

WINDS FROM JAPAN

The Licensing Executives Society Japan

CRISPR patent battles – Who will be the final winner?

By Jinzo Fujino *

CRISPR-Cas9 is a technique widely used for genome editing in not only eukaryotic cells in humans and plants, but also prokaryotic cells in bacteria. Since 2012, many patent applications have been filed in this cutting-edge technical field. The US Patent and Trademark Office (USPTO) has so far issued more than 300 patents with CRISPR-related claims to more than 500 inventors from nearly 100 institutes and organizations. The European Patent Office (EPO) has issued more than 100 such patents to approximately 250 inventors from about 60 institutions.

Reportedly, there are more than 4,500 patent families filed around the world. Most of them are still pending. One of the active players in this field is The Broad Institute which is a laboratory jointly established by the Massachusetts Institute of Technology (MIT) and Harvard University. Broad holds more than 40 key CRISPR patents in the United States, Europe, China and elsewhere.

In actuality, however, it was UC Berkley (UCB) that filed relevant applications earlier than Broad. UCB's team headed by Dr. Jennifer Doudna filed patent applications in May 2012 for methods and compositions for modifying a target gene which do not limit uses in eukaryotic cells. Seven months later, in December 2012, Broad' team headed by Dr. Feng Zhang filed patent applications with requests for accelerated examination to cover genome editing by CRISPR-Cas9 in eukaryotic cells and utilizing

the systems. Since then, Broad has obtained 20 patents for CRISPR-Cas9, as well as three for CRISPR-Cas12 while UCB has totaled 16 patents on CRISPR-Cas9. Broad and UCB are under interference procedures in the United States to determine who is the first inventor of CASPR-Cas9.

What has happened in Japan?

Japan is not exceptional for CRISPR patent races. Broad has already obtained 8 CRISPR-related patents here. Some of its applications are pending before the Japan Patent Office and some appeals are before the court. On February 25, 2020, the Intellectual Property High Court (IPHC) handed down two appeal cases: one in favor of Broad and the other in its disfavor.

The two patent applications at issue were derived from Broad's PCT/US2013/074743 which relates to CRISPR-Cas9 systems for use in eukaryotic cells. The JPO rejected them for the lack of novelty and inventive step and Broad appealed the JPO decision to the IPHC. On appeal, the court ruled one in Broad's favor and another in JPO's favor.

1) Novelty of tracr Sequences

As a basis for rejection of Application No. 128599/2016 entitled Crispr-Cas systems and methods for altering expression of gene products, the JPO cited a patent application PCT/US2013/073307 to Sigma-Aldrich (Citation 1) and an article in the American journal "SCIENCE" (Citation 2). On appeal, the court concluded that the JPO's rejection was erroneous on the following reasonings.

Focusing on “the length of trans-activating CRISPR RNA (tracr) sequences”, the present invention includes, as one of the elements of the invention, tracr sequences consisting of 30 or more nucleotides. With this element, efficiency of genome-editing has increased to cause a feature of the present invention. On the other hand, Citation 1 simply discloses the following: (i) the guide RNA contains 3 regions from the first to the third; (ii) a stem length is 6 to 20 base pairs; (iii) the third region is generally longer than 4 nucleotides, say, 5-60 nucleotides; and (iv) the length of the second and the third regions of the guide RNA is somewhere between around 30-120 nucleotides.

According to the description in the patent specification, the length of the tracr sequence corresponds to the length of the third region and one half of the stems in the second region of Citation 1. However, Citation 1 does not suggest anything about a technical idea to define the length of tracr sequences (or the length of the third region and one half of the stems in the second region).

And further, as of the date of priority to this invention, there is no evidence to show a common sense among those who skilled in the art that tracr sequences should be longer than 30 nucleotides. For these reasons, we cannot say that Citation 1 has descriptions to suggest a structure to include a tracr sequence in the length of 30 or more nucleotides. Neither we can say that a reference to an engineers’ common sense would be tantamount to such a description.

2) Inventive Step of tracr Sequences

The IPHC reviewed the article “A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity” (Citation 2) to determine whether it bars the Application at issue from issuing a patent in view of inventive step. A point of difference between the present invention and Citation 2 is that the length of tracr sequences is 30 or more in the present invention while the length of tracr sequences in Citation 2 is 26 nucleotides. The court elaborated on this point as follows.

