【2009 年 第 83 回大会 学会賞】「論文部門」受賞

Unintended Transfer of Rejected Outcomes from Potential Research

——A Case Study of R&D Process for Anti-hypertensive Drug Discovery——

Tokai University Kyoko Kameoka

1. INTRODUCTION

This paper explores how and why a potential but dead-end research outcome was unintentionally taken over from a Japanese firm to an overseas firm, resulting in creation of an innovative product between non-cooperative firms.

Recently, most of the literatures discuss "Open Innovation" which represents innovation through value creation by integrating some external and internal ideas. Conventional innovation takes place in a closed intra-company cycle of making investments in inventing new technology, launching new products based on new technology, making reinvestments in research and development (R&D) from increased sales and profits from such new products. As firms accelerate time-to-market, life-cycle gets shorter and competition with overseas firms aggravates. Under the circumstances, many researchers invent or discover a new technology to start their own business, and firms have more difficulties to gain profits from investments in R&D than before. The existing innovation cycle is getting unsustainable (Chesbrough, 2003).

What and how do firms exchange in the process of open innovation? Some firms in the software development field occasionally venture to open their innovation for free without patenting, although it is not very common in any other fields (von Hippel, 2005). Letting competitors adopting a technology would overtly or covertly lead to development and productization of derivative versions based on the innovation to make it de facto standard of the industry. In other development fields, certain firms provide competitors with their technical information as informal transaction to obtain competitors' know-how in turn (von Hippel, 1998).

As stated above, the cooperative relationship under which technical information and/or knowledge are exchanged have been assumedly built among firms in order to create open innovation. Yet, transfer processes of technical information vary with industries even if firms are cooperative. For instance, patented technological information and/or research outcomes in biotechnology are traded in the market. In short, patenting plays an important role in insuring inventors' rights (Arora, et al., 2001). Therefore, whole concepts of cooperative relationships between/among firms differ by virtue of industries.

Viewing open innovation from the perspective of inter-firm relationships, a question arises about a possibility to establish innovation without any collaboration among firms. If open innovation takes place under noncollaboration, what processes and mechanisms exist?

Based on the above research question, we analyze the R&D process for the hypertension drug BLOPRESS® developed by Takeda Pharmaceutical Company (hereinafter called as Takeda) and

NEW-LOTAN® (in the US: COZAAR® or HYZAAR®) developed by a major US chemical company DuPont-Merck. Through the analysis of the case, the paper attempts to elucidate this unconventional innovation process and examines the mechanism; a research outcome which a firm failed to productize was made public as a patent information; and then an overseas firm which did not know the fact cited the patent to develop the research outcome; and the overseas firm successfully made a breakthrough product. Nevertheless, the original inventing firm could ensure the profitability through world-wide cutthroat competition after that the prominent research outcome was unintentionally transferred to a competitor. In light of this fact, the paper gives an implication of an impact on firms from disclosure of information.

Section 2 will sort out prior literatures on innovation creating process and inter-firm relationship to present a framework in the paper. Section 3 will introduce specific cases and Section 4 examines the process and mechanism of creating innovations as seen in the case and presents an implication. At last, we will come to a conclusion and describe open issues.

2. Preceding Researches on Open Innovation

This section overviews preceding researches on inter-firm relationships which create open innovations to frame the paper in this research field.

"Open innovation processes combine internal and external ideas into architectures and systems. Open Innovation processes utilize business models to define the requirements for these architectures and systems. The business model utilizes both external and internal ideas to create value, while defining internal mechanisms to claim some portion of that value (Chesbrough, 2003)." His idea includes both technology and market, but the paper mainly focuses on technology.

Technology itself is not recognized as a valuable thing until it is productized (Chesbrough, 2003). Consequently, when a firm can hardly create a value by productizing its own technologies, firms have come to incorporate external technology after identifying their own lacking portions of internal technology. This lies behind open innovation.

Firms need to identify characteristics of their lacking technologies and knowledge first, because differences determine how firms acquire them from outsiders, in other words, inter-firm relationship. For example, Tidd, et al. (1997) indicated that if a firm wants to obtain the base of a noncompetitive technology from outsiders, the firm need technical licensing, consignment agreement or collaborative relationship with its customers and/or suppliers. This is because procurement from outside is better than in-house development from the points of technological levels and costs when the base of outsider's technology is recognized as their core competence. If a firm wants to obtain a key of a certain technology, the firm promotes in-house R&D or sets up a joint venture to maximize competitive advantage. As for an emerging technology, a firm will wait and see after funding to universities or handling in-house R&D. Thus inter-firm relationships vary with the characteristics of technology (Tidd and Trewhella, 1997).

