


# SYNGAP RESEARCH FUND

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Collaboration. Transparency. Urgency.

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J. M. G. 3/11/21

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**Principal Investigator:**

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**Milestones:**

AIM 1: Determine the specific disruption by cell type of glutamatergic and GABAergic function caused by SYNGAP1 mutations in cells derived from patients with neurodevelopmental disease.

Results are an implementation of an experimental model featuring cultures containing excitatory and inhibitory neurons in different combinations of patient and control cell types. A comprehensive analysis of cell-specific functions in each of these combinations will be produced.

- By the end of Year 1, generation of glutamatergic and GABAergic cell lines with their correspondent isogenic controls.
- By the end of Year 2, characterization of electrical activity by 2-D multi-electrode arrays of excitatory and inhibitory neurons and characterization of their functional interaction in patient and isogenic controls.

AIM 2: Determine the molecular signatures of SYNGAP1 disruption in excitatory and inhibitory synaptic signaling at a single-cell proteome resolution.

Results are use of the experimental model established in Aim 1 to analyze changes in cell-specific proteomes with single-cell resolution and determine changes in excitatory and inhibitory protein interactomes. Additionally, a network propagation analysis will be produced to predict targets that can restore synaptic function and describe how inhibitory and excitatory signaling is regulated.

- By the end of Year 1, characterization and proteomic profiling for excitatory and inhibitory neurons from patients and isogenic controls.
- By the end of Year 2, computational biology integration of results obtained in Aims 1 and 2, electrical and biochemical activity for each cell type and interaction among inhibitory and excitatory neurons. Identification of new targets and starting of initial test-screens for translational applications.

**Terms and Conditions**

Attached.

## Grant Award Agreement Terms and Conditions

**Recitals:** SynGAP Research Fund ("SRF") is a California nonprofit public benefit corporation exempt from U.S. federal income tax pursuant to Section 501(c)(3) of the Internal Revenue Code of 1986, as amended (the "Code"). SRF was formed for the charitable purpose of improving the quality of life of SYNGAP1 patients through the research and development of treatments, therapies and support systems. SRF desires to provide funding to the Institution in the form of the Award in furtherance of its charitable purposes under the terms and conditions set forth herein, which are intended to provide SRF with adequate assurance that such funding will be used for the intended purposes and consistent with SRF's tax-exempt status. By accepting this Award, the Institution agrees to accept such funding and to carry out the intended purposes of the Award, in furtherance of SRF's purposes, on the terms and conditions set forth herein.

**Award:** The Award will be made to the Institution. The Institution is responsible for disbursing funds to the Awardee (typically the Principal Investigator). In accepting the Award from SynGAP Research Fund, the Awardee and the Institution agree to expend the Award exclusively for the purposes as set forth in the Research Project application submitted and pursuant to the milestones and reporting obligations described herein (the "Award Purposes").

The Award Period starts and ends on the dates set out above, and has been approved at the level of funding indicated below:

Year 1: Start Date: 3/1/2021, End Date: 2/28/2022, Total: \$65,000

Year 2: Start Date: 3/1/2022, End Date: 2/28/2023, Total: \$65,000

At the sole discretion of SRF, the Award Period and/or funding level may be increased and/or extended subject to need, available funds and approval by SRF's Board of Directors. The Institution acknowledges SRF has no obligation to make any additional grants or provide any other financial support to the Institution.

**Payment Schedule:** Payment will be disbursed in two payments. The first payment will be made promptly upon the execution of this Grant Award Agreement. The second payment will be made on January 1, 2022, provided that applicable targets, milestones, and reporting deliverables as described herein are met prior to such date.

**No-Cost Extension:** The Research Project shall be carried out in accordance with the milestones described herein. In the event that these milestones are not met within the time frame established herein, SRF and the Institution may mutually agree to extend the Award Period and corresponding payment dates set forth in the Payment Schedule, provided work towards completion of the milestones continues and there is no additional expense to SRF.

