How can We Promote Development of New Drugs from Academic Knowledge?: Focusing on Corporate Perspective on Contribution of Basic Research to Innovation

Koichi Sumikura[1], Hiromi Saito[1,2]
[1]National Graduate Institute for Policy Studies, Tokyo, Japan
[2]Chiba University, Chiba, Japan

***Abstract*--It is well understood that academic knowledge generated from basic research at university contribute to innovation in industrial sector. In order to demonstrate the degree to which academic knowledge contributes to innovation, we conducted multiple surveys on private corporations. Based on the results of our surveys, we have found the existence of a recognition gap between inventors and business managers with respect to contribution of academic knowledge to innovation. The reason for this gap is the potential disconnect in information between inventors and business managers concerning the application of academic knowledge.**

I. BACKGROUND AND RESEARCH FRAMEWORK

Basic research conducted at national universities and public research institutions (when referred to in this paper, "universities" include public research institutions, unless otherwise specified), also referred to as "academic research," has received large amounts of public funding in Japan; in particular, investment of public funds has accelerated since the enactment of the "Science and Technology Basic Law" adopted in September 1996 and the "Science and Technology Basic Plan (1996–2000)" in October 1997. Since then, the government has begun placing greater emphasis on the aspects of basic research that can be translated into industrial applications and provide a return to society, as shown in [1].

It is well known that academic knowledge born from basic university research and its contribution to innovation in corporations, as shown in [2]. Such academic knowledge contributes to the appearance of new products or services hat afford tangible benefits to society. However, the dramatic growth of patenting and licensing of publicly funded research had stimulated debates in science and technology policy, especially in the United States as shown in [3].

Figure 1. shows a conceptual framework of this study. Academic knowledge has both of promoting and impeding effects on innovation in corporations. In this paper, based on this framework, we try to answer to the following research questions. The first question is to what extent academic knowledge is contributing to corporate innovation. The second question is to what extent academic knowledge is impeding corporate innovation.

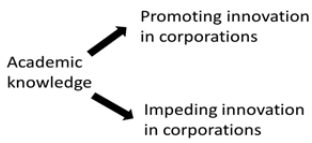

Figure 1. Conceptual framework of this study.

For the promoting effect, [4] and [5] evaluated its extent by the surveys in which the targets of surveys were individual corporations. Here we carry out an inventor survey to grasp perceptions of inventors who are actually absorbing academic knowledge in their daily R&D activities as well as a corporation survey to grasp the status in Japanese market. The extent to which industry evaluates contribution of academic knowledge to innovation is assumed to differ by the role of the person who responds. In discussing the degree to which university basic research contributes to innovation, it is likely that the degree of contribution recognized will be over or under-estimated unless it is based on this premise.

In considering the impact of academic knowledge on innovation in corporations, along with the positive impact as above, we also have to notice the negative impact that hinders corporate R&D, because existence of patents, know-hows or materials arisen from academic research may significantly delay R&D of corporations. Reference [6] tried to see the effects of research tool patents and licensing on biomedical innovation by interviewing 70 experts to find little evidence that university research had been impeded by concerns about patents on research tools. In our inventor survey we specifically analyze whether patents, know-hows or materials produced by academic research impede R&D activities of corporations in Japanese market.

II. REVIEW OF THE PREVIOUS STUDIES

According to [7], depending on the industry in question, it is necessary to cultivate an ability to absorb and adapt new and external information to increase the propensity to realize innovation for commercial application, known specifically as "absorptive capacity." Conducting basic research internally can contribute to a company's efforts to improve its absorptive capacity, allowing it to broaden its own base of knowledge, discover and understand external sources of new knowledge, and tie these activities to the development of new products and benefits.

Thus, for companies, to what extent does external knowledge generated from basic academic research results contribute to company innovation? While some research has been conducted to find clear answers to this question based on evidence, several different approaches have been taken. Reference [8] identified a positive correlation between university research expenditure and corporate patent applications by analyzing chronological data from different U.S. states. According to corporate questionnaire surveys carried out by [4], [5], without the results gleaned from

academic research, 13-15% of new products would not have been developed, or the appearance of these products would have been delayed considerably. In addition, [9] demonstrated that 73% of the academic papers cited in patents filed by U.S. companies were produced by university, or other public research institutions, indicating that academic research offers large contributions to industry.