Technology and knowledge are sometimes induced to exchange through another cooperative relationship which differs from alliance, licensing and joint venture as mentioned above. Taking software development for example, software houses sometimes go public about their innovation with free of charge, because they have incentive to make the innovation a de facto standard through network externalities (von Hippel, 2005). It is observed in non-software development fields that a certain firm goes open about their technological information for the purpose of making it become de facto standard. For the same reason, the Japanese audio company Victor disclosed their technical information about Video Home System (VHS) for home-use VCRs. The disclosure led Victor's system

become a de facto standard, and the system had with a competitive edge over the beta system (Cusumano, Mylonadis and Rosebloom, 1992).

Technological information and knowledge is not always transferred from sender to receiver but sometimes reciprocally exchanged via informal transactions among firms. If engineers judge some external know-how as beneficial to them, they will share their own technical information or know-how even with competitors to receive the valuable know-how in turn (von Hippel, 1997). Individual engineers communicate directly and informally with each other across firms, whereas firms are rivals and seemingly have no cooperative relationship.

When firms attempt to have collaborative relationships with scientists' communities, firms need not only funding to them but also establishing personal exchanges. If a firm needs outcomes from basic research for seeking new technology, it is crucial for the firm to be located near scientists' communities (Audretsch and Feldman, 1996). Joint research and co-authoring academic papers with scientists constitute an important method for firms to advance in-house R&D (Cockburn and Henderson, 1998).

Furthermore in the biotechnology industry, firms often build a network with scientists who work for universities and research institutions to connect the learnings from them with firm's research outcomes (Powell, et al., 1996; Zucker, et al., 2002; Owen-Smith and Powell, 2004; Smith and Bagchi-Sen, 2006). On the other hand, if some conflicts occur among scientists and are not appropriately settled, knowledge spillover may happen through the flow of researchers (Audretsh and Stephan, 1991). This situation does not directly cause the following, but since technological information in the biotechnology industry is sold and bought in the market, it is indispensable for biotech firms to secure inventors' proprietary rights by patent (Arora, et al., 2001).

From the view of the inter-firm relationships on open innovation, previous literatures discuss on the assumption that there exists collaboration with outsiders or the personal networking and liaison with research institutions. However, if a firm has no relationship with outsiders, is it impossible for the firm to acquire external technological information and knowledge in order to create open innovation? As Levin, et al. (1987) argues that even confidentiality and patent protection have a difficulty ensuring appropriability of benefits from corporate R&D, research outcomes and technical information are unavoidably spilt over.

To be sure, such spilt research outcome or patent information is not always those which can compensate insufficiencies for a firm to create innovation. Instead, whether or not they can evaluate the spilt technology or information which are incorporated into their R&D and will be proficiently utilized depends on the firm's capability. Speculating about this condition, open innovation will possibly take place under non-cooperative relationship between firms, yet real success is likely to require some conditions or mechanism.

So far, few previous literatures discussed open innovation from view of non-cooperative relationship among firms. The paper examines a case to explore how and why an innovation took place by transferring research outcomes under the non-cooperative relationship between firms. The paper picks up a phenomenon that two firms seem to collaboratively solve a problem on research without any virtual connection between them, resulting in innovation. The paper addresses the phenomenon as "unintended transfer of research outcomes." The paper also elucidates the implication that a firm can make profits from a "second-in-class" product by utilizing their accumulated technology, even if the firm discloses their potential but rejected research outcomes.

3. CASE STUDY

The section describes the respective R&D processes for antihypertensive drugs: NU-LOTAN

manufactured by DuPont-Merck[1] and BLOPRESS by Takeda. The former is the first drug which brings down the blood pressure with a different action mechanism from conventional antihypertensive drugs so that it was called as breakthrough medicine. In Japan, DuPont-Merck obtained manufacturing approval of NU-LOTAN in July 1998 and Takeda did it for BLOPRESS in February 1999. After that, another 3 firms[2] obtained approvals in Japan. Finally, Takeda has boasted the top sales with BLOPRESS in all the kinds of medicine in Japanese market since 2005 (*Yakuji Handbook, 2009*: Handbook of Clinical Medicine).

The summary of this case is as follows. (1) DuPont succeeded in commercializing a research outcome which Takeda failed to productize, creating breakthrough medicine. (2) However, those two firms had no cooperative relationship such as information exchange, alliance or joint research. (3) It was published patent information that served as the intermediary between two firms. And (4) Takeda disclosed their prominent information to the public, resulting in conceding DuPont's innovation with a breakthrough medicine. Takeda, however, has secured profits from an improved new drug. Then, the following describes how the breakthrough medicines were developed and productized.

