and assignees, by the patents granted during the period of 1991 to 2002. The entities are ranked based on the times cited.

Impact Index. Times cited of cited entity over the number of patents granted to the cited entity. The index is to show the depth of the research impact of cited entity.

Bradford's Law. Bradford's Law is originally used to identify the essential journals in different subject area by the numbers of articles issued that are related to particular topics. The journals are sorted descending by the number of articles, dividing the journals into 3 zones and the titles in each zone generate certain amount of articles. The journals in the first zone are seen as the core titles, highly relate to the chosen subject. The relevance of the ones located in the further zones is decreasing by the distance from the core zone. The numbers of titles in each zone could be presented by the equation, $1:ak:ak^2$. In this study, the assignee is used in Bradford's Law instead of periodical, and the assignees are sorted by the numbers of patent granted.

Patent Coupling. Count the numbers of share citations of each pair of assignees. Based on the numbers of share citations, Coupling Index (CI) and Coupling Strength (CS) are calculated for each pair. CI is the ratio of the number of shared citations over the sum of citations of paired assignees. The higher coupling index presents closer correlation between two paired assignees. Each assignee will get the CS that is the sum of the coupling index of the assignee's coupling pairs.

$$CI_{ij} = C_{ij} / (C_i + C_j)$$

CI_{ij} is the coupling index of entities I and J, C_i is the number of patent citations of entity I, C_j is the number of patent citations of entity J, C_{ij} is the number of shared patent citations of entities I and J.

$$CS_i = \sum_{j=1}^n CI_{ij}$$

CS_i is coupling strength of entity I, CI_{ij} is the coupling index of entities I and J, the number of entity J could be from 1 to n, n is the number of core assignees minus 1.

Results

Basic analysis

Annual growth. 13,055 genetic engineering patents were retrieved by the patent classification numbers. In average, 1,088 patents were granted each year. 1991 is the year granted the least number of patents during the period of 1991 to 2002 (258 patents) and 2001 is the year granted the most patents (1,998 patents). Comparing to the previous year, the numbers of patent increased significantly in 1993, 1996, 1997 and 1998. From the viewpoint of the cumulative number of patents, the patents were doubled every 2 years before 1998 and the growth was slowed down afterwards. Although the number of patents granted each year is still over 1,500, the increasing rate was limited.

From the patents granted annually, the 12-year period could be divided into three time zones, pre 1995, from 1995 to 1997, and post 1997. Before 1995, the number of patents granted annually was under 500, the numbers of patents granted started to increase rapidly from 1995 to 1997. The period of 1998 to 2002 was the most productive period, there were over 1,500 patents issued annually during this period. By the annual increasing rate, three zones could be labeled as Initial Period, Developing Period, and Developed Period. The Initial Period was from 1991 to 1995 and the number of patents granted every year was below 500. The Developing Period was from 1996 to 1998 and the numbers of patents increased dramatically, the average increasing rate was 63.71%. The Developed Period was from 1999 to 2002 and the average number of patents granted annually was 1,847. Figure 1 is a visual of the results of annual count and distribution of Initial, Developing and Developed Periods.

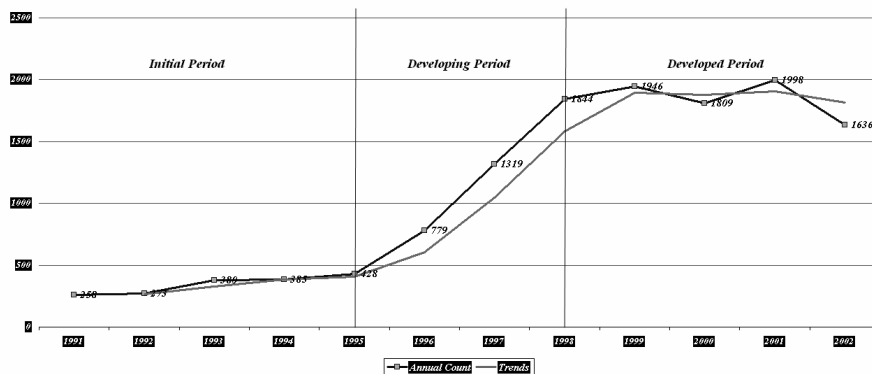


Figure 1. Annual patent count – Patents granted to Japan, Korea and Taiwan from 1991 to 2002