From the survey results [4], [5], it is believed that there is a higher probability that the knowledge from basic academic research is applied in the field of drug and medical products industry. In addition, the proportion of products that would not have been developed if not for the results of academic research was estimated at an average of 15% across all industries between the years 1986 and 1994, whereas the figure was 31% for drugs and medical products —the highest percentage of all industries examined in the surveys. According to the survey results [10], the pharmaceutical industry is where science is most entwined with business. Reference [11] demonstrated that companies in the biotechnology industries are more reliant on public research and basic academic science than companies in other industries based on an analysis of patent references by post-IPO (Initial Public Offering) U.S. biotechnology companies. From these results, it is clear that there is a strong connection between academic research and innovation, especially with respect to companies in the pharmaceutical and biotechnology industries.

As stated previously, [7] determined that conducting basic research internally was effective as a method by which companies increase their absorptive capacity with respect to external knowledge. By interviews with members of pharmaceutical companies, [12] demonstrated that companies that are aiming at utilizing the results of publically funded research have to conduct joint research with the researchers receiving public funding, rather than just to concentrate on investing internal basic research. The analysis of pharmaceutical industry in [12] further demonstrated a positive correlation between the number of papers co-authored with publicly funded researchers and the corporate performance, represented by the number of important patents by unit of research expenditure.

It is demonstrated in [13], by focusing on the star scientists in genetics who had published numerous academic papers or belong to the top 112 U.S. universities, that the number of patent application and the frequency of patent citation are higher in the companies that have joint publications with the star scientists than others. An analysis of biotechnology related companies in Japan [14] demonstrated that the productivity of corporate research activity becomes higher by working with the university star scientists. Reference [14] also indicated by comparing Japan with the U.S. that the star scientists in the U.S. are more likely to conduct research in corporate laboratories, whereas Japanese star scientists are more likely to conduct research in their own laboratories with corporate researchers.

Based on the status of patent applications jointly-filed by universities and Japanese pharmaceutical companies, [15] demonstrated that making a tie with academic research improves corporate R&D performance, using an indicator of propensity to capture basic research. However, [15] found no evidence that the frequency of utilization of academic research had a significant positive impact on the number of novel drug products developed, suggesting the existence of disconnect between the development of new drugs by pharmaceutical companies and the effective use of academic research.

Thus, what is the extent of the economic and social impact of public research funding in the field of pharmaceuticals and biotechnology? It is stated in [16] that the rate of return to public funding of biomedical sciences may be as high as 30% per year. In addition, [17] indicated that the National Institutes of Health (NIH) funding of basic academic research, potential market size and industry R&D expenses offered a positive contribution to the development of new drugs. Through this research, [17] estimated that the 1% increase of public funding on basic research results in 1.8% increase in new drugs. Actually, there are numerous new drugs developed based on academic research results. According to [18], of all the vaccine and drug products that received Food and Drug Administration (FDA) approval over the past 40 years, 153 were developed from public academic research activities, demonstrating the economic and social impact of the public support for basic life sciences research in the U.S.

Of course, outside of the cases where academic knowledge arisen from public funding is directly contributing to the development of new drugs, it may offer a greater indirect impact on corporate R&D by providing a hint to overcome bottlenecks in or a research tool for the development of new products. Accordingly, in order to gain a more sophisticated understanding of the impact of academic knowledge on innovation in corporations, it is necessary to consider the whole picture including these indirect contributions.

On the basis of this background, this paper will discuss whether university research is affecting on innovation in corporations positively or negatively, respectively, focusing on inventors of pharmaceutical and biotechnology companies in Japan.

III. METHODS

To approach the question, to what extent academic knowledge derived from basic research contributes to innovation in corporations, we conducted a questionnaire survey while referring to prior research works. One of the prior studies we cited was [4] and [5], the studies investigating the proportion of products whose development was never completed or was significantly delayed due to a lack of academic research results. In following this precedent, we also included in our survey the questions designed to pinpoint the proportion of products or services that would have never been developed without the results of research

conducted by academia.