3-1. New Molecular Entity Discovered by Takeda[3]

For the past 100 years and more, the research on anti-hypertensive drug has been approached in three ways. They were: (1) angiotensin-converting enzyme (ACE) inhibitor, (2) renin inhibitor and (3) angiotensin II receptor antagonist (ARB). In 1981, the first approach became successful after a long time research. In response to this, many pharmaceutical firms in the world focused on the research for ACE inhibitor and this approach seemed to be a mainstream for research on the anti-hypertensive drug.

Yet, in 1978, Takeda discovered a fundamental skeleton (essential part) of a chemical structural formula which would possibly become an ARB as mentioned in the above (3). The chemical compound was elaborated by a new synthesis approach which was found as a basic research outcome in the R&D center. Originally, the chemical compound was not elaborated for targeting at a specified medical remedy for some specific diseases so that Takeda's researchers tested its drug efficacy. Then, it exhibited diuretic effect. As they continued to test the chemical compound with decreasing dose, they confirmed that it could reduce blood pressure but could not act as a diuretic[4]. These test results clarified that the new molecular entity (NME) inhibits the activity of angiotensin II (a hormone which constricts a blood vessel). The NME was supposed to be a breakthrough drug, so-called an innovative product, but the research outcome was turned out not as originally planned but as a result of persistent efforts through repeated experiments. The NME served as a beginning of R&D activity for angiotensin II receptor inhibitor (ARB) at Takeda.

The above research outcome had a significant meaning in the medical study. As a background of it, ARB had been studied worldwide and the target of the studies was a peptide compound which consisted of long chemical bonds of amino acids. Therefore, a molecular of ordinary ARB was too big to make an oral drug, and as a result, putting ARB into practical use was considered to be infeasible. However, the NME, which was discovered by Takeda, was non-peptide with small molecular weight; conventional theories had not recognized it. Pharmaceutical firms as well as research institutes had never found such a NME which was to be a base of non-peptide ARB. Takeda's discovery was so valuable from the worldwide view.

In Japan, academia's opinions, however, were divided whether or not they could recognize the hypertensive action of the non-peptide NME as ARB. The discovery was hard for them to accept, but Takeda continued to make chemical compounds based on the non-peptide NME, synthesizing three types of candidate ARB compounds which had more effective functions. In November 1980, Takeda filed for a patent on those compounds (US Patent No.435504). After that, the applications were

approved to be published on October 19, 1982. The reason Takeda applied a patent was to protect their right.

The patented chemical compound was verified its efficacy by testing with a cell fragment, but clinical trials to human patients could not verify its efficacy. Such an outcome happens often in drug discovery process. Also, the worldwide mainstream of the research of those days was ACE inhibitors as described previously. Therefore, continuance or termination of the ARB research was a controversial issue in Takeda. At last, the R&D project for ARB was terminated in 1982. A patent for the NME was approved but the productization aborted.

3-2. Productization by DuPont

Around the same time in 1980, then-the-largest chemical firm DuPont studied the peptide type of angiotensin II receptor inhibitor. Now DuPont offers licensing for drugs only, but at that time the firm had a pharmaceutical department for drug discovery. They had studied peptide-type compounds for a long time, recognizing that peptide was not suitable for oral drug, because the molecular of peptide was too big to be absorbed in a human body. In general, peptide is an injectable drug so that pharmaceutical firms are in difficulty to administer peptide at clinical trials.

Despite repeated experiments, DuPont's research on the peptide-type ARB did not proceed in solving the problem of low absorbed fraction. The ARB project members had a deadline coming up. If they could not solve the problem, they had to abort the project. Then, one researcher found a patent description about non-peptide ARB compound invented by Takeda, which was disclosed one and half year passed after filing. It was October 1982.

DuPont had to verify the reliability of the information from Takeda on their own, because they did not have any collaborative relationship with the foreign company. First, DuPont synthesized the chemical compound exactly the same as described in a patent description to verify its antihypertensive action by testing (Cabri and Di Fabio, 2000; Naka, 1999; Nishikawa, 2007). The test result demonstrated a slight ARB activity, and DuPont terminated the research for the peptide agent to determine to proceed to the R&D for non-peptide agent (Duncia, et al., 1990).

DuPont commenced to search a potential chemical compound with more functionality based on the Takeda's patent information. DuPont synthesized various compounds for further modifications. It also established a joint venture with Merck to aim for synergy in R&D and marketability (Cabri and Di Fabio, 2000). They found a one compound through trial and error by adding various molecules to increase binding force by a factor of ten. They systematically searched the correlations between chemical structure and activity, finding a chemical compound with binding force which was 1,000 times stronger than the first compound (Duncia, et al., 1990). The success of synthesis process allowed DuPont to produce drug with small quantity of chemical compounds, and therefore, the drug showed fewer side-effects.

