

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.

SIGMA-ALDRICH CO., LLC,

Application 15/456,204,

Senior Party.

Patent Interference No. 106,133 (DK)
(Technology Center 1600)

BROAD CONTINGENT MOTION 2
(to add claims 52-54 of Broad's 403 application)

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

2 Junior Party, The Broad Institute, Inc., Massachusetts Institute of Technology, and
3 President and Fellows of Harvard College (“Broad”), contingent upon the grant of Broad Motion
4 1, moves pursuant to 37 C.F.R. §§ 41.121(a)(1)(i) and 41.208 and Standing Order ¶ 203.2 to add
5 Broad Application No. 16/177,403 (“403 application”), allowable claims 52-54, to this
6 Interference and designate those claims as corresponding to Proposed Count 3.

7 Independent claim 52 of the 403 application recites a method to cleave both strands of
8 DNA in a eukaryotic cell and repair them through integration of a template polynucleotide (a
9 “Donor Template Integration” claim). Claim 52 is generic as to RNA and so encompasses both
10 dualRNA and sgRNA embodiments of CRISPR-Cas9 systems. Dependent claims 53 and 54 each
11 separately specify either a dualRNA or sgRNA embodiment of claim 52 respectively. The claims
12 of the 403 application are indicated as allowable as of the Office Actions dated October 5 and
13 November 15, 2021.

14 Given that these claims are allowable, these Donor Template Integration claims are
15 appropriate for addition to this Interference if it is redeclared with Proposed Count 3. Both halves
16 of Proposed Count 3 are limited to integration of polynucleotide template, i.e., are Donor Template
17 Integration claims. Thus, it would be proper to add the allowed claims of the 403 application here.

18 **II. DESCRIPTION OF APPENDICES**

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

20 **III. ARGUMENT**

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

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

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

12 **B. The Broad Application Should Be Added To The Interference**

13 Claim 52-54 of the 403 application should be added to the interference contingent upon the
14 grant of Broad Motion 1 to substitute Proposed Count 3 for Count 1. The claims are as follows:

15 52. A method comprising: introducing into, or expressing in, a eukaryotic cell
16 having a DNA molecule,
17 (I) a Cas9 protein or one or more nucleotide sequences encoding the Cas9
18 protein,
19 (II) an RNA or one or more nucleotide sequences encoding the RNA, the
20 RNA comprising: (a) a first RNA comprising a first ribonucleotide
21 sequence and a second ribonucleotide sequence, and (b) a second RNA,
22 and
23 (III) a template polynucleotide,
24 wherein, the second RNA forms an RNA duplex with the second
25 ribonucleotide sequence, and wherein, in the eukaryotic cell, the first
26 ribonucleotide sequence directs the Cas9 protein to a target sequence of the
27 DNA molecule, whereby the Cas9 cleaves both strands of the DNA molecule
28 and the cleavage is repaired by integration of the template polynucleotide into
29 the DNA molecule in the eukaryotic cell.

30 53. The method of claim 52, wherein the first RNA and the second RNA are
31 not fused or linked by intervening nucleotides.

32 54. The method of claim 52, wherein the first RNA and the second RNA are
33 fused or linked by intervening nucleotides.

34 Independent claim 52 recites use of a CRISPR-Cas9 system to cleave both strands of DNA in a
35 eukaryotic cell and repair them through integration of a template polynucleotide. It encompasses
36 both dualRNA and sgRNA embodiments. Dependent claims 53 and 54 each specify either

1 dualRNA or sgRNA embodiments of independent claim 52 respectively.

2 All of Sigma’s involved claims are directed to methods of integrating a donor
3 polynucleotide sequence into the chromosomal sequence of a eukaryotic cell. Broad similarly has
4 issued and allowed Donor Template Integration claims covering subject matter requiring the use
5 of a donor polynucleotide to repair double-stranded cleavage in connection with a eukaryotic
6 CRISPR-Cas9 system. (These are specified and discussed in Motion 1.)

7 Sigma has argued through prosecution of its claims (as well as in related applications), and
8 now in Interference 106,132 (“132 Interference”), that Donor Template Integration claims are
9 directed to a distinct invention from claims that specify other forms of cleavage and repair. *See,*
10 *e.g.*, Ex. 2124 (132 Sigma Mot. 1) at 4:14-23, 6:23-29; Ex. 2074 (October 13, 2020 Applicant
11 Remarks) at 8-9 (“Applicant has concluded that CRISPR cleavage + donor integration claims, as
12 more specifically recited in the new claims presented herein, are patentably distinct from CRISPR
13 cleavage-only claims.”). Thus, Proposed Count 3, which is limited to Donor Template Integration
14 subject matter, defines the common subject matter of the parties to the Interference.

