# International Waldenstrom's Macroglobulinemia Foundation

# **2024 Educational Forum** IMMERSE, EXPLORE, SOAR!

# Welcome to Day Two of the 2024 Educational Forum

May 3-5, 2024 Hyatt Regency Lake Washington



2024 Educational Forum

May 3 - 5, 2024

# Thank You to Our Ed Forum Sponsors!



2024 Educational Forum

May 3 - 5, 2024

# **Supporting Sponsors**







2024 Educational Forum

May 3 - 5, 2024

## **Premier Sponsors**



## Spharmacyclics® An AbbVie Company Johnson&Johnson



2024 Educational Forum

May 3 - 5, 2024

## **Title Sponsor**

# BeiGene



May 3 - 5, 2024

# Todd Zimmerman, MD

#### Senior Medical Director, Medical Affairs BeiGene



2024 Educational Forum

May 3 - 5, 2024

# International Waldenstrom's Macroglobulinemia Foundation

# **2024 Educational Forum** IMMERSE, EXPLORE, SOAR!

# Steven Ansell, MD, PhD

Dorotha W. and Grant L. Sundquist Professor in Hematologic Malignancies Research Mayo Clinic IWMF Scientific Advisory Committee Chair



2024 Educational Forum N

May 3 - 5, 2024



# **Overview of IWMF Funded Research** (past, present, and future)



# 20 years ago.....

- No models of Waldenstrom macroglobulinemia
- Poor understanding of the biology of the disease
- No research specific to WM
- All drugs used in WM were borrowed from other diseases.

# Enter the IWMF!

- 2005 Convened a workshop to discuss tools needed
- 2015 First Roadmap meeting in partnership with LLS
- 2024 Most recent update of the Roadmap priorities



# **Roadmap priorities**

- **Signaling –** What pathways do WM cells use for communication?
- **Immunology/immunotherapy** How can we better use our own immune system to fight WM?
- **Tumor microenvironment –** How does the bone marrow/tumor environment affect WM cells?
- "Omics" What else can we learn about genomics, epigenomics, and mutations in WM cells?
- IgM Monoclonal Gammopathy of Undetermined Significance (MGUS) – prevent or suppress progression.



# Funding mechanisms

- IWMF-LLS Strategic Roadmap Initiative grants
- IWMF-LLS Enhanced Research Roadmap Initiative
- Robert A. Kyle Career Development award program
- IWMF Research Seed Money
  Initiative
- IWMF-LLS Companion Initiative



## IWMF-LLS STRATEGIC RESEARCH ROADMAP INITIATIVE

- IWMF partnered with Leukemia and Lymphoma Society (LLS) in 2015 to create a Strategic Research Roadmap Initiative for WM
- Continues to demonstrate commitment to search for a cure
- Defines the five focus areas in basic biomedical research where we are seeking RFPs

## IWMF-LLS STRATEGIC RESEARCH ROADMAP INITIATIVE (continued)

- Added companion projects to the initiative for basic science projects within a clinical trial
- Awards for a maximum of \$480,000 over two years
- Issued Requests for Proposals annually currently funding eight projects
- Multi-institutional proposals welcome

## **RESEARCH SEED MONEY INITIATIVE**

- Established IWMF Research Seed Money Initiative in 2022 to offer investigators opportunities to develop pilot projects
- Intended to allow investigators to define objectives and test pilot hypotheses to prepare for larger grant applications through IWMF/LLS Strategic Research Roadmap Initiative
- Awards up to \$90,000 for one year
- Approved four new Seed Money Grants in June

## ENHANCED RESEARCH ROADMAP INITIATIVE (NEW 2022)

- Mirrors IWMF-LLS Strategic Research Roadmap Initiative with a twist
- Award funded at aggregate of up to \$1.5 million over 3 to 4 years

# Robert A. Kyle Career Development award

The Award Program recognizes the 50+ years of impactful contributions by Dr. Robert Kyle to the field of Waldenstrom's macroglobulinemia.



