



National Institute of
Neurological Disorders
and Stroke

Team Science Opportunities at NINDS: Introducing the new COMBINE program

*Collaborative Opportunities for Multidisciplinary, Bold, and
Innovative Neuroscience (COMBINE)
(RM1, RFA-NS-23-027)*

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For more information, visit <https://www.ninds.nih.gov/funding/about-funding/ninds-grant-mechanisms/RM1-team-science>

You can also email your NINDS Program Official or NINDSTeamScience@nih.gov

Team Science Opportunities at NINDS



1. Why team science?
2. Your options to support team science at NINDS: MPI R01, NINDS P01, NINDS COMBINE RM1
 - Overview of differences
 - Practical Considerations
3. Introducing the NINDS COMBINE Program (*RFA-NS-23-027*)
 - Key features
 - Is this a good fit for your collaboration?
 - Examples of funded awards
4. Next Steps

What will not be covered?



Which topics are within NINDS mission and/or would be a good fit for the different funding mechanisms?

Reach out to your Program Officer

- Because topics are often shared across institutes and NIH programs, we highly recommend that you check on this with us by *sharing us your project summary or draft of aims.*

“Stronger together through interdisciplinary team science”

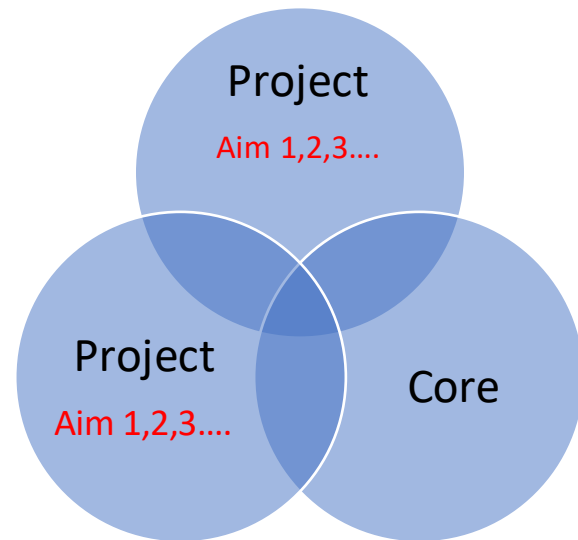


A team science approach expands our ability to pursue **complex and challenging** problems in neuroscience research in a *comprehensive, interdisciplinary, rigorous, and mechanistic* manner.

Comparison of NINDS Team Science mechanisms



P01 Program Project



- Multiple Projects+Cores
- *Team-specific* features and resources
- Single Special Emphasis Panel

R01 Parent



- Multiple Aims
- Not team-specific
- Multiple study sections

RM1 COMBINE



- 1 goal/**multiple aims are non-responsive**
- *Team-specific* features and resources
- Single Special Emphasis Panel
- Larger scale, more complex than R01

Which funding opportunity is best for me?

Practical considerations for NINDS team applications



1. Structure and scale:

- Do you have multiple aims (R01), single aim/goal (COMBINE RM1), or multiple projects/cores (P01)?
- What is your proposed budget? (>500k DC R01 and all P01 applications need prior approval with NINDS; Contact NINDSTeamScience@nih.gov for responsiveness)
- Do you have 3-6 MPIs? (COMBINE RM1 only); R01 and P01 have no specified PI #

2. What is your timeline?

- R01 and P01 have 3 receipt dates per year; COMBINE RM1 has 1 receipt date/year (Oct 2024)

3. Responsiveness Criteria:

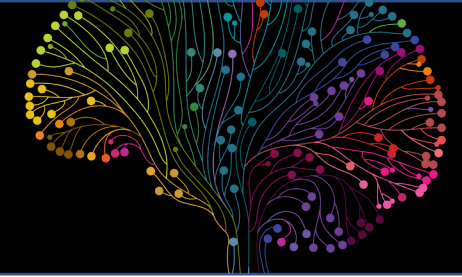
- Note the responsiveness and non-responsiveness criteria which vary across mechanisms; For example, P01 and RM1 do not accept specific types of clinical trials; RM1 COMBINE has restrictions about epidemiological studies and projects not fully NINDS'

