

Filed on behalf of: Junior Party, Broad

Paper No. ____

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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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3 **Cases**

4 *In re Deckler*, 977 F.2d 1449 (Fed. Cir. 1992) 8

5 *Ex parte Tytgat*, 225 USPQ 907 (Bd. Pat. App. & Inter. 1985) 8

6 **Rules and Regulations**

7 37 C.F.R. § 41.121(a)(1)(i) 1

8 37 C.F.R. § 41.208(a)(2)..... 1

9 Standing Order ¶ 203.2 1

10 MPEP § 2308.03 7

1 **I. STATEMENT OF THE RELIEF REQUESTED**

2 Pursuant to 37 C.F.R. §§ 41.121(a)(1)(i) and 41.208(a)(2) and Standing Order (“SO”)
3 ¶ 203.2, Junior Party, The Broad Institute, Inc., Massachusetts Institute of Technology, and
4 President and Fellows of Harvard College (“Broad”) contingent upon the grant of Broad Motion
5 1, moves to add Broad applications 15/160,710 (“710 Application”) (allowable claims 1, 40, and
6 41) and 15/430,260 (“260 Application”) (allowable claims 74, 94, and 95) to the Interference and
7 designate the allowable claims as corresponding to Proposed Count 2. Allowable claim 1 of the
8 710 Application and allowable claim 74 of the 260 Application are claims that are generic as to
9 the RNA configuration and thus, should be added to the Interference, along with their dependent
10 claims that specify either dual-molecule RNA or single-molecule RNA, if the PTAB adopts
11 Proposed Count 2.

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

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

1 to single-molecule RNA, but are generic as to the RNA configuration and its entitlement to future
2 generic RNA claims.

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

8 **II. DESCRIPTION OF APPENDICES**

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

10 **III. ARGUMENT**

11 **A. The Legal Requirements To Add Applications**

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

- 14 (1) Identify the application or patent to be added;
- 15 (2) Certify that a complete copy of the application file for the application or
16 patent has been served on all opponents except if it belongs to the opponent or if
17 the Office has posted it electronically;
- 18 (3) Indicate which claims of the patent or application should be designated as
19 corresponding to the count and show how the claims correspond to the count(s);
20 and
- 21 (4) Explain whether there are alternative remedies; if so, why alternative
22 remedies are not adequate; and what attempts, if any, have been made to have the
23 examiner recommend declaration of another interference involving the application
24 or patent sought to be added to the interference.

25 **B. The Broad Applications Should Be Added To The Interference**

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

1 designate the claims as corresponding to Proposed Count 2.

2 Proposed Count 2 reads as follows:

3 **Proposed Count 2**

4 Broad application 15/160,710, claim 1

5 or

6 ToolGen application 14/685,510, claim 85.

7 MF1; Broad Motion 1 at 4. Allowable claims 1, 40, and 41 of the 710 Application and 74, 94, and
8 95 of the 260 Application should be added and designated as corresponding to Proposed Count 2.

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

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

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

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

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

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

18 Claim 1 of the 710 Application (the Broad half of Proposed Count 2) and claim 74 of the
19 260 Application are parallel independent claims, with claim 1 being a system claim and claim 74
20 being a method claim. Each claim encompasses subject matter wherein the RNA components are
21 either separate molecules (dual-molecule RNA) or part of a single-molecule RNA (sgRNA). The
22 other limitations of these two claims mirror limitations in currently involved claims designated as
23 corresponding to Count 1. The dependent claims (claims 40 and 41 of the 710 Application and
24 claims 94 and 95 of the 260 Application) each specifically cover one of the two alternative species

1 within the genus, where the first RNA and the second RNA either “are” fused or linked by
 2 intervening nucleotides (claims 41 and 95) (*i.e.*, are limited to single-molecule RNA) or “are not”
 3 fused or linked by intervening nucleotides (claims 40 and 94) (*i.e.*, are directed to dual-molecule
 4 RNA). Thus, the species claims also correspond to Proposed Count 2, which is generic as to the
 5 RNA configuration.

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

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

Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)	Claim 1 of 15/160,710	Claim 40 of 15/160,710	Claim 41 of 15/160,710
1. An engineered CRISPR-Cas-system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:	1. An engineered CRISPR-Cas-system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:	40. The engineered CRISPR-Cas system of claim 1,	41. The engineered CRISPR-Cas system of claim 1,
I. a Cas9 or a nucleotide sequence encoding the Cas9, and	I. a Cas9 or a nucleotide sequence encoding the Cas9, and		

Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)	Claim 1 of 15/160,710	Claim 40 of 15/160,710	Claim 41 of 15/160,710
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,	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 first RNA and the second RNA are not fused or linked by intervening nucleotides.	wherein the first RNA and the second RNA are fused or linked by intervening nucleotides.
wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.	wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.		

