Filed on behalf of: **Junior Party, Broad** Paper No. ____
By: Steven R. Trybus
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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; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; 8,999,641, and Application 14/704,551),

Junior Party,

v.

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, UNIVERSITY OF VIENNA, and EMMANUELLE CHARPENTIER
(Application 13/842,859),

Senior Party.

Patent Interference No. 106,048 (DK)

BROAD et al. PRIORITY STATEMENT

BROAD PRIORITY STATEMENT

Pursuant to Bd.R. 204(a), Junior Party, The Broad Institute, Inc., et al. (collectively "Broad") states with respect to Count 1:

(a) Broad's earliest corroborated conception of the invention of Count 1 took place at least as early as February 4, 2011, in Cambridge, Massachusetts, United States of America, Exhibit A;

(b) Broad's earliest corroborated actual reduction to practice of the invention of Count 1 took place at least as early as March 6, 2011, in Cambridge, Massachusetts, United States of America;

(c) Broad's earliest corroborated diligence with respect to the invention of Count 1 began no later than February 4, 2011;

(d) Pursuant to Bd.R. 204 (a)(2)(iv), the attached, Broad Exhibit A is a copy of the earliest document, upon which Broad will rely to show conception of the invention of Count 1.

Dated: May 23, 2016

Respectfully submitted,

/Steven R. Trybus/

Steven R. Trybus
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CERTIFICATE OF FILING

I hereby certify that on the 23rd day of May, 2016, a true and complete copy of the foregoing BROAD et al. PRIORITY STATEMENT is being filed via the Interference Web Portal.

/Steven R. Trybus/

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Exhibit A

Print Form

BROAD INSTITUTE

CONFIDENTIAL MEMORANDUM OF INVENTION

This is an important document requiring careful attention
ALL QUESTIONS SHOULD BE ANSWERED
(Attach additional pages as needed)

1. Invention Title:

Multiplexed genome engineering

2. Project Information:

Core Faculty: Zhang Lab
Broad Program/Platform

Feng Zhang
Principal Investigator

3. General Subject Matter (check all that apply):

a)
- ☐ Small molecule/compound
- ☐ New use, existing drug
- ☐ Improvement of existing drug
- ☒ Method/process
- ☐ Database
- ☒ Gene/protein sequence
- ☐ Biological Materials
- ☒ Other: Gene therapy, biotechnology, synthetic biology
- ☒ Diagnostic
- ☒ Research tool
- ☐ Algorithm/software

b) KEYWORDS	c) COMPOUND IDENTIFIERS
genome engineering	
site-specific nuclease	
gene knock-out	
CRISPR	

4. Funding Sources:

Please include all sources of funding to any contributor for the research that led to this invention.

☐ US Govt ☐ Commercial/Private ☒ Broad ☐ Personal ☐ Other

Name of Sponsor	Grant Number	Broad Account Number	Title
Broad Institute/McGovern Inst		2000024	Startup Funding

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CONFIDENTIAL MEMORANDUM OF INVENTION

5. CONTRIBUTORS:

Please list all individuals who made any contribution to the conception of the invention or reduction of the invention to practice.

NAME & EMPLOYER	E-MAIL – PHONE	HOME ADDRESS – CITIZENSHIP	CONTRIBUTION (CHECK ALL THAT APPLY)
Feng Zhang Broad Institute	Personal Information REDACTED	Personal Information REDACTED	☐ Discussions ☒ Lab research ☒ Theory ☐ Provided materials ☐ Assay dev't
			☐ Discussions ☐ Lab research ☐ Theory ☐ Provided materials ☐ Assay dev't
			☐ Discussions ☐ Lab research ☐ Theory ☐ Provided materials ☐ Assay dev't
			☐ Discussions ☐ Lab research ☐ Theory ☐ Provided materials ☐ Assay dev't
			☐ Discussions ☐ Lab research ☐ Theory ☐ Provided materials ☐ Assay dev't

6. DESCRIPTION OF THE INVENTION:

(a) What problem does this invention solve? How was the problem solved in the past? What was the disadvantage to be overcome? If this invention is better than prior technologies, state the known advantages of the invention.

