ROBERT A. KYLE CAREER DEVELOPMENT AWARD
FROM THE IWMF
2025 Request for Proposals

To fulfill its vision of a world free from Waldenstrom's macroglobulinemia (WM), the International Waldenstrom's Macroglobulinemia Foundation (IWMF) acknowledges the crucial role of nurturing a new generation of WM researchers to ensure continuous progress in the field. The primary objective of the Kyle Career Development Awards is to inspire and provide support to talented young investigators with a background in hematology and/or oncology, encouraging them to either enter or persist in their work within the realm of Waldenstrom's research. In this regard, the IWMF is delighted to announce the fifth year of the Robert A. Kyle Career Development Award for Waldenstrom's Macroglobulinemia, which serves as a tribute to Dr. Robert Kyle's significant contributions to the field of plasma cell disorders and Waldenstrom's macroglobulinemia over the past 50+ years.

Program Structure

- Each grant will be of two (2) years in duration, with a direct cost of $75,000 per year for a maximum total direct cost of $150,000 per grant.
- A 5% institutional related overhead (indirect) cost will also be provided, to a maximum of $7,500 per grant.
- The total Grant Award is 157,500.

Research Focus

The IWMF Robert A. Kyle Career Development Award Initiative is a mechanism designed to promote research that will ultimately identify the cause and cure of Waldenstrom's macroglobulinemia (WM). WM research funded by the Kyle Initiative should be guided by the pillars listed below. While clinical trials are not funded by this mechanism, coordination with clinical trials samples and outcomes is encouraged.

- **WM Cell Biology**: Includes research into signaling pathways driving the growth and survival of WM. Also includes are preclinical testing of novel therapeutic strategies and research into signaling mechanisms related to recurrent somatic mutations such as MYD88, CXCR4 and ARID1A as well as WM specific dysregulation of novel and established pathways such NF-kB, ERK, and PI3K/AKT.

- **T-Cell Based Therapeutics**: Includes development and preclinical testing of CAR-T and bi- and tri-specific antibodies, as well as the development of novel therapeutic strategies that promote immune anti-WM engagement. Also includes proposals to overcome T-cell anergy and counter the immunosuppressive effects associated with myeloid derived suppressor cells and similar mechanisms.

- **Microenvironmental Research**: Like many indolent lymphomas, WM cannot survive without the support of its local environment. This pillar supports research into identifying these dependencies and assessing their therapeutic potential. It also supports the development of organoids and xenograft models that can support long-term primary WM cultures for research and testing. This includes changes in microenvironmental composition, signaling, and spatial relationships associated with disease progression and response. In addition to T-cell exhaustion and immune dysregulation studies from the previous pillar, it also supports the development of organoids and xenograft models that can support long term primary WM cultures for research and testing.

- **Genomic, Epigenomic, and Transcriptional Research**: Supports bulk, single cell, and spatial studies to better understand the biology of WM evolution from MGUS to symptomatic disease, as well as mechanisms driving primary and acquired therapeutic resistance. This pillar further supports related research into identification of high-risk features, novel target identification, and biological characterization of WM disease manifestations such as Bing Neel Syndrome and transformation.

- **Proteomics**: This pillar is distinct from the previous one as it focuses on protein properties and modifications that impact key WM signaling pathways or can be used for prognostic testing in a manner distinct from the underlying genetics. It also supports protein-based research into the causes and treatment of cryoglobulinemia, cold agglutinins, amyloid, demyelinating neuropathy, and other complications associated with the IgM paraprotein.

The International Waldenstrom's Macroglobulinemia Foundation (IWMF)

The IWMF is a patient-founded and volunteer-led nonprofit organization that is dedicated to a simple but compelling vision and mission:

- Vision – A World Without WM (Waldenstrom's macroglobulinemia).
- Mission – Support and educate everyone affected by Waldenstrom's macroglobulinemia (WM) while advancing the search for a cure.

The IWMF currently has a worldwide membership, with Support Groups and affiliate organizations on virtually every continent.

Today the IWMF:

- Provides support to patients and their caregivers.
- Enables patients to communicate with one another.
- Sponsors patient educational forums and webinars about WM that feature prominent physicians and researchers.
- Publishes booklets and fact sheets on WM and its treatment.
- Supports research aimed at improving treatments and ultimately, finding a cure for WM.

The IWMF has invested $27 million dollars on WM basic science research since 1999. We have just approved $3,126,500 for 11 projects that are starting this year.

For more information, visit the IWMF website at http://www.iwmf.com

IWMF Research

The IWMF supports research to understand the biology of WM, with the goals of improving

quality of life for WM patients, discovering new treatments, and ultimately, finding a cure.

IWMF funding for research has helped to provide insight into understanding the basic biology and genetics of WM. This research in turn has played a significant role in the development of treatments and treatment guidelines in current use, as well as potential new drugs still in the pipeline.

How to Apply for a Research Grant

The grant application process for the Robert A. Kyle Career Development Award will follow standards that already exist for previous IWMF-funded research grants, as well as NIH review guidelines:

Submissions: An application for a research project can be submitted for the Robert A. Kyle Career Development Award via email (timelines and addresses listed below). The project description, significance, Aims, six-month timelines and scientific approach should not exceed 12 pages in length and follow the Research Application Cover Sheet noted below and also located on the IWMF website at www.iwmf.com/research/applying-research-grant. Additional pages should include references, biographical sketches, detailed budget with justification, list of other projects, and appendices as necessary. Following a review process that may take up to 2-3 months, the award will be made to the successful applicant(s).

