SYNGAP RESEARCH FUND

Collaboration. Transparency. Urgency.

BCM

Baylor College of Medicine

SRF Grant 19/1

Checks to: Baylor College of Medicine

Address:
PO Box 301207
Dallas, TX 75303-1207

GRANT AGREEMENT

THIS GRANT AGREEMENT (the "Agreement"), effective the 1st day of December, 2018 (hereinafter the "Effective Date"), is entered into by and between Baylor College of Medicine (hereinafter "Baylor") and SynGap Research Fund, Incorporated, with principal offices located at 1270 Lincoln Ave, Palo Alto, CA 94301 (hereinafter "Sponsor"), governing research to be conducted at Baylor in the laboratory of Dr. Jimmy Holder (hereinafter "Principal Investigator").

1) TERM

This Agreement shall commence on the Effective Date, and terminate on the 30th day of November, 2021.

2) RESTRICTED GRANT

Sponsor hereby grants to Baylor one-hundred and thirty thousand dollars ($130,000.00), subject to the terms and conditions set forth herein (the "Grant").

Baylor agrees to use the Grant solely for the purposes of conducting the Principal Investigator's scientific research project entitled "*Development Of iPSC Lines For The Purpose Of Understanding How SynGap1 Patient Mutations Impact SynGap Protein Levels And Human Neuron Function*," with the ultimate objective of making genetic discoveries and developing new therapies for the treatment and cure of patients with SynGap1 mutations (the "Research Project"). Baylor will devote the time, effort, and resources to the Research Project necessary to accomplish the milestones in the timeframe set forth in Exhibit A of this Agreement. The Grant shall not be used for any other purpose or program without the express prior written approval of Sponsor.

The Grant will be used over the Term in accordance with the budget set forth in Exhibit A to this Agreement. If unspent funds remain at the end of the term, BCM will return unspent funding.

Baylor shall hold the Grant in a separate restricted fund, the principal and income of which shall be expended by Baylor solely for the Research Project.

3) PAYMENT SCHEDULE

The Grant shall be paid in accordance with the following payment schedule:

Payment 1: $43,333, payable on December 1, 2018 or within two weeks of the date this Agreement is executed, whichever is later.

Payment 2: $43,333, less any surplus identified in the first year report, payable within one month of the receipt of an annual progress report (due November 1, 2019) or on December 1, 2019, whichever is later.

Payment 3: $43,334, less any surplus identified in the second year report, payable within one month of the receipt of an annual progress report (due November 1, 2020) or on December 1, 2020, whichever is later.

4) REPORTS AND DELIVERABLES

Baylor will complete annual progress reports, due on the 1st day of November of each year, which will describe Baylor's progress toward specific aims during the year of the report, as identified in the proposal from the appendix. A final progress report will be due 30 days after the completion of the project.

5) INTELLECTUAL PROPERTY AND THE SHARING OF DATA

With respect to any intellectual property that Baylor creates, develops, conceives, or reduces to practice, independently or jointly with others, under this Grant Agreement and to which the Sponsor does not have ownership rights, including without limitation iPSC lines and any associated data ("Intellectual Property"), Baylor hereby grants to Sponsor a worldwide, perpetual, paid- up, royalty-free, irrevocable, non-exclusive license for noncommercial research and education applications of such Intellectual property, and all applications required to meet Sponsor's charitable obligations (the "License"). To the extent Baylor's ability to grant the foregoing License with respect to any specific Intellectual Property is subject to the consent of a third party (i.e., Baylor jointly creates, develops, conceives, or reduces to practice any Intellectual Property with a third party that (i) is not a party to this Agreement and (ii) has superior rights to Baylor in such Intellectual Property), Baylor shall undertake reasonable efforts to obtain such consent.

With respect to research data, which shall include the recorded factual material commonly accepted in the scientific community as necessary to validate research findings (but not any preliminary analyses, drafts of scientific papers, plans for future research, peer reviews, or communications with colleagues), Baylor shall retain all rights in said data but shall provide timely and unrestricted access to the data to Sponsor.

