FOUNDATION FIGHTING BLINDNESS

Letter of Intent Guidelines

Individual Investigator Research Awards– Targeted Call for New Proposals

The Foundation Fighting Blindness (FFB) expects to fund a limited number of Individual Investigator Research Awards to be awarded in June 2026.

If you are interested in being considered for an award, submit a letter of intent (LOI) and a short, no longer than five pages, Curriculum Vitae (NIH Biosketch is acceptable) to FFB by October 16, 2025, via the FFB application portal [**https://www.onlineapplicationportal.com/blindness**].

The following sections must be entered into the designated application portal fields:

1. Title of Project
2. FFB Research Priority Area (RPA) (ONE ONLY, see below)
3. Inherited Retinal Degenerative Disease(s) (or dry AMD) that this research impacts and why this research is important to and will make a significant difference in achieving the Foundation's mission. (Word limit: 200 words.)
4. Overall research, goals and hypothesis to include the Specific Aims and rationale proposed for FFB Grant funding (it is recommended that the specific aims are listed and rationale stated) (Word limit: 500 words.) Applicants **must propose** a research plan that is both **realistic** and **achievable** within a three-year timeframe and a $300,000 budget. Your proposal should show a well-structured plan that emphasizes **feasibility** and **impact**.
5. Stage of Development
6. Overall Description of Application: Describe the research plan. (Word limit: 600 words.) If figures are to be included, a maximum of 3 figures or tables can be uploaded separately to the Figures Upload page.
7. Curriculum Vitae for the Principal Investigator. A 5-page NIH biosketch format is acceptable. Curriculum Vitae is not included in the word limits.

8. Reference List
9. Figures Upload (upload files must be in .doc or pdf format)

A budget is not required with the letter of intent.

All applicants must have an ORCID iD and include it in their application. If you don't have one, you can register for free at https://orcid.org/register.

If you use AI tools to help with your application, you are responsible for ensuring the accuracy, originality, and integrity of all submitted content.

Executive Summary:
Individual Investigator Research Awards are intended to support research with the greatest potential to advance treatments and cures for **inherited retinal degenerative diseases (IRD)** and **dry age-related macular degeneration (dAMD)**.
To address critical gaps in dAMD research, proposals must aim to understand the pathophysiologic mechanisms that drive the transition from aging to early-stage dry AMD. Proposals must:

- Focus on early, dry AMD
- Use animal or cellular models that best represent AMD pathobiology
- Demonstrate that the outcomes will have a direct impact on advancing AMD research and treatment

The Foundation has identified **Research Priority Areas (RPAs)** that align with its mission. This targeted postdoctoral opportunity aims to address specific gaps within these RPAs related to retinal diseases. While proposals that directly address the areas of particular interest will receive priority consideration, the Foundation will also consider highly novel research that may fall outside these defined goals. In such cases, the Letter of Intent (LOI) must clearly articulate how the proposed research could lead to prevention, treatments, or cures for inherited retinal degenerative diseases and dAMD.

(**NOTE**: studies focused on wet AMD and diabetic retinopathy are **not** eligible for support by the Foundation Fighting Blindness).

Individual Research Awards are available in the following Research Priority Areas:

Research Priority Areas

1. **Genetic Technologies**

Objective: To develop viral and non-viral delivery system(s) for genes and complex constructs (e.g. editing tools, mRNA and proteins), and the development of RNA editing techniques.
Applications that target the following areas are of interest:

- Improve gene therapy delivery methods by
    a. understanding the hurdles associated with gene delivery by subretinal injection, intravitreal injection, suprachoroidal, and subconjunctival injection, and develop tools to overcome them
    b. develop non-viral delivery tools (e.g., lipid nanoparticles)
    c. develop alternative viral vectors (in addition to AAV)
- Develop tools for effectively and efficiently transducing all relevant retinal cell types (e.g., cell-specific plasmids, novel capsids) that permit improved control of expression levels
- Implement strategies for delivering complex constructs (large DNA, gene editing tools, mRNA, or protein)
- Advance RNA editing techniques
- Establish metrics by which the efficiency of delivery (viral or non-viral) and the efficiency of editing (DNA/RNA) can be quantified and measured across delivery platforms
- Understand the impact of gene augmentation in a diseased retina
- Develop standardized methods for quantifying vector genomes and total protein that can be compared among groups/studies, including analysis of dose-response effects on treatment efficacy and toxicity.
- Develop manufacturing techniques that are affordable/scalable

2. **Restorative Therapies (includes cell-based approaches, visual prosthetics and optogenetics)**

Objective: To restore sight after photoreceptor loss by strategies to rescue or replace degenerating or dead retinal cells, optimize visual prostheses,

and develop optogenetic strategies to confer light sensitivity to neuronal cells in the absence of fully functional photoreceptors.
Applications that target the following areas are of interest:

- Optimize cell transplantation by identifying the best preparation and purification methods for donor tissue, determining how to enhance cell survival and function, and establishing the necessary immune suppression regimen.
- Improve understanding of transplanted cells by studying the role of biomaterials, measuring the function of donor RPE and photoreceptors after transplantation, and assessing the importance of cytoplasmic transfer versus transplant survival.
- Optimize optogenetic approaches by identifying the best non-photoreceptor cell for optimal outcomes
- Evaluate the potential of visual prostheses, including understanding how these therapies interact with remaining retinal cells and circuitry.