DuPont also filed some patents concerning methodology through synthesizing processes (Cabri and Di Fabio, 2000). This type of patents fortified DuPont-Merck's advantage, because followers' approaches for searching compounds were limited in order to avoid infringing the patented methods of synthesis.

DuPont was not the only one company that noticed Takeda's patented research outcome. Park Davis (merged with Pfizer in 2000) also proceeded with the research based on the Takeda's lead compound. Park Davis found a chemical compound to apply a patent for it in 1987 around the same time when DuPont filed a patent. Both Park Davis and DuPont accelerated the development for ARB drug (Naka, 1999). As a result, DuPont's compound demonstrated anti-hypertensive action via the oral route, while Park Davis' compound did not (Wong, et al., 1991). Both firms filed patents for their own lead compound but after patenting, their NMEs (new molecular entity) were developed to show the

different test results.

In 1989, DuPont presented the research outcome about AII type ARB at Gordon Research Conferences in the US. In 1980's, the mainstream of theory for anti-hypertensive drug supported ACE inhibitor and ARB was considered as impossible. The DuPont's research outcome received an enthusiastic researchers' response.

No one from Takeda attended the conference, but a Japanese doctor who attended it made an inquiry about the Takeda's lead compound. Because he thought that Takeda must have found something effective compound because even DuPont found the NME of ARB,. Receiving the inquiry, Takeda was astonished and in turn asked information about DuPont's invention. Takeda immediately decided to revive the terminated ARB project. This prompted worldwide research by approximately 60 pharmaceutical companies involving Takeda. More than 600 patent applications were filed for the ARB drug from 1989 to 1994 they faced fierce competition (Naka, 2000; Nishikawa, 2007).

3-3. Fierce Competition over Improved New Drug Development

Takeda resumed its ARB project in about one month later than other pharmaceutical firms which attended the above Gordon Research Conferences. Both development speed and product's functionality were critical to catch up with DuPont's research outcome and to survive the worldwide fierce competition over the ARB drug. Takeda positioned the ARB as the top-priority drug, focusing on the development. As the result, Takeda productionized it in eight years which was the shortest R&D period for the company.

In Japan, Takeda obtained the second manufacturing approval following DuPont, and after that, three firms were also approved to produce ARB drugs. Among many competitors, Takeda's BLOPRESS has shown top sales at the time of shipment in the Japanese market for not only anti-anti-hypertensive drug but also drugs for all diseases since 2005.

There are some reasons for BLOPRESS to be a profitable me-too drug. One of the reasons was its high functionality. BLOPRESS required 8-12 mg dose per day. On the meanwhile DuPont's NU-LOTAN required dosing about 40mg a day. A drug price for hypertension was fixed. If a low-dose drug can have the same effect as a high-dose drug, the manufacturing cost will be cheaper for a low-dose drug to gain a certain effect. Patients can take less frequent dose. These factors caused patients and doctors to prefer BLOPRESS to other makers' products.

Takeda successfully optimized BLOPRESS as "prodrug" so that even low dose could work effectively. Prodrug is a compound that, on administration, must undergo chemical conversion by metabolic processes before becoming an active pharmacological agent. The absorption rate of BLOPRESS was originally 3%, but after becoming prodrug the rate was raised up to 50-60%. Unless otherwise making prodrug was successful, 100-200 mg administration was necessary for BLOPRESS, which was definitely less competitive in comparison with 40-mg administration.

Then, what is driving force for Takeda to successfully make BLOPRESS prodrug? This comes from accumulated knowledge and experiences of researchers in Takeda. Utilizing prior research outcomes, they added a substituent group into the previous stage compound of BLOPRESS. This synthesis came up not from data base matching but researchers' experience; researchers formulated a hypothesis about a substituent group which they speculated about to improve the compound's functionality. They actually synthesized a substituent group to verify its function in a step-by-step fashion. The critical point was the speed of development, that is to say, how fast a hypothesis in an early development stage is formulated and how fast it leads to optimization.