As an educational institution, Baylor shall be free to publish the results of the project in scientific or other journals, and to present at professional conferences and meetings. After first publication, Baylor will make available the cells generated under this agreement to academic researchers solely for non-profit academic research and teaching purposes.

6) HUMAN SUBJECTS

All research under this grant that involves human subjects will follow all relevant laws and regulations and will have the approval of the Baylor Institutional Review Board (IRB) before any human subjects are enrolled.

7) **USE OF NAME**

No party to this Agreement shall use the name, logo, symbol, or marks of the other party, or the name of any employee, staff member, student, or agent of the other party, in advertising, promotional material, or any form of publicity without prior written approval of the party whose name is to be used.

8) **NO WARRANTIES**

In connection with the project, each party shall be responsible for its negligent acts or omissions and the negligent acts or omissions of its employees and agents. Baylor is conducting basic research, with no warranties, implied or express, including warranties of merchantability or fitness for a particular purpose or of non-infringement of patents or other proprietary rights. Any deliverables provided under this Agreement are provided "as-is."

9) **INDEMNIFICATION**

Baylor shall indemnify, defend, and hold harmless Sponsor and its members, directors, officers, employees, agents, and contractors and the heirs, personal representatives, successors, and assigns of each of them from and against any and all liability, loss, expense, attorney's fees, claims or suits arising from or in any way connected with any willful malfeasance or grossly negligent act or omission of Baylor and/or its agents, officers or employees in connection with performance of this Agreement, except for any claims arising from Sponsor's gross negligence or willful malfeasance.

Sponsor shall indemnify, defend, and hold harmless Baylor and its members, directors, officers, employees, agents, and contractors and the heirs, personal representatives, successors, and assigns of each of them from and against any and all liability, loss, expense, attorney's fees, claims or suits arising from or in any way connected with any Sponsor's grossly negligent or willfully malfeasant use of any deliverables, reports, or other items provided pursuant to this Agreement, except for any claims arising from Baylor's gross negligence or willful malfeasance.

[*Signature Page to Follow*]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the Effective Date.

SYNGAP RESEARCH FUND, INCORPORATED

By: _____

Name:

Title J. Michael Graglia
Managing Director,
SRF

BAYLOR COLLEGE OF MEDICINE

By: Leanne Scott

Name: Leanne Scott, Ph.D.

Title: Sr. Director, Sponsored Programs

EXHIBIT A

Research Project: Annual Budget and Timeline

Budget:

Post-doctoral fellow (50% effort)	$32,000	$32,000	$32,000	$96,000
Supplies and services - Holder				
iPSC reprogramming	$1,333	$1,333	$1,333	$4,000
iPSC consumables	$5,000	$5,000	$5,000	$15,000
Molecular Biology reagents	$5,000	$5,000	$5,000	$15,000
Total per year	**$43,333**	**$43,333**	**$43,333**	**$130,000**

Timeline:

Year 1

- Create three subclones of induced Pluripotent Stem Cells (iPSCs) in test patient's ("Test Patient") blood line
- Perform quality control of iPSC subclones (flow cytometry, karyotype
- immunofluorescent staining of pluripotency markers)
- Differentiate iPSCs into neurons
- Validate neuronal differentiation (immunofluorescent staining of neuronal lineage)
- Begin CRISPR/Cas9 correction of mutation

Year 2

- Complete CRISPR/Cas9 correction of Test Patient's mutation
- Validate specificity of genomic editing (exome sequencing)
- Determine molecular consequence of Test Patient's mutation on *SYNGAP1*/SynGAP expression
- Compare SynGAP abundance in Test Patient's line with other individuals with *SYNGAP1* mutations

Year 3

- Evaluate for neuroanatomical abnormalities in Test Patient's line compared with genetically corrected control line
- Compare neuroanatomical differences in Test Patient's line versus other *SYNGAP1* mutant lines
- Evaluate for cell signaling abnormalities in Test Patient's line versus genetically corrected control line
- Compare cell signaling abnormalities in Test Patient's line versus other SYNGAP1 mutant lines