ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

POLICLINICO DI
SANT'ORSOLA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Bologna

Aggressive
Lymphoma
Workshop

Bologna, Royal Hotel Carlton
May 8-9, 2023

Genomic classification of DLBCL

Roland Schmitz, Ph.D.
Justus Liebig University Giessen

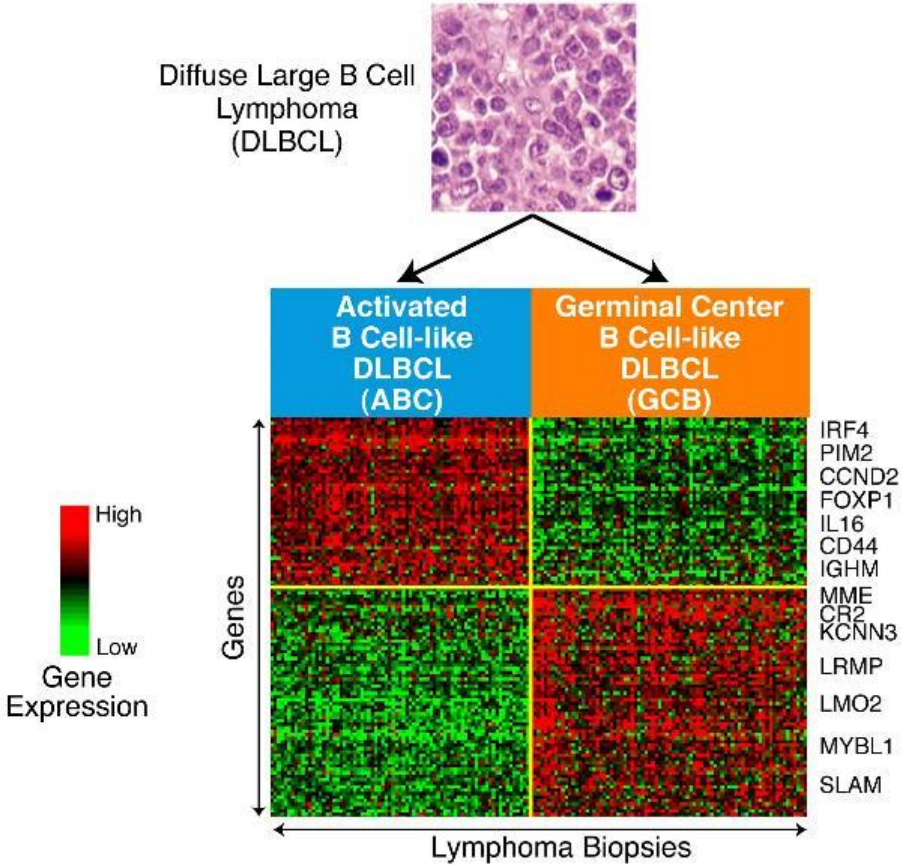
President: **Pier Luigi Zinzani**

Disclosures

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
NONE	-	-	-	-	-	-	-

Dissecting Cancer Into Molecularly and Clinically Distinct Subtypes by Gene Expression Profiling

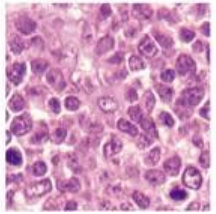


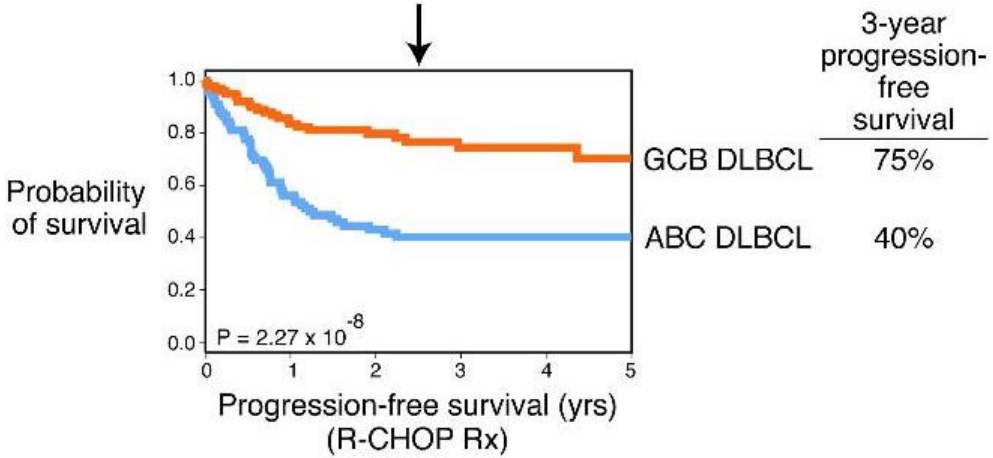
Subtype-specific gene expression signatures