It is understandable that, when compared, tracr sequences longer than 26 nucleotides are preferable to those shorter than the

threshold of 26 nucleotides. However, Citation 2 has no description about a preference of longer tracr sequences to shorter ones in terms of the threshold of 26 nucleotides. And further, there is no evidence to show a presence of an engineers’ common sense as of the date of priority to the present invention, namely, the longer tracr sequences are, the better their efficiencies are. Even if descriptions in Citation 2 and the engineers’ common sense are taken into account, we cannot conclude that the disclosure in Citation 2 on 26 nucleotides would motivate those who skilled in the art to change it to a longer length, say, 30 or more nucleotides in view of increasing efficiency of genome-editing.

Also, there exist no technical papers or patent literatures which refer to its applicability to eukaryotic cells, not in vitro, of CRISPR-Cas systems derived from immunes acquired in bacteria and archaea as mentioned in the summary of Citation 2. It appears that tracr sequences longer than 30 or more nucleotides have an increased efficiency of genome-editing in eukaryotic cells. It is worth appreciating that this fact is beyond the expectation or anticipation of those who skilled in the art.

The tracr sequence is a specifying matter of the present invention. Arguably it is a matter to distinguish the present invention from Citation 2. It is not easy for those who skilled in the art to conceive the tracr sequence longer than 30 or more nucleotides, from descriptions in Citation 2 or the then engineers’ common sense.

3) Inventive Step of tracr Sequences

Another patent application which was rejected by the JPO is Application No. 117740/2016 entitled “Engineering of systems, methods and optimized compositions for sequence manipulation.” Regarding the present invention as being identical to PCT/US2013/073307 (Citation 1), the IPHC upheld the JPO’s decision of refusal. The court reasoned as follows.

Citation 1 describes in detail methods for constructing each vector (i)-(iii) in Examples 1-3. Example 4 specifically describes ways of experiments to ascertain the insertion of donor sequences (GFP genes) into target sequences and in their

vicinity. It is understandable from the results of experiments in Example 4 that a combination of RNA-guiding endonuclease including NLS, guiding RNA and donor polynucleotides are inserted into eukaryotic cells to cut and repair the double-stranded DNA at the target site. Results of experiments in Example 5 do not obstruct such understanding.

And further, the vector system including above-mentioned vectors (i)~(iii) is equipped with technical means to carry out a proper transcription, translation and nuclear transfer of gene in eukaryotic cells as well as means for editing target sequences in eukaryotic cells. It is understandable that this function of cutting and editing target sequences in eukaryotic cells is available in the vector system. If so, it can be assumed that Citation 1 has ample descriptions to let those who skilled in the art know the disclosure of an early invention there and understand its practicability. Such descriptions are enough to preclude later applications from being patented.

Latest development overseas

In the United States, the PTO initiated a second round interference involving claims to CRISPR-Cas9 systems for use in eukaryotic cells on June 24, 2019. This proceeding involves patent applications of CVC (UC Berkeley, the University of Vienna, and Emmanuelle Charpentier) and Broad's patents which were involved in the first interference. Reportedly, in the second interference, the PTO designated

Broad and its collaborators, MIT and Harvard, as the senior parties and UCB as the junior party. In interference practice, the senior party is generally presumed to be the "first to invent." Because Broad's inventions go back to 2011, an interference proceeding under the old law is conducted.

On January 16, 2020, the EPO Board of Appeal dismissed Broad's appeal of an earlier Opposition Division decision which denied Broad's reliance on its U.S. priority provisional application for one patent in Europe based on a technical formality. Reportedly, it concerns the interpretation of rules concerning inventorship, i.e., what happens when the names of inventors differ across international applications. Now that several other patents are connected to this application, it is assumed that the decision may affect nine of Broad's 21 CRISPR-Cas9 patents in Europe.

In China, the State Intellectual Property Office has allowed 3 of Broad's patent applications. Broad expects a further grant of patents based on pending applications. UCB also has patents in China where patents are subject to invalidation proceedings after they are issued.

According to a press release by Broad, it has been, along with its collaborators, allowed and granted 8 CRISPR patents in Australia, 4 CRISPR patents in South Africa, 3 CRISPR patents in Russia, 2 CRISPR patents in Israel and 2 CRISPR patents in Singapore.

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*\* Editor / Office of Fujino IP Management*

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# LES Japan Online Mini-Annual Conference

**By Yasuo Fujii, Ph.D.\***

The LES Japan Annual Conference 2020 was held online due to the coronavirus pandemic. While being just a two-hour online conference called “Online Mini-Annual Conference”, it was very successful having a valuable keynote lecture and panel discussion under the positive theme of “Innovation for IP Activities after COVID-19!”.