3. **Novel Medical Therapies**

Objective: To support research directed toward developing drugs to retain retinal function and structure in retinal degenerative diseases, including better functional testing of drug effectiveness, and novel drug delivery systems.
Applications that target the following areas are of interest:

- Develop and optimize models for high throughput screening and drug repurposing.
- Assess and improve therapeutic approaches by examining therapies that enhance cellular metabolism.
- Overcome challenges in therapy development for complex genetic IRDs and optimize delivery systems for efficacy and reduced toxicity.
- Identify and utilize non-invasive methods for tracking disease progression and therapeutic benefit.
- Understand the role of the microbiome in IRDs and explores if targeting the microbiome (e.g., antibiotics, bacterial consortia) can alter the disease course.
- Identify and develop gene-independent and gene-agnostic approaches based on common mechanisms of degeneration.
- Identify non-drug therapies (e.g. red light) to treat IRDs.
- Develop non-invasive delivery modalities (topical or systemic), especially for IRDs with early onset of disease.

4. **Clinical: Structure and Function**

Objective: Develop improved technology and standardized processes to establish relationships between clinical retina function and retina structure in retinal degenerative diseases and to enable early disease detection, utilizing the Foundation's Clinical Consortium to expand patient populations and expedite clinical trials.

Applications that target the following areas are of interest:

- Develop outcome variables for clinical trials, including functional testing, retinal imaging, and candidate surrogate endpoints.
- Develop clinical procedures to help diagnose and phenotype patients with IRDs.
- Conduct multimodal studies to link function to underlying pathology.
- Understand the role of inflammation in IRDs and efforts to control inflammation after genetic or stem cell therapies.
- Utilize imaging, psychophysics, and electrophysiology to understand mechanism of loss in specific mutations.
- Understand the causes and prevention of CME in IRDs Understand relationships between rod and cone loss in IRDs.
- Understand the role of the RPE in IRDs.

5. **Genetics**

Objective: To improve abilities to identify disease-causing mutations in inherited retinal disorders, in part by integrating comprehensive genetic testing into routine clinical care. To identify inherited risk factors for age-related macular degeneration (AMD) and the relative contributions of associated genetic and non-genetic factors (e.g., lifestyle), sufficient to use such knowledge in developing treatments and preventions.

Applications that target the following areas are of interest:

- Identify disease-causing genotypes in unsolved IRD cases, including the role of non-coding mutations, mosaicism, and various forms of inheritance.
- Classify pathogenic variants of uncertain significance in IRD genes using novel analytic methods, including AI-assisted modeling.
- Understand factors contributing to clinical variation in patients with identical disease-causing genotypes, such as genetic, environmental, and lifestyle factors.

- Promote inclusion of underrepresented populations in clinical trials to address research gaps and provide direct benefits to all affected individuals.

6. **Cell and Molecular Mechanisms of Disease**

Objective: To improve our understanding of the nature and cause of disease in inherited retinal degenerations so that improved therapies for the prevention of vision loss can be developed.
Applications that target the following areas are of interest:

- Identify shared mechanisms and pathways across IRDs and between IRD and AMD for gene agnostic approaches.
- Determine the genes that modify IRD phenotypes and how their activity can be modulated to affect disease pathophysiology.
- Improve the generation and characterization of organoids and animal models to better model the macula.
- Utilize spatial-omics approaches for a better understanding of the macula and other topological heterogeneity in the retina.
- Identify biomarkers that can predict disease onset and monitor disease progression and determine if they are shared or unique based on genotype.
- Enhance access to fresh AMD tissue and RP donor tissue to improve understanding of disease mechanisms.
- Understand the role of nuclear and mitochondrial DNA damage in IRD pathophysiology and how it can be targeted to ameliorate disease phenotypes.

Eligibility:

Applicants must hold a Ph.D., M.D., D.M.D., D.V.M., D.O., O.D., or equivalent degree and have a faculty position or equivalent at a domestic or foreign: non-profit organization, or public or private institution, such as a university, college, medical school, hospital, research institute, or laboratory. Individuals from underrepresented racial, ethnic and gender groups, as well as individuals with disabilities, are always encouraged to apply.

Award:

The award will total $300,000 over three years.. The award may be used to support the salaries of research trainees (graduate students, postdoctoral

or clinical fellows), technical staff and research supplies. Partial support for the Principal Investigator's salary is permitted but is not to exceed **20% of the total annual award**.

A budget is not required for the letter of intent. The Foundation Fighting Blindness does not provide funds for equipment or indirect administrative costs.

Letter of Intent Submission:
Applicants must submit the completed LOI electronically by October 16, 2025, 11:59 PM EST via the FFB Application Portal. Access the FFB Application Portal through the FFB website:
https://www.fightingblindness.org/grants-and-award-programs

Use the print application tab to preview your application in pdf format. Your signature will be added to the pdf when the submit application page is completed.

Email confirmation of the submitted application will be sent immediately from blindness@onlineapplicationportal.com. Add this address to your safe sender list to avoid emails being sent to your SPAM folder.

PLEASE USE YOUR OWN E-MAIL ADDRESS IF POSSIBLE WHEN SUBMITTING THE LETTER OF INTENT SO THAT WE CAN INFORM YOU IN A TIMELY FASHION IF YOUR APPLICATION HAS BEEN SELECTED FOR SUBMISSION OF A FULL PROPOSAL. IN ADDITION, PLEASE ADVISE US AS SOON AS POSSIBLE OF CHANGES IN E-MAIL ADDRESSES.

The Letters of Intent will be reviewed for scientific quality, training potential, and relevance to FFB's mission and current research priorities. If your letter of intent is selected, the FFB will contact you to request a full application in January 2026. The deadline for full applications will be approximately March 6, 2026.