The subjects of the questionnaire were primarily company management staff or operations staff involved in similar duties. Surveys geared towards management staff or a management division (hereafter, "management" shall, unless otherwise specified, also refer to administrative staff) have the advantage of requiring only one questionnaire be sent to each company. Thereby, numerous companies can be surveyed simultaneously. However, since the questionnaires will not be answered by those actually participating in the activities creating the inventions (e.g., internal scientists, R&D employees, etc.), by absorbing information from a variety of sources, another questionnaire specifically targeting inventors needed to be sent separately in order to assess the actual situation at the R&D sites. Surveys targeting inventors were sent to each individual inventor.

Here we provide a detailed explanation of the two survey methods implemented.

A. Corporation survey

We independently designed our questionnaire and entrusted the implementation of the survey to the Teikoku Data Bank (TDB). Specifically, the "TDB Economic Climate Survey," administered monthly by TDB, was used. The surveys were conducted via the Internet. The survey targets were Japanese companies of all industry types; if companies agreed to participate in the survey, they received a survey form. The survey period was from December 17th, 2008 to January 5th, 2009.

The survey company sent out requests via postal mail, providing written notification of a URL that respondents could access where they would be able to view the questions and enter their responses. The requests were sent to the head offices of each company; individual departments were not specified. We anticipated that approximately 50% of the respondents would be members of management, but individuals who were not managers could also respond. The survey encompassed requests to 20,455 companies, resulting in valid answers from 10,731 companies. The response rate was 52.5%.

Companies that conducted neither internal nor external research activities were excluded from analysis based on this initial question, and the companies remaining made a sample size of 5,360.[1]

B. Pharmaceutical/biotechnology company inventor survey

Pharmaceutical/biotechnology company inventor surveys targeted Japanese companies in the pharmaceutical or biotech industries (as well as large-scale biotech start-up firms). Large-scale pharmaceutical companies were determined based on the top ten companies with the highest revenues in 2008 (according to IMS drug product market statistics; foreign companies were excluded). With regard to biotech start-ups, the 23 listed biotech start-ups as of September 2009 were identified. We focused on the patent applications of these companies (filed after 2005), and by using Patent Result Co., Ltd.'s "BizCruncher," we identified the inventors of patents of particular importance at each company according to Patent Score indicator.[2] For the 10 major pharmaceutical companies, 15 individuals were selected for each. Of these, two inventors stationed overseas were excluded (for a total of 148 inventors). For the 23 biotech start-ups, basically 15 individuals were selected for each but some did not have the minimum of 15 inventors as of 2005. For those companies as many inventors as available were excluded (the result was a total of 184 inventors selected from biotech start-up companies). Thus, a total of 332 inventors were identified, and surveys were sent to each inventor using the posting address of the department of the companies they were affiliated. The number of the returned mail due to unknown addressees were 6 large pharmaceutical companies and 23 from inventors in biotech start-ups. The survey period was from December 1st to 18th, 2009, with some reminder letters sent after this period. Of the 332 target respondents, the final sample size was 160 inventors (including 6 non-responders), with a collection rate of 48%.

Of the 154 valid respondents, 71 were from the 10 major pharmaceutical companies, 82 were from the 23 biotech start-ups, and 1 from unknown. All 71 inventors who were abstracted from the major pharmaceutical companies still belong to the companies at present. Concerning the 82 inventors who were abstracted from the biotech start-ups, the 65 are working for their companies, 2 were retired, and the other 15 are working for the university and public research institutes. In summary, approximately 90% of the respondents are inventors at companies. This survey, in accordance with its original purpose, can be regarded as summarizing the opinions of the inventors working at corporations.

IV. RESULTS

A. Results of corporation survey

Our survey included the questions designed to find out the extent to which academic knowledge contributes to the realization of innovation in companies in the form of new products or services. In concrete, respondents are requested to answer to the question, "What percentage of the products or services of your company do you believe would not have been produced if it were not for the results of research conducted at universities or public research institutions? Precise figures are not necessarily required and your best estimate is acceptable," by choosing from "all (100%)," "very large (30-100% though not 100%)," "large (10-30%)," "moderately large (3-10%)," "moderately small (1-3%)," "small (0.3-1%)," "very small (0-0.3% though not zero)," or

[1] For detailed results, please refer to [19].