### ROBERT A. KYLE CAREER DEVELOPMENT AWARD

- Vital to provide funding to support career development of next-generation researchers for WM
- In 2021, added Robert A. Kyle Career Development Award Program, recognizing the 50+ years of Dr. Kyle's impact to the field of plasma cell disorders and WM
- Awards up to \$157,500 over two years
- Currently funding four Robert A. Kyle Career Development Award projects

#### 2023 Robert A. Kyle Career Development Award Recipient



#### Jithma Abeykoon, MD

- Senior Associate Consultant, Division of Hematology, Department of Internal Medicine, Mayo Clinic, MN
- Assistant Professor, Mayo Clinic College of Medicine and Science
- Earned medical degree from University of Kansas
- Completed Internal Medicine residency and Hematology and Medical Oncology fellowship at Mayo Clinic, MN
- Research focused on DNA damage repair pathways in cancer, where he aims to understand better the disease biology of hematologic malignancies such as Waldenström's macroglobulinemia.

#### 2023 ROBERT A. KYLE CAREER DEVELOPMENT AWARD

Title: Defining the Prognostic Significance of TP53 Alterations in Waldenström Macroglobulinemia and Exploiting them for Therapeutic Benefit

#### BACKGROUND

- Waldenström Macroglobulinemia (WM) is a treatable but incurable B-cell lymphoplasmacytic lymphoma.
- Recently, studies have reported that TP53 mutations in up to 30% of WM patients and this mutation is associated with a poor prognosis.
- How these *TP53* alterations are acquired and evolve and their impact on treatment response is unclear.
- Thus, there is an unmet need to delineate the prognostic and therapeutic characteristics of patients with *TP53*-altered WM by using a larger cohort of patients and also to find novel treatment strategies for patients with TP53 mutated WM.

#### AIMS

- 1. Assessment and categorization of *TP53* alterations and to understand its prognostic and therapeutic significance in Waldenström Macroglobulinemia using a large cohort of patients.
- 2. Exploit *TP53* alterations in WM for therapeutic benefit by targeting DNA damage repair pathways in cancer cells.

#### 2023 Robert A. Kyle Career Development Award Recipient



#### Maria Luisa Guerrera, MD

- Instructor in Medicine, Harvard Medical School and Dana-Farber Cancer Institute
- Physician-Scientist with clinical experience in diagnosis and treatment of hematological diseases including Waldenström's Macroglobulinemia
- Earned MD degree, University of Pavia, Italy, where she completed 5-year clinical fellowship in hematology
- Joined Bing Center for Waldenström's Macroglobulinemia, Dana-Farber Cancer Institute, for postdoctoral research fellowship
- Research focuses on uncovering mechanisms underlying WM oncogenesis and disease evolution, especially in MYD88 mutated disease, and discovering novel therapeutical targets and their functions



### **29<sup>th</sup> Annual** IWMF Educational Forum

MAY 3-5, 2024 Hyatt Regency Lake Washington | Renton, WA



#### **Robert A. Kyle Career Development Awardee**

#### Maria Luisa Guerrera, MD

Instructor in Medicine at Dana-Farber Cancer Institute and Harvard Medical School Dr. Treon lab







#### What I have learned so far

Looking beyond

Curiosity

Imagination

Adaptation skills

Fun

Family

Belonging

Exploring

Community

Experiences

Love

Ex

#### What I have learned so far

#### **Humanistic studies**

- Ancient Greek
- Latin
- Philosophy
- Art history
- Italian Literature
- Theater





«Considerate la vostra semenza: fatti non foste a viver come bruti, ma per seguir virtute e canoscenza".»

«Consider the seed from which you sprang: you were not made to live like brutes, but for the pursuit of virtue and knowledge.»

Dante Alighieri, Divine Comedy 'Inferno', Canto XXVI

# 

#### MD training in Italy (University of Pavia)

Alessandro Volta Camillo Golgi, 1906 Nobel Prize in Physiology or Medicine Adolfo Ferrata and Edoardo Storti

#### Germany (University of Bonn)

What I have learned so far

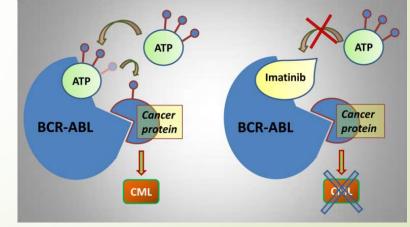
Pavia



#### A Lab of Her Own

Sheltered in her bedroom during WWII, Rita Levi-Montalcini discovered how the nervous system is wired.