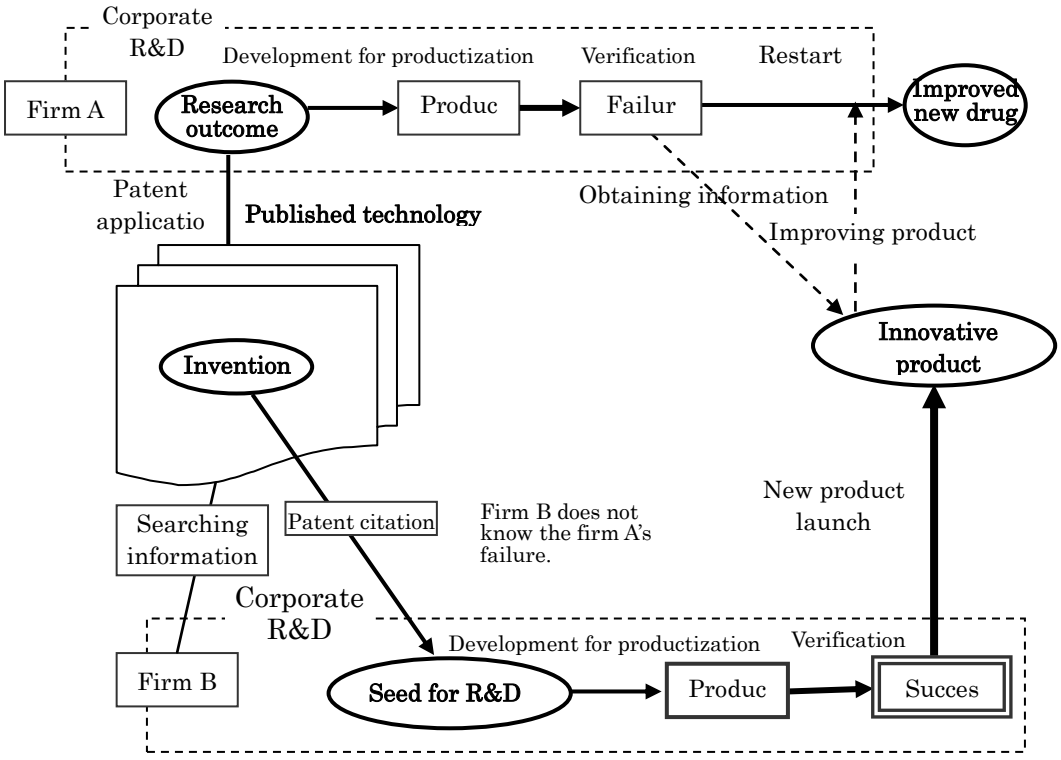
As described above, the speed of the development was determined by Takeda's internal experiences in synthesizing compounds. Generally, it takes about one month to create one compound. As for BLOPRESS, there were seven alternative positions to set a certain substituent group to be

attached. If researchers synthesized a compound one-by-one adding a substituent group to one position out of seven alternatives, it would take seven months in the worst case. However, Takeda could specify the most optimal position at the first month, because they had quick wits coming from their experiences but could not explain the reason theoretically. In Takeda's case, young researchers, who were ex-members of the old ARB project, became leaders to promote the new ARB project where they could utilize their experiences and knowledge cultivated in the ex-project.

The other driving force of development came from the improvement of assaying technique. A pharmacology group in Takeda had been assaying compounds to verify if they had anti-hypertensive function even after the ex-ARB project was terminated, because the methodology of assay itself was continually applicable for ACE inhibitor drug as well as ARB drug. The pharmacology group had been improving assaying technique through the development of another type of anti-hypertensive drug to conduct verification test in large doses and to set appropriate criteria. This inherited technique could drive the Takeda's ARB project accelerated to stay one step ahead of competitors. Furthermore, doctors who took in charge of clinical trials were as also those who were involved in the previous ARB project and adhered to the existing procedures. These factors substantially contributed to acceleration of the development.

Takeda's competitive advantage was not only from explicit research outcomes but also from individual expertise, knowledge and know-how on experiments accumulated in the R&D groups. The flow of drug discovery process driven and taken-over by Takeda and DuPont is shown in Figure 1.

Figure 1 Unintended Transfer of Rejected Outcomes from Potential Research



4. DISCUSSION

This section elucidates from the case that how and why an innovation took place through

"unintended transfer of rejected outcomes from potential research." The case also implies that the disclosure of technical information is not always adverse to the firm's interests rather than advantageous over competitors who solved the firm's bottleneck problem, if the firm could utilize their accumulated technology.

4-1. Unintended Transfer of R&D Outcomes

How does a firm obtain necessary technical information and knowledge from externals under non-collaborative relationship with them? As the case study indicates, such knowledge transfer happens on occasion. In fact everyone can use patented technologies for one's R&D activities, unless otherwise they take a trade with the patent or infringe it (Nagaoka, 2001). Provided that, it is essential they can evaluate the technology which can be used but are not sure its applicability to the firm's technology.

