UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THE BROAD INSTITUTE, INC., MASSACHUSETTS INSTITUTE OF TECHNOLOGY, and PRESIDENT AND FELLOWS OF HARVARD COLLEGE,

Patents 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356; 8,889,418; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; 8,999,641; and 9,840,713; and Applications 14/704,551 and 15/330,876,

Junior Party,

v.

TOOLGEN, INC.,

Application 14/685,510,

Senior Party.

Patent Interference No. 106,126 (DK)
( Technology Center 1600)

BROAD CONTINGENT MOTION 2
(to add claims 1, 40, and 41 of 15/160,710 and claims 74, 94, and 95 of 15/430,260)
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I. STATEMENT OF THE RELIEF REQUESTED

Pursuant to 37 C.F.R. §§ 41.121(a)(1)(i) and 41.208(a)(2) and Standing Order ("SO") ¶ 203.2, Junior Party, The Broad Institute, Inc., Massachusetts Institute of Technology, and President and Fellows of Harvard College ("Broad") contingent upon the grant of Broad Motion 1, moves to add Broad applications 15/160,710 ("710 Application") (allowable claims 1, 40, and 41) and 15/430,260 ("260 Application") (allowable claims 74, 94, and 95) to the Interference and designate the allowable claims as corresponding to Proposed Count 2. Allowable claim 1 of the 710 Application and allowable claim 74 of the 260 Application are claims that are generic as to the RNA configuration and thus, should be added to the Interference, along with their dependent claims that specify either dual-molecule RNA or single-molecule RNA, if the PTAB adopts Proposed Count 2.

Broad notes that in the event that the PTAB denies Broad Motion 1 and proceeds with Count 1, claim 41 of the 710 Application and claim 95 of the 260 Application are both limited to single-molecule RNA ("sgRNA") configurations and thus also correspond to Count 1.

The allowable claims in the 710 and 260 Applications exemplify the problem and unfairness with proceeding with Count 1. As shown by the allowance of these claims (and prior issued claims), Broad’s specifications fully describe and enable the invention of eukaryotic CRISPR-Cas9 systems with generic RNA, using either single- or dual-molecule RNA configurations. Count 1, however, prevents Broad from using its early dual-molecule RNA proofs, and it also unfairly puts Broad’s entitlement to generic RNA claims at risk. Broad invented eukaryotic CRISPR-Cas9 systems long before ToolGen even allegedly began working with eukaryotic single-molecule RNA CRISPR-Cas9 systems. But if ToolGen somehow prevailed with respect to Count 1, which it should not, Broad could lose its involved claims that are not limited
to single-molecule RNA, but are generic as to the RNA configuration and its entitlement to future
generic RNA claims.

In such a situation, the USPTO and third parties likely could argue under MPEP § 2308.03
that interference estoppel prevents Broad from continuing to pursue generic and dual-molecule
RNA claims—despite the fact that proceeding with Count 1 limited the PTAB to considering only
single-molecule RNA proofs in determining priority. To prevent this unfairness, the PTAB should
grant this Contingent Motion 2 along with Broad Motion 1.

II. DESCRIPTION OF APPENDICES

Appendix A is a List of Exhibits Cited. Appendix B is the Statement of Material Facts.

III. ARGUMENT

A. The Legal Requirements To Add Applications

SO ¶ 203.2 specifies the requirements for a motion to add an application to an interference
and provides that the motion must:

(1) Identify the application or patent to be added;

(2) Certify that a complete copy of the application file for the application or
patent has been served on all opponents except if it belongs to the opponent or if
the Office has posted it electronically;

(3) Indicate which claims of the patent or application should be designated as
corresponding to the count and show how the claims correspond to the count(s); and

(4) Explain whether there are alternative remedies; if so, why alternative
remedies are not adequate; and what attempts, if any, have been made to have the
examiner recommend declaration of another interference involving the application
or patent sought to be added to the interference.

B. The Broad Applications Should Be Added To The Interference

Contingent upon the PTAB granting Broad Motion 1 to substitute Proposed Count 2 for
Count 1, this motion is to add Broad Application 15/160,710 (allowable claims 1, 40, and 41)
and Broad Application 15/430,260 (allowable claims 74, 94, and 95) to the Interference and
designate the claims as corresponding to Proposed Count 2.