Navigating the COMBINE (RM1) Program, RFA-NS-23-027



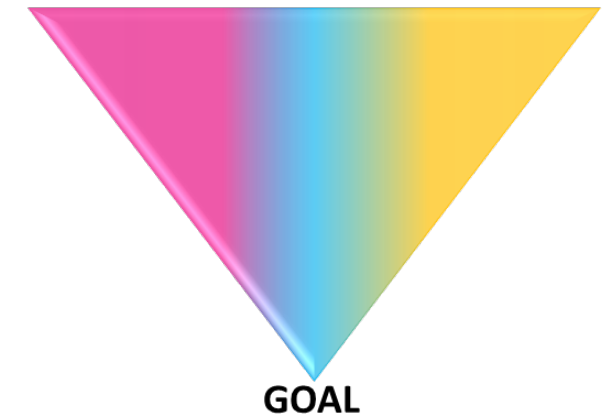
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Key Features of the NINDS COMBINE program (What is new? - highlighted in yellow)



- **Transformative 5-year goal** *fully within NINDS mission*
 - Bold, impactful, and challenging
 - *Single, focused goal*
 - Only achieved via interdisciplinary team science
 - **Multiple aims are non-responsive**
- **3-6 MPIs integrating distinct viewpoint/expertise**
 - ≥ 2.4 cal mo/yr effort each
 - Subject to [SCR policy](#)
- Sufficient scope and complexity (vs MPI R01)
 - **~\$500K - \$1.5M DC**
- Integration of team science and research strategy
 - Team Management
 - Enhancing Diverse Perspectives

PI Expertise #1 PI Expertise #2 PI Expertise #3



NINDS COMBINE (RM1) Program, RFA-NS-23-027: What are we looking for?



- ✓ Goal
- Approach
- Scale

➤ Bold and impactful

- **Transformative** objective with **defined 5-year outcomes**
- A goal that challenges existing paradigms, overcomes long-standing roadblocks to progress, and/or develops new synergies between different scientific fields



➤ Challenging

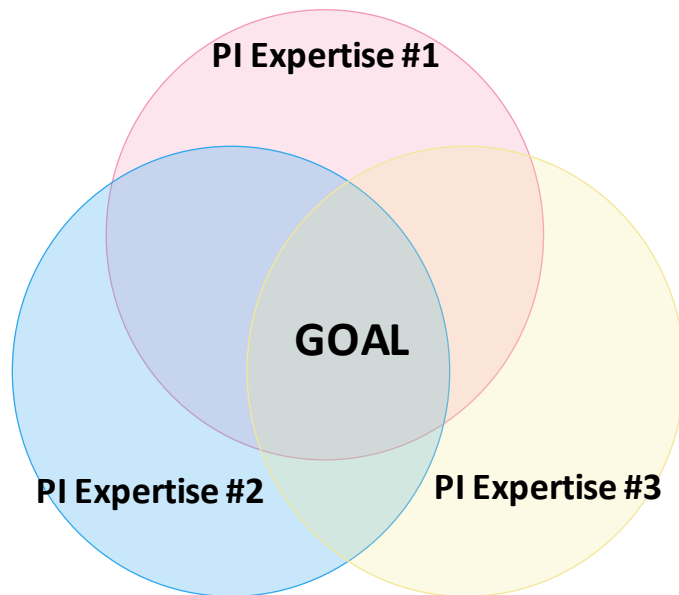
- Can only be achieved through a team-based approach
 - Why is a team science approach needed to address the research question?
- Applications will *assume some degree of risk*
- Generally, more ambitious and innovative than traditional NIH applications.
- Feasibility will be assessed; applicants should carefully manage any risk in the premise and/or approach.

NINDS COMBINE (RM1) Program, RFA-NS-23-027: What are we looking for in the MPIs?