**Restricted Fund; Accounting:** The Institution shall hold the Award funds in a separate restricted fund, the principal and income (if any) of which shall be expended by Institution and Awardee solely for the Award Purposes. Although the Award funds need not be physically segregated, the funds and any income thereon shall be accounted for separately in the Institution's books and records.

The Institution or the Awardee, as applicable, shall (i) keep records of all of its receipts and expenditures of the Award funds, (ii) maintain a systematic accounting record of the receipt and disbursement of the Award funds and shall maintain substantiating documents (such as bills, invoices, cancelled checks, etc.) in its files for at least four (4) years after the Award funds have been fully spent, and (iii) make its books and records relating to the Award available to SRF for inspection, copying and auditing at reasonable times during the Award Period and for three (3) years after the Award funds have been fully spent, to confirm the Institution's and Awardee's compliance with their respective obligations under this Grant Award Agreement. Any onsite visit or audit shall be conducted at SRF's expense, following prior 30 day written notice, during normal business hours and no more than once in any 12-month period.

**Copyrights:** The copyrights in all written materials, photographs, drawings, software, and other works subject to copyright protection created or generated in the direct performance of this Grant Award Agreement shall be owned by the Institution. All such copyrighted works shall include a formal acknowledgement of SRF funding under this Agreement. The Institution shall provide at least one hard copy and an electronic copy of each such copyrighted work to SRF. SRF encourages the Institution to publish and disseminate any such copyrighted works. To the extent Institution has the legal right to do so, Institution grants SRF a perpetual, royalty-free,

nontransferable, non-exclusive right and license to use, reproduce, make derivative works, display, and perform publicly any copyrights or copyrighted material (including any computer software and its documentation and/or databases) first developed and delivered under this Grant Award Agreement for noncommercial research and education purposes in furtherance of SRF's charitable purposes.

**Patents:** The Institution will have the right to elect title to the patent rights in inventions resulting from the direct performance of this Grant Award Agreement. With respect to any intellectual property that the Institution conceives and first reduces to practice, independently or jointly with others, in the direct performance of this Grant Award Agreement and to which SRF does not have ownership rights as a joint inventor/owner, the Institution hereby grants to SRF a worldwide, perpetual, paid-up, royalty-free, non-exclusive license for noncommercial research and education applications of such intellectual property in furtherance of SRF's charitable purposes.

**Data:** 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), the Institution shall retain all rights in said data but, provided Institution has the legal right to do so, shall provide timely and unrestricted access to the data to SRF.

All materials created as part of the Research Project will be openly shared with the scientific community for noncommercial research and education use, including at the direction and request of SRF.

**Publications:** SynGAP Research Fund must be acknowledged as a source of funds in any publication dealing with the work carried out as part of the Research Project. SRF retains the right to publicize the Award, to publicly report on the Award's progress and outcomes of the Research Project as SRF deems appropriate, and to include any information about the Award, including the Institution's name, in its public reports, and SRF may make such information available on its website and part of press releases, public reports, speeches, social media, newsletters, tax returns and other public disclosures. Nothing in this Grant Award Agreement shall be deemed to grant any right to any of the trademarks, trade name or other intellectual property or good will of SRF.

**Recognition and Terminology:** If the Award type is in support of a postdoctoral fellowship, the recipient must be recognized as a "SynGAP Research Fund Fellow" or "SRF Fellow" in any materials referencing the fellowship.

**Reporting:** Reporting must occur every 6 months during the course of the Award Period. Reports should include:

1. Progress made towards the expected milestones and any significant accomplishments
2. Any setbacks or challenges to the project
3. Any significant staffing or other changes that may impact the outcome or long-term potential of the project
4. An accounting of how Award funds are being used

In addition, upon the completion of the Research Project, a final report shall be provided to SRF describing the outcome of the Research Project, including material findings and observations, an accounting of the expenditure of the Award funds, and whether any Award funds have not been spent. SRF may, in its sole discretion, determine whether Award funds remaining after the completion of the Research Project either must be returned to SRF or may be used towards another mutually agreeable purpose that is consistent with SRF's charitable purposes.