[2] Patent Score of a given patent indicates its visibility to others, based on the indicators such as willingness of applicant to establish exclusive right, recognition of patent examiners as prior technology, and degree of attention from competing parties. http://www.patentresult.co.jp/about-patentscore.html

"nothing (0%)."

The results of the company survey are displayed in Figure 2. By reviewing the answers of all the companies in the company survey, regardless of industry types, we can see that an overwhelmingly large number of respondents chose "nothing" for the extent of contribution received, indicating that Japanese companies in general are placing little value on the potential contributions of academic knowledge.

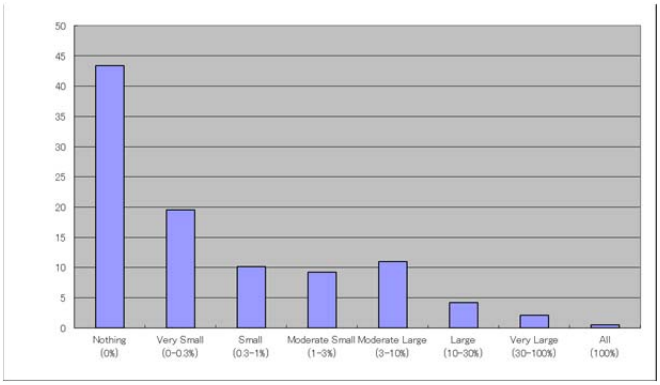

Figure 2. The rating of the extent of contribution of academic knowledge to innovation. The answers of all the companies in the company survey, regardless of industry types. N=5173.

B. Results of inventor survey and comparison of the responses between corporations and inventors

In terms of the question above, Figure 3 is a comparison of the result of pharmaceutical companies extracted from the responses to the corporation survey and that of the Pharmaceutical/biotechnology company inventor survey. The results of the inventor survey indicated higher ratings of the contributions of academic knowledge. As a result, a gap was observed with respect to views on the importance of academic knowledge between business managers and inventors involved with R&D activities in companies.

However, here we should notice that there were only 23 pharmaceutical companies within the scope of the companies targeted in the corporation survey, and that the companies targeted in the corporation survey are different from the ones to which the inventors targeted in the inventor survey belong.

When the responses across all companies, displayed in Figure 2, and the responses from pharmaceutical/biotech companies, displayed in Figure 3, are compared, more than 40% of Japanese companies provided the response of "nothing" regarding the extent of contribution of academic knowledge to innovation, while among the responses received from pharmaceutical companies the answer "moderately large" was most frequent. This is consistent with the prior research as in [4], [5], [10] respectively suggesting that with respect to pharmaceutical companies there is a smaller gap between academic research and business activities than in other industries.

Comparison of the one by pharmaceutical companies (N=23) in the company survey and the one by inventors (N=149) in the pharmaceutical/biotechnology inventor survey.

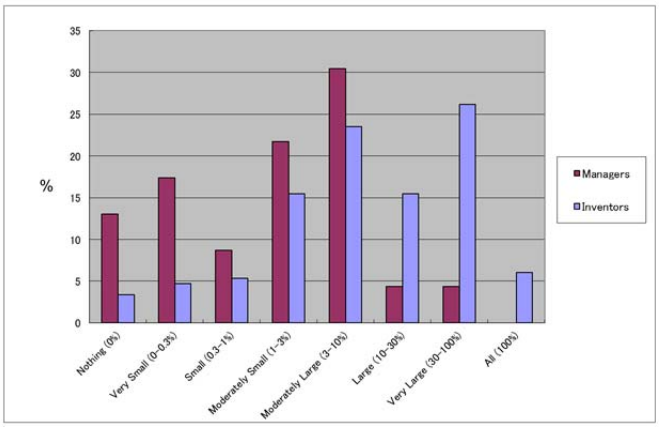

Figure 3. The rating of the extent of contribution of academic knowledge to innovation in company.

C. Impeding effects

Concerning the following questions in the pharmaceutical/biotech inventor survey, we compared the responses from 71 inventors who belong to the major pharmaceutical companies and the responses from 65 inventors who belong to the biotech start-ups.

