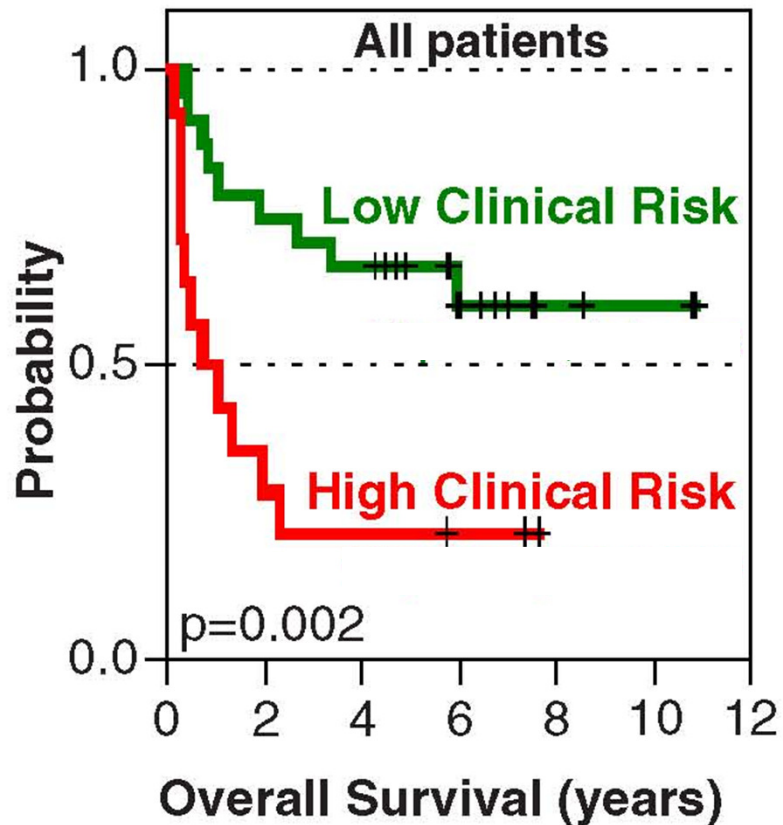


Cellular Redox Environment as a Target for Cancer Prognostics and Treatment

Margaret M. Briehl, Ph.D.
Professor of Pathology

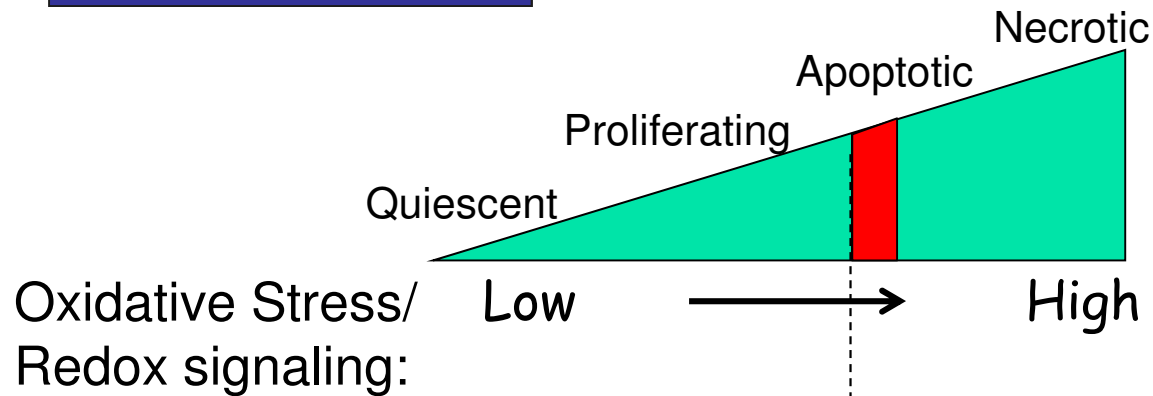
Diffuse Large B Cell Lymphoma (DLBCL)