Rita Levi Montalcini, 1986 Nobel Prize in Physiology or Medicine



Gleevec (Imatinib) in Chronic Myelogenous Leukemia

#### What I have learned so far



Hematology Clinical Fellowship in Italy (Pavia)

Wide range of hematological diseases
 Clinical research focus on indolent lymphomas and WM
 Luca Arcaini and Marzia Varettoni
 Incredible human experiences with the patients

Pavia



#### What I have learned so far

97



Boston



Postdoctoral Research Fellowship Instructorship in Medicine

Bing Center for Waldenström's Macroglobulinemia

MYD88 mutated and wild-type Waldenström's Macroglobulinemia: characterization of chromosome 6q gene losses and their mutual exclusivity with mutations in CXCR4

Maria Luisa Guerrera, Nickolas Tsakmaklis, Lian Xu, Guang Yang, Maria Demos, Amanda Kofides, Gloria G. Chan, Robert J. Manning, Xia Liu, Jiaji G. Chen, Manit Munshi, Christopher J. Patterson, Jorge J. Castillo, Toni Dubeau, Joshua Gustine, Ruben D. Carrasco, Luca Arcaini, Marzia Varettoni, Mario Cazzola, Steven P. Treon, Zachary R. Hunter

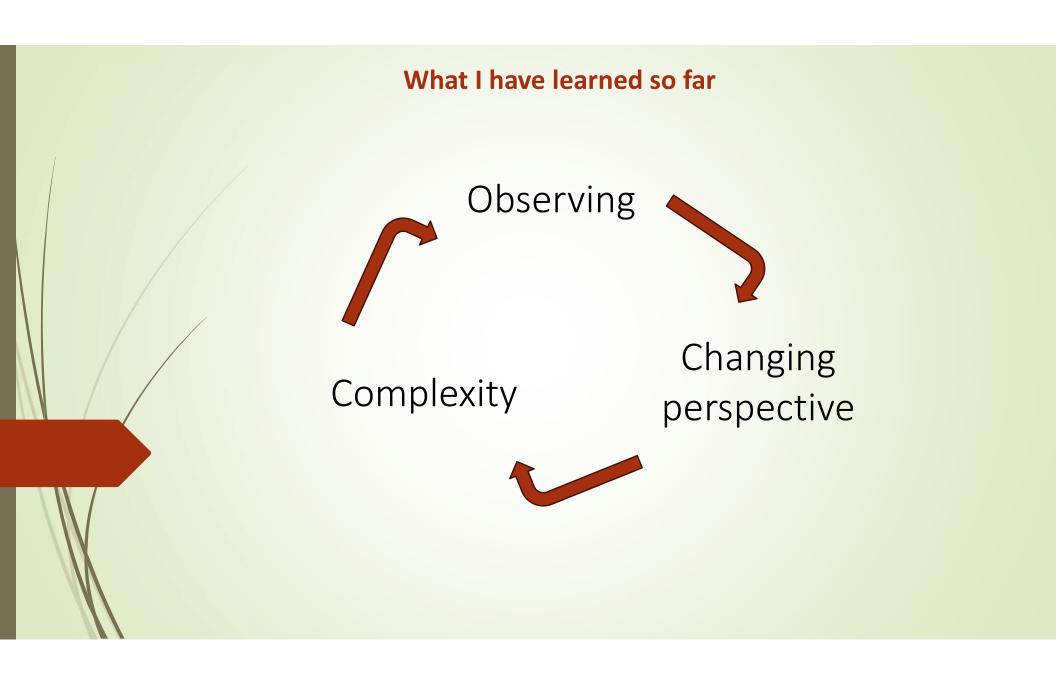
Vol. 103 No. 9 (2018): September, 2018 https://doi.org/10.3324/haematol.2018.190181

