Request for Applications

The ASAP Collaborative Research Network

CRN 2025 RFA | Scientific Track

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Opportunity

The Aligning Science Across Parkinson's (ASAP) Initiative invites applications from collaborative teams to join the ASAP Collaborative Research Network (CRN), an international, multidisciplinary, multi-institutional network of research teams working to address high-priority research questions in an effort to advance our understanding of Parkinson's disease (PD) and drive new ideas into the R&D pipeline. **For this cycle, applications within the Scientific Track that focus on dissecting the mechanisms that contribute to PD heterogeneity will be considered.** All applications must fall into one of the following six focus areas:

1. **Aging:** Examining PD in the Context of Aging
2. **Co-pathologies:** Understanding How Co-Pathologies Can Influence PD Pathogenesis and Progression
3. **Environmental Risk:** Role of Environmental Risk Factors in Contributing to Disease Pathogenesis
4. **Circuit Biology:** Understanding the Circuit Biology Driving Clinical Symptom Presentation (With an Emphasis on Non-motor Symptoms)
5. **Clearance:** Role of Clearance Mechanisms in PD
6. **Seeding:** Identification of Factors Influencing Seeding in the Alpha-Synuclein Seed Amplification Assay

Background

The ASAP Initiative

ASAP is a Parkinson's disease-focused, global initiative that aims to address key knowledge gaps in PD research to reinvigorate the PD research pipeline. ASAP is managed by the Coalition for Aligning Science (CAS) and implemented through the Michael J Fox Foundation for Parkinson's Research (MJFF). Led by Nobel laureate Dr. Randy Schekman, and Dr. Ekemini Riley, ASAP works with MJFF to leverage the Foundation's grant administration and grantmaking infrastructure to receive applications, administer the review process and execute grant awards to projects selected for funding.

ASAP is on a mission to accelerate the pace of discovery and inform the path to a cure for Parkinson's disease (PD) through collaboration, generation of research-enabling resources, and data-sharing. The ASAP initiative provides funding opportunities to the scientific community in support of higher-risk, large-scale, ambitious projects to spur discovery for PD research. To learn more, please visit our website and read about the initiative.

Goals of the ASAP Collaborative Research Network

Parkinson's Disease is a multisystem disorder encompassing motor and non-motor symptoms, which is why we support a collaborative, multidisciplinary approach to significantly increase our understanding of the disease. We will continue to build upon the international, multidisciplinary network of collaborating investigators first established by ASAP in 2020. In our efforts, we seek to:

- **Attract** diverse talent from relevant fields outside of PD and neurodegeneration, as well as young investigators who will infuse fresh ideas and perspectives to PD research.
- **Support** productive, meaningful collaborations to achieve goals that supersede the expertise or capabilities of any one lab.
- **Drive** intense focus to the selected research themes to accelerate discovery.
- **Embrace** the values of openness and transparency as a means of accelerating outcomes and improving the reproducibility and impact of research findings.

We encourage a forward-thinking approach to research that is not constrained by long-held hypotheses and dogma, and that is conducted in an environment of trust. As such, we seek to bring together investigators who are enthusiastic about working transparently in a highly collaborative network -- one that includes field experts working with investigators with no previous record of PD research, who prioritize innovation over safe bets, and who are willing to risk testing unconventional ideas.

Award Overview

Research Focus and Scope

The CRN 2025 Scientific Track will focus on supporting high-priority, mechanism-focused projects to drive new ideas into the Parkinson's disease R&D pipeline. **This RFA is centered around dissecting the mechanisms that can contribute to PD heterogeneity,** with a specific focus on one of the six following areas outlined below.