- | | |
|-------------------------------------|----------|
| <input type="checkbox"/> | Goal |
| <input checked="" type="checkbox"/> | Approach |
| <input type="checkbox"/> | Scale |

- **Innovative combination** of **distinct** fields/expertise
 - 3-6 MPIs to pursue a **single** goal or problem
- **Essential contributions** from each of the MPIs
 - Reflected in Aims, Budget, Leadership Plan, Team Management Plan
 - Bandwidth: ≥ 2.4 cal mo/yr; subject to SCR policy
- **Integrated and equitable efforts** from MPIs
 - Must not be dominated by a single individual
 - Not a collection of individual efforts or interrelated and parallel projects



NINDS COMBINE (RM1) Program, RFA-NS-23-027: What are we looking for in the structure?



- Goal
- Approach
- Scale



- A truly **integrated** collaborative project
 - All contributions and pieces are essential to the goal.
 - *Deletion test-if you remove a piece, the goal falls apart*
 - Pursuing 1 single focused goal
 - Multiple aims are non-responsive
 - Distinguishes the COMBINE program from R01 and P01.
- Substantial and **integrated** contributions across the PD/PIs.
 - Not a collection of individual or series of efforts.
 - Not interrelated and parallel projects.
 - *Will a series or several separate R01s, or a multi-component P01 be a better fit?*
 - *What is the value added/Why do these pieces needed to be studied together?*
- Intentional about **integrating** efforts
 - Includes activities, planned outcomes, approaches, experiments, and/or frameworks that act as “glues”
 - Integrate and combines efforts across disciplines and team members.
 - *What is unifying all these pieces together that is necessary to achieve the specified goal?*

NINDS COMBINE (RM1) Program, RFA-NS-23-027: What are we looking for in terms of scale?



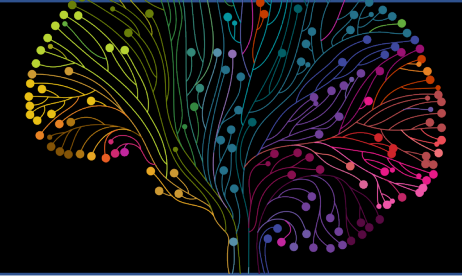
- Goal
- Approach
- Scale

PI Expertise #1 PI Expertise #2 PI Expertise #3



- **Shared leadership** across 3-6 MPIs
 - Each with a distinct scientific viewpoint or expertise necessary to pursue the interdisciplinary approach
- Scale will likely benefit from **resources for team management**
 - E.g. Program manager, data scientist
 - Can be requested under the "Team Management Plan" and included in budget)
- Scale will benefit from **expanded page limit**
 - Research Strategy (15-page max)
 - Additional Attachments
 - Team Management Plan
 - Timeline and Benchmarks for Success
 - Plan for Enhancing Diverse Perspectives)

Application Structure is **different** from typical NIH applications



TRANSFORMATIVE. INNOVATIVE. INTEGRATED.

- Address “**how will the project challenge existing paradigms, overcome long-standing roadblocks to progress, and/or develop new synergies between different scientific fields?**”
- Be intentional about **integrating** efforts: Highlight activities, planned outcomes, and/or frameworks that act as “glues”, serving to integrate and combine efforts across disciplines and team members.
- Applications will assume some degree of risk and are in general more ambitious and innovative than traditional NIH applications. Because feasibility will be assessed, applicants should carefully manage any risk in the premise and/or approach.

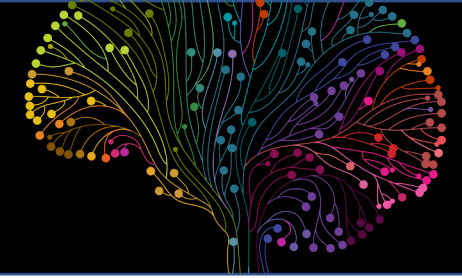
Specific Aims and 15-page Research Strategy: structured differently (see Section IV).