In general, when firms exchange technical information and knowledge under collaborative relationship, they tend to anticipate something associated with them. In other words, since some sort of collaborative relationship exists during that exchange, personal knowledge and accumulated technology of externals are possibly transferred including "trust" and "reciprocity" toward peers and partner firms. If there is no collaborative relationship between firms, obtaining technological information and knowledge from external firms may represent risk-taking to some extent. Therefore, in that situation, a firm may well tend to search a determinate technology and/or research outcome which they are familiar with in order to minimize the risk. DuPont's behavior in this case indicates that they had capabilities for reproducing and verifying an external research outcome.

As described above, it is of pivotal importance that researchers be able to screen the firm-specific valuable information from the crowd of patented technologies under the limited time and budget. Collecting patent information can be recognized as searching a seed for future research, but at the same time, the seed might be a failed outcome as Takeda's case. Typically, viewing patent publications for searching leading-edge technology seems to be beneficial to all the firms, but screening capability is also required to determine whether or not the patent information is applicable to the firm's technology. The case actually indicates that it was only two firms in the world that cited the Takeda's patent to start their studies. In the meanwhile, DuPont succeeded in developing NU-LOTAN so that more than 60 firms cited DuPont's patent to aim at an improved new drug, engaging in fierce competition. There is a great difference between two patent citations.

The fact demonstrates that DuPont was assumed to have such an evaluation capability for premature technology as understanding of potential value of Takeda's patent, since DuPont had accumulated peptide studies for a long time. DuPont was also vigilant, since they did not start their ARB project until they could successfully reproduce the Takeda's outcome, verifying its efficacy. Additionally, DuPont as a major chemical company could make use of the core business; they procured an in-house catalytic agent which could proceed in experiments. It was another advantage for successful productization.

Through the above process, DuPont created an innovative product. Takeda's prominent discovery was not productized and became an obscure research outcome, but the disclosure of Takeda's patent led DuPont to take over the research outcome, bringing an innovative product. There was no collaborative relationship between two firms contrary to the definition of open innovation, yet the innovation happened to take place under unintentionally taking over a research outcome from Takeda to DuPont, not knowing adverse party's conditions. Needless to say, it was essential that DuPont had the salient information screening capability through accumulated technologies, utilizing all the chemical company's specific resources.

4-2. New Significance of Published Patent Information

Conventional literatures on innovation delivered by patents have not referred in particular to the details and/or value of inventions in patent publications, but rather those inventions were doubtlessly considered to be valuable to every firm.

For instance, as a representative innovation study in 1980's, Levin, Klevorick, Nelson and Winter (1987) investigated how appropriability from the benefits of research outcomes can be obtained and whether or not patents can function as a measure of obtaining appropriability by respective industries. The study focused on the private firms' economic incentive when they promote in-house R&D investment rather than investment on academia and public research institutes. Among them, especially the pharmaceutical industry seems to secure their appropriability by patents. Definitely, patented technology and/or invention are secured from free usage. However, it is also feasible that patented technologies are incorporated into other firms' technological seed for their own development while avoiding infringement of the patent. Prior literatures have not touched upon this arguments.

As the case study indicated, if an original inventor could not prove the value of their own patented invention, and more if some firm is capable of evaluation for the invention, the "capable firm" would utilize it for their original innovation. As a matter of fact, published patent information may have a searching function for advanced technologies.

4-3. Conditions on Profitability When Disclosing Proprietary Technology

Contrary to DuPont which produced an innovative product, why could Takeda be the most profitable after fierce competition despite the one of 60 followers in the world? In this case, DuPont solved a bottleneck problem on behalf of Takeda so that the latter could step forward to an advanced development stage to improve the efficacy. That is to say, Takeda had already accumulated considerable amount of technologies, knowledge and experiences, leading to elaborate the DuPont's product with higher quality and resulting in the survival from competition. As described in section 3-3, once researchers have acquired technologies and knowledge through their prior researches, since such knowledge is dependent on them and will be possibly utilized for another researches. Moreover, such knowledge is not always utilized by extraneous researchers, even if it is stored as database. In this case, it is assumed to be one of critical factors for catching up with the DuPont's product that Takeda's original ARB project researchers came back to new ARB project.

Originally, Takeda applied for a patent while they recognized the world widely prominent new molecular entity (NME), which had not been discovered by academia, would be known to all the competitors. From the view of disclosing any technological information, the incentive of the firm's behavior was presumed to aiming at a "fast-second" from the beginning, unless otherwise it aimed at acquiring the technological standards. When appropriability for profit from a patent is not secured, an original inventor will have an incentive to voluntarily disclose the invention, if acting as a second mover will be advantageous to a first mover who was in difficulty for achievement of its commercialization (Fraja, 1993).