Proposed Count 2 reads as follows:

**Proposed Count 2**

Broad application 15/160,710, claim 1

or

ToolGen application 14/685,510, claim 85.

MF1; Broad Motion 1 at 4. Allowable claims 1, 40, and 41 of the 710 Application and 74, 94, and 95 of the 260 Application should be added and designated as corresponding to Proposed Count 2.

1. **Identification Of Applications To Be Added**

The applications to be added are: (1) Broad’s 710 Application (allowable claims 1, 40, and 41) and (2) Broad’s 260 Application (allowable claims 74, 94, and 95).

2. **Copies Of The Applications Have Been Posted By The Office**

The 710 and 260 Applications have been posted by the Office electronically, are available on Public PAIR, and are exhibits here. See MFs 2-4; Exs. 2063 and 2065.

3. **The Claims That Should Be Designated As Corresponding To Count 2**

Claims 1, 40, and 41 of the 710 Application and claims 74, 94, and 95 of the 260 Application should be designated as corresponding to Proposed Count 2.

Claim 1 of the 710 Application (the Broad half of Proposed Count 2) and claim 74 of the 260 Application are parallel independent claims, with claim 1 being a system claim and claim 74 being a method claim. Each claim encompasses subject matter wherein the RNA components are either separate molecules (dual-molecule RNA) or part of a single-molecule RNA (sgRNA). The other limitations of these two claims mirror limitations in currently involved claims designated as corresponding to Count 1. The dependent claims (claims 40 and 41 of the 710 Application and claims 94 and 95 of the 260 Application) each specifically cover one of the two alternative species
within the genus, where the first RNA and the second RNA either “are” fused or linked by intervening nucleotides (claims 41 and 95) \( (i.e., \text{are limited to single-molecule RNA}) \) or “are not” fused or linked by intervening nucleotides (claims 40 and 94) \( (i.e., \text{are directed to dual-molecule RNA}) \). Thus, the species claims also correspond to Proposed Count 2, which is generic as to the RNA configuration.

With respect to claim 1 of the 710 Application, it is the Broad half of Proposed Count 2, and thus, necessarily corresponds to Proposed Count 2. The correspondence to Proposed Count 2 of all the claims sought to be added via this Motion is demonstrated in the claim charts below:

**Claim Chart Showing Correspondence Of Claims 1, 40, and 41 of the 710 Application**

<table>
<thead>
<tr>
<th>Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)</th>
<th>Claim 1 of 15/160,710</th>
<th>Claim 40 of 15/160,710</th>
<th>Claim 41 of 15/160,710</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. An engineered CRISPR-Cas-system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:</td>
<td>1. An engineered CRISPR-Cas-system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:</td>
<td>40. The engineered CRISPR-Cas system of claim 1,</td>
<td>41. The engineered CRISPR-Cas system of claim 1,</td>
</tr>
<tr>
<td>I. a Cas9 or a nucleotide sequence encoding the Cas9, and</td>
<td>I. a Cas9 or a nucleotide sequence encoding the Cas9, and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)</td>
<td>Claim 1 of 15/160,710</td>
<td>Claim 40 of 15/160,710</td>
<td>Claim 41 of 15/160,710</td>
</tr>
<tr>
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</tr>
<tr>
<td>II. an RNA or a nucleotide sequence encoding the RNA, the RNA comprising (a) a first RNA comprising (i) a guide sequence capable of hybridizing to a target sequence of the DNA molecule adjacent to a Protospacer Adjacent Motif (PAM) in the eukaryotic cell and (ii) a tracr mate sequence, and (b) a second RNA comprising a tracr sequence capable of hybridizing to the tracr mate sequence, wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.</td>
<td>II. an RNA or a nucleotide sequence encoding the RNA, the RNA comprising (a) a first RNA comprising (i) a guide sequence capable of hybridizing to a target sequence of the DNA molecule adjacent to a Protospacer Adjacent Motif (PAM) in the eukaryotic cell and (ii) a tracr mate sequence, and (b) a second RNA comprising a tracr sequence capable of hybridizing to the tracr mate sequence, wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.</td>
<td>wherein the first RNA and the second RNA are not fused or linked by intervening nucleotides.</td>
<td>wherein the first RNA and the second RNA are fused or linked by intervening nucleotides.</td>
</tr>
</tbody>
</table>