Alizadeh et al. Nature 2000

Dissecting Cancer Into Molecularly and Clinically Distinct Subtypes by Gene Expression Profiling

Diffuse Large B Cell Lymphoma (DLBCL)

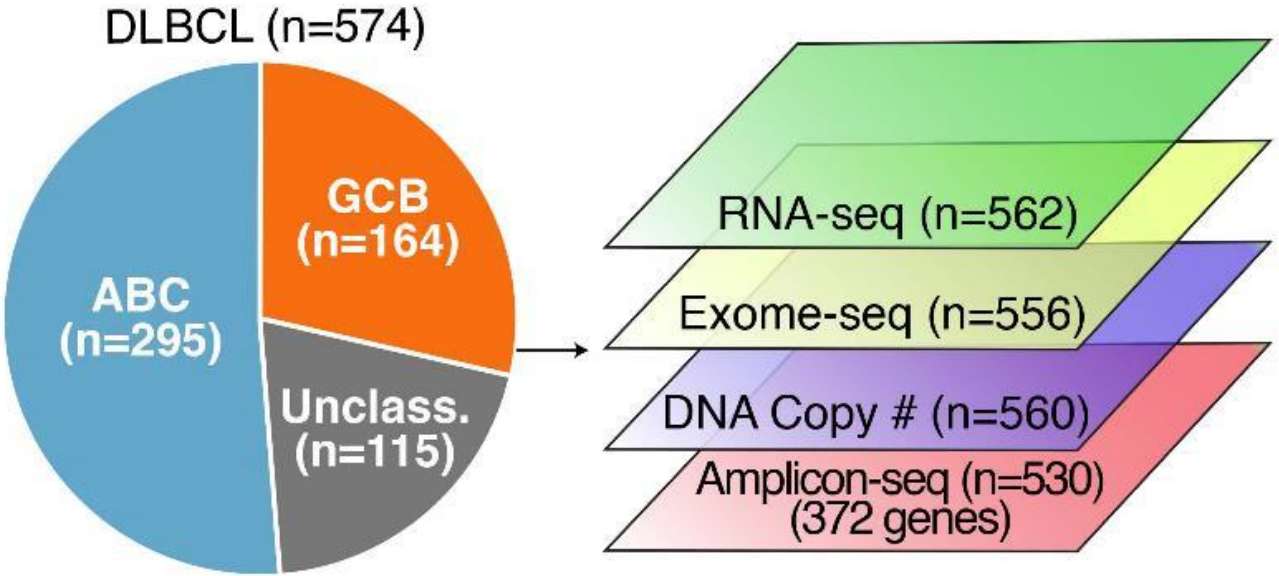