However, a firm cannot always become a second mover, even if the firm discloses their secret research outcomes, since R&D for drug discovery includes too much uncertainty. Thus, Takeda is presumed that they did not apply a patent in order to become a second mover from the beginning but they aimed to insure the proprietary right. Unless otherwise patent protection, Takeda was concerned about losing the proprietary right, when some competitors would discover the same new molecular entity as Takeda did.

Given this perspective, even if a firm discloses their research outcome which was not solved its bottleneck problem, the firm would possibly gain back benefit from the disclosed outcome when satisfying specific conditions. The fact implies that many Japanese firms with cutting-edge

technology try to fence off their technologies so called putting them into a “black box,” but in occasion, patenting their un-commercialized technologies with novelty for disclosure would be beneficial rather than remaining such a potentially prominent research outcome as unused, because it would result in creating another chance for development.

5. CONCLUSION

The paper elucidates the process and the mechanism of innovation which was created through patented technology transfer under non-collaborative relationship. From the view of problem solving, a firm could indirectly solve a bottleneck problem in an in-house research outcome by unintentionally consigning it to an external firm except for alliance or joint research. The problem solving flow indicates that a successful inventor (anonymous consignee) produces the “first-in-class” product and an original inventor (unintentional consigner as well as follower) produces the “best-in-class” product.

In general, open innovation has been discussed as a pattern from obtaining external technology, utilizing for internal knowledge and technology, and thereby leading to successful commercialization. The external technology is, however, often premised on the “usable as is.” It could be rare that through an innovation process, a firm cites patent information to develop it for success of innovation, and the firm did not know the technology in the patent had failed. Nevertheless, it is understandable that patented technology is not always commercialized. In this sense, such an innovation process as shown in the case may occur in any of non-pharmaceutical industries.

The case study implies the economic appropriability through innovation in the following manner. When a firm’s research outcome which failed in commercialization is taken over by a competitor through patent publication but the competitor did not know the fact of failure, the firm will possibly get profitability by improving the competitor’s product with its knowledge and technology accumulated through the past researches. In light of success, a firm may hesitate to file a patent application for its discovery even if it failed for productization, because the firm would never success by itself and some competitor would pick up the discovery to succeed in productization. Yet, from the view of a follower, the firm remains in the position of competitive advantage, being capable of producing a quality product by utilizing its inherited and associated knowledge and technology as organizational capability.

When it comes to the technological “black-box” to which most Japanese firms tend to prefer as R&D strategy, a shelved technology should be reconsidered how to handle them. Disclosing technological information, which includes a problem that a firm could not solve, is not always disadvantage. Consigning the problem-solving to competitors may possibly lead to breakthrough for consigner’s better research outcome. That is to say, consignment may become a kind of strategy under certain circumstances. The essential is to evaluate the circumstances. Furthermore, even if a firm does not get directly profitable, the disclosed research outcome would lead profit social welfare eventually.

As managerial agenda, we should discuss that in what circumstances a firm would open unsolved problems including discoveries or inventions. The paper suggests as one hint that a firm disclosing or discovering a technology should reside in the network where the firm catches external information about R&D in the world, and in such case, disclosure will become simple technology transfer.

(1) In 1991, the joint company DuPont Merck Pharmaceutical Company was established, but DuPont dissolved the joint business to take over the Merck’s equity for $2.6 billion in 1998 (*Nikkei Business*, in the June 8 issue in 1998, pp.24-25). At present, Merck manufactures and sells NU-LOTAN (COZAAR or HYZAAR in the US) and DuPont licenses it to Merck. See the DuPont website:

http://www.dupontrefinish.eu/dupontrefinish/com/en/PDF/2009_DuPont_DataBook.pdf.

(2) Another three firms and names of products are DIOVAN manufactured by Novartis, MICARDIS discovered and developed by Boehringer Ingelheim and sold by Astellas (in Japan), and OLMETE (in Japan and EU, BENICAR in the US) manufactured by Daiichi Sankyo.

(3) This section consists of interviews for Mr. Naka and Mr. Nishikawa who were researchers of Takeda Pharmaceutical Industry, and some descriptions cited from Naka (2000), Naka (1999) and Nishikawa (2007). The interviews were conducted to Mr. Naka on March 13, 2007 and to Mr. Nishikawa on July 24, 2007.

(4) A drug, which acts as a diuretic, promotes exhausting water from a body so that water in blood would decrease and the blood pressure as well.