1. Examining PD in the Context of Aging
2. Understanding How Co-Pathologies Can Influence PD Pathogenesis and Progression
3. Role of Environmental Risk Factors in Contributing to Disease Pathogenesis
4. Understanding the Circuit Biology Driving Clinical Symptom Presentation (With an Emphasis on Non-motor Symptoms)
5. Role of Clearance Mechanisms in PD
6. Identification of Factors Influencing Seeding in the Alpha-Synuclein Seed Amplification Assay

Proposals that do not fit these six focus areas will not be considered. **All proposals across the six subthemes within the scientific track must have a tie to human biology,** meaning that the project must demonstrate the relevance of biological discoveries to human Parkinson's disease, which can be demonstrated through:

- Generation of disease biology hypotheses using human data (e.g., genetic, clinical, biomarkers)
- Validation assessment of biological/mechanistic hypotheses in human biospecimens and/or

- Leveraging human PD relevant models to improve translatability of biological hypotheses

Please read below to learn about our focus areas, and what we define as in scope versus out of scope for each of the six respective research focus areas.

1. **Examining PD in the Context of Aging**

   Advanced age is the best-established risk factor for PD; however, it is still unclear how aging-influenced processes contribute to the underlying pathogenesis of PD. This call will support discovery efforts to understand pathogenesis and progression of PD in the context of biological aging, exploring whether targets for aging-influenced processes are involved in changing the timing of onset, features, and rate of progression of PD. For this call, a variety of well-validated models can be utilized from *in vitro*, *in vivo*, *in silico*, and human cohorts.

   - **In scope:** The types of applications we seek to fund would focus on the following areas of study:
     - Investigating whether factors proposed to rejuvenate the aging brain can influence PD disease onset and rate of progression
     - Exploring compensatory biological mechanisms associated with aging and their impact on PD disease progression
     - Studying interactions between PD risk genes, biological sex, and age in PD onset and progression to understand what specific characteristics may mediate progression, clinical presentation, pathology, or reduced penetrance in PD
     - Projects positioned to transform our understanding of the mechanisms involved in Early Onset PD (EOPD), individuals who are diagnosed with Parkinson's before age of 50.
   - **Out of scope:**
     - Prospective studies requiring new or active cohort recruitment (however existing aging cohorts and available data can and should be leveraged)
     - Studies with a primary focus other than PD biology, including general studies of aging, or studies focused on non-PD neurodegenerative disease

2. **Understanding How Co-Pathologies Can Influence PD Pathogenesis and Progression**

   Human postmortem data has demonstrated that co-pathology exists between PD, Lewy Body Dementia, and Alzheimer's disease. This theme aims to better understand the mechanisms that impact the drivers and downstream effects of co-pathologies in the context of PD development and progression. Although the primary focus is on neurodegenerative co-pathologies, exploration into other known co-occurring conditions, such as Inflammatory Bowel Disease, can also be considered.

- **In scope:** The types of applications we seek to fund would focus on the following areas of study:
    - Human pathology studies or other models that can help us understand the specific temporal and spatial sequence of co-pathology in the brain within different neurological diseases in physiologically relevant conditions (e.g., how do physiologically relevant levels of Tau, amyloid beta, TDP43, and/or alpha-synuclein interact and influence disease processes or pathogenesis.)
    - Meaningfully address whether co-pathologies contribute to converging mechanisms of PD through risk, manifestation, and progression, vs independent coincident disease states with discrete clinical and molecular features.
    - Examining the role of different cell types in the brain in response to various protein aggregates associated with neurodegenerative diseases
- **Out of scope:**
    - Studying the phenomenology in patient populations to examine the temporal onset of protein aggregate pathologies without investigating the underlying mechanisms driving these changes
    - Projects primarily focused on diseases other than PD or projects that do not have a direct link to PD

3. **Role of Environmental Risk Factors in Contributing to Disease Pathogenesis**

Environmental factors including exposure to pesticides, industrial chemicals, and other toxins have been linked to an increased risk of developing PD. A greater understanding of the mechanisms through which these various environmental triggers (in isolation and in combination) impact PD risk and the converging/diverging interactions of these mechanisms with known genetic, age-related, biological sex-related, and other pathogenic pathways would uncover key therapeutic targets/prevention strategies for the broad PD population. This theme seeks to understand how various suspected environmental triggers influence processes implicated in PD and/or novel pathways not previously linked in PD.

