IWMF-LLS ENHANCED RESEARCH ROADMAP INITIATIVE

2025 Request for Proposals

The International Waldenstrom's Macroglobulinemia Foundation (IWMF) and the Leukemia & Lymphoma Society (LLS) are proud to announce new and larger funding for a grant proposal under the Enhanced Research Roadmap Initiative. This type of proposal requires more effort, time, or resources than the previous two (2)-year IWMF-LLS Strategic Research Roadmap Initiative grants.

Program Structure

- Each grant will be at least two (2) years and can be up to four (4) years in duration, with a maximum total direct cost of $1,250,000 per grant.
- A 20% institutional related overhead cost (to a maximum of $250,000 per grant) will also be provided.
- The total Grant Award is $1,500,000.

Research Focus

The IWMF/LLS Enhanced 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 Roadmap 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-driven, nonprofit organization that is dedicated to a simple but compelling vision: A world without Waldenstrom's macroglobulinemia (WM). Our mission is to 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.

To accomplish this vision and mission, the IWMF offers patients with WM, caregivers, family members, and friends six invaluable services:

- **Information** from our website and our publications written in a patient-friendly way to promote understanding of our rare disease.
- **Education** at our annual Educational Forum and periodic webinars to help patients and caregivers learn about our disease from WM researchers and clinicians.
- **On-going updates** about WM and the IWMF sent through our **quarterly *IWMF Torch*** magazine and our **NEWS releases.**
- Peer **support** from others who've been where you are.
- **Information** for medical professionals who may have limited experience with our rare disease.
- **Research** directed to better treatments while we search for a cure.

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

The Leukemia & Lymphoma Society (LLS)

LLS is a US-based foundation focused on developing, and providing access to, therapies to cure

or control leukemia, lymphoma, Hodgkin's disease, and myeloma as well as improve the quality of life of patients and their families. The organization has funded blood cancer research for the past 60 years to strive toward these goals.

For more information, visit the LLS website at http://www.lls.org

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 Enhanced Roadmap Initiative 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 within the Enhanced Research Roadmap Initiative 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 four to six months, awards will be made to successful applicants.

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. Applicants should have an independent research or academic position. Applicants need not be US citizens, and there are no restrictions on applicant age, race, gender, or creed. Applications from non-academic facilities, postdoctoral positions, and the National Institutes of Health are not eligible.

Multi-institutional Collaborations: Multi-institutional or multi-disciplinary applications are encouraged. This can be in the form of a single application with Co-Principal Investigators or collaborators from different institutions or different sections within one institution. In these

types of collaborations, the project contract will go to only one Principal Investigator and their facility. That Principal Investigator be in charge of obtaining letters of collaboration, sending intermittent reports, receiving IWMF payments and disbursing it to collaborators, and other contract needs. Alternatively, two (or more) institutions can submit separate stand-alone applications and indicate that the applications are linked, in the event that they are both selected for funding.

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 are ranked according to NIH review criteria. The final decision for funding is made by the IWMF Board of Trustees. Generally speaking, at this stage a decision to fund a proposal is based on funding availability. Applicants will be notified by the IWMF as soon as a decision is made.

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 Principal Investigator every six (6) 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 Principal 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 webinar is required yearly where the researcher will give a scientific presentation with slides to the IWMF Research Committee and selected members of our Scientific Advisory Committee (SAC), then there will be a live Q & A. The webinar will be 4-6 weeks after the due date of the yearly progress reports. 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. There will be a last webinar at this time. The

Principal 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

The total grant will be up to $1,500,000 in the aggregate. The maximum total direct costs may be up to $1,250,000, and indirect costs may be up to $250,000. The granting period must be specified by the Principal Investigator and should be at least two (2) years and can be up to four (4) years in duration. This gives the Investigator the flexibility to apply for a shorter grant (e.g., two years to test a hypothesis, with funding of $625,000/year in direct costs), or a longer-term project (e.g., four years, with funding of $312,500/year in direct costs).

A detailed budget and budget justification should provide itemized detail for each major category for all the years of the program. This budget can be summarized for year one and extrapolated for the remaining years. All totals and subtotals should be included.

Permissible direct costs include the following with the specified limitations:

- Personnel expenses including salary, wage, 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 technical staff (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 twenty percent (20%) above the total direct costs. For sponsoring institutions that do not need to use all of these funds for indirect costs, the funds can be applied to the Grantee's/Principal Investigator's stipend, fringe benefits cost, or to only request their true indirect costs.

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

Review Criteria

An application will be judged on these criteria:

- As an Enhanced Roadmap proposal, the application must clearly demonstrate that the project exceeds the scope of the traditional Roadmap grants, including greater scientific impact and greater resources required to carry out the research.
- 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.
- Preliminary data to indicate the likelihood of project success
- Thoughtful and clear presentation.
- The overall plan for bringing the research findings to clinical application.
- Experience, background, and qualifications of investigator(s).
- Adequacy of resources and environment (facilities, data management, data analysis, etc.).
- 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	March - April, 2025
Notification of Awards	May - June, 2025
Projects must start from	July 1, 2025 to February 26, 2026

Submit All Correspondence to

All proposals and other correspondence regarding the Enhanced Research Roadmap Initiative 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.