Who Can Apply: Applicants must hold an MD, PhD, or equivalent degree and work in domestic or foreign non-profit organizations, such as universities, colleges, hospitals, or laboratories, that have a teaching curriculum and mentoring program with senior investigators who have a track record in the B-cell or plasma cell malignancy fields. Applicants should be junior faculty members and/or post-doctoral fellows who have had a focus in clinical research on B-cell or plasma cell malignancies for at least two (2) years. Applicants need not be US citizens, and there are no restrictions on applicant age, race, gender, or creed. Applications from non-academic facilities and the National Institutes of Health are not eligible.

Review Process: Research proposals are reviewed by an independent committee composed of selected members of the IWMF Research Committee, the IWMF Scientific Advisory Committee (SAC) and other experts in the field. This committee may in turn respond to the research proposal applicant(s) with questions and/or request clarification regarding certain aspects of the proposal itself. The proposals will be ranked using established NIH review criteria. Awards will be made based on funding availability. Applicants will be notified by

the IWMF as soon as a decision is made. Grant recipients will be invited to the IWMF Educational Forum to be acknowledged by and meet the attendees. the IWMF reimburses a grant recipient's expenses for attendance at the Ed Forum.

Payment Policy: The IWMF Treasurer will pay a pro rata amount for six months at the start of the project. Future payments will be made at designated six-month intervals after each Interim or Final Progress Report and accompanying Lay Summary has been received and the IWMF Research Committee has reviewed it for satisfactorily meeting the IWMF reporting guidelines (see below). Payments will be made after all guidelines have been met.

Reporting Requirements: Progress Reports are required to be submitted to the IWMF by the Investigator every six months for the duration of the project. Interim Progress Reports must be submitted no later than 30 days after the six-month period ends. Such Progress Reports will describe the activities and results with respect to each specific Aim that has occurred during the preceding six-month period. Each Progress Report will include a proposed path forward over the next six-month period. Project Aims should not be changed during the research process without prior notification, justification, and agreement of the IWMF Research Committee. The Investigator must show in the reports that he or she is performing the obligations stated in the submitted and approved research proposal for each reporting period. Deviations from the six-month timelines need to be explained to ensure that the project is on track. A Final Progress Report which describes the results and findings as they relate to the stated goals of the project for the full term of the project is required no later than 45 days after the project ending date. The Investigator should expect on occasion to receive requests for clarification of Progress Reports. A Lay Summary must accompany each Interim Progress Report and the Final Progress Report. The reports must be submitted in Microsoft Word or PDF file format. A final detailed expenditure report must also be sent no later than 90 days after the project ending date.

Budget

A detailed budget and budget justification should provide itemized detail for each major category for all the years of the project. This budget can be summarized for year one and extrapolated for the remaining year. All totals and subtotals should be included. The maximum annual direct costs cannot exceed $75,000. The Indirect cost will be up to 5% of the project's direct cost. The aggregate costs over two (2) years cannot exceed $157,500.

Permissible direct costs include the following with the specified limitations:

- Personnel expenses including salary or stipend with fringe benefits.
- In total, no more than forty percent (40%) of the direct costs may be requested for the salary and fringe benefit expenses of professional staff with a post-graduate degree (i.e., MD, PhD, DVM) regardless of function or role. This restriction does not apply to supportive technical staff for the project (lab assistants, nurses, etc.).
- Supplies and materials requests should be itemized by category. Equipment purchase requests must identify each item of equipment with an acquisition cost of more than $500.

Permissible indirect costs (often referred to as institutional overhead, IDC, M&A, G&A, or pooled costs) are those costs incurred for common or joint objectives that cannot be readily identified with a particular project (general maintenance, utilities, library, etc.). Indirect costs are limited to five percent (5%) of total direct costs. For sponsoring institutions that do not choose to use these funds for indirect costs, these funds can be applied to the Grantee's/Investigator's stipend or fringe benefits cost.

Impermissible costs include membership dues, tuition, books, journals, and publication costs.

Review Criteria

An application will be judged on these criteria:

- The probability of an advance in prevention, diagnosis, or treatment in the near-term.
- The conceptual basis upon which the proposal rests.
- The novelty of the concept and strategy.
- Thoughtful and clear presentation.
- The overall plan for bringing the research findings to clinical application.
- Experience, background, and qualifications of the investigator.
- Adequacy of resources and environment (facilities, data management data analysis, etc.).
- Adequacy of provisions for protection of human subjects.
- Access to sufficient patient samples (if appropriate to the project), either from the investigator's own institution or from documented collaborations must be adequate. If an investigator does not have access to sufficient samples, the IWMF encourages the investigator to collaborate with another researcher or bone marrow banks who will share samples with them pre-proposal. You may contact the IWMF

before submitting the proposal to discuss ways to obtain samples. Failure to have adequate samples and therefore lack of scientific levels may result in a cancellation of the project.

Timeline

Email Call for Proposals	July 17, 2024
Application Deadline	February 26, 2025 (**No exceptions**)
Review of Submitted Applications Completed & Notification of Awards	March – April, 2025
Award Winners will Receive the Award at the 2025 IWMF Educational Forum in Florida	May – June, 2025
Anticipated Funding Start Date	July 1, 2025 to February 26, 2026

Submit All Correspondence to

All proposals and other correspondence regarding the Robert A. Kyle Career Development Award should be sent to the following two individuals:

- Dr. Tom Hoffmann, IWMF Research Committee, thoffmann@iwmf.com
- Robin Tucker, IWMF Finance Director, rtucker@iwmf.com

The IWMF Office will acknowledge receipt of each proposal within one business day via email. If you do not receive such an acknowledgment, please contact Robin Tucker, IWMF Finance Director, at rtucker@iwmf.com or call the IWMF Office at 941-927-4963.

Good luck and thank you for your interest!