NEUROIMAGING AND CSF BIOMARKER PROGRAM

FUNDING OPPORTUNITY DESCRIPTION

The aim of this RFP is to further develop and validate established biomarkers for which there is a clear clinical need in Alzheimer's disease and related dementias. This RFP prioritizes biomarkers with a **defined context of use**, a clear advantage over other relevant biomarkers, and a path to commercialization and/or clinical use.

Specifically, this RFP focuses on:

- Developing novel PET ligands for clinical trials
- Supporting novel CSF biomarkers
- Validating innovative MRI approaches in larger cohorts
- Developing novel measures of functional activity such as EEG

*Peripheral biofluids and digital/ocular approaches are supported through the **Diagnostics Accelerator RFP**.*

Novel biomarkers of neuroinflammation, synaptic integrity, autophagy and TDP-43 are high priority. Other target areas of interest include:

- Neuronal loss
- Vascular injury and blood-brain barrier integrity
- Mitochondria and metabolic function
- Protein misfolding
- Oxidative stress
- White matter changes
- Lewy body dementia
- Other novel targets supported by compelling biological rationale and connection to disease

The ADDF has limited interest in CSF measures of amyloid and tau.

UPCOMING DEADLINES

ELIGIBILITY

AWARD INFORMATION

FUNDING PRIORITIES

The ADDF focuses on advancing drug development for Alzheimer's and related dementias and the biomarker tools that aid in this process. This RFP prioritizes biomarker programs that define a specific use and have potential for commercial and clinical translation, with an emphasis on clinical trials (see the Evaluation section below). The RFP supports advancement of neuroimaging and CSF biomarkers that can do one or more of the following:

1. **Demonstrate target engagement for novel therapeutics**
   Biomarkers that can serve as direct measures of target engagement for novel drugs in clinical

development. High priority will be given to projects advancing biomarkers that can be used as specific companion biomarkers for therapies currently in the development pipeline. Identification of such therapies strengthens an application.

2. **Detect signs of disease earlier and monitor progression**
   Programs developing sensitive biomarkers that can detect disease earlier than currently available biomarkers. This includes biomarkers that can predict and monitor conversion from cognitively healthy to mild cognitive impairment (MCI) or MCI to Alzheimer's disease. We also seek prognostic markers that can predict rates of cognitive decline.
3. **More accurately diagnose and distinguish between dementia subtypes**
   Many types of dementias can present with similar clinical features, and patients often show overlapping pathologies. At present, it is challenging to distinguish between dementia subtypes and proteinopathies. Biomarkers that can distinguish between subtypes and stratify patients in clinical trials are of high priority.

MODALITY-SPECIFIC PRIORITIES

Neuroimaging:

- **Positron emission tomography (PET):** These projects should focus on ligands for target engagement and pharmacodynamic measurements of novel and repurposed therapeutics. This RFP will support pharmacokinetics, safety, synthesis, and clinical development of novel PET ligands. The investigative team should include individuals with experience in developing PET ligands for human use.
- **Magnetic resonance imaging (MRI):** The proposed structural or functional approach should already have proof-of-concept data in *human patients* and be translatable for clinical use. Approaches that can measure novel targets and are significant improvements upon what is currently available in MR techniques are of higher priority.
- **Magnetic resonance spectroscopy (MRS):** The ability to detect specific molecules or proteins relevant to disease or a specific drug in development should be demonstrated in the preliminary data section of the application.

Cerebrospinal fluid (CSF) biomarkers can be a single analyte or panel of analytes; however, the proposed signature should have proof-of-concept data in *human patient samples* and the specific analyte combination should be well justified.

Functional activity measures applicable to this RFP include electroencephalogram (EEG), magnetoencephalography (MEG), and transcranial magnetic stimulation (TMS). Only highly novel techniques or analyses for EEG, MEG and TMS will be considered. These proposals must meet the following criteria:

- The proposed approach is an improvement on already existing functional measures used in clinical practice for diagnosing and monitoring dementias
- The biomarker and its biological connection to the disease should be established and clearly described
- Proof-of-concept data should be completed in human patients

Other novel approaches: The biomarker should already be identified and validated in at least a small number of human samples.

EXPECTATIONS AND EVALUATION

APPLICATION SUBMISSIONS

Review the **Application Instructions** for steps on applying.

LOG IN OR CREATE ACCOUNT

We encourage you to contact us if you would like to discuss your proposed project and receive initial feedback.

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