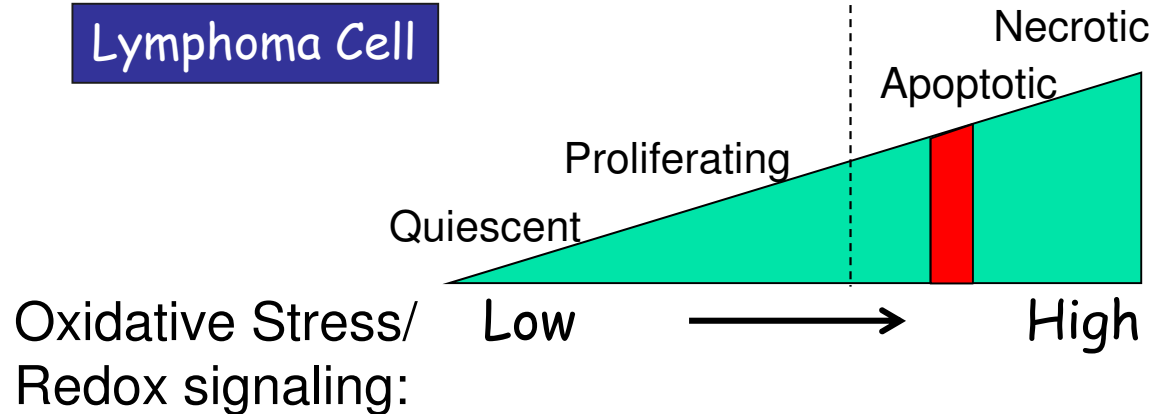
- Standard therapy cures ~50% of patients
- Remaining patients have a high probability of death within 5 years
- Clinical features are somewhat predictive of treatment outcome
- Clinical features do not inform the underlying biology

Model & Translational Studies

Normal Lymphocyte

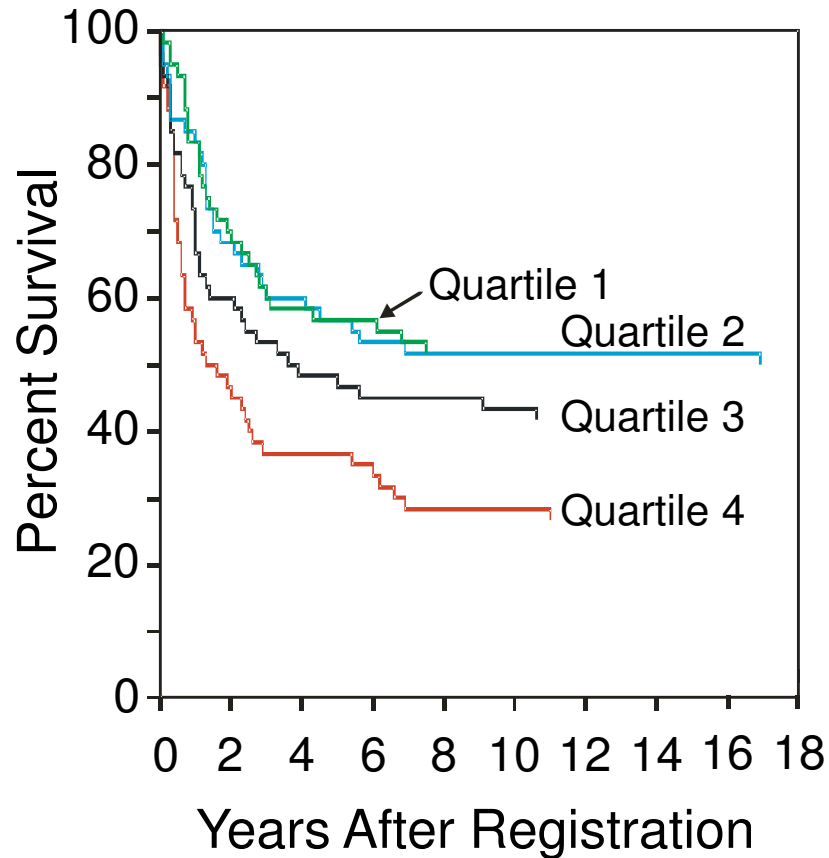


Lymphoma Cell



1. How does the redox state contribute to treatment resistance?
2. What is the mechanism for altered redox signaling altered in lymphoma cells?
3. How do we capitalize on the redox state of lymphomas to improve cure rates?