**Solution Bood advances** issues - Latest articles - Guidelines Collections

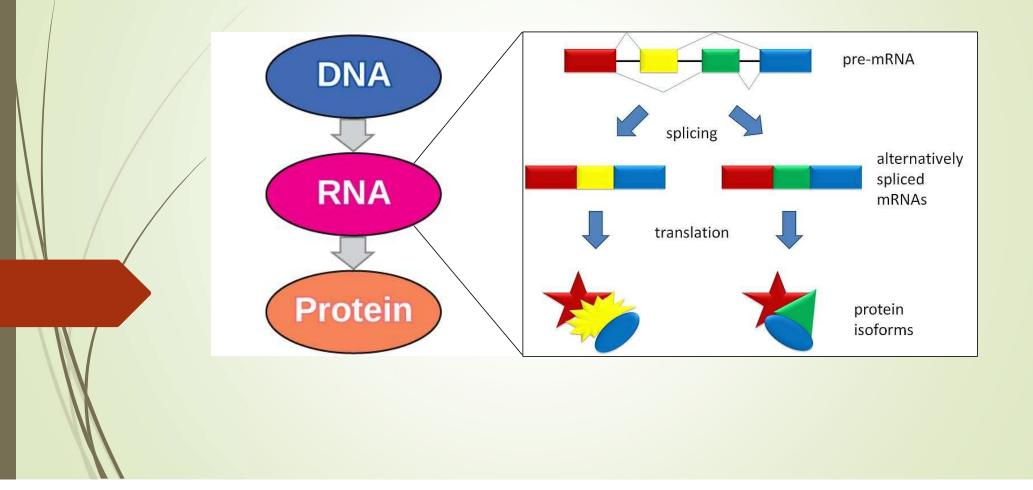
LYMPHOID NEOPLASIA I NOVEMBER 5, 2019

Human *MYD88*<sup>L255P</sup> is insufficient by itself to drive neoplastic transformation in mature mouse B cells

Tomasz Sewastianik, Maria Luisa Guerrera, Keith Adler, Peter S. Dennis, Kyle Wright, Vignesh Shanmugam, Ying Huang, Helen Tanton, Meng Jiang, Amanda Kofides, Maria G. Demos, Audrey Dalgarno, Neil A. Patel, Anwesha Nag, Geraldine S. Pinkus, Guang Yang, Zachary R. Hunter, Petr Jarolim, Nikhil C. Munshi, Steven P. Treon, Ruben D. Carrasco



#### Let the journey take us inward into our biology



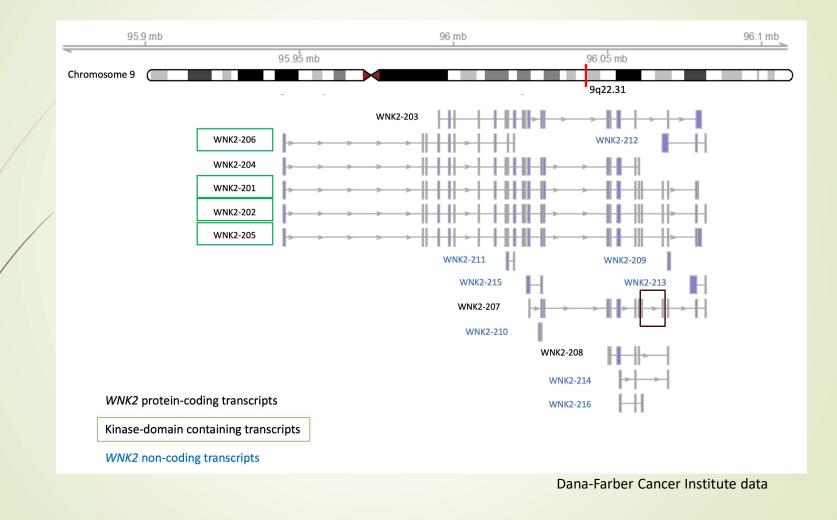
iene	200 -	Chrom	Start	End	LogFC Del6q	LogFC CXCR4 <sup>mt</sup>
FAMIIOC		chr2	38813	41627	-3.61	-3.29
WNK2		chr9	95947211	95947892	-1.88	-4.92
SGCD		chr5	155135062	155135118	-1.87	-3.26
CCDCI4I		chr2	179694483	179699167	-1.67	-1.30
PKHDILI	150 -	chr8	110374705	110374882	-1.56	-1.47
EML6 🔶		chr2	54952148	54952395	-1.49	-1.03
ZNF214		chr11	7020548	7022786	-1.39	-1.85
SYTL2 S		chr11	85405264	85406383	-1.32	-1.30
CHorf92	100 -	chr11	111164113	111169391	-1.\$1	-0.91
ILI7RB	100	chr3	53880576	53880675	-1.26	-2.04
ZNF215		chr11	6947653	6947916	-1.19	-1.29
ZNF804A 2		chr2	185463092	185463797	-1.12	-0.69
LINC00271 🛱		chr6	135818938	135819138 👔	-0.99	-0.69
CDK14	50 -	chr7	90095737	90095827	-0.76	-0.57
FOXO3		chr6	108881025	108881218	-055	-0.54
CYP4V2		chr4	187112673	187113191	1000	-0.53
IGF2R		chr6	160390130	160390427	-0.53	-0.43
EPS15		chrl	51819934	822518	-0.39	-0.37
HRK	0 -	-cirri2	117299020	117299271	1.84	2.02