Examining the growth of the patents and it is found that the numbers of patents cumulated slowly during the Initial Periods and increased rapidly during the Developing Period, the growth pattern during these two periods fit the exponential curves and this pattern continued at the first two years of the Developed Period and the growth curve turned into linear curve two years later (Figure 1). Although this study does not include the data after 2002, it was predicted that the numbers of patents granted each year continued declining and it stepped into Withdrawn Period after 2002 based on the curves shown in Figure 1 and Figure 2 and this was confirmed by the numbers of patents granted in 2003 and 2004.

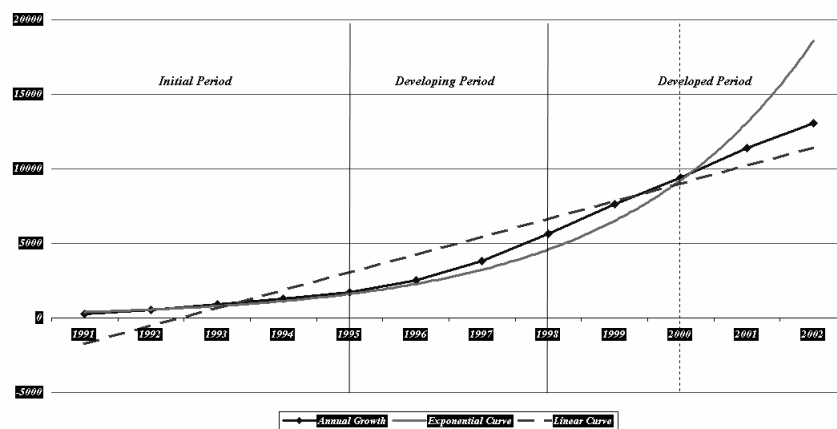


Figure 2. The growth of JKT own patents – from 1991 to 2002

Productivity and research impact analyses by countries. 42 countries are identified by the assignee country of 13,055 patents. Among those countries, United States owns the most number of patents, 75% (9,843) of patents were granted to U.S. Next to U.S., Japan is ranked at the second place and was granted 765 patents. German, Great Britain and France are the other top five productive countries; each of them was granted more than 400 patents. The other two countries which will be reviewed further in this article, Korea and Taiwan, each owns 50 and 26 patents, are listed the 14th and 17th.

13,055 patents referenced the prior arts of 18,490 USPTO patents and the cited patented were cited 63,954 times. 50 cited countries are recognized from the 18,490 cited patents. Among the cited countries, U.S. is the most cited country, were cited 52,247 times. Japan was cited 2,276 times and is listed the second place. The other top five cited countries include Great Britain, Netherlands and German. Korea and Taiwan is listed 18th and 22nd and were cited 38 and 28 times.

U.S. holds the distinguish research strength in genetic engineering research, both in productivity and research impact. Besides U.S., Japan also demonstrates the competitiveness in genetic engineering research based on the number of patents granted to Japan and times cited of patents comparing to other countries. Although the genetic engineering research in Korea and Taiwan is not as competitive as Japan, these two countries are advanced in the research among rest of the Asian countries both in research productivity and impact.

The productivity of Japan, Korea and Taiwan

Patent count of Japan, Korea and Taiwan. The number of patents granted to Japan, Korea and Taiwan is 841. It is about 70 patents granted to these three countries each year. Among them, Japan holds the majority of the patents. 765 (90.96%) patents were granted to Japan, 63 in average from 1991 to 2002. 1998 is the most productive year for Japan in genetic engineering research, 131 patents were granted that year. Japan also showed innovation capacity in 2001 and 1999, 104 and 94 patents were granted in these two years. Korea and Taiwan are not as productive comparing to Japan, each of them holds 50 (5.95%) and 26 (3.09%) patents. Both of Korea and Taiwan were not granted patents early on in the period of 1991 to 2002. It was till 1993 before Korea was granted the first patent and Taiwan was not granted USPTO patent until 1995. Both countries did not demonstrate strong strength in getting patents in any particular year.