The first question is, "Have you ever had the following experiences concerning your company's R&D?", asking to select an answer from "1: R&D was delayed more than one month due to the existence of patent rights/know-how or the non-smooth contract, 2: R&D was required to be modified due to the existence of patent rights/know-how or the non-smooth contract, 3: R&D was made to stop due to the existence of patent rights/know-how or the non-smooth contract, and 4: No such experience." As a result, the similar percentage of inventors of both the major pharmaceutical companies and the biotech start-ups selected the answer "d: No such experience," as shown in Figure 4. Judging from this percentage of answers, there was not a large difference between the inventors of these two types of companies.

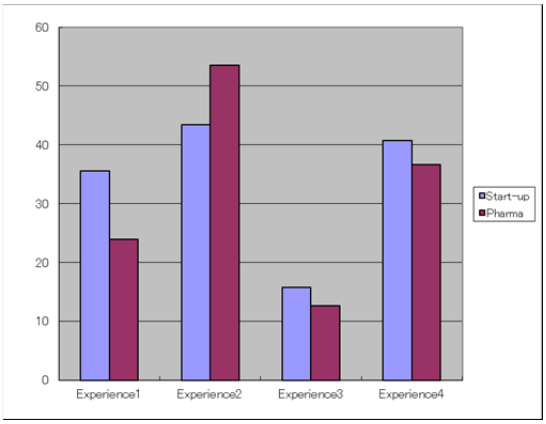

Figure 4. The percentage of the respondents having the experiences that R&D was impeded due to the existence of patent rights/know-how or the non-smooth contract.
1: R&D delayed, 2: R&D required to be modified, 3: R&D stopped, 4: No such experience.

In addition, targeting to the respondents that answered they had experiences of impediment of R&D to the question above, the second question "which of the following factors lead your company's R&D to be delayed, modified or stopped at that time?," asking for the respondents to select an answer from "1: patent right held by university and public research institute, 2: know-how held by university and public research institute, c: material held by university and public research institute, d: patent right held by company, e: know-how held by company, and f: material held by company." As a result, it was proven that the patent right held by a company have a greater influence on other company's R&D, but there was a lower possibility that the patent right held by university might impede corporate R&D. However, it was also found that the patent right, know-how or material held by university had greater influence on the biotech start-ups' R&D than on the major pharmaceutical companies' R&D (Figure 5).

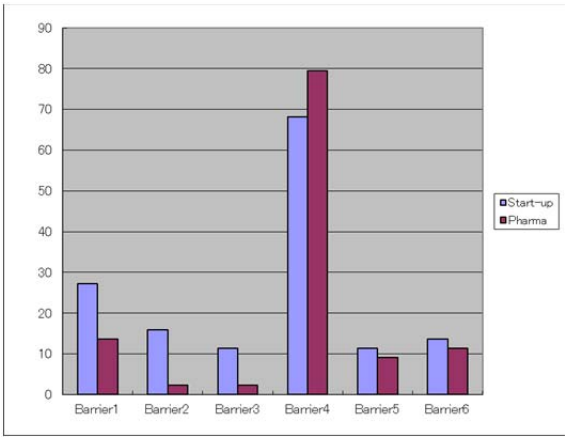

Figure 5. The percentage of the respondents having the experiences that R&D was impeded due to the following factors.
1: patent right held by university and public research institute, 2: know-how held by university and public research institute, 3: material held by university and public research institute, 4: patent right held by company, 5: know-how held by company, 6: material held by company.

The following issues were suggested by both the analysis of data from the pharmaceutical/biotech inventor survey and the comparison of the responses from the inventors in the major pharmaceutical companies and the ones from the inventors in the biotech start-ups. The patent held by companies had the greatest influence on corporate R&D, but the possibility that the patent held by universities impedes it is not high. However, the patent right, know-how and material held by university had greater influence on the biotech start-ups' R&D than on pharmaceutical companies' R&D.

V. DISCUSSION

As described in the first chapter, our research questions were (1) to what extent academic knowledge is impeding corporate innovation and (2) to what extent academic knowledge is contributing to corporate innovation.

As for (1), while the previous study of [6] showed there was little evidence that university research had been impeded by patents on research tools, on the contrary, our inventor survey specifically showed that the patents, know-hows or materials produced by academic research does not impede R&D activities of corporations so much in Japanese market. However, we should take a notice that the patent right, know-how and material held by university had larger influence on the biotech start-ups' R&D than on pharmaceutical companies' R&D.