- **Specific Aims Page:** *Multiple aims are inappropriate as the research plan must be focused on pursuing a single focused goal.*
- **Research strategy** (15-page max). Use subheadings: "Importance of the Research and Appropriateness for the NINDS COMBINE program" and "Approach and Experimental Design".

3 Other Attachments: The success of team science hinges on:

- **Well-managed team interactions** (**Team Management Plan** is complementary to MPI Leadership Plan).
- **Clear Timelines and Benchmarks for Success**
- **Evidence of commitment** to diversity, equity, and inclusion (**Plan for Enhancing Diverse Perspectives (PEDP)**)
 - Definition of “diverse perspectives” is broad
 - Unique and customized to the proposal; Summary of strategies+ timeline/milestones+approach to assess progress

What topics will **not** be a good fit? (Section I)



- Research that is **not fully within the NINDS mission**
- Better fit **for other Institutes and/or specific funding opportunities**
 - e.g., Better fit for other programs (BRAIN, HEAL, etc)-
 - “The COMBINE RM1 has fixed and limited budget commitments, so funding priorities will include considerations where the research might better fit special funding programs like the NIH BRAIN initiative, HEAL Initiative, ADRD, and other active programs.”
- Applications in which the **primary goal is to create, maintain, expand, and/or disseminate resources or infrastructure**
- Considerations about **translational and clinical** types of applications:
 - Applications that propose to discover and develop a small molecule, biologic therapeutic, or therapeutic device to treat neurological and/or neuromuscular disorders (covered by [NINDS Division of Translational Research Programs](#)).
 - Development and validation of biomarkers for use in clinical trials or in clinical practice. These types of applications are already covered by the NINDS Biomarker Program funding opportunities (PAR-22-089 and PARs-21-056, 057, 058, and 059), see: [NINDS: Focus On Biomarkers Research](#).
 - Clinical trials designed to answer specific questions about safety, tolerability, efficacy and/or effectiveness of pharmacologic, behavioral, biologic, surgical, or device (invasive or non-invasive) interventions (e.g., phase I, phase II, phase III, or pivotal clinical trials). Such designs should be submitted to an NINDS clinical trial-specific funding announcement (see [NINDS: Clinical Research](#)). If planning a clinical trial, **this NOFO will only accept mechanistic or BESH (Basic Experimental Studies Involving Humans) types of clinical trials**. Understanding the distinction between mechanistic, BESH, and efficacy trials can be difficult. PIs are strongly encouraged to discuss any planned clinical trial in consideration for this opportunity with the scientific program contact to avoid errors in interpretation.
 - **Clinical research projects with an inherently team science approach (e.g., applications in which the primary goal is multi-site clinical epidemiological or observational studies, genetic studies, or comparative effectiveness research)**. NINDS will continue to consider these large projects as a separate, unsolicited independent investigator-initiated projects (i.e., R01/U01 applications). For comparative effectiveness research projects, see: [PAR-22-076: Prospective Observational Comparative Effectiveness Research in Clinical Neurosciences \(UG3/UH3 Clinical Trial Not Allowed\)](#) .

Non-responsive applications will not proceed to reviewed and will be withdrawn. Please consult us!

6 NINDS COMBINE Awards (2023)



- [Systems-Level Approach to Neuronopathic Lysosomal Storage Disorders](#)
- [Targeting Dysregulated RNA Splicing in Neurodegenerative Diseases](#)
- [Targeting Cell-type Specific Disease Phenotypes to Promote CNS Repair](#)
- [Brain Glucose Deficiency: Mechanisms and Modulation](#)
- [Resilience to Cognitive Decline and Resistance to Alzheimer's Disease and Related Neurodegenerative Diseases in Individuals from Colombia with Autosomal Dominant Dementias](#)
- [Reexamining the Role of Dendrites in Neuronal Function](#)

