UC Irvine 趙 Chao Family Comprehensive Cancer Center

Infection-Related Immune Responses and MGUS: A Multi-Ethnic, Multi-Site Study

Mallory Bernstein, MSc

MPIs: 5R01CA260615-05
Wendy Cozen, DO, MPH (UC Irvine)
Kim Bertrand, ScD, MPH (Boston University)
Pinkal Desai, MD, MPH. (Cornell University)

Collaborator: Phil Felgner, PhD (UC Irvine)

2026 Scientific Retreat

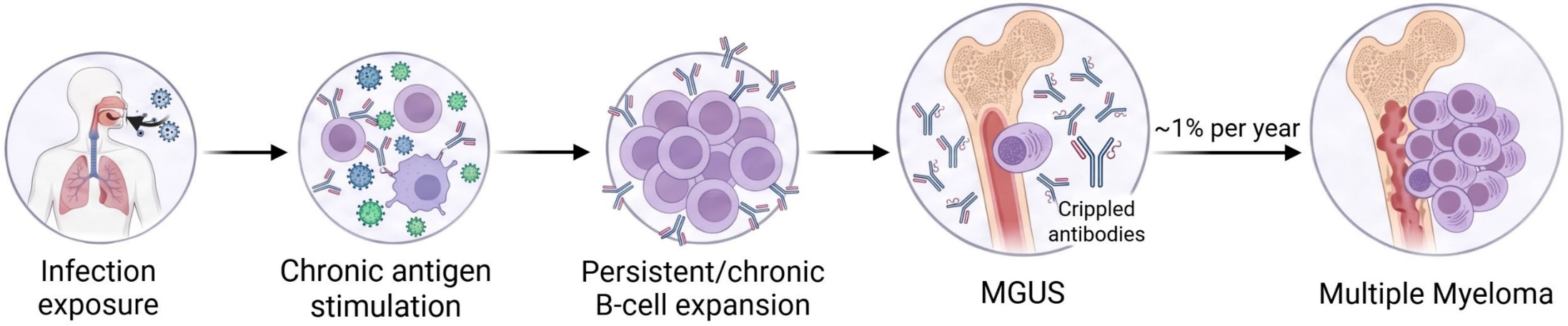
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Rationale: Could persistent immune stimulation help explain MGUS?

Monoclonal Gammopathy of Undetermined Significance (MGUS) is the precursor of Multiple Myeloma (MM).

Disparities are present before myeloma develops.

MGUS offers an opportunity to study earlier disease biology.



Working Hypothesis: Exposure to chronic infectious agents may produce persistent B-cell stimulation, influencing MGUS development.

Study Design: Design and Analysis

The Multiethnic Cohort Study

Understanding ethnic differences in cancer to prevent it in all populations

BLACK WOMEN'S HEALTH STUDY

SCCS

The Women's Health Initiative

Provided Serum and Questionnaires

1,403 MGUS cases
43.5% Black, 41.6% White

1,524 controls
44.7% Black, 40.0% White

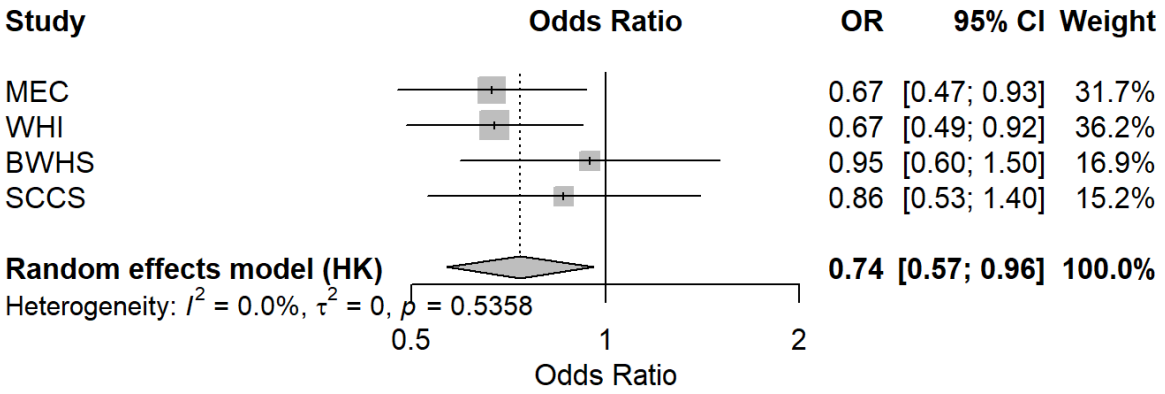
- Cross-Sectional, Nested Case-Control Study
- Performed IgG serum microarray: *HSV-1, CMV, EBV, VZV*
- Examined Highest vs lowest reactivity tertiles (T3 vs T1)
- Adjusted cohort models ➔ random-effects meta-analysis