15 Broad has proposed using independent claim 52 of the 403 application as the Broad portion
16 of Proposed Count 3. MF 1. There is thus no question that the claims sought to be added here
17 would correspond to Proposed Count 3 and that adding them to the Interference is proper.

18 **1. Identification Of Application To Be Added**

19 The application to be added is Application No. 16/177,403, which contains allowed
20 claims 52-54. MF 2.

21 The claims of the 403 application were first indicated as allowable on October 5, 2021,
22 pending declaration of an interference, and prosecution was suspended. Ex. 2075 (403
23 prosecution history). Applicants subsequently conducted an interview on October 7, 2021 and
24 discussed potential amendments to the claims, those amendments were subsequently filed on

1 October 15, 2021. *Id.* After consideration, the Examiner entered those Amendments on
2 November 15, 2021 and continued suspension of prosecution pending declaration of an
3 interference. *Id.* MF 5-7.

4 **2. Copies Of The Application Have Been Posted By The Office And**
5 **Served On Sigma As An Exhibit**

6 The 403 application has been posted by the Office electronically, is available on Public
7 PAIR, and a complete copy of the 403 application file has been served on Sigma as Exhibit 2075
8 here. *See* MF 3-4; Ex. 2075 (403 prosecution history).

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

10 Claims 52-54 of the 403 application should be designated as corresponding to Proposed
11 Count 3. The claims of the 403 application are indicated as allowable in the Office Actions of
12 October 5, and November 15, 2021. MF 5-7. Given that claim 52 is the Broad half of the Proposed
13 Count 3, there is no question of correspondence to Proposed Count 3.

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

15 Pursuant to Standing Order ¶ 203.2, Broad is not aware of any alternative remedies that
16 exist, and Broad did not request the declaration of another interference, given the existence of this
17 Interference and Broad's Motion 1. The subject matter of these claims is the subject matter of
18 Proposed Count 3, and so another interference, or any other alternative remedy, is not available
19 and would not be appropriate.

20 Upon adoption of Proposed Count 3 based on the grant of Broad Motion 1, the 403
21 application claims 52-54 should be added and designated as corresponding to Proposed Count 3.

1 **IV. CONCLUSION**

2 For the foregoing reasons, contingent upon Broad Motion 1 being granted and Proposed
3 Count 3 being substituted for Count 1, this motion should be granted.

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5 Dated: December 3, 2021

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Respectfully submitted,

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APPENDIX A: LIST OF EXHIBITS CITED

Ex.	Description
2074	Excerpts of U.S. Patent Application 15/456,204, Chen et al., dated March 10, 2017
2075	U.S. Patent Application 16/177,403, Zhang et al., dated May 20, 2016 (the '403 Application).
2124	Paper 482, Sigma Motion 1 (to Substitute Proposed Count 2 for Count 1), Interference 106,132, November 19, 2021.

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

2 **1.** Proposed Count 3 reads as follows:

3 **Proposed Count 3**

4 Broad application 16/177,403, claim 52

5 or

6 Sigma Application 15/456,204, claim 31.

7 Broad Motion 1 at 6-7.

8 **2.** The application to be added is 16/177,403, allowed claims 52-54. Ex. 2075 (403
9 prosecution history).

10 **3.** The 403 application has been posted by the Office electronically and is available
11 on Public PAIR. *See id.*

12 **4.** A complete copy of the application file for Broad’s 403 application has been
13 served on Sigma as Exhibit 2075 here. *Id.*

14 **5.** The claims of the 403 application were first indicated as allowable on October 5,
15 2021, pending interference, and prosecution was suspended. *Id.*

16 **6.** Applicants subsequently conducted an interview on October 7, 2021 and
17 discussed potential amendments to the claims, which were subsequently filed on October 15,
18 2021. *Id.*

19 **7.** After consideration, the Examiner entered the Amendments on November 15,
20 2021 and continued suspension of prosecution pending interference. *Id.*

CERTIFICATE OF FILING AND SERVICE

I hereby certify that on December 3, 2021, a true and complete copy of the foregoing **BROAD CONTINGENT MOTION 2** (to add claims 52-54 of Broad's 403 application) is being filed and served by 8:00 pm ET via the Interference Web Portal (SO ¶ 105.3; Paper 27 at 11). Service copies are being sent by email by 11:00 pm ET to counsel for Senior Party as follows:

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