As for (2), our results of comparison of the responses across all companies and pharmaceutical/biotech companies were consistent with the previous study [5] showing that the proportion of products that would not have been developed or significantly delayed if not for the results of academic research was higher in drugs and medical products than in all industries mean. In addition, in this study we also inquired the responses of inventors in pharmaceutical/biotech companies and found that inventors are rating contributions of academic knowledge to innovation more highly than business managers.

Regarding the extent to which academic knowledge contributes to innovation, one reason for the recognition gap between inventors and business managers is that although inventors are referring to academic knowledge in the form of various sources of information, such as published papers, they are not reporting existence of each individual piece of those academic knowledge to business managers. It results in that contribution of academic knowledge does not reach the awareness of management. As a result, management is only aware of knowledge produced by the company internally during the course of development of products or services, even when such products or services were developed in part through the introduction of external knowledge that contributed to the innovation, particularly when there is no clear joint agreement or patent licensing contract concluded between the company and a university. As a result, when discussing the significance of academic research, we should be careful not to overestimate the opinion of business managers who tend to disregard contribution of academic knowledge to innovation.

In addition to the ones described above, the recognition gap on contribution of academic knowledge to innovation between inventors and business managers might be caused by the fact that even if inventors introduce academic knowledge to corporate R&D activities it is difficult to produce new products or services to the market, especially in pharmaceutical/biotechnology industries. In the development of medical products, in particular, it is necessary to first conclude both nonclinical and clinical testing phases. Even in cases where academic knowledge contributes to the development of drug seeds, there are many cases where such knowledge offers no contribution to the subsequent commercialization of the product. As a result, it is possible that a recognition gap is then formed between inventors and

business managers based on this reality. This is consistent with the possibility of the existence of a non-continuous phase between the R&D activities aimed at the creation of new drugs and the entry of such products into the market, demonstrated in [15].

Nevertheless, it is also possible that the causality is opposite. Because of the recognition gap between inventors and business managers in terms of the possibility that academic knowledge contribute to the development of new drugs, even when academic knowledge that can be used for internal product development exists, it might be difficult for management to utilize those knowledge to decide on investment on large-scale development for the commercialization of such knowledge (that is, a "follow-on" investment). This feature can also potentially decrease the frequency of the development of new drugs based on academic knowledge.

If the findings described above are made into a formula, it is possible that a negative environment, such as in Figure 6, may be created. More specifically: (i) the recognition gap between inventors and business managers concerning the degree of contribution of academic knowledge to innovation in company, will result in company managers underestimating the impact of academic knowledge; (ii) managers will become hesitating to decide on follow-on investment on R&D by introducing academic knowledge; and, (iii) successful development of new products or services (e.g., medical products in the case of pharmaceutical or biotechnology companies) will be hampered. As such, (iv) there will be no opportunities for academic knowledge to contribute to innovation, and therefore, business managers will not rate academic knowledge highly. This is observed as a vicious circle and leaves us with the question as to what are the best measures for dismantling this negative environment and shifting to a virtuous circle.

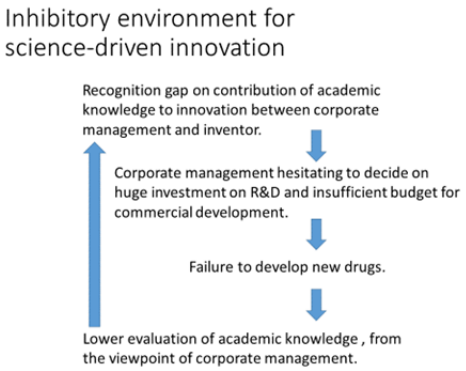

Figure 6. Vicious circle surrounding the development of new drugs based on academic knowledge.