2 Claim Chart Showing Correspondence Of Claims 74, 94, and 95 of the 260 Application

<table>
<thead>
<tr>
<th>Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)</th>
<th>Claim 74 of 15/430,260</th>
<th>Claim 94 of 15/430,260</th>
<th>Claim 95 of 15/430,260</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. An engineered CRISPR-Cas system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:</td>
<td>74. A method comprising: introducing into, or expressing in, a eukaryotic cell having a DNA molecule,</td>
<td>94. The method of claim 74,</td>
<td>95. The method of claim 74,</td>
</tr>
<tr>
<td>I. a Cas9 or a nucleotide sequence encoding the Cas9, and</td>
<td>(I) a Cas9 protein or a nucleotide sequence encoding the Cas9 protein, and</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Broad Half of Proposed Count 2</strong> (Broad application 15/160,710, claim 1)</td>
<td><strong>Claim 74 of 15/430,260</strong></td>
<td><strong>Claim 94 of 15/430,260</strong></td>
<td><strong>Claim 95 of 15/430,260</strong></td>
</tr>
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</tr>
<tr>
<td>II. an RNA or a nucleotide sequence encoding the RNA, the RNA comprising (a) a first RNA comprising (i) a guide sequence capable of hybridizing to a target sequence of the DNA molecule adjacent to a Protosparse Adjacent Motif (PAM) in the eukaryotic cell and (ii) a tracr mate sequence, and (b) a second RNA comprising a tracr sequence capable of hybridizing to the tracr mate sequence, wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.</td>
<td>(II) an RNA or a nucleotide sequence encoding the RNA, the RNA comprising: (a) a first RNA comprising a first ribonucleotide sequence and a second ribonucleotide sequence, and (b) a second RNA, and wherein the second RNA forms an RNA duplex with the second ribonucleotide sequence, and wherein, in the eukaryotic cell, the first ribonucleotide sequence directs the Cas9 protein to a target sequence of the DNA molecule, whereby the Cas9 cleaves or edits the DNA molecule or alters expression of at least one product of the DNA molecule in the eukaryotic cell.</td>
<td>wherein the first RNA and the second RNA are not fused or linked by intervening nucleotides.</td>
<td>wherein the first RNA and the second RNA are fused or linked by intervening nucleotides.</td>
</tr>
</tbody>
</table>

As set forth in the above claim charts and in the Seeger Declaration, all of the claims sought to be added correspond to Proposed Count 2. MFs 7-8; Ex. 2454, Seeger Decl. ¶¶ 203-06.

4. **No Other Remedy Would Be Adequate**

The reasons why Proposed Count 2 should be substituted for Count 1 are set forth in full in Broad Motion 1. Count 1 is limited to only a single-molecule RNA configuration. Proposed Count 2 is directed to a generic RNA CRISPR-Cas9 system for use in a eukaryotic cell wherein
components of the RNA are either on separate molecules (dual-molecule RNA) or are part of a single-molecule RNA (sgRNA). Unlike Count 1, Proposed Count 2 allows Broad the opportunity to present its earliest and best proofs, and permits Broad to establish that it was first to invent systems and methods for using CRISPR-Cas9 in eukaryotic cells. As shown above, claims 1 (the Broad half of Proposed Count 2) and 40 of the 710 Application and claims 74 and 94 of the 260 Application correspond to Proposed Count 2. Those claims are in allowable condition as acknowledged in Office communications dated April 5, 2021. MFs 5-6; Exs. 2063 and 2065.

No relief other than adding these generic and dual-molecule RNA claims (and substituting Proposed Count 2 for Count 1) would be adequate. These allowable claims are to the same, broader, CRISPR-Cas9 inventions that do not limit the RNA configurations and so encompass dual-molecule RNA configurations as were used in Broad’s earliest experiments. Thus, the subject matter of these claims is precisely what Broad was first to invent and is entitled to priority on. They include the dual-molecule RNA configurations that were the subject matter of Dr. Zhang’s experiments in 2011, all of which occurred substantially before his and ToolGen’s later, single-molecule RNA work in 2012.

If the PTAB denies Motion 1 and this motion, proceeding in this Interference with Count 1 would prevent Broad from using its dual-molecule RNA proofs associated with its earliest experiments to show priority. Should Broad lose the Interference (whether due to the unfair restriction on proofs or for other reasons), then the USPTO and third parties may still argue that interference estoppel destroys Broad’s entitlement to generic and dual-molecule RNA claims such as claims 1 and 40 of the 710 Application and claims 74 and 94 of the 260 Application—despite Count 1 limiting the priority proofs to the single-molecule RNA species.