This invention addresses three specific needs in the genome engineering and biotechnology field:
1. Site-specific gene knockout in the endogenous genome: This need is currently addressed using site-specific nuclease technologies based on zinc finger and TAL effectors. The advantage of the described technology is that it does not require elaborate design and can be used to simultaneously knockout multiple genes within the same genome.
2. Site-specific genome editing: This need is currently addressed using natural or artificial site-specific nucleases or recombinases. The advantage of the described technology will be able to introduce site-specific double strand breaks to facilitate homologous recombination at the targeted genome loci.

(b) What is the key concept on which the invention is based? What are the distinguishing novel features of the invention?

The key concept of this invention is based on the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) found in many microbial organisms. Enzymes associated with the CRISPR complex use short RNA sequences to recognize specific target sites on the host genome and performs site-specific cleavage. The key novel feature of this invention is that it does not rely on the design of site-specific DNA binding proteins (i.e. zinc finger or TAL effector) and can be easily targeted to multiple sites through the use of multiple sequence-specific CRISPR spacer elements.

(c) What are the currently envisioned uses for the invention? Give a detailed description of how to use for each proposed application.

1. Generation of isogenic lines of mammalian cells for the study of genetic variations in disease.
2. Generation of genetically-modified animal models, either transgenic or viral-mediated delivery
3. Genome modification of microbes, cells, plants, animals or synthetic organisms for the generation of biomedically, agriculturally, and industrially useful products.
4. Gene therapy
5. Biological research tool, for understanding the genome: gene knockout
6. many others that depend on the basic ability of editing and rewriting the DNA content of genomes, as well as targeted inactivation of DNA-based organisms. Also may be used as therapeutic for targeting specific strains of bacterial infections, viral

(d) Please include, as appropriate, generic structures and/or ranges of conditions involved, expected primary and secondary therapeutic indications, and any other products that might be used in combination with your invention.

The described invention serves as a basic platform for enabling targeted modification of DNA-based genomes. It can interface with many delivery systems not limited to viral, liposome, electroporation, microinjection, and conjugation.

(e) Please indicate what you believe to be the closest prior art, including patents and publications.

Only one patent directly related: US 2010/0093617 A1

Other related art include anything pertaining to Zinc Finger or TAL Effector-based genome targeting. RNAi for targeted gene inactivation is also a related art.

7. Detailed Examples and/or Drawings; Chemical Name, Compound Tracking Number and Structure

(a) Attach drawings, sketches, flow sheets of syntheses, etc. showing the contemplated scope, and examples of how the invention is made and operates.

(b) For compounds, attach a sheet showing the chemical name, Compound Tracking Number and structure of any compounds within the contemplated scope of the invention. For nucleic acid sequences or polypeptides, include sequence listings if available.

8. Record of Invention:

EVENT	(APPROXIMATE) DATE	WHERE RECORDED (Notebook #, page #)	BY WHOM
Initial idea	2/4/2011	Electronic	Feng Zhang
First written description/ diagram	2/8/2011	Electronic	Feng Zhang
First reduction to practice			

9. Stage of Development:

☒ Concept ☒ Initial, promising result ☐ Proof of concept ☐ *In vitro* data ☐ Animal data

Please describe your plans for this project for the next year (include funding information).

Currently research is being conducted in my laboratory to rapidly test the efficiency of CRISPR system for sequence-specific genome modification. We anticipate to obtain proof of concept in 2 to 3 weeks.

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10. Outside Technology:

Please indicate whether any outside technology and/or material was used in the research that led to this invention. Please also indicate whether the research that led to this invention is covered by any third party agreements. Please attach any relevant agreements.

Third Party Material? (biological materials, compounds, vectors, cell lines, reagents, processes, methodology, natural products, other)	Material: Source:	MTA? ☐ Y ☐ N (Please explain)
Third Party Software?	Source:	License:
Sponsored Research Agreement?	Parties:	
Collaboration Agreement?	Parties:	
Confidential Disclosure Agreement?	Parties:	

11. Publications and Disclosures in the Field:

Please indicate whether any aspect of your invention has been publicly disclosed or used. Please attach any available publications.