From the technologies points of views, Japan has research gains in all three areas covered in this study, "Mutation and genetic engineering", "Preparation of peptides and proteins" and "Measuring and testing processes involving nucleic acids". More patents granted to the "Mutation and genetic engineering", especially the techniques relate to DNA recombinant. Based on the numbers of patents granted to Japan in these three area; DNA recombinant of "Mutation and genetic engineering" was the focusing technique of the first two periods and it started to show changes in 1998, more patents were granted in "Measuring and testing processes". In 2001, the number of patents that relate to "Measuring and testing processes" was higher than the number of patents granted in "Mutation and genetic engineering". As the "Preparation of peptides and proteins", the number of patents was listed at the third place throughout the 12 years. As for the patents granted to Korea, the techniques involved with DNA recombinant of "Mutation and genetic engineering" and the techniques relate to "Preparations of peptides" were granted more patents. Among 26 patents granted to Taiwan, more patents relate to DNA recombinant technique.

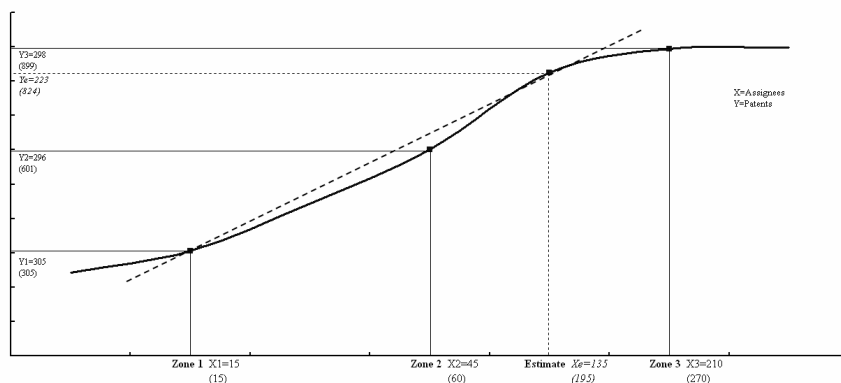
JKT research base and collaboration. Regarding the assignees and inventors as the research base of each country, this section further analyze the size of research communities of Japan, Korea and Taiwan by counting the numbers of assignees and inventors from these three countries. There are 270 assignees from Japan, Korea and

Taiwan, 235 assignees of them are Japan based institutions or individuals, 26 assignees are Korea based and 9 are Taiwan based. Comparing to the innovation population, the number of assignees from Japan takes 11.51% of the total number of assignees (2,042 assignees identified from 13,055 patents), 1.27% for Korea and 0.44% for Taiwan. As for the inventors, 1,706 inventors are from Japan, 155 inventors from Korea and 66 inventors from Taiwan. They take 11.30%, 1.03% and 0.44% of the total number of inventors (15,102 inventors).

From the viewpoint of co-ownership of the patent rights, it shows more cooperative efforts in the research community of Japan. The average number of assignees of patents is 1.12. 13.5% of the patents granted to Japan are owned by multiple assignees, 10.2% of the patents granted to Korea are co-owned, and only 4% of the patents are owned by multi-assignee. Although there is one tenth of patents are shared by multiple assignees, Japan is the only country among the three countries that cooperates with other countries and U.S. is the principle country that co-owns patents with Japan. As for the inventors, most of the patents granted are team effort achievement. The average number of inventors is 3.7; the average number of inventor of Korea is close to 4. For the cooperation, the inventors from Korea and Taiwan tend to work with the inventors from the same area. Only limited patents are invented with the cross nations' efforts. In the contrast to less inner-cooperation of the inventors from Korea and Taiwan, there are more patents invented under the cooperation effort.

JKT assignees. 270 assignees are identified from patents granted to Japan, Korea and Taiwan. Among them, 235 assignees are Japan based institutions or individual, 26 assignees are Korea based and 9 are from Taiwan. Comparing the numbers of patents owned by the assignees, majority of the assignees own limited numbers of patents. There are 252 assignees with less than 10 patents. Among them, 142 (52.40%) assignees own 1 patent, 50 (18.45%) assignees own 2 patents and 18 (6.64%) assignees own 3 patents. The percentage of the assignees with less than 10 patents is 92.99% and only small portion, 19 (7.01%); of assignees own more than 10 patents.