[References]

Audretsch, D. B. and M. P. Feldman. 1996. R&D Spillovers and the Geography of Innovation and Production. ***The American Economic Review***, Vol. 86, No. 3, pp.630-640.

——— and P. E. Stephan. 1999. Knowledge spillovers in biotechnology: sources and incentives. ***Journal of Evolutionary Economics***, 9, pp.97-107.

Arora, A, A. Fosfuri and A. Gambardella. 2001. ***Market for Technology***. The MIT Press, London.

Cabri, W. and R. D. Fabio. 2000. ***From Bench to Market***. Oxford University Press, NY.

Chesbrough, H. W. 2003. ***Open Innovation***, Harvard Business School Press, Boston.

Cockburn, I. M. and R. M. Henderson. 1998. Absorptive Capacity, Coauthoring Behavior, and the Organization of Research in Drug Discovery. ***The Journal of Industrial Economics,*** Vol. 46, No. 2, pp.157-182.

Cusumon, M., Y. Mylondais and R. Rosenbloom. 1992. Strategic Maneuvering and Mass-Market Dynamics: The Triumph of VHS over Beta. ***Business History Review,*** Vol. 66, pp.1-94.

De Fraja, G. 1993. Strategic spillovers in patent races. ***International Journal of Industrial Organization***, Vol. 11, No. 1, pp.139-146.

Duncia, J. V., A. T. Chiu, D. J. Carini, G. B. Gregory, A. L. Johnson, W. A. Price, G. J. Wells, P. C. Wong, J. C. Calabrese and P. B. Timmerman. 1990. The Discovery of potent Nonpeptide Angiotension II Receptor Antagonists: A New Class of potent Antihypertensives. ***Journal of Medicinal Chemistry,*** 33, pp.1312-1329.

Levin, R. C., A. K. Klevorick, R. R. Nelson, and S. G. Winter. 1987. Appropriating the Returns from Industrial Research and Development. ***Brookings Papers on Economic Activity,*** No. 3, pp.784-831.

Naka, T. 1999. Angiotensin II Receptor Antagonist. ***Success Stories of Factor Studies for Circulatory Control Peptide in Japan,*** Nihon Rinsho Press, pp.65-70. (in Japanese)

——— 2000. Angiotensin II Receptor Antagonist Drug. ***Protein, Nucleic Acid and Enzyme***, Vol. 45, No. 6, pp.204-208. (in Japanese)

Nagaoka, S. 2001. Intellectual Property Right and Innovation. In Hitotsubashi Innovation Research Center (Eds), ***Introduction to Innovation Management***, Nihon Keizai Shinmun, Inc., pp.334-359. (in Japanese)

Nishikawa, K. 2007. "Development of ARB (Basic edition) - Lead Compound Discovered from Research for Diuretic Drug. ***Blood Pressure,*** Vol. 14, No. 5, pp.71-83.

Owen-Smith, J. and W. W. Powell. 2004. Knowledge Networks as Channels and Conduits: The effects of Spillovers in the Boston Biotechnology Community. ***Organization Science***, Vol. 15, No. 1, pp.5-21.

Powell, W. W., K. W. Koput and L. Smith-Doerr. 1996. Interorganizational Collaboration and the Locus of Innovation: Networks of Learning in Biotechnology. ***Administrative Science Quarterly,*** 41, pp.116-145.

Smith, H. L. and S. Bagchi-Sen. 2006. University-Industry Interactions: the Case of the UK Biotech Industry. ***Industry and Innovation,*** Vol. 13, No. 4, pp.371-392.

Tidd, J. and M. J. Trewhella. 1997. Organizational and technological antecedents for knowledge acquisition and learning. ***R&D Management,*** 27, 4, pp.359-375.

United States Patent, 4355040, Furukawa, et al. Oct. 19, 1982. Hypotensive Imidazole-5-Acetic Acid Derivates.

von Hippel, E. 2005. ***Democratizing Innovation.*** The MIT Press.

——— 1988. ***The Sources of Innovation.*** Oxford University Press.

Wong, P. C., S. D. Hart, J. V. Duncia and P. B. Timmermans. 1991. Nonpeptide angiotesin II receptor antagonists*. Studies with DuP753 and EXP3174 in dogs. ***European Journal of Pharmacology,*** 202, pp.323-330.

Yakuji Handbook. (Handbook of Pharmaceutical Affairs) 2007, Jiho. (in Japanese)

Zucker, L. G., M. R. Darby and J. S. Armstrong. 2002. Commercializing Knowledge: University Science, Knowledge Capture, and Firm Performance in Biotechnology. ***Management Science,*** Vol. 48, No. 1, pp.138-153.