To answer this question, we would like to consider solution measures by following the example of a representative drug, Actemra,[3] which is the first therapeutic antibody developed through joint research conducted by Osaka University (Professor Tadamitsu Kishimoto) and Chugai Pharmaceuticals. We asked Dr. Kishimoto to speak about the factors contributing to the success of the industry-academia partnership formed during the development of Actemra.[4] Particularly important is the fact that Dr. Kishimoto explained the potential of the IL-6 therapeutic antibody drug product directly to the president of Chugai Pharma. Dr. Kishimoto's passion paid off, and Chugai Pharma decided to install a 10-ton tank for production purposes at its Utsunomiya Plant. As a result, this investment was used as a determining factor in Roche's decision to partner with Chugai Pharma, and thanks to this partnership with Roche, it was possible to implement a 4,100 subject clinical trial in 40 countries with a budget of 30 billion yen. The ultimate result was that Actemra's use spread across the globe. We can see that the installation of this tank at the Utsunomiya Plant was an important step that became the premise for Roche's trial. This became possible in particular due to the long-standing trust relationship between Dr. Kishimoto and the president of Chugai Pharma. We believe that the key to the success of Actemra was overcoming the recognition gap between company managers and inventors regarding the contribution of academic knowledge to innovation, and creating an environment where those overseeing academic research can directly influence the top management of companies.

The success factors of the Actemra case, described above, can provide some clues for breaking away from the vicious circle, illustrated in Figure 6, and fostering the virtuous circle in Figure 7. More specifically, if there is academic knowledge that will lead to the implementation of innovation through follow-on investment, then: (i) through direct communication between academic researchers and top management, the recognition gap between management and inventors of the extent of contribution offered by academic knowledge to company innovation can be narrowed, allowing managers to correctly value academic knowledge and the potential developments offered by it; (ii) management decisions to execute follow-on investment in R&D can result from the introduction of academic knowledge to management; and, (iii) new products or services (in the case of pharmaceutical and biotech companies, drug products) can be successfully developed. Hence, (iv) the rating of the contribution of academic knowledge to company innovation by managers will increase; and, (v) decisions concerning the introduction of academic knowledge will be better facilitated, and as innovation based on the application of academic knowledge is realized, a more virtuous circle is likely to be formed. Validation of this model requires future study.

[3] Refer to [20] to [25] for further details.

[4] Interview was carried out on January 22nd, 2013.

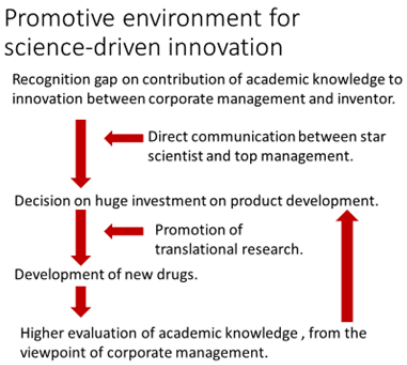

Figure 7. A measure for creating a virtuous circle in an environment supporting the creation of new drugs based on academic knowledge.

VI. CONCLUSION

As stated above, in this paper, we have a new finding, the existence of a recognition gap between inventors and business managers with respect to the contribution of academic knowledge to innovation in corporations, based on the results of our surveys. The reason for this gap is the potential disconnect in information between inventors and business managers concerning the application of academic knowledge, as well as the potential disconnect reflecting the tall hurdles between research conducted by companies and commercialization of the results. Against this backdrop, we cite the example of the case of the development of Actemra, and based on this example, examined what kinds of measures might be needed in the future to promote the development of new drug products from academic knowledge.

Academic research is an essential activity to accumulate knowledge for society and pass it on to those who come later. Almost no one would disagree with this activity in itself. Nevertheless, it is also a fact that academic research is conducted through a portion of the limited capital resources allotted to researchers from the government. Thus, in order for academic research to continue without interruption, it must establish and demonstrate not only conceptual theories but also concrete evidence of the legitimacy and value of allocating public capital to it. The societal and economic impact offered by academic research, demonstrated through evidence gathered from various corners, contributes to the cultivation of a societal consensus regarding the value of academic research.

REFERENCES

[1] Fujisue, K., "Promotion of academia-industry cooperation in Japan — establishing the "law of promoting technology transfer from university to industry" in Japan," *Technovation*, 18, 371-381, 1998.

[2] Rosenberg, N. and Nelson, R.R., "American universities and technical advance in industry," *Research Policy* 23, 323-348, 1994.