Applied the Bradford's Law to analyze the distribution of productivity among assignees and 16 core assignees are identified. The assignees are sorted descending by the numbers of patents granted and divide the 270 assignees into three groups. The number of patents granted to the assignees in each zone is from 295 to 305. It is found 15 assignees in the core zone and the estimate number of assignees in the third zone is off. According the original Bradford's Law equation, the estimate number of assignees is 135 and the number of patents is 824. The adjustment could be made to the original equation, $1:ak:1.5 \times ak^2$, 'a' equals to 15 and 'k' equals to 3. Figure 3 is a graphic presentation of the results of the Bradford's Law analysis.



Zone	No. of assignees	Total assignees	No. of patents	Total patents	Equation
1	15	15	305	305	$1 \times a$ ($a=15$)
2	45	60	296	601	$1 \times a \times k$ ($k=3$)
3	210	270	298	899	$1 \times a \times k^2 \times 1.5$

Figure 3. Distribution of assignees' productivity – Bradford's Law analysis

Table 1. Patent count of the most productive assignees

Rank	Assignee	Patent	%	Countries
1	Takeda Chemical Industries, Ltd.	45	5.35%	JP
2	Hitachi, Ltd.	40	4.76%	JP
3	Takara Shuzo Co., Ltd.	28	3.33%	JP
4	Suntory Limited	27	3.21%	JP
5	Ajinomoto Co., Inc.	23	2.73%	JP
5	Sumitomo Chemical Company, Limited	23	2.73%	JP
7	Institute of Physical and Chemical Research	15	1.78%	JP
7	Japan Tobacco Inc.	15	1.78%	JP
9	Kyowa Hakko Kogyo Co., Ltd.	14	1.66%	JP
9	Chemo-Sero-Therapeutic Research Ins	13	1.55%	JP
9	Mitsubishi Chemical Corporation	13	1.55%	JP
9	Mochida Pharmaceutical Co., Ltd.	13	1.55%	JP
13	Canon Kabushiki Kaisha	12	1.43%	JP
13	Kirin Beer Kabushiki Kaisha	12	1.43%	JP
13	National Science Council	12	1.43%	TW
13	Toyo Boseki Kabushiki Kaisha	12	1.43%	JP

Based on the result of Bradford's Law analysis, 16 core assignees are identified. Except National Science Council of Taiwan, the other 15 assignees are Japan based institutions and 14 out of 16 assignees are private sectors. The number of patents

granted to the core assignees is from 12 to 45. Among them, Takeda Chemical Industries is ranked at the first place. There are 45 patents granted to Takeda. Hitachi is listed the second place with 40 patents. The assignees listed at the third place to fifth place are Takara Shuzo, Suntory, Ajinomoto and Sumitomo Chemical. The numbers of patents granted to those companies are 28, 27, 23 and 23. Table 1 lists the 16 priority assignees and the results of patent count.

Comparing the numbers of patents granted to the top 5 assignees, Takeda, Hitachi, Takara, Suntory, Ajinomoto and Sumitomo over the 12 years period, no assignee was granted more than 10 patents each year. Takeda is listed at the first place with 45 patents and the productive period for Takeda was from 1996 to 2000. During the period of 1996 to 2000, Takeda was granted more patents than other assignees were. However, it started to show some changes after 1999. Hitachi, which was granted 40 patents and listed at the second place among 270 assignees, was granted more patents than Takeda in 1999, 2001 and 2002. Takara is ranked at the third, and most of the patents granted to Takara were issued after 1998. Both Ajinomoto and Sumitomo were not granted patents during early period, the patents granted to these two assignees were issued during the period from 1997 to 2001. Institute of Physical & Chemical Research and Japan Tobacco both listed at the seventh place, Institute of Physical & Chemical Research did not get any patent until 1998 and patents granted to Japan Tobacco were issued around the period of 1997 to 2002. Although Kyowa, Chemo-Sero, and Mochida were granted patents through out the whole period, more patents were granted from 1997 to 1999. The distribution of patents granted to Mitsubishi is similar to Kyowa, Chemo-Sero and Mochida, but there is not particular period that Mitsubishi got more patents. Canon, Kirin and Toyo were all ranked at the thirteenth with 12 patents and none of them were granted patents before 1996. National Science Council of Taiwan, the only non-Japan based institution among priority assignees, holds 12 patents, which were granted after 1995.