- **In scope:** The types of applications we seek to fund would focus on the following areas of study:
    - Identifying converging mechanisms of suspected external environmental risk factors (e.g., viruses, toxins, chemical) on PD development and/or progression including examination of gene-environment interactions, and impact of environment on genetic penetrance
    - Identifying pathways that are protective from the neurotoxic effects of environmental PD triggers
    - Understanding how biological sex differences and/or age-related differences contribute to these converging environmental mechanisms

- **Out of scope:**
    - Prospective studies to identify and characterize epidemiology or relative risk of the PD exposome
    - Meta-analysis of existing epidemiological data without a focus on experimental work to evaluate specific mechanistic hypotheses
    - Identification of new environmental risk factors in large epidemiological cohorts
    - Survey and questionnaire methodologies to identify de novo environmental risk factors
    - Observational studies evaluating the correlation of lifestyle factors to PD susceptibility/risk

4. **Understanding the Circuit Biology Driving Clinical Symptom Presentation (With an Emphasis on Non-motor Symptoms)**

   PD is largely identified based on the hallmark motor clinical symptoms of rigidity, bradykinesia, and tremor, but clinical presentation varies widely, and non-motor symptoms can be equally or more debilitating to patients. Better efforts in modeling the various motor and non-motor symptoms that recapitulate the key temporal aspects of disease progression will be critical to identifying the mechanisms and circuits that play a role in the development of these symptoms. Modulation of these circuits and pathways using novel technologies could then be tested as potential treatment strategies for people with PD. Through this theme, we will prioritize applications that can connect preclinical and clinical dataset findings to better explore and understand how heterogeneity in PD circuit biology manifests as symptomatic heterogeneity.

   - **In scope:** The types of applications we seek to fund would focus on the following areas of study:
     - Manipulation of circuits to understand the mechanisms underlying functional changes to circuits contributing to PD non-motor behaviors. For these projects, preference will be given to those studies that prioritize the unmet needs of the PD patient community (e.g., sleep, pain, cognitive dysfunction, etc.)
     - We encourage individuals to apply existing toolkits to glean insights into PD circuit pathology. However, if strong justification is made for why a new tool is needed to answer the research question proposed, this can be included provided the rationale is given.
   - **Out of scope:**
     - Studies that do not have a direct link to human PD datasets
     - Human studies that cannot be completed in three years
     - Circuits that only focus on well-studied motor symptoms

- Development of new tools to query the circuits without strong justification and relevance to PD

5. **Role of Clearance Mechanisms in PD**

Considerable evidence supports the hypothesis that pathological aggregates may initiate organelle damage and precipitate events that lead to dopaminergic cell death. Although progress has been made in defining the nature of this damage and identifying factors that may connect the damage to neuronal death, the challenge remains to define those unique targets that may offer opportunities for therapeutic intervention. Expanded research in basic discovery is essential to elucidate the pathways of protein aggregate turnover, spread or removal (e.g., autophagy, glymphatic clearing, etc.), and to advance these discoveries to specific molecules as drug targets. ASAP will prioritize applications that address the role of these mechanisms in mediating Parkinson's-relevant pathology and selective vulnerability of dopaminergic neuron populations.

- **In scope:** The types of applications we seek to fund would focus on the following areas of study:
  - Studying the pathways of aggregate turnover on a molecular or systems level, with a focus on specific targets and pathways linked to these clearance mechanisms (This should not be a discovery expedition to identify new targets)
  - Studying PD-related alterations in autophagy and the ubiquitin proteasome system through novel approaches (imaging, immunoassays, molecular assessment of autophagic pathways, etc.)
  - Studying the role of sleep abnormalities in impacting glymphatic system
  - Studying PD-specific alterations in established clearance mechanisms as a potential factor in selective vulnerability
- **Out of scope:**
  - Studying pathways that cannot be directly linked to PD biology
  - Identifying new autophagy/ubiquitin proteasome pathway modifiers through screening assays

6. **Identification of Factors Influencing Seeding in the Alpha-Synuclein Seed Amplification Assay**

The identification of alpha-synuclein Seed Amplification Assay (SAA) as a biomarker of PD provides a biological anchor, enabling a clearer biological definition of the disease beyond its clinical diagnosis. However, the exact alpha-synuclein species detected by the assay, relevance of the observed amplification products to disease pathology, and whether additional co-factors influence seeding ability remain unknown. This theme calls for a comprehensive study on human biomaterials to identify and characterize the seeding agent, investigating the process for seeding biologically relevant aggregates,

and interrogating the presence of these species throughout the body to understand the systemic relevance of alpha-synuclein in PD pathology.