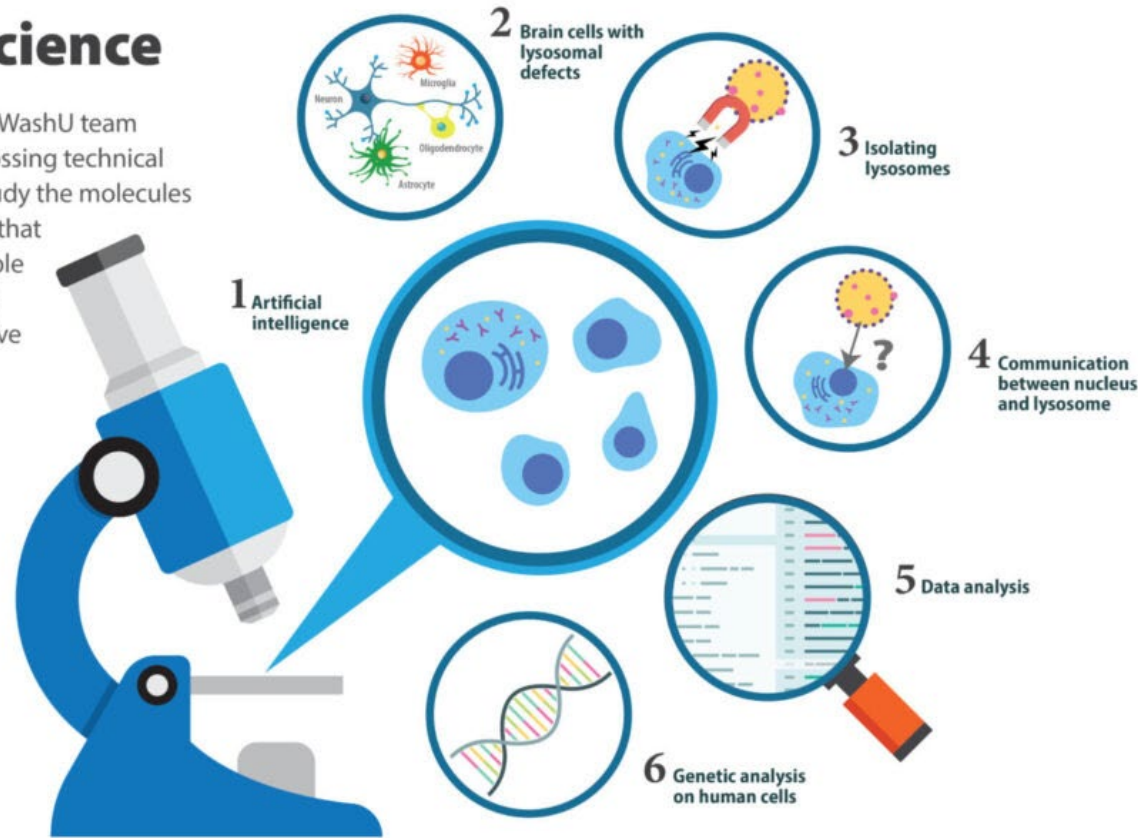


Systems-Level Approach to Neuronopathic Lysosomal Storage Disorders *1RM1NS132962-01*



Team science

Multidisciplinary WashU team committed to crossing technical boundaries to study the molecules inside brain cells that may be responsible for fatal pediatric neurodegenerative diseases.



Resources & Next Steps



- **Questions?**
- Questions from the live audience
 - View the NOFO: RFA-NS-23-027
 - Please see our Website and FAQs
 - Email: NINDSTeamScience@nih.gov

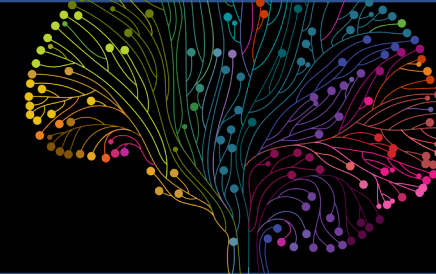


<https://www.ninds.nih.gov/funding/about-funding/types-research-support/team-or-multi-component/collaborative-opportunities-multidisciplinary-bold-and-innovative-neuroscience-combine-rm1-clinical>