The Conference started with opening remarks by Mr. Hiroki Saito, President of LES Japan. Mr. Saito expressed his expectation that innovation will overcome the threat posed by COVID-19, a threat that has never happened before. Mr. Saito also expressed his sincere appreciation for all healthcare professionals and introduced the LES Japan website (<https://www.lesj.org/>) which hosts a short movie expressing such appreciation.

Subsequently, the opening speech was given by Ms. Audrey Yap, President of LES International. Ms. Yap introduced the theme for her Presidential year, entitled “*LET’S Innovate!*”. In this regard, Ms. Yap expressed her great expectations for Japan to provide innovations, giving several examples of specific technologies developed by Japanese companies.

Then the keynote lecture was given by Dr. Fumihiko Matsuda, Professor at Kyoto University. Dr. Matsuda pointed out the current problems regarding the measures taken against COVID-19 - mainly based on a lack of understanding of actual infection status, effective actions, and the accuracy of test kits. Dr. Matsuda introduced his research into developing highly reliable antibody testing, which has been ongoing as collaborative research with Institut Pasteur. Dr. Matsuda expressed his strong intention to make the novel antibody testing be practical in real-world usage.



Dr. Fumihiko Matsuda

Subsequently, a panel discussion was held with the theme “IP Activities amid COVID-19 Pandemic and Role of Intellectual Property Department for New Normal thereafter” by the moderator: Mr. Toshiya Watanabe (Professor, at the University of Tokyo), and panelists: Mr. Shohei Imai (Corporate Vice President, General Manager of Intellectual Property Strategy Division, FUJIFILM Holdings Corporation), Mr. Kazushi Takemoto (Senior General Manager, Intellectual Property Department, SUNTORY HOLDINGS LIMITED), Mr. Kenichi Nagasawa (Managing Executive Officer, Head of Corporate Intellectual Property & Legal Headquarters, CANON INC.), and Mr. Hirokazu Bessho (Head of Supervisory Unit, Intellectual Property and Standardization Supervisory Unit, HONDA MOTOR CO., LTD.).



Mr. Toshiya Watanabe



Mr. Shoei Imai



Mr. Kazushi Takemoto



Mr. Kenichi Nagasawa



Mr. Hirokazu Bessho

The panelists introduced the ongoing measures in their companies amid the COVID-19 pandemic and they also gave their opinions in several aspects including teleworking, possible changes in business, and intellectual property strategies.

The moderator asked the panelists a question about how the management resources should be adapted to the new normal situation. Answers from the panelists included: activities for increased social liability, increased value of virtually obtained data, the necessity in construction of IP portfolios for new business related to digital transformation, and the necessity

in creating new value for newly developing, post-COVID-19 market.

The panel discussion indicated that changes in society due to the COVID-19 pandemic will provide the motivation for innovation and that new businesses which adapt to such changes will also develop the new IP strategies.

At the end of the Conference, Mr. Mitsuo Kariya, Organizing Committee Chair announced that the LES Japan 42nd Annual Conference will be held on July 9-10, 2021 at the Convention Hall Oumi annexed to the Lake Biwa Otsu Prince Hotel in Otsu city, Shiga prefecture.



Venue beside Biwa Lake

We hope to see you in Otsu soon!

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** Editor / Patent Attorney, Haruka Patent & Trademark*

IP News from Japan

By Shoichi Okuyama, Ph.D.*

Patent filings fall 10% in April and May

The Japan Patent Office (JPO) publishes the numbers of filings in different categories each month. The July figures were released on September 30, 2020. The numbers of filings for patents, utility models, designs, and PCT applications with the JPO as the receiving office are shown in the table below.

A state of emergency was declared for densely populated areas such as Tokyo and Osaka on April 7, 2020, and was lifted on May 21, 2020. According to statistics published by the Tokyo Metropolitan Subway, the number of passengers

decreased about 70% during the state of emergency.

The monthly numbers of patent applications were down even before the pandemic due in part to 15% increases in examination fees in April 2019, although the April and May 2020 figures do seem to show effects of the pandemic.

In addition, the Design Act underwent a major overhaul that took effect in April this year. It was expected there would be more design filings because subject matters of design registrations were expanded, but the pandemic overshadowed this.

While the annual figures remain to be seen, the recent downward trend in numbers of patent and design filings may continue.