Pathogen	Antigen
HSV-1	gG
CMV	gB
CMV	pp28
CMV	pp52
CMV	pp65
CMV	pp150
EBV	Early Antigen
EBV	EBNA-1
EBV	Extract Antigen
EBV	p18 (VCA)
VZV	gB
VZV	gE (Shingrix)
VZV	gH/gL
VZV	ORF9

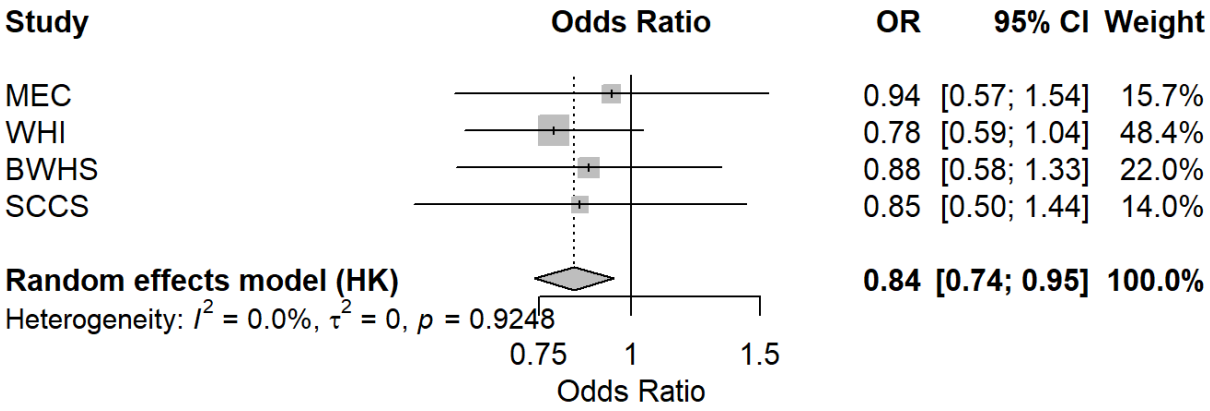
Results: Two antigen responses showed inverse associations with MGUS

All other antigen serum reactivity meta-analyses were null

EBV early antigen



CMV pp65



OR compares T3 vs T1 and association with MGUS

Results Summary: Signals differ by risk of MGUS progression to MM

Significant Associations • Non-IgM MGUS • modified Mayo Clinic MGUS risk classification • compared with controls

	Low-Risk Non-IgM MGUS			Intermediate/High-Risk non-IgM MGUS		
Antigen (T3 vs T1)	Meta-Analysis OR (95% CI)	p	p (FDR)	Meta-Analysis OR (95% CI)	p	p (FDR)
EBV EA	0.74 (0.52-1.05)	0.07	0.27	0.66 (0.36-1.21)	0.12	0.33
CMV pp65	**0.82 (0.70-0.97)**	**0.03**	0.23	0.98 (0.52-1.86)	0.94	0.94
EBV p18 (VCA)	1.12 (0.66-1.91)	0.53	0.75	**1.23 (1.06-1.43)**	**0.02**	0.14
VZV gB	1.27 (0.81-1.98)	0.19	0.43	**1.37 (1.10-4.98)**	**0.02**	0.14
VZV gH/gL	**1.16 (1.02-1.31)**	**0.03**	0.24	0.70 (0.46-1.08)	0.07	0.28
	OR compares T3 vs T1 and association with low risk MGUS			OR compares T3 vs T1 and association with intermediate/high risk MGUS		

Conclusion: Antibody-response differences merit follow-up

Observation 1: Only two antigens were significantly statistically inversely associated with MGUS (EBV EA and CMV pp65).

Observation 2: However, when stratified by risk of progression to MM, serum reactivity to several antigens differed by risk of progression level.

The inverse associations between serum reactivity to EBV EA and CMV pp65 and MGUS may reflect diminished antigen-specific humoral responses in individuals with MGUS, although these findings alone are not definitive for immunoparesis. The positive association between serum reactivity and low- but not high-risk MGUS suggests immune dysregulation may be associated with MGUS risk of progression to MM.

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Thank You!