From the viewpoint of techniques, Takeda, Takara, Ajinomoto, Chemo-Sero and Mitsubishi focus more on the development of the techniques involve with DNA recombinant; Hitachi, Institute of Physical & Chemical Research, Canon and Toyo are focusing on the measuring and testing processes. Besides the DNA recombinant, Suntory, Japan Tobacco, Kyowa and Kirin applied the DNA recombinant techniques to the preparations of protein and were granted similar amount of patents in both technologies. Mochida and National Science Council of Taiwan were granted patents in three areas and no specializing technique from the numbers of patents granted to. Examining the techniques involved with the patents granted over those years, there is not evidence shows the technology shifting.

The research impact of Japan, Korea and Taiwan

Citation count of Japan, Korea and Taiwan. 1,146 cited patents granted to Japan, Korea and Taiwan. 1,111 of them were granted to Japan, 25 patents granted to Korea and 9 patents were granted to Taiwan. The impact indexes are 1.45(Japan), 0.50(Korea), and 0.35 (Taiwan). Most of the cited patents were cited less than 5 times. There are only a few of the patents were cited more than 10 times. The ones granted to Japan were cited 2,216 times, Korea owns cited patents were cited 36 times and those granted to Taiwan were cited 26 times. The most 3 cited patents are co-owned by multi-assignees and at least one of the co-assignees is Japan based institution. The first two most cited patents are granted to Cancer Institute and U.S. based institutions, John Hopkins University and University of Utah. The third highly cited patent were granted to Tasuku Honjo and Ono Pharmaceutical, one is based at Kyoto and the other one is based at Osaka. Most of the highly cited patents were granted to the Japan based institutions. Only very few patents belong to non-Japan based institution or co-owned by Japan based institution and non-Japan based institution. 472 cited patents granted to Japan were issued before 1991, those cited patents were cited 921 times and the average times cited were 1.95. 639 cited patents granted to Japan were granted after 1991 and were cited 1,395 times and the average times cited were 2.03. The cited patents granted to Korea and Taiwan, were all issued after 1991 and the average times cited were 1.44 and 1.11.

The patents granted to Japan, Korea and Taiwan, were highly cited by US. The patents were cited 1,688 times by U.S. Besides U.S., the cited patents were self-cited by the patents granted to the same countries. Japan patents were self-cited 273 times, the ones granted to Korea were self-cited 3 times and the ones belong to Taiwan were self-cited 9 times. Use the number of patents granted as based for the Impact Index, the self-cited impact index is higher than ones of other countries.

JKT cited assignees. 334 cited assignees from Japan, Korea and Taiwan were identified from the 1,146 cited patents. Among the cited assignees, 309 assignees are from Japan, 17 assignees are from Korea and 8 assignees are from Taiwan. Besides cooperating with Japan based institutions, a few Japan assignees co-own cited patents with assignees from other area, mainly the assignees from US. Among them, Cancer Institute from Japan co-owns several cited patents with John Hopkins University and University of Utah. Korea and Taiwan do not share co-ownership with assignees from other countries. Only one of the cited patents granted to Korea is co-owned by the assignee from Korea and United States. All the cited patents owned by Taiwan, are solely owned by Taiwan based institutions. Majority of the cited assignees were cited limited times. 269 out of 334 assignees, 80.54%, were cited less than 10 times. Among them, 127 (38.02%) assignees were cited once, 48 (14.37%) assignees were cited twice and 35 (10.48%) assignees were cited three times. Among 334 cited assignees, only 10