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

Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)	Claim 74 of 15/430,260	Claim 94 of 15/430,260	Claim 95 of 15/430,260
1. An engineered CRISPR-Cas-system in a eukaryotic cell having a DNA molecule, the CRISPR-Cas system comprising:	74. A method comprising: introducing into, or expressing in, a eukaryotic cell having a DNA molecule,	94. The method of claim 74,	95. The method of claim 74,
I. a Cas9 or a nucleotide sequence encoding the Cas9, and	(I) a Cas9 protein or a nucleotide sequence encoding the Cas9 protein, and		

Broad Half of Proposed Count 2 (Broad application 15/160,710, claim 1)	Claim 74 of 15/430,260	Claim 94 of 15/430,260	Claim 95 of 15/430,260
II. an RNA or a nucleotide sequence encoding the RNA, the RNA comprising <ul style="list-style-type: none"> (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, 	(II) an RNA or a nucleotide sequence encoding the RNA, the RNA comprising: <ul style="list-style-type: none"> (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 the first RNA and the second RNA are not fused or linked by intervening nucleotides.	wherein the first RNA and the second RNA are fused or linked by intervening nucleotides.
wherein the guide sequence directs the Cas9 to the target sequence, whereby the DNA molecule is cleaved or edited in the eukaryotic cell.	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.		

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

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

5 The reasons why Proposed Count 2 should be substituted for Count 1 are set forth in full
 6 in Broad Motion 1. Count 1 is limited to only a single-molecule RNA configuration. Proposed
 7 Count 2 is directed to a generic RNA CRISPR-Cas9 system for use in a eukaryotic cell wherein

1 components of the RNA are *either* on separate molecules (dual-molecule RNA) or are part of a
2 single-molecule RNA (sgRNA). Unlike Count 1, Proposed Count 2 allows Broad the opportunity
3 to present its earliest and best proofs, and permits Broad to establish that it was first to invent
4 systems and methods for using CRISPR-Cas9 in eukaryotic cells. As shown above, claims 1 (the
5 Broad half of Proposed Count 2) and 40 of the 710 Application and claims 74 and 94 of the 260
6 Application correspond to Proposed Count 2. Those claims are in allowable condition as
7 acknowledged in Office communications dated April 5, 2021. MFs 5-6; Exs. 2063 and 2065.

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

16 If the PTAB denies Motion 1 and this motion, proceeding in this Interference with Count
17 1 would prevent Broad from using its dual-molecule RNA proofs associated with its earliest
18 experiments to show priority. Should Broad lose the Interference (whether due to the unfair
19 restriction on proofs or for other reasons), then the USPTO and third parties may *still* argue that
20 interference estoppel destroys Broad’s entitlement to generic and dual-molecule RNA claims such
21 as claims 1 and 40 of the 710 Application and claims 74 and 94 of the 260 Application—despite
22 Count 1 limiting the priority proofs to the single-molecule RNA species.

23 That is because, as MPEP § 2308.03 explains, interference estoppel provides that “a losing

1 party is barred on the merits from seeking a claim that would have been anticipated or rendered
2 obvious by the subject matter of the lost count.” *Id.* (citing *In re Deckler*, 977 F.2d 1449 (Fed. Cir.
3 1992); and *Ex parte Tytgat*, 225 USPQ 907 (Bd. Pat. App. & Inter. 1985)).

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

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

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

22 **IV. CONCLUSION**

23 For the foregoing reasons, contingent upon Broad Motion 1 being granted and Proposed
24 Count 2 being substituted for Count 1, this motion should be granted, the 710 and 260 Applications

1 added to the Interference, and the allowable 710 application claims 1, 40, and 41 and allowable
2 260 application claims 74, 94, and 95 designated as corresponding to Proposed Count 2.

3
4 Dated: May 28, 2021

Respectfully submitted,

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APPENDIX A: LIST OF EXHIBITS CITED

Ex.	Description
2063	U.S. Patent Application 15/160,710, Zhang, May 20, 2016 (the '710 Application)
2065	U.S. Patent Application 15/430,260, Zhang, February 10, 2017 (the '260 Application)
2454	Declaration of Christoph Seeger, executed May 28, 2021

1 **APPENDIX B: STATEMENT OF MATERIAL FACTS**

2 **1.** Proposed Count 2 reads as follows:

3 **Proposed Count 2**

4 Broad application 15/160,710, claim 1

5 or

6 ToolGen application 14/685,510, claim 85.

7 Broad Motion 1 at 4.

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

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

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

14 **5.** Claims 1, 40, and 41 of the 710 Application are in allowable condition as
15 acknowledged in an Office communication dated April 5, 2021. Ex. 2063 at April 5, 2021 Office
16 Communication, page 2. (Part 4 at PDF pp. 230, 253).

17 **6.** Claims 74, 94, and 95 of the 260 Application are in allowable condition as
18 acknowledged in an Office communication dated April 5, 2021. Ex. 2065 at April 5, 2021 Office
19 Communication, page 2. (Part 36 at PDF p. 248).

20 **7.** Claims 1, 40, and 41 of the 710 Application correspond to Proposed Count 2. Ex.
21 2454, Seeger Decl. ¶¶ 203-06.

22 **8.** Claims 74, 94, and 95 of the 260 Application correspond to Proposed Count 2.
23 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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