

NIH AD Summit 2018 Yields Research Recommendations

More than 3,000 experts from government, academia, industry, and nonprofit organizations met at the National Institutes of Health (NIH; Bethesda, MD) and by videocast on May 24 for the Alzheimer's Disease (AD) Research Summit 2018: Path to Treatment and Prevention. The summit was convened by the National Institute on Aging (NIA). Participants endorsed almost 100 recommendations that provide a roadmap for an integrated, multidisciplinary research agenda intended to inform priorities for AD and related dementias. The recommendations are designed to guide continued efforts to build a collaborative research environment capable of delivering urgently needed cures for people at all stages of the disease. A reoccurring theme at the summit and in the recommendations was a "precision medicine" approach to AD treatment and prevention, targeting interventions that can address the underlying disease processes and symptoms with sufficient flexibility to be tailored to individual risk profiles.

"This is a critical time in Alzheimer's research, with new opportunities to build upon what we have learned," said NIA Director Richard J. Hodes, MD, "We must continue to foster creative approaches that leverage emerging scientific and technological advances, establish robust translational infrastructure for rapid and broad sharing of data and research tools, and work with funding partners and other stakeholders to cultivate and sustain an open science research ecosystem."

The research recommendations build on the framework established by previous NIA/NIH summits in 2012 and 2015. Recommendations from these meetings served as the basis for developing research implementation milestones detailing specific steps and success criteria for NIH and other stakeholders in the development of effective treatments for and prevention of AD. These milestones span the AD research spectrum, including basic, translational, clinical, and health services research, and have served as guidelines for development of the NIH Alzheimer's Disease Bypass Budget.

Sessions at the meeting focused on: (1) novel mechanistic insights into the complex biology and heterogeneity of AD; (2) enabling precision medicine for AD; (3) translational tools and infrastructure for predictive drug development; (4) emerging therapeutics; (5) understanding the impact of the environment to advance disease prevention; (6) advancing disease monitoring, assessment, and care; and (7) building an open science research ecosystem to accelerate AD therapy development.

More than 80 experts on AD and other complex diseases joined forces as speakers and cochairs, and, through a multistep process, developed a series of new research recommendations that address the topics of each summit session and the overarching programmatic themes of the summit: (1) enabling precision medicine research to understand disease heterogeneity; (2) enhancing research rigor, reproducibility, and translatability; and (3) enabling rapid translational

learning through open science systems and incentives. The new recommendations expand the 2012 and 2015 research frameworks and will serve as the basis for updating research implementation milestones. The recommendations will also guide the public and private sectors toward meeting the research goals of the National Plan to Address Alzheimer's Disease, with the ambitious goal of identifying effective interventions to treat and prevent AD by 2025.

Nuclear and molecular imaging and theranostic applications form essential and integral parts of many of the recommendations, especially those aimed at understanding the mechanisms of AD development and surveillance of novel treatments. Imaging was specifically mentioned in calls for efforts to:

- Determine structural variations of pathogenic peptides collected from well-phenotyped, diverse cohorts to inform the development of structure-specific imaging agents and inhibitors with therapeutic potential;
- Continue to establish new cohorts that include participants across diverse socioeconomic backgrounds at increased or decreased risk of dementia and incorporate collection of novel clinical data (imaging, personal wearables, and sensors for in-home monitoring);
- Expand biorepository infrastructures to enable storage and wide distribution of clinical data and biosamples for deep molecular phenotyping, collected from diverse populations. ... These resources should include biorepositories for samples and clinical data from ongoing clinical trials to support multiomic data generation;
- Provide support for high-cost capital equipment/core facilities and staff training to make high-throughput technologies such as molecular profiling, cryoelectron microscopy, advanced human brain imaging, and other emerging technological capabilities available for wide use.
- Accelerate development of the next-generation central nervous system imaging ligands and biofluid molecular signatures targeting a variety of disease processes (neuroinflammation, bioenergetic/metabolic compromise, oxidative stress, synaptic pathology) that can be used as research tools or developed into diagnostic, prognostic, theranostic, or target engagement biomarkers. These reagents should be made available as open-source research tools for target validation and as enabling tools for predictive drug development.

The complete recommendations are available at: <https://www.nia.nih.gov/research/recommendations-nih-ad-research-summit-2018>.

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