The screenshot shows the NIH website interface. At the top, there is a navigation bar with links for Health Information, Funding, Current Research, News & Events, and About NINDS. Below the navigation bar is a search bar and a language selector for 'Información en Español'. The main content area is titled 'Frequently Asked Questions for NINDS COMBINE RM1'. On the left side, there is a sidebar menu with various funding categories, including 'Collaborative Opportunities for Multidisciplinary, Bold, and Innovative Neuroscience (COMBINE) (RM1)'. The main content area has tabs for 'View', 'Edit', and 'Revisions'. Below the tabs, there are several sections: 'Funding Opportunity Description', 'Application', 'Investigators', 'Review', and 'Funding'. An 'Expand all' button is visible on the right side of the content area.



Supplemental information



FAQs (COMBINE RM1 Program)



➤ **Is my topic X within NINDS mission?**

Because topics are often shared across institutes and NIH programs, we highly recommend that you check on this with us by sharing us your project summary or draft of aims.

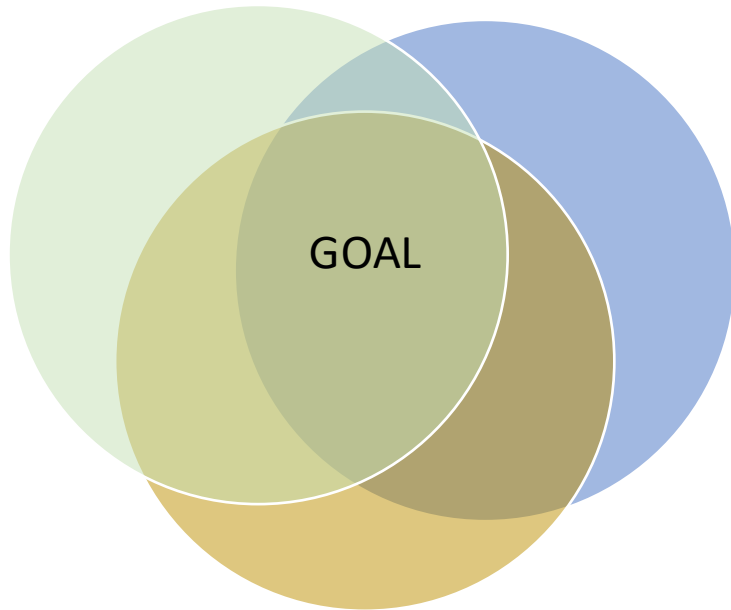
➤ **Is this RFA for a single site? Can it be for multisites? Are PIs expected to be from different institutions or can they all be from the same place? Can the team be made up of different disciplines within a single department? Would it be OK for form a team consisting of expertise on each step of an entire biological process? Who should be on the team?**

The science should drive the type of collaboration and the team/expertise composition. Being in different vs same institution/departments could differ in logistical considerations, so this should be accounted for in the team management plan.

➤ **Is there a recommended effort for the Pis?**

Programs of this level of complexity are expected to require significant effort from all PDs/Pis involved. Generally, each PD/PI should devote at least 2.4 person months (i.e., the equivalent of 20% effort on a full-year appointment, 26.7% on a 9-month appointment, or 40% on a 6-month appointment) throughout the duration of the award.