assignees were cited more than 40 times and the sum of times cited takes one third of the total times cited. Applying the Bradford's Law on the analysis of cited assignees, core cited assignees identified are all Japan based institutions. Hitachi is the most cited assignee among them. Hitachi was cited 277 times (81 cited Patents), including 20 self-citing, and the impact index is 6.93. Among the 81 cited patents owned by Hitachi, there are 9 cited patents cited over 10 times and most of them relate to the measurement process. Some of the electron methods were original used in the automotive engineering was applied to analyze the nucleic acid. The researches relate to the measurement procedures done by Affymetrix, EXACT Sciences, Visible Genetics, California Institute of Technology, etc. were affected by the procedures invented by Hitachi. Fuji is the second most cited assignee, with 57 cited patents and cited 133 times. The impact index is 19.00, the highest among the 10 most cited assignees. 42 out of 57 cited patents owned by Fuji were issued before 1991 and were cited more times comparing the ones issued after 1991. Besides self-citing, Fuji's patents were mostly cited by the patents granted to Carnegie Mellon, Affymetrix and Hyseq. The processes involved with the patents are all relate to the measurement procedures for analyzing nucleic acid.

Ajinomoto is at the third place with Mitsubishi and Takeda; all three cited assignees were cited 86 times and the impact indexes are 3.74, 6.62 and 1.91. Most of 33 cited patents owned by Ajinomoto were cited limited times. Two cited patents showed more impact on others, one relates to the DNA recombinant and was issued in 1988, and the other one is the procedure of formation compounds at specific position of RNA and was issued in 1991. The former was cited 13 times and the latter was cited 17 times. Ajinomoto shows more research impact on the assignees that are based in Japan, including the research done within Ajinomoto. Differing from Hitachi and Fuji, Ajinomoto demonstrated higher impact on the development of formation compounds. Among 35 cited patents owned by Mitsubishi, 26 were issued after 1991. The one cited most was issued in 1996 and relates to the reproducing technique. The second highly cited patent was issued in 1982 and the technique deals with measuring procedure. Although the cited patents are not measuring procedure related, the detecting procedure Mitsubishi revealed during the transformed process have research impact on the measurement processes invented later on. Among the citing assignees, Promega is the major citing assignee comparing to others. Comparing the self-citing with other top 5 cited assignees, Mitsubishi has the lowest self-citing rate. Besides 11 self-cited times, FMC, Chiron and Genentech are 3 major citing assignees of Takeda. From viewpoint of technologies, Takeda shows more research impact on the modification of DNA or RNA fragments.

Cancer Institute, Kyowa, Wakunaga, Asahi and Chemo-Sero-Therapeutic are listed 6th to 10th cited assignees. Cancer Institute only holds patent rights to 10 cited patents, but with two highly cited patents. The 10 cited patents were totally cited 71 times. The average times cited are 7, the highest among the top 10 cited assignees. Two key patents

were cited 27 and 24 times, both of them were issued in 1994. Different genes were disclosed in these two patents and the mutations procedures were used by other similar inventions, especially the research done by EXACT Sciences. Most cited patents owned by Kyowa were cited once or twice, even the most cited Kyowa patent were cited 5 times only. The times of self-citation takes one third of the times cited. Kyowa's cited patents involved with the processes of forming peptides and proteins, and the ones influenced others more deal with DNA recombinant. 13 cited patents granted to Wakunaga Seiyaku and were cited 47 times. Only 4 cited patents with limited times cited were issued after 1991. The two cited most both related to the procedure of "Oligonucleotide derivatives" and were issued in consecutive years, one is in 1986 and another one is in 1987. Wakunaga's recent patents mainly deal with nucleic acid measurement. The techniques involved with the patents effected by Wakunaga's patents mainly focus on the improvement of measuring procedure. 26 cited patents were granted to Asahi. Except the one dealing with the formation process, most of Asahi cited patents were cited less than 5 times. 15 out of 26 cited patents were only cited once. Chemo-Sero-Therapeutic Research Institute holds 21 cited patents. Most of cited patents belong to Asahi and Chemo are deal with the procedures of purification of antigen and the methods were used as foundation of producing recombinant protein. Examining the cross-citation among the 10 most cited assignees, there is no evidence shows there is citation relationship exists even there are similarities of the researches done by these 10 cited assignees. Table 2 shows the results of basic citation count of the 10 most cited assignees.