That is because, as MPEP § 2308.03 explains, interference estoppel provides that “a losing
party is barred on the merits from seeking a claim that would have been anticipated or rendered obvious by the subject matter of the lost count.” *Id.* (citing *In re Deekler*, 977 F.2d 1449 (Fed. Cir. 1992); and *Ex parte Tytgat*, 225 USPQ 907 (Bd. Pat. App. & Inter. 1985)).

Because the single-molecule RNA subject matter of Count 1 is a species of the broader generic subject matter claimed by Broad in the applications it seeks to add contingently via this motion, the USPTO and third parties could argue Count 1 anticipates or renders broader, generic claims obvious. Similarly, the single-molecule RNA Count 1 recites all of the elements of a dual-molecule RNA CRISPR system (it merely *adds* a covalent linker to that system). Thus, the USPTO and third parties could argue that Count 1 anticipates or renders obvious dual-molecule RNA claims such as dependent claim 40 of the 710 Application and dependent claim 94 of the 260 Application. Accordingly, if those arguments were accepted, interference estoppel could prevent Broad from continuing to pursue the generic and dual-molecule RNA claims it here seeks to add, even though current Count 1 limits Broad to single-molecule RNA proofs rather than its earliest proofs.

Put differently, under Count 1, the PTAB would be resolving Broad’s entitlement to priority to the generic eukaryotic CRISPR-Cas9 invention by asking an overly narrow question—which party first invented the *single-molecule* RNA species of eukaryotic CRISPR-Cas9 systems.

If Broad Motion 1 is granted (as it should be), the applications identified herein should be added and the allowable claims designated as corresponding to Proposed Count 2; no other relief would be adequate as these allowable claims are to the same broad, eukaryotic subject matter as Proposed Count 2.

**IV. CONCLUSION**

For the foregoing reasons, contingent upon Broad Motion 1 being granted and Proposed Count 2 being substituted for Count 1, this motion should be granted, the 710 and 260 Applications
added to the Interference, and the allowable 710 application claims 1, 40, and 41 and allowable
260 application claims 74, 94, and 95 designated as corresponding to Proposed Count 2.

Dated: May 28, 2021

Respectfully submitted,

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Counsel for Junior Party
APPENDIX A: LIST OF EXHIBITS CITED

<table>
<thead>
<tr>
<th>Ex.</th>
<th>Description</th>
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<tbody>
<tr>
<td>2063</td>
<td>U.S. Patent Application 15/160,710, Zhang, May 20, 2016 (the ’710 Application)</td>
</tr>
<tr>
<td>2454</td>
<td>Declaration of Christoph Seeger, executed May 28, 2021</td>
</tr>
</tbody>
</table>
APPENDIX B: STATEMENT OF MATERIAL FACTS

1. Proposed Count 2 reads as follows:

**Proposed Count 2**

Broad application 15/160,710, claim 1

or

ToolGen application 14/685,510, claim 85.

2. The applications sought to be added are Broad applications 15/160,710 (allowable claims 1, 40, and 41) and 15/430,260 (allowable claims 74, 94, and 95). Exs. 2063 and 2065.

3. The 710 Application has been posted by the Office electronically and is available on Public PAIR. See Ex. 2063.

4. The 260 Application has been posted by the Office electronically and is available on Public PAIR. See Ex. 2065.


7. Claims 1, 40, and 41 of the 710 Application correspond to Proposed Count 2. Ex. 2454, Seeger Decl. ¶¶ 203-06.

8. Claims 74, 94, and 95 of the 260 Application correspond to Proposed Count 2. Ex. 2454, Seeger Decl. ¶¶ 203-06.
CERTIFICATE OF FILING AND SERVICE

I hereby certify that on May 28, 2021, a true and complete copy of the foregoing BROAD CONTINGENT MOTION 2 (to add claims 1, 40, and 41 of 15/160,710 and claims 74, 94, and 95 of 15/430,260) is being filed and served by 5:00 pm PT /8:00 pm ET via the Interference Web Portal and by agreement served by email on Senior Party by 8:00 pm PT / 11:00 pm ET to:

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