IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	17/638,355	Conf. No.: 6265
First Named Inventor	:	Feng Zhang, et al.	
Filed	:	February 25, 2022	
TC/AU	:	1633	
Examiner	:	Katherine R. Small	
Customer No.	:	198696	
Docket No.	:	BROD-4800US	
Title	:	CRISPR-ASSOCIATED MU TRANSPOSASE SYSTEMS	

AMENDMENT AND RESPONSE

FILED VIA EFS-WEB

Commissioner:

In response to the Non-Final Office Action mailed June 6, 2025 ("Office Action"), please enter and consider the amendments and remarks.

Certificate of EFS-WEB Transmission pursuant to 37 C.F.R. § 1.8

I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO, on September 5, 2025.

/Christopher D. Southgate/
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AMENDMENT TO THE CLAIMS

1. (Currently amended) An engineered system for inserting a donor polynucleotide into a target polynucleotide, the system comprising:
   a. one or more CRISPR-associated Mu transposases, wherein the one or more CRISPR-associated Mu transposases comprise a MuA, a MuB, a MuC, or a combination thereof;
   b. one or more Cas proteins, wherein the one or more Cas proteins comprise one or more Type I Cas proteins; and
   c. a guide molecule that can form a complex with the Cas protein and direct~~ing~~ sequence-specific binding of the guide-Cas protein complex to the target polynucleotide.

2. (Canceled)

3. (Canceled)

4. (Original) The system of claim 3, wherein the one or more Type I Cas proteins comprises Cas5, Cas6(i), Cas6(ii), Cas7, Cas 8, or a combination thereof.

5. (Original) The system of claim 1, wherein the one or more Cas proteins lacks nuclease activity.

6. (Original) The system of claim 1, wherein the one or more Cas proteins has nickase activity.

7. (Original) The system of claim 1, further comprising a donor polynucleotide.

8. (Withdrawn) The system of claim 6, wherein the donor polynucleotide comprises a polynucleotide insert, a left element sequence, and a right element sequence.

9. (Previously Presented) The system of claim 6, wherein the donor polynucleotide:
   a. introduces one or more mutations to the target polynucleotide,
   b. corrects a premature stop codon in the target polynucleotide,
   c. disrupts a splicing site,
   d. restores a splice site, or

e. a combination thereof.

10. (Original) The system of claim 9, wherein the one or more mutations introduced by the donor polynucleotide comprises substitutions, deletions, insertions, or a combination thereof.

11. (Original) The system of claim 9, wherein the one or more mutations cause a shift in an open reading frame on the target polynucleotide.

12. (Withdrawn) The system of claim 7, wherein the donor polynucleotide is between 100 bases and 30 kb in length.

13. (Original) The system of claim 1, wherein the target polynucleotide comprises a protospacer adjacent motif on 5' side of the target polynucleotide.

14. (Withdrawn) The system of claim 1, further comprising a targeting moiety.

15. (Currently amended) An engineered system for insertion of a donor polynucleotide into a target polynucleotide, the system comprising one or more polynucleotides encoding:
    a. one or more CRISPR-associated Mu transposases, wherein the one or more CRISPR-associated Mu transposases comprise a MuA, a MuB, a MuC, or a combination thereof;
    b. one or more Cas proteins, wherein the one or more Cas proteins comprise one or more Type I Cas proteins; and
    c. a guide molecule that can form a complex with the Cas protein and direct binding of the guide-Cas protein complex to a target polynucleotide.

16. (Withdrawn) The system of claim 15, further comprising a donor polynucleotide.

17. (Withdrawn) The system of claim 16, wherein the donor polynucleotide comprises a polynucleotide insert, a left element sequence, and a right element sequence.

18. (Withdrawn) The system of claim 1, comprising one or more polynucleotides or encoded products of the polynucleotides in one or more loci in Table 6 or 7.

19. (Withdrawn) The system of claim 1, comprising one or more polynucleotides or encoded products of the polynucleotides or fragments thereof in Table 8 or 9.

20. (Previously Presented) A vector comprising the one or more polynucleotides of claim 15.

21. (Previously Presented) An engineered cell comprising the system of claim 1.