Redox Scores and Outcome in DLBCL



Redox Score

Q1

Q4

High

Low

Antioxidant Defenses

Low

High

Oxidative Stress Response

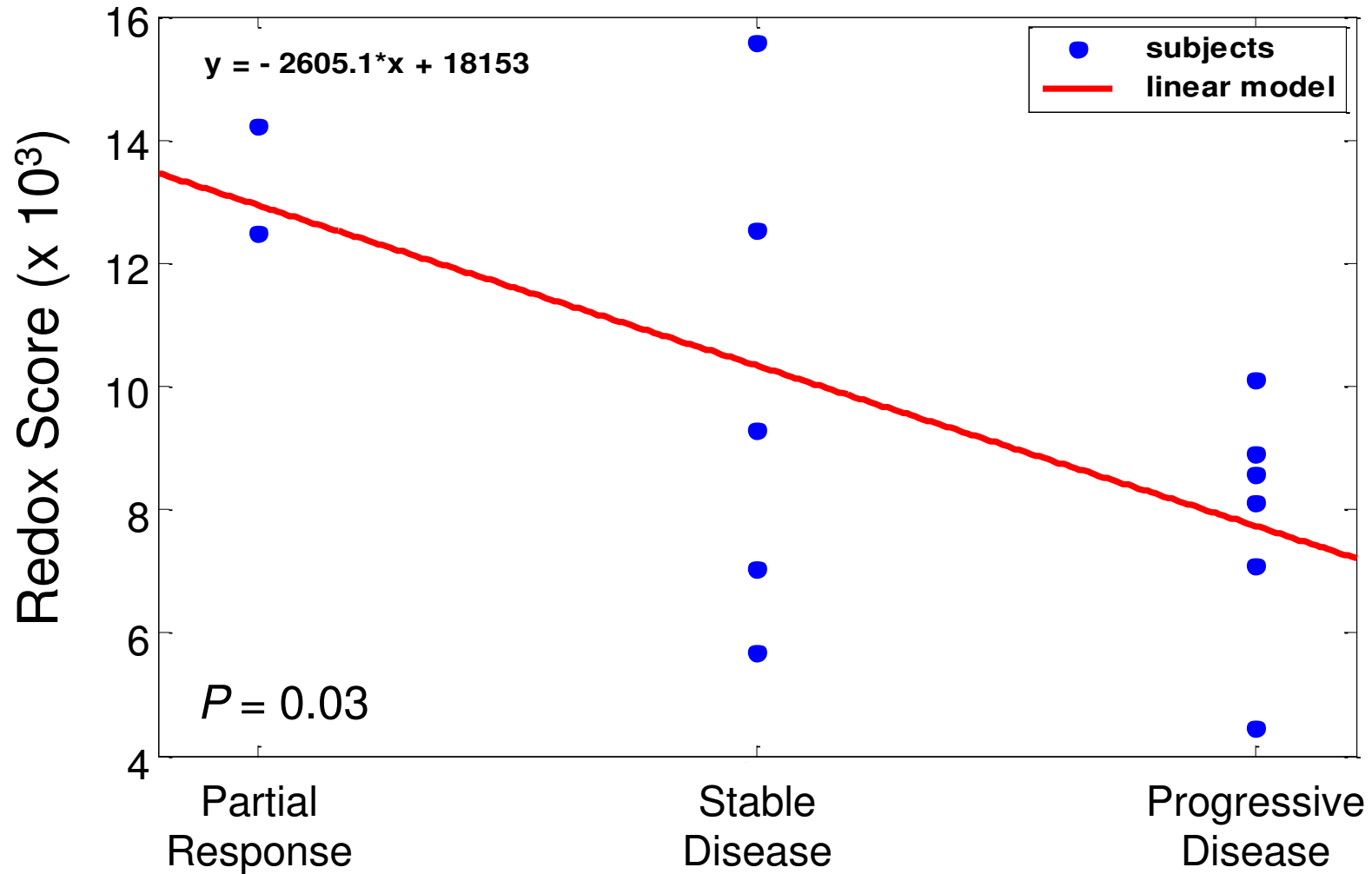
Low

High

Maintenance of Redox-Regulated Transcription Factors

Quartiles 1 or 2 vs. 4, $P < 0.01$

Redox Score Predicts Lymphoma Response to the Redox-Targeted Drug Imexon





NADPH Oxidase Gene SNP and Treatment Outcome in Aggressive Lymphomas

Cohort	Genotype	Events/Patients	HR (95% CI)	P value
Discovery (n=327)	GG/AG	157/274	1.00 (reference)	0.06
	AA	24/53	0.66 (0.43 – 1.02)	
Validation (n=504)	GG/AG	165/423	1.00 (reference)	0.05
	AA	26/81	0.66 (0.44 – 1.01)	
Meta-Analysis	GG/AG	322/697	1.00 (reference)	<0.01
	AA	50/134	0.66 (0.49 – 0.89)	

Discovery: SWOG clinical trials, aggressive lymphomas, anthracycline based therapies

Validation: Mayo Rochester patients, DLBCL, R-CHOP

Partnership for Native American Cancer Prevention (NACP)



- Objective: Alleviate cancer health disparities among Native Americans in the southwest
- Four components
 - Research – 3 projects, each with an NAU & UA PI
 - Training – recruit Native American students for training activities from pre-college to post-graduate
 - Outreach – cancer education and input on community priorities
 - Evaluation – tracks progress toward specific aims



Alignment with Areas of Excellence

- **Precision Health:** mechanistic studies of redox-based approaches to guide treatment for lymphoma patients
- **Health Disparities:** developing a workforce of Native American health care providers and cancer researchers



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