Table 2. Citation count of the most influential assignees

Assignee	Times cited	Number of cited patents	Average times cited	Impact Index
Hitachi, Ltd.	277	81	3.42	6.93
Fuji Photo Film Co., Ltd.	133	57	2.33	19.00
Ajinomoto Co., Inc.	86	33	2.61	3.74
Mitsubishi Kasei Corporation	86	35	2.46	6.62
Takeda Chemical Industries, Ltd.	86	58	1.48	1.91
Cancer Institute	71	10	7.10	6.45
Kyowa Hakko Kogyo Co., Ltd.	50	33	1.52	3.57
Wakunaga Seiyaku Kabushiki Kaisha	47	13	3.62	5.22
Asahi Kasei Kogyo Kabushiki Kaisha	46	26	1.77	4.60
The Chemo-Sero-Therapeutic Research Institute	43	21	2.05	3.31

None of the cited assignees from Korea and Taiwan is listed on the list of core-cited assignees. Goldstar is the most cited assignee among Korea based assignees; it was cited 6 times by U.S. based institutions and individuals. The technologies involved with cited patents granted to Goldstar are not genetic engineering related. They are measuring techniques related and were cited by the patents involved with nucleic acid measuring methods. National Science Council is the most cited assignees among

Taiwan based assignees; it was cited 12 times by Taiwan based and US based institutions. The technology of cited patents granted to National Science Council is nucleic acid measurement related.

Correlation analysis of core assignees

Correlation analysis is done for core assignees only. 20 priority assignees identified by the results of productivity and impact analysis are included in this section. The research method used in the correlation analysis is 'Patent Coupling'. The correlation among various assignees is defined by the ratio of the numbers of shared patent citations over the total numbers of patent citations. Two indexes are calculated for the 20 core assignees, Coupling Index (CI) and Coupling Strength (CS). CI is computed for the coupling pairs to show the depth of correlation based on the number of shared patent citations. CS, that the sum of the CIs of assignee's coupling pairs, is calculated for each core assignee. 190 coupling pairs are formed with the 20 core assignees. It is found that there are limited shared patent citations among the 20 core assignees. 23 (12.11%) out of 190 pairs shared patent citations. There is no shared patent citation among the other 167 pairs. Among the 190 coupling pairs, the pair of Toyo and Wakunaga gets the highest coupling index 0.123. The techniques of the patents granted to both Toyo and Wakunaga are involved with the nucleic acid testing technologies. Besides the pair of Toyo and Wakunaga, the pairs of Asahi and Kyowa, Mitsubishi and Chemo, Canon and Hitachi, and Mitsubishi and Takara also have higher coupling indexes, 0.064, 0.043, 0.034, and 0.032. Asahi and Kyowa cited the patents that involve the genetic engineering techniques. The pair of Mitsubishi and Chemo shares the patent citations that relate the transformation of proteins. The pairs of Canon-Hitachi and Mitsubishi-Takara share the patent citations with the nucleic acid measuring techniques. Table 3 shows the coupling indexes of the top 10 pairs.

Table 3. Top 10 patent coupling pairs

Index rank	Coupling pair	Coupling Index
1	Toyo – Wakunaga	0.123
2	Asahi – Kyowa	0.064
3	Chemo – Mitsubishi	0.043
4	Canon – Hitachi	0.034
5	Mitsubishi – Takara	0.032
6	Asahi – Takeda	0.031
7	Asahi – Wakunaga	0.026
8	Japan-Tobacco - Takara	0.025
9	Kirin – Takara	0.023
10	Ajinomoto – Kyowa	0.018
10	Hitachi – Mitsubishi	0.018

Reviewing the CS of the core assignees, Wakunage, Toyo, Takara, Asahi and Mitsubishi are the top 5 core assignees with close correlation with other core assignees. Cancer Institute, Fuji, the Institute of Physical and Chemical Research, NSC (Taiwan) and Sumitomo do not share any patent citations with other core assignees. Even Cancer Institute, Fuji and Sumitomo all involve the development of the nucleic acid measuring techniques; there is no shared patent citation among those assignees. Although other core assignees share patent citations with others, the numbers of coupling pairs are limit and the CS is lower than 1. The only assignee differs from others is Hitachi. Hitachi shares same patent citations with other 6 core assignees, but the numbers of shared patent citations are very limited and the CS is 0.92. Contrast to Hitachi, Kyowa only has shared patent citations with the other three core assignees. With the high Coupling Index with Asahi, the CS of Kyowa is 0.95.