22. (Withdrawn) The engineered cell of claim 21, comprising one or more insertions made by the system or the vector.

23. (Withdrawn - Previously Presented) The engineered cell of claim 21, wherein the cell is a prokaryotic cell, a eukaryotic cell, or a plant cell.

24. (Withdrawn - Previously Presented) The engineered cell of claim 21, wherein the cell is a mammalian cell, a cell of a non-human primate, or a human cell.

25. (Withdrawn - Previously Presented) An organism, or a population thereof, comprising the engineered cell of claim 21.

26. (Withdrawn – Currently amended) A method of inserting a donor polynucleotide into a target polynucleotide in a cell, the method comprises introducing to the cell:

a. one or more CRISPR-associated Mu transposases, wherein the one or more CRISPR-associated Mu transposases comprise a MuA, a MuB, a MuC, or a combination thereof;
b. one or more Cas proteins, wherein the one or more Cas proteins comprise one or more Type I Cas proteins; and
c. a guide molecule capable of binding to a target sequence on the target polynucleotide, and designed to form a CRISPR-Cas complex with the one or more Cas proteins; and
d. a donor polynucleotide,

wherein the CRISPR-Cas complex directs the one or more CRISPR-associated Mu transposases to the target sequence and the one or more CRISPR-associated Mu transposases inserts the donor polynucleotide into the target polynucleotide at or near the target sequence.

27. (Withdrawn) The method of claim 26, wherein the donor polynucleotide:

a. introduces one or more mutations to the target polynucleotide,
b. corrects a premature stop codon in the target polynucleotide,
c. disrupts a splicing site,
d. restores a splice cite, or
e. a combination thereof.

28. (Withdrawn) The method of claim 26, wherein the one or more mutations introduced by the donor polynucleotide comprises substitutions, deletions, insertions, or a combination thereof.

29. (Withdrawn) The method of claim 26, wherein the one or more mutations causes a shift in an open reading frame on the target polynucleotide.

30. (Withdrawn) The method of claim 26, wherein the donor polynucleotide is between 100 bases and 30 kb in length.

31. (Withdrawn) The method of claim 26, wherein one or more of components (a), (b), and (c) is expressed from a nucleic acid operably linked to a regulatory sequence.

32. (Withdrawn) The method of claim 26, wherein one or more of components (a), (b), and (c) is introduced in a particle.

33. (Withdrawn) The method of claim 32, wherein the particle comprises a ribonucleoprotein (RNP).

34. (Withdrawn) The method of claim 26, wherein the cell is a prokaryotic cell, a eukaryotic cell, or a plant cell.

35. (Withdrawn) The method of claim 26, wherein the cell is a mammalian cell, a cell of a non-human primate, or a human cell.

REMARKS

Status of the Claims

Claims 1, 4–22, and 26–35 are pending, with claims 1, 15, and 26 being independent. Claims 1, 15, and 26 are amended. Claims 2–3 are canceled without prejudice or disclaimer as to the subject matter recited therein. Claims 8, 12, 14, 16–19, 22, and 26–35 are withdrawn as being drawn to a non-elected invention. No new matter has been added.

Objections to the Drawings

In the Office Action, the Examiner objects to the drawings for formality issues. Applicants submit replacement sheets of the drawings to address these issues. Accordingly, withdrawal of the objection is respectfully requested.

Claim Rejections Under 35 U.S.C. §102(a)(1)

In the Office Action, the Examiner rejected claims 1, 3-7, 9-11, 13, 15, and 20 under 35 U.S.C. §102(a)(1) as allegedly being anticipated by Qi (WO 2019/051278 "Qi") and claims 1, 2, 5, 6, 7, 9, 10, and 15 under 35 U.S.C. §102(a)(1) as allegedly being anticipated by Mellor (WO 2017/123758 "Mellor").

Applicant respectfully traverses the rejections.

Applicant has amended claim 1 to incorporate all the limitations of claims 2 and 3, now canceled. Accordingly, the Applicant submits that the rejections under 35 U.S.C. § 102(a) do not apply to the claims as currently presented. Withdrawal of the rejections is respectfully requested.