Subtype-specific response
To chemotherapy

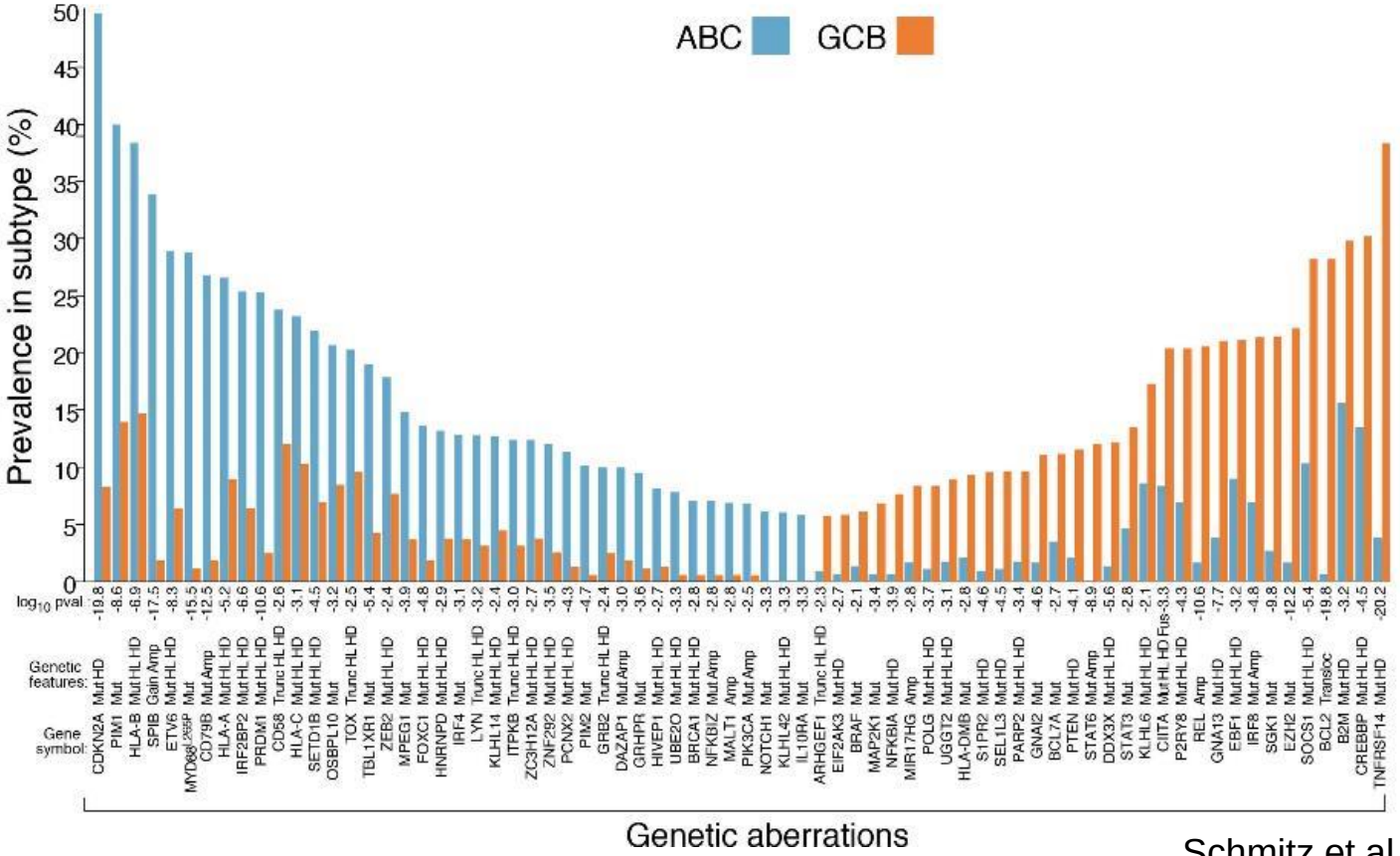
Alizadeh et al. Nature 2000

Building a Genetic Classification of DLBCL