[3] Sampat, B. N., "Patenting and US academic research in the 20th century: the world before and after Bayh-Dole," *Research Policy,* 35, 772-789, 2006.

[4] Mansfield, E., "Academic research and industrial innovation," *Research Policy,* 20, 1-12, 1991.

[5] Mansfield, E., "Academic research and industrial innovation: An update of empirical findings," *Research Policy,* 26, 773-776, 1998.

[6] Walsh J. P., Arora A. and Cohen W. M., "Effects of Research Tool Patents and Licensing on Biomedical Innovation," in Cohen and Merrill (eds.), *Patents in the Knowledge-Based Economy.* The National Academies Press, Washington, DC.: 285-340, 2003.

[7] Cohen, W. M. and D. A. Levinthal, "Absorptive capacity: A new perspective on learning and innovation," *Administrative Science Quarterly*, 35(1), 128–152, 1990.

[8] Jaffe, A. B., "Real effects of academic research," *The American Economic Review*, 79(5), 957-970, 1989.

[9] Narin, F., Hamilton, K., Olivastro D., "The increasing linkage between U.S. technology and public science," *Research Policy*, 26, 317-330, 1997.

[10] Klevorick, A. K. et al., "On the sources and significance of interindustry differences in technological opportunities," *Research Policy*, 24, 185-205, 1995.

[11] McMillan S. G. et al., "An analysis of the critical role of public science in innovation: the case of biotechnology," *Research Policy*, 29, 1-8, 2000.

[12] Cockburn, I. M. and Henderson, R. M., "Absorptive Capacity, Coauthoring Behavior, and the Organization of Research in Drug Discovery," *Journal of Industrial Economics*, 46(2), 157-182, 1998.

[13] Zucker, L. G. et al., "Commercializing knowledge: university science, knowledge capture, and firm performance in biotechnology," *Management Science,* 48(1), 138-153, 2002.

[14] Zucker, L. G. and Darby, M. R., "Capturing technological opportunity via Japan's star scientists: Evidence from Japanese firm's biotech patents and products," *Journal of Technology Transfer*, 26, 37–58, 2001.

[15] Saito, H. and Sumikura, K., "An Empirical Analysis on Absorptive Capacity Based on Linkage with Academia," *International Journal of Innovation Management*, 14(3), 491-509, 2010.

[16] Cockburn, I. M. and Henderson, R. M., "Publicly Funded Science and the Productivity of the Pharmaceutical Industry," *NBER Chapters*, in: Innovation Policy and the Economy, 1, 1-34, 2001.

[17] Toole, A. A., "The impact of public basic research on industrial innovation: Evidence from the pharmaceutical industry," *Research Policy*, 41, 1-12, 2012.

[18] Stevens, A. J. et al., "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines," *New England Journal of Medicine*, 364(6), 535-541, 2011.

[19] Saito, H. and Sumikura, K., "How Are Fruits of Research in Universities and Public Research Institutes Used?: Brief Overview of the GRIPS Firm Survey," GRIPS Discussion Paper, 2010.

[20] Osugi, Y., "Development of tocilizumab, the first made-in-Japan antibody drug," *Journal of Industry-Academia-Government Collaboration,* 9(4), 11-16, 2013. (Japanese)

[21] Ito, K., "Story of development of new drug in Japan (2) tocilizumab (Actemra)," *International Pharmaceutical Intelligence*, 970, 20-23, 2012. (Japanese)

[22] Osugi, Y.; *Birth of a new drug, Actemra, the first made-in-Japan antibody drug.* Iwanami Shoten, 2013. (Japanese)

[23] Sumikura, K., "Contribution of university basic research to development of new drugs: case study," *the 11th annual research meeting of the Intellectual Property Association of Japan*, 2013. (Japanese)

[24] Hara, Y., Osugi, Y., Nagaoka, S., "Actemra–the first antibody drug by Japanese corporation that reformed therapeutics of rheumatoid arthritis," in Nagaoka (eds.), *Creating New Drugs.* Nikkei BP, Tokyo.: 281-319, 2016. (Japanese)

[25] Kishimoto, T., Nagaoka, S., Akaike, S., "Toward successful university-industry cooperation," *Hitotsubashi Business Review*, 61(3), 170-178, 2013. (Japanese)