Anticipated Presentation?	☐ Y ☐ N	Date:	
Manuscript Prepared?	☐ Y ☐ N	Submission Date:	
Article or Abstract	☐ Y ☐ N	Journal: Submission Date:	Print Publication Date: Online Publication Date:
Oral Disclosure	☐ Y ☐ N	Date: Occasion:	Handouts/written materials? ☐ Y
Thesis	☐ Y ☐ N	Presentation Date:	Date Shelved:
Press Release	☐ Y ☐ N	Date:	Publication:
Web Site	☐ Y ☐ N	Date:	URL:
Discussion with Industry Representative?	☐ Y ☐ N	Location: Date:	Individuals/Company:
Poster Presentation	☐ Y ☐ N	Date:	Occasion:
Has invention been used, tested or offered for sale outside of the Broad?	☐ Y ☐ N	Date:	Location:
Other?	☐ Y ☐ N		

12. Commercial Interest:

Please list any companies or commercial contacts that might be interested in this invention. Please also list any products you believe would be competing products to this invention.

Some potential applications:

Many life science tools companies will be interested in commercializing this tool: Life Technology (Invitrogen), Stratagene, Sigma, Qiagen, Sangamo, Cellectis.

Pharmaceutical companies will be interested in licensing this for use in their drug discovery/development process: Merck, Pfizer, Roche, Astra-Zeneca, etc.

Medical, gene therapy, bioenergy, agricultural, and industrial biotechnology companies will use this as a primary product or as a core technology for developing useful strains of cells and organisms: DuPont/Pioneer, Amgen, Monsanto, and many other smaller biotechs.

BROAD INSTITUTE

CONFIDENTIAL MEMORANDUM OF INVENTION

13. Signatures of Contributors:

All contributors employed by the Broad Institute, Inc. ("Broad") hereby assign all right, title and interest in this invention to Broad and agree to execute all documents as requested to assign said rights to Broad. All contributors employed by an entity other than Broad assign their rights pursuant to their own employment agreement or as otherwise agreed upon.

I/We hereby declare all statements made herein are true and complete to the best of my/our knowledge. I/we hereby further agree to cooperate in securing intellectual property protection and commercialization of the disclosed invention.

Feng Zhang	7CC-5011/REDACTED
Print Name	Broad Location/Phone
Feng Zhang Digitally signed by Feng Zhang DN: c=US, st=Massachusetts, o=Massachusetts Institute of Technology, ou=Client CA v1, cn=Feng Zhang, email=REDACTED Date: 2011.02.13 13:59:56 -05'00'	Feb 13, 2011
Signature	Date
Print Name	Broad Location/Phone
Signature	Date
Print Name	Broad Location/Phone
Signature	Date
Print Name	Broad Location/Phone
Signature	Date

14. Authorization:

Principal investigator, if not a named contributor.

Print Name of Supervisor	
Signature of Supervisor	Date

Supervisor's comments as to importance and plans for future research:

This invention addresses three specific needs in the genome engineering and biotechnology field:
1. Site-specific gene knockout in the endogenous genome: This need is currently addressed using site-specific nuclease technologies based on zinc finger and TAL effectors. The advantage of the described technology is that it does not require elaborate design and can be used to simultaneously knockout multiple genes within the same genome.
2. Site-specific genome editing: This need is currently addressed using natural or artificial site-specific nucleases or recombinases. The advantage of the described technology will be able to introduce site-specific double strand breaks to facilitate homologous recombination at the targeted genome loci.
3. DNA sequence-specific interference: This technology can be used to inactivate the genome of deleterious DNA-based organisms, such as microbes, viruses, or even cancerous cells, by directly introducing breaks at specific sites in the genome of these organisms.

Envisioned uses:
1. Generation of isogenic lines of mammalian cells for the study of genetic variations in disease.
2. Generation of genetically-modified animal models, either transgenic or viral-mediated delivery
3. Genome modification of microbes, cells, plants, animals or synthetic organisms for the generation of biomedically, agriculturally, and industrially useful products.
4. Gene therapy
5. Biological research tool, for understanding the genome: gene knockout
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