#### My Robert A. Kyle Award: studying WNK2

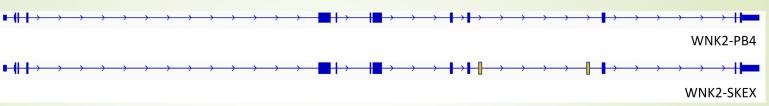
WNK2 is one of the top dysregulated genes in MYD88 mutated WM and is aberrantly expressed in early stages of disease

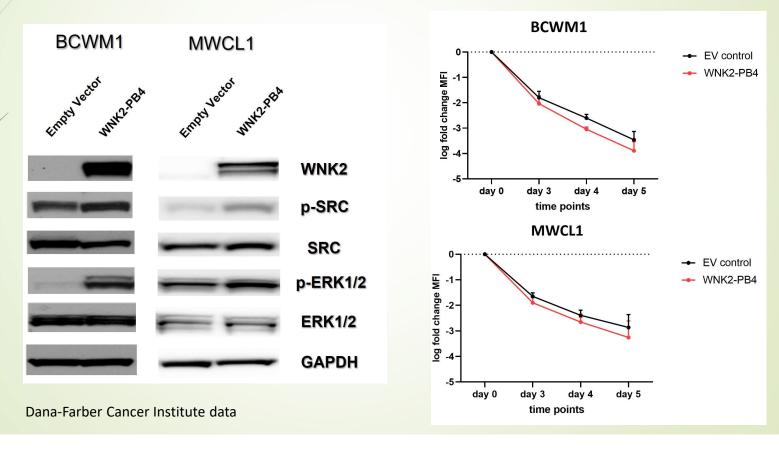
WNK2 may be involved in the malignant trasformation of MYD88 mutated cells

#### My Robert A. Kyle Award: studying WNK2









#### **THANK YOU!**



#### **29<sup>th</sup> Annual IWMF Educational Forum** MAY 3-5, 2024

Hyatt Regency Lake Washington | Renton, WA



#### All WM patients and their families



**Dana-Farber** 

**Cancer** Institute

COMPLEXITY







## **Remembering Glenn Cantor**

- Joined IWMF Board of Trustees in 2020
- Served on IWMF Scientific Advisory Committee (SAC) and Research Grants Review Committee
- Served as Science Writer & Editor for IWMF's *Torch* Magazine
- Tireless advocate for finding and engaging the best and brightest next generation researchers for WM

# IWMF is proud to announce the <u>Glenn Cantor Memorial Early</u> <u>Career Researcher Fund</u>

- Created by the Cantor Family
- Will help ensure that the IWMF continues to attract the best and brightest next generation researchers to WM while recognizing the incredible contributions that Glenn made to the global WM community

Thank You to the Cantor Family!

# Glenn Cantor Early Career Research Fund

Supports new investigators