- **In scope:** The types of applications we seek to fund would focus on the following areas of study:
  - Biochemical and biophysical analysis within human brain, CSF, and other biomaterials to identify the seeding factor for alpha-synuclein SAA and map/understand the distribution of this factor across different biosamples (e.g., CSF vs. blood vs. brain regions vs peripheral tissues).
  - Characterizing the structural and biological relevance of seed amplification products.
  - Identification of cofactors (e.g., lipids, proteins, or nucleic acids) that influence alpha-synuclein seeding ability and understand how these co-factors interact with alpha-synuclein to modulate aggregation
  - Investigating the molecular and cellular mechanisms underlying the human seeding/aggregation process, both in vitro (in the SAA) and in preclinical models.
  - Proposals focused on novel optimization and improvement of synuclein SAA can be part of the proposal but must be connected to a dedicated research strategy into understanding seeding activity.
  - Comparison and mechanistic analysis of SAA across the PD clinical spectrum (e.g., REM Sleep Behavior Disorder, Multiple System Atrophy, Dementia with Lewy Bodies)
  - Mapping the presence and distribution of alpha-synuclein seeding species across tissues and fluids (e.g., brain, CSF, peripheral tissues) to investigate how distribution relates to PD pathology and disease progression.
  - Proposals including development of novel tools and methods to enhance isolation, characterization, or analysis of alpha-synuclein seeding species in SAA can be considered as long as justification is provided as to why this is needed.
- **Out of scope:**
  - Studying alpha-synuclein post translational modifications in animal model systems without a clear focus on leveraging preclinical models to understand human synuclein and SAA assay performance (this is a human focused call.)
  - Proposals focused on understanding the endogenous function of alpha-synuclein.
  - Clinical projects seeking support to perform synuclein SAA analysis without clearly specified research goals on uncovering the molecular drivers of seeding.

Team Composition

Teams are required to be multidisciplinary and multi-institutional. Unlike "Center Grants" that play to the strengths of a single institution, this research network intends to establish teams comprising the best researcher expertise to address key knowledge gaps, regardless of their geographical location or institutional affiliation. The ASAP CRN encourages applications which leverage diverse expertise to creatively overcome challenges in Parkinson's research.

For a more detailed description of ASAP Team roles and a summary of Institutional and Core Leadership eligibility criteria, please see the corresponding ASAP Team Application & Budget Guidelines document.

Funding Available

Applicant teams may request funds up to $3 million USD total costs per year to support up to a three-year research plan, for a total of up to $9 million USD in total costs. Total costs are inclusive of a maximum 15% indirect rate applied to the team's direct costs.

Key Dates

JANUARY 15, 2025	Online application portal opens for Letter of Intent (LOI) submission
MARCH 20, 2025	LOI submission deadline (6 PM EST)
WEEK OF JUNE 2, 2025	Notification of invitation to submit full proposals
AUGUST 7, 2025	Full proposal deadline (6 PM EST)
WEEK OF NOVEMBER 3, 2025	Earliest notification of invitation to interview
NOVEMBER 2025	Finalist virtual interviews held
JANUARY 2026	Anticipated Notice of Award
JUNE 2026	Anticipated Project start date

Grant Terms and Policies

Grant Terms

- **Use of Funds** – Funds may be used for scientific and technical personnel, supplies and standard equipment needs directly related to the successful execution of the proposed scope or work. However, funds may not be used for laboratory or facility renovation.
- **Carryover Funding** – Unused research funds may be carried over to the following year. If unused funds amount to ≥ 5% of the total award amount for any project year, a budget

reallocation request must be submitted and approved before funds are permitted to be carried over. A one-time request for no-cost extension (NCE) will be considered at the end of the project period.