2020	January	February	March	April	May	June	July
Patent and Utility Model	21,437 (-2.1)	24,213 (-6.8)	37,541 (-3.3)	21,317 (-10.9)	20,056 (-9.5)	25,918 (0.5)	23,656 (-6.1)
Design	2,306 (6.6)	2,294 (-2.4)	2,514 (-14.1)	2,870 (-2.1)	2,310 (-4.3)	2,869 (-0.7)	3,046 (15.0)
PCT RO	3,844 (8.2)	4,723 (6.7)	6,412 (-0.3)	3,386 (-10.3)	3,145 (-15.4)	4,241 (3.3)	3,853 (-6.1)

Figures in parentheses are percentile changes from the same month last year.

Warning: Retweeting may be copyright infringement

On July 21, 2020, the Supreme Court of Japan handed down a puzzling decision in a case that involves requests for disclosure of identifying information of originators based on the Act of Restrictions on the Liability of Internet Service Providers.¹ The plaintiff-appellee was a professional photographer and the defendant-appellants were Twitter Inc. and its Japanese subsidiary. In this case, the plaintiff asked for information on those who *retweeted* a tweet that included an unauthorized copy of plaintiff's picture. A person who was not involved in this case (person A) had uploaded the plaintiff's picture without plaintiff's authorization on Twitter, and those who were associated with five

twitter accounts retweeted that tweet. The Supreme Court found infringement on moral rights of the plaintiff and affirmed an IP High Court decision that ordered the defendants to disclose the email addresses of the holders of five Twitter accounts. The actors of infringement were found to be those who retweeted, not Twitter Inc. nor its Japanese subsidiary.

As we know, with Twitter, a picture may be shown with its upper and lower parts cropped in certain cases, and a truncated version of the original text may be shown, so that viewers can recognize that it is not an original tweet. In this case, the photographer placed his picture on his website with "Reproduction strictly prohibited" in the upper-right portion of the picture and © plus his name at the bottom-right. When person A

¹Shorthand for the Act, which has a much longer official name.

uploaded his picture, the entire picture appeared in the tweet, but when the tweet was retweeted, as shown on a PC monitor or smart phone, the upper and bottom portions were cropped, and the warning and copyright notice was not visible. Retweeting does not make a new copy of the picture. It merely creates a link to the originally uploaded picture. When a viewer clicks the cropped picture, the whole picture becomes visible. Those who retweeted had no control over this phenomenon. Nevertheless, the Supreme Court found copyright infringement.

The Japanese Copyright Act has two prongs of protection: copyrights as economic rights and personal moral rights. The moral rights consist of three categories: rights of making the work public (Art. 18), rights of determining the indication of the author's name (Art. 19), and rights of preserving the integrity of the work (Art. 20). In this particular case, the Supreme Court took up only the issue of the author's name. Initially, before the district court, five issues were argued and the court decided on those issues and found no infringement on the part of those who retweeted, but at the IP High Court, infringement was found on rights to preserve the work's integrity and indicate the author's name.

This is not a straightforward copyright infringement case. Those who originally

uploaded the picture and subsequently retweeted were not parties to this case, whereas the final finding of liability would depend on the determination of willfulness or gross negligence on their part. The email addresses of those who retweeted will be disclosed to the plaintiff, but it will be another matter whether the plaintiff can reach suspected infringers. The Supreme Court has discretionary power whether to take up a case and can reject a petition for acceptance of an appeal without explanation.

To this author, it is a mystery why the Supreme Court took up this case, only to affirm the original IP High Court decision. If person A is held liable for a clear act of infringement, that may have been sufficient for the protection of the copyright holder. As a result of this decision, which may be plausible as a legal theory, another unnecessary constraint has been placed on numerous and unaware Internet users. Now millions of Twitter users in Japan have to be mindful of complicated copyright issues when retweeting, otherwise they may be subject to information disclosure orders.

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## Editors' Note

This issue includes articles, "CRISPR patent battles - Who will be the final winner?" by Mr. Jinzo Fujino, "LES Japan Online Mini-Annual Conference" by Mr. Yasuo Fujii, and "IP News from Japan" by Mr. Shoichi Okuyama.

Thank you for supporting "*WINDS from Japan*." This newsletter will continue to provide you with useful information on activities at LES Japan and up-to-date information on IP and licensing activities in Japan.

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<https://www.lesj.org/en/winds/new.php>  
(YF)

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