Provisional Obvious-Type Double Patenting Rejections Based On Co-pending Applications

In the Office Action, the Examiner provisionally rejected claims 1, 3, and 5 on the grounds of non-statutory double patenting as allegedly being unpatentable over:

i. claims 1, 7, 11, 29, and 37 of co-pending Application No. 17/928,355;

ii. claim 1of co-pending Application No. 19/043,619;

iii. claim 1 of co-pending Application No. 18/269,813;

iv. claim 1 of co-pending Application No. 18/248,252; and

v. claim 1 of co-pending Application No. 17/773,104.

Applicant respectfully disagrees and traverses these rejections.

The issue of whether there is indeed double patenting is contingent upon whether the remarks herewith are considered and entered, and, if so, whether the Office believes there is overlap with claims ultimately allowed in the application. Upon a finding of otherwise allowable subject matter, where the provisional double patenting rejection is the only issue remaining in prosecution, and the Office believes there is overlap with claims ultimately allowed in the application, a Terminal Disclaimer will be considered only to expedite prosecution. Otherwise, Applicant respectfully requests that the non-statutory double patenting issues be held in abeyance until an agreement is reached regarding allowable subject matter.

No Waiver

All of Applicant's arguments and amendments are without prejudice or disclaimer. Applicant may not have addressed each specific rejection of the independent and dependent claims because Applicant submits that the independent claims are allowable, as discussed above. Applicant has not acquiesced to any such rejection and reserves the right to address the patentability of any additional claim features in the future.

CONCLUSION

Applicant submits the foregoing as a complete response to the Office Action. Applicant submits that this Amendment and Response places the application in condition for allowance and respectfully requests such action. If any issues can be resolved with an Examiner's Amendment or a telephone conference, please contact the Applicant's representative at (478) 292 5119.

No additional fees are believed due for consideration of this paper. However, the Commissioner is hereby authorized to charge any fee deemed necessary for consideration of this paper, including any extension of time fees or additional claim fees, or to credit any overpayment, to Deposit Account Number 50-5193, reference number BROD-4800US.

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

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17/638,355	**09/05/2025 03:02:59 PM Z ET**	**BROD-4800US**

Title of Invention

CRISPR-ASSOCIATED MU TRANSPOSASE SYSTEMS

Application Information

APPLICATION TYPE	Utility - U.S. National Stage under 35 USC 371	PATENT #	-
CONFIRMATION #	6265	FILED BY	COLLEEN SULLIVAN
PATENT CENTER #	72174034	FILING DATE	02/25/2022
CUSTOMER #	198696	FIRST NAMED INVENTOR	Feng Zhang
INTL. APPLICATION #	-	INTL. FILING DATE	-
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	CHRISTOPHER SOUTHGATE

Documents

TOTAL DOCUMENTS: 3

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US.pdf		8	-	184 KB
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-A....pdf	(1-1)	1	Amendment/Request for Reconsideration-After Non-Final Rejection	103 KB
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-CLM.pdf	(2-5)	4	Claims	126 KB

2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-REM.pdf	(6-8)	3	Applicant Arguments/Remarks Made in an Amendment	161 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US.pdf	BDCC74AA9D2F683F00C4F021E3F1FA270663AAC687FE0B6ED94FF453DA8EB4FF4B8D0C77D771E5B7B03B1A1D6F3E67E565187BDE1A5112ED0C35A99E97409111
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-A....pdf	903ABE1FE1AF21FABB4D056A9DC02C192F55F9C321A687C857372D8E7560A10C45D474ED43664DE492F9A01CB0F2C7ED7079EC5A4F324DDA9A9375338E20E095
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-CLM.pdf	9E8109D9CDB72B1E49E0F5CFDEDDFA0E2EC019E3E184519E5BF9B4E9CDE66CC5FFEF70C6E1AFAE609AB9B7429907117E65FF295D451AE5B5B7F42143A1DAD00D
2025-09-05_Final_BI_10596_Response_NFOA_BROD_4800US-REM.pdf	09185D846ACC69AD027024E56E8CB8252E4E2E97EBD352EFA9A47E3EE512EB046AC528C44AE51204617B6A95D6154E91B0995A1B6CF4F2558A020D86B003B242

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.