- **Reporting Requirements** – ASAP supported research programs require scheduled updates on progress and outcomes throughout the grant duration. Progress reports are due annually or at other times as deemed necessary by ASAP and MJFF for project evaluation. Progress report forms will be provided by MJFF approximately two months before they are due. Investigators may also be asked to interact regularly with ASAP and/or MJFF staff and advisors to discuss elements of the project on an ongoing basis throughout the project duration.
- **Intellectual Property** – ASAP will not retain any rights to funded projects, other than the right to publicly discuss any data, published results, and intellectual property that result from the research.
- **Open Science**− All Teams must comply with the ASAP Open Science Policy outlined below. This policy is non-negotiable.

ASAP Open Science Policy

The ASAP Open Science Policy is divided into five (5) main requirements:

1. **Share research outputs.** Data, code, and protocols generated as part of an ASAP-funded study must be deposited in a discipline-specific, community-recognized repository by the time of publication, with information to facilitate reuse and a license that allows for reuse. Key lab materials generated as part of an ASAP-funded study must be registered by the time of publication.
2. **Identify research inputs.** Data, software, protocols, and key lab materials used in a study–but which were not generated as part of an ASAP-funded study–must be unambiguously identified in the study's publication.
3. **Ensure immediate open access.** Preprints must be posted no later than the date a manuscript is submitted to a journal. Preprints and publications must be immediately publicly available with a CC-BY or CC0 license and include an Availability Statement outlining where all research outputs (Requirement 1) and research inputs (Requirement 2) can be accessed.
4. **Acknowledge ASAP.** Manuscripts and other research outputs that were partially or fully funded by ASAP must acknowledge ASAP. Manuscripts must include an ORCID and ASAP affiliation for all authors who received funding from ASAP.
5. **Share outputs with the ASAP network.** All ASAP-funded research outputs, including manuscripts, must be shared on the ASAP grantee virtual platform, no later than the time of publication. Manuscript drafts must be sent to the ASAP Open Science Team no later than the time of preprint.

For more details, please go to https://parkinsonsroadmap.org/open-science-policy/

Cost Policy

Please see the ASAP CRN 2025 Team, Application, and Budget Guidelines for more information regarding subawards, indirect costs, and allowable costs vs. unallowable costs.

Application Process

There are three stages for this funding opportunity: (1) letter of intent (LOI), (2) full proposal, and (3) finalist (virtual) interview.

LOIs are due no later than March 20, 2025 by 6pm EST. Following evaluation, teams selected to submit full proposals will be notified in June 2025. Invited full proposals will be due August 7, 2025. Finalists will be interviewed virtually by ASAP leadership in November 2025. **Awardees will be notified of final funding decisions in January 2026.**

All applications must be completed and submitted through MJFF online portal at https://grants.michaeljfox.org/s_Login.jsp. We strongly recommend that applicants familiarize themselves with the online portal in advance of any deadlines. No exceptions will be made for technical or institutional difficulties in preparation or submission. For detailed application instructions, please visit the online portal for more information.

As a reminder, CAS and MJFF are partnering to implement this ASAP RFA. As such, applicants may hear from ASAP staff that are from either CAS or MJFF with follow-up needs or questions pertaining to their submissions.

LOI Instructions

A brief letter of intent is required for funding consideration (no more than five [5] pages). Applicants must use the template available on the ASAP website. In addition to the five-page template, applicants must follow each tab within the online portal and fill in the designated areas. Note: no budget is collected at this stage. The LOI consists of the following sections:

1. **Project Description**
    - Descriptive project title
    - Project summary (100 words maximum)
    - Scientific goals and strategy (500 words maximum)
    - Statement of impact and alignment with ASAP initiative goals (100 words maximum)
2. **Team Summary**
    - List of Team investigators
    - Description of each investigator's role on the project (100 words maximum per investigator)
    - Description of the collective expertise and resources that the investigators bring to the Team

- Collaboration history of each investigator including reference to past intra-Team collaboration where relevant (review the LOI template for specific parameters)
- Historical adherence to open science practices (review the LOI template for specific parameters)