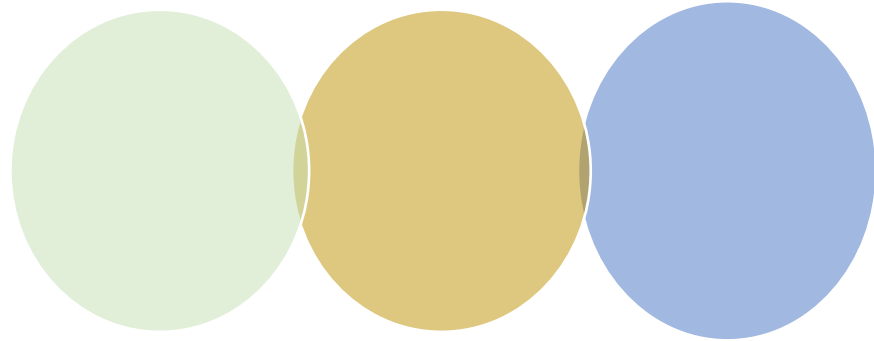
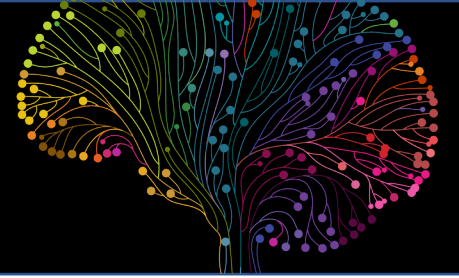
Ideal COMBINE Program



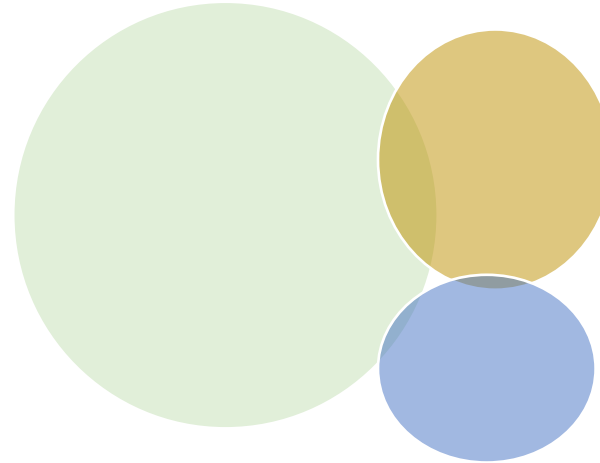
3-6 MPIs **integrating and combining** distinct expertise necessary to solve a **single, focused, transformative** goal within 5-years

Thoughtful plan for managing the team and feasibility and for incorporating diverse perspectives

What characteristics/features will **not** be a good fit?



- Not well-integrated
- A collection of individual, parallel, or series of efforts (Better off as a P01 or multiple/series of R01s)
- Plan is not cohesive; **multiple aims (non-responsive)** instead of a single, focused goal
- Some pieces are not essential to the goal, or not necessary to study altogether. (minimal impact to the project if deleted)



- A dominant PI plus supporting roles from the other PIs
- Does not have 3-6 MPIs with distinct expertise and viewpoint

- Overly broad; open-ended types of projects
- Goal is not well-defined or has a low likelihood of being completed within 5 years

How is the COMBINE RM1 different from the P01 and MPI R01?



	NINDS <u>P01</u>	Parent R01	NINDS <u>COMBINE Program</u>
Purpose	Synergy, collaboration, team science efforts (Parallel/interrelated efforts)	Efforts from single lab to small teams	Synergy, collaboration, team science efforts (integrated and interdisciplinary)
Structure	Interrelated projects; Multi-component (minimum of 3 research components-projects + cores)	1 set of aims; 12-page research strategy	1 goal (multiple aims not allowed) + 15-page Research Strategy + 3 "Other Attachments" (Team Management Plan (3-page max), Timeline and Benchmarks for Success (2-page max), and Plan for Enhancing Diverse Perspectives (1-page max, PEDP))
Review	Review each component + overall ; NINDS SEP	Review 1 project; CSR	Review 1 project + Other Attachments (3); NINDS SEP
Leadership	PPG director- established leader, driver of the project	Depends on the project	Emphasis on multi-PI collaboration and shared leadership across 3-6 MPIs
Team science-specific features	Coordination by an administrative core; diversity as a scorable criteria	MPI specific language	Coordination described in the team management plan; diversity as a scorable criteria; Can allot resources for a program manager/coordinator and for intra-team data management; specific review criteria
Due dates	3x per year (~May, June, January)	Standard dates	Once per year: October 8, 2024 (May Council)