**Indemnification:** The Institution shall indemnify, defend, and hold harmless SRF and its directors, trustees, officers, employees, agents, and contractors and the heirs, personal representatives, successors, and assigns of each of them from and against any and all third-party demands, claims, actions, suits, losses, damages (including property damage, bodily injury, and wrongful death), arbitration and legal proceedings, judgments, settlements, or costs or expenses (including reasonable attorneys' fees and expenses) (collectively, "Claims") directly arising out of the acts or omissions of the Institution and/or its directors, trustees, officers, employees, agents, sub-grantees, sub-contractors, contingent workers and affiliates, the Awardee and/or any other staff working on the Research Project (collectively, the "Institution Parties"), with respect to this Grant Award Agreement, except to the extent such Claims arise from SRF's gross negligence or willful misconduct. The Institution agrees that any activities by SRF in connection with the Award or the Institution Parties' activities to achieve the Award Purposes, such as SRF's review or proposal of Award activities and expenditures, shall not

modify or waive SRF's rights under this paragraph. SRF may, at its own expense, employ separate legal counsel to monitor and participate in the defense of any Claim.

### **Limitation of Liability**

Notwithstanding anything to the contrary contained herein, to the maximum extent permitted by law, in no event will either party be responsible for any incidental, consequential, indirect, special, punitive, or exemplary damages of any kind, lost goodwill, lost profits, lost business or other indirect economic damages, whether such claim is based on contract, negligence, tort (including strict liability) or other legal theory, as a result of a breach of any warranty or any other term of this agreement, and regardless of whether a party was advised or had reason to know of the possibility of such damages in advance. Additionally, Institutions total liability under this agreement shall not be in excess of the total amount of Commitment paid by SRF to Institution under this agreement.

**Termination:** In addition to any other grounds for termination set forth in this Grant Award Agreement, SRF, in its sole discretion, may, upon 30 day written notice to the Institution and the Awardee, revoke this Award and cancel payment of future unpaid balances if at any time any of the following occurs: (1) the Institution becomes insolvent or files a voluntary petition in bankruptcy, (2) any third party files an involuntary petition in bankruptcy against the Institution, (3) any act by one or more of the Institution's creditors to access the Award funds in any manner, or (4) SRF determines, in its discretion, that (a) the Institution or Awardee is acting or has acted inconsistently with applicable law or the terms and conditions of this Grant Award Agreement, (b) SRF is not reasonably satisfied with the progress towards achieving the Award Purposes (including in the event that the milestones are not achieved within the desired timeline), (c) there is a change in the Awardee or any other staff who are material to carrying out the Award Purposes, (d) there is a change in the Institution's tax-exempt or non-profit status, or (e) the Institution or Awardee is acting in a manner that could damage the reputation of SRF.

**Miscellaneous:** This Grant Award Agreement is binding on and shall inure to the benefit of the Institution, its successors and assigns, and upon SRF's representatives, successors and assigns. The Institution may not assign, transfer or subcontract any of its obligations under this Agreement without the prior written consent of SRF. This Grant Award Agreement is executed in and shall be governed by the laws of the state of California. This Grant Award Agreement may be amended at any time by written agreement signed by each party. Awardee and Institution are responsible for all currency conversion fees. All notices or other communications required hereunder shall be made to the addresses identified on the first page of this Grant Award Agreement or at such addresses as a party may designate by written notice to the other party. This Grant Award Agreement may be executed by the parties in separate counterparts and delivered by facsimile or e-mail with scan attachment, each of which when so executed and delivered shall be an original, but all such counterparts shall together constitute one and the same instrument.

### **Trademarks**

Neither party shall use the name, trade name, trademark or other designation of the other party or its affiliates in connection with any products, promotion or advertising without the prior written permission of the other party.