3. **Letter of commitment signed from each investigator.**

Full Proposal Instructions

Full proposal submissions are by invitation only and based on the outcome of LOI review. A weblink and additional instructions for online submission will be provided to selected applicants during the week of June 2, 2025. Full proposals are **due no later than Tuesday, August 7, 2025.**

LOI Checklist

For a more detailed description of ASAP Team roles and a summary of Institutional and Core Leadership eligibility criteria, please see the corresponding ASAP Team Application & Budget Guidelines document. Below we have summarized key eligibility criteria for the LOI stage for your convenience:

- ❑ The Core Leadership of the proposed team consists of one (1) Coordinating Lead PI and between two (2) and four (4) additional Core Leadership Co-Investigators.
- ❑ The Core Leadership of the proposed team are employed at one Primary Institution with up to four (4) subawardee institutions.
- ❑ At least one (1) Core Leadership Co-Investigator must be an early career investigator (ECI) within one (1) to seven (7) years of their first independent appointment. For the purposes of this award, an ECI should have attained their first independent appointment no earlier than 01/01/2019 and no later than 01/01/2025.
- ❑ The overall team represents at least two (2) different scientific disciplines.
- ❑ Each member of Core Leadership holds a doctorate, such as a PhD, MD, or equivalent degree.
- ❑ The Coordinating Lead PI holds an academic appointment and is in an independent faculty position or equivalent. Applicants from the private sector must hold a Senior Scientist position or equivalent.
- ❑ All Core Leadership Co-Investigators are in an independent faculty position or equivalent. Applicants from the private sector must hold a Senior Scientist position or equivalent.

Review and Selection Process

ASAP will evaluate all applications for both scientific merit and alignment with the ASAP mission. All projects will be externally reviewed by a panel of experts who are familiar with our program goals and have deep expertise in our program's scientific focus areas. Final decisions will be made by ASAP staff and Executive Leadership in consultation with external advisors. There is no expectation that a set number of awards will be granted; selection of awardees will be based on the following criteria:

- **Quality** of the proposal, expertise, and capacity of the collaborative group for addressing the proposed project. There should be evidence of synergy and substantive contributions from all assembled members of the research team – i.e., not simply a collection of individual projects.
- **Potential impact** of the research questions being addressed in the application.
- **Focus on mechanism-focused projects.** The CRN 2025 Scientific Track will focus on supporting high-priority, mechanism-focused projects to drive new ideas into the Parkinson's disease R&D pipeline that fall under the six subthemes outlined above.
- **Degree** to which the proposed work brings in new ideas to the field and stimulates potential new avenues of investigation.
- **Diversity** of the proposed scientific team.
- **Demonstrated collaborative potential** of the proposed Team as evidenced by co-authorships, past collaborations among at least two (2) members of the Team, as well as relevant contributions to other successful research collaborations in the recent past.
- **Commitment to open science and active research community engagement.** These values may be demonstrated through service on committees and editorial boards, past history of open science practices (including but not limited to sharing of research outputs such as data, code, protocols, lab materials, etc, publication of open access articles, and use of preprint servers)
- **Leadership capacity of the Coordinating Lead PI.** The Coordinating Lead investigator's vision, leadership qualities, willingness to collaborate, and demonstrated ability to bring together and lead a multidisciplinary team of experts to a successful conclusion will be a critical factor.

Confidentiality

The review process will be performed under confidentiality among all parties involved except as necessary for our evaluation or to comply with any applicable laws. All LOIs received in response to this ASAP RFA will be subjected to review and only applicants whose LOIs are determined to best fit the criteria specified in the RFA will be invited to submit full applications. In order to expedite the LOI review process, written critiques will not be provided to applicants who are not invited to the full application stage.

Successfully funded proposals will be made publicly available and/or shared across the ASAP Collaborative Research Network and/or or with other grantees or collaborators. Lay project summaries will be publicly communicated on ASAP and/or MJFF websites. Unfunded proposals submitted to ASAP will remain confidential. Application materials will not be returned to applicants.

Contact

Inquiries concerning this funding opportunity are encouraged to avoid submission complications. For administrative and programmatic inquiries, please contact grants@parkinsonsroadmap.org. We encourage questions well in advance of the deadline.