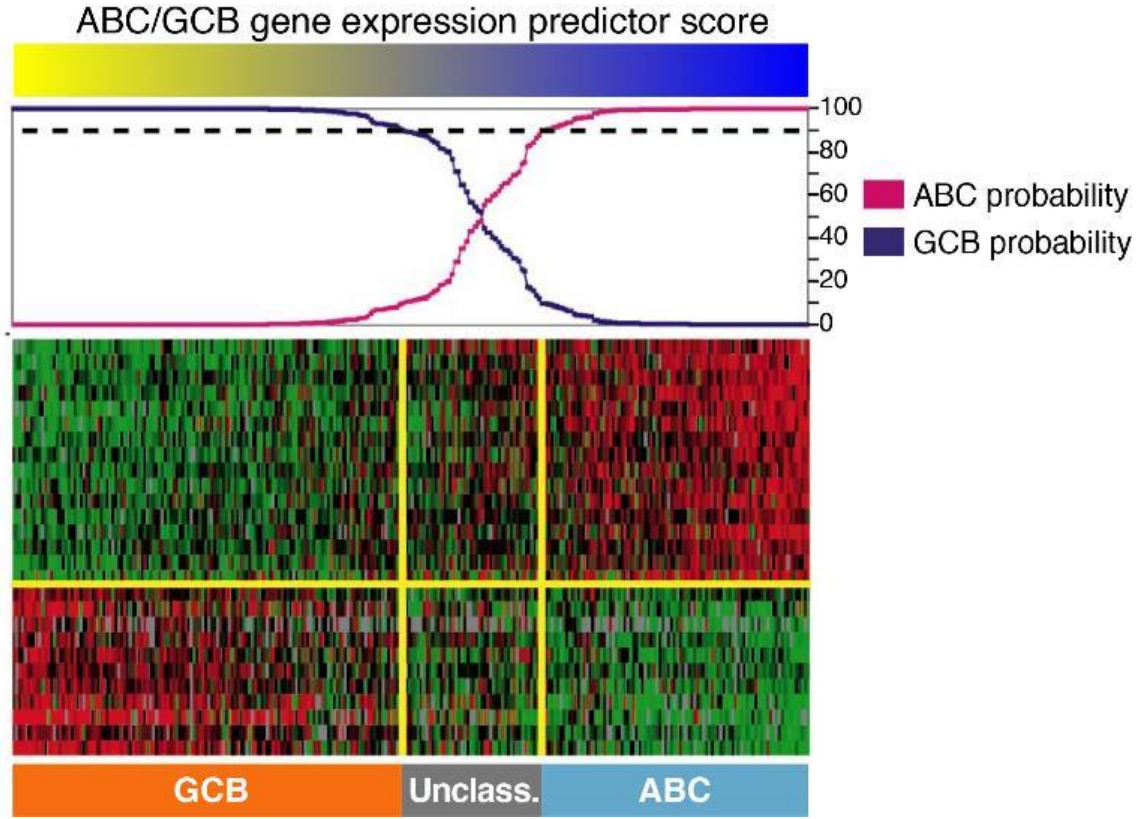
Schmitz et al. NEJM 2018

Extensive Genetic Differences Between ABC and GCB DLBCL



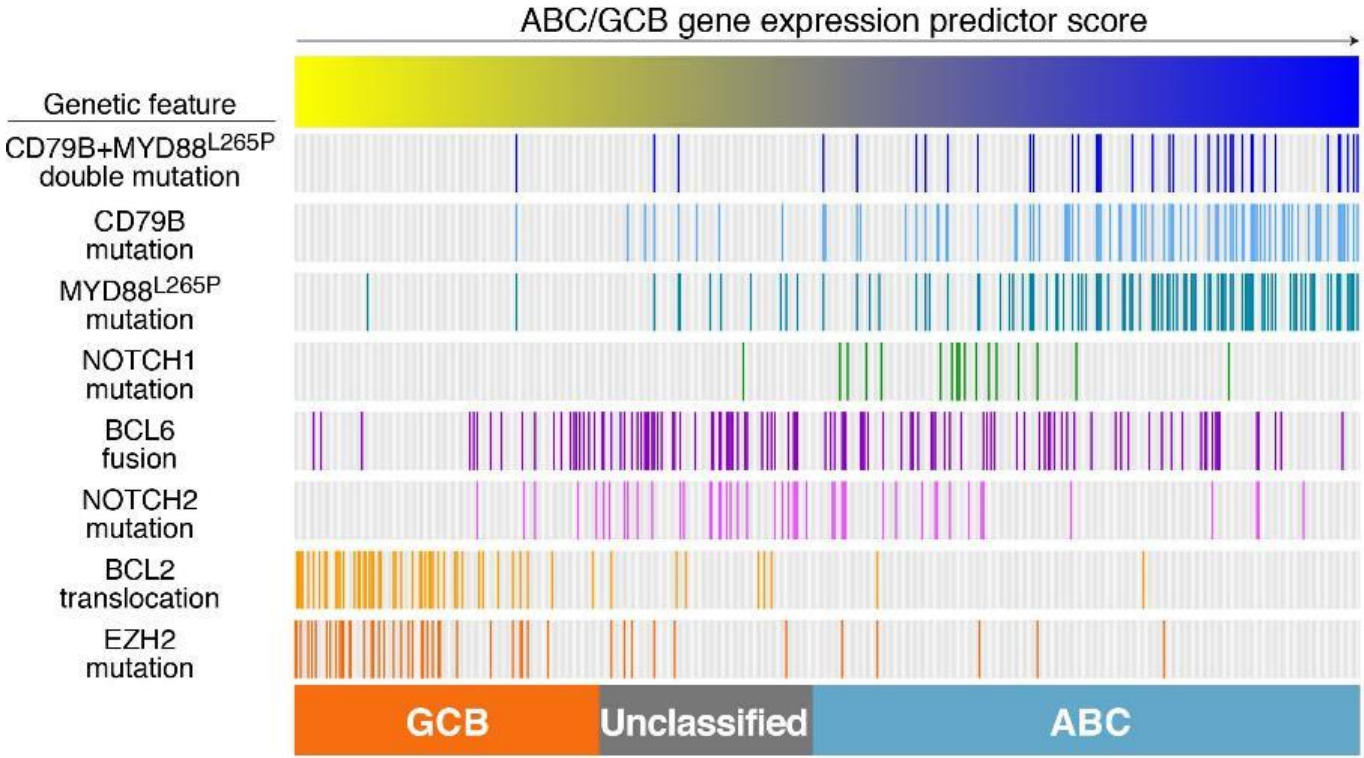
Schmitz et al. NEJM 2018

Defining