The further correlation analysis and hierarchical classifying are done for the 20 core assignees. 4 clusters with similar technologies characters are found from the analysis. The size of the cluster includes 3 to 4 assignees. The first cluster includes Asahi, Kyowa and Takeda that emphasizes the development of genes encoding animal proteins. The second cluster contains Canon, Hitachi and Mochida, which focus the technique of nucleic acid measurement. The third cluster is comprised by Japan Tobacco, Takara and Kirin, mainly involves the technologies of introduction of genetic materials. Ajinomoto, Chemo, Mitsubishi and Suntory form the fourth cluster the only cluster involves both techniques of genetic encoding animal proteins and introduction of genetic materials. Table 4 shows the 4 clusters including the assignees, the focus techniques and the sum of Coupling Index. Cancer-Institute, Fuji and Sunimoto form another cluster. Although these 3 assignees do not share the same citation patents, they involved in the development of similar techniques, nucleic acid measurement.

Table 4. Technological clusters – Results of patent coupling analysis

Cluster	Assignees	Technical name	CI – Sum
C1	Asahi, Kyowa, Takeda	Genes encoding animal proteins	0.095
C2	Canon, Hitachi, Mochida	Nucleic acid measurement	0.045
C3	Japan-Tobacco, Takara, Kirin	Introduction of genetic materials	0.048
C4	Ajinomoto, Chemo, Mitsubishi, Suntory	Genetic encoding animal proteins/ Introduction of genetic materials	0.085

Conclusion

From the patent productivity and research impact, Japan is the leading country in genetic engineering research in the three Asia countries and also owns the innovation human resources. Korea holds the second place with double amount of patents comparing to the ones granted to Taiwan. From the viewpoint of technologies, Japan owns patents in “Mutation and genetic engineering”, “Preparation of peptides and

proteins” and “Measuring and testing processes involving nucleic acids”. Differs from Japan, Korea gains more patents involve DNA recombinant and preparations of peptides, and Taiwan obtains more patents in DNA recombinant technique.

For the 270 assignees, the core assignees that are high productive in genetic engineering research are all Japan based institutions. Takeda Chemical, Hitachi, Takara, Suntory and Ajinomoto are the top 5 productive assignees. National Science Council is the most productive Taiwan based assignee; Korea Institute of Science & Technology and Korea Kumho Petrochemical are the two productive Korea based assignees. The core productive assignees also have higher research impact than the non-core assignees. Among them, Hitachi was most cited. Fuji, Ajinomoto, Mitsubishi and Takeda are the other 4 most cited assignees. There is no evidence shows that the assignees from Korea and Taiwan have significant research impact on the development of genetic engineering research comparing to the ones from Japan.

From the results of patent coupling analysis, Wakunage, Toyo, Takara, Asahi and Mitsubishi have greater Coupling Strength among the core assignees, which means higher correlation with other assignees. As for the patent coupling pairs, Toyo and Wakunage, Asahi and Kyowa, Chemo and Mitsubishi, Canon and Hitachi, Mitsubishi and Takara are the 5 coupling pairs with highest Coupling Index. Comparing the techniques involved, four correlation clusters could be identified, such as the cluster includes Asahi, Kyowa and Takeda that focus on the development of genes encoding animal proteins. Even with the shared citation patents, it is found that the assignees are self-contained in the technology development, with low patent coupling.

This study reveals the development of the genetic engineering research of Japan, Korea and Taiwan by taking patent bibliometrics approach. The results show that the analyses of patent information could be also used in assessing the technology research to identify the productive countries and core assignees. The same approach could be taken in analyzing the research performances in other areas. Absolute numbers of patents and patent citations were used for indicators in this study. Other relative indicators could be applied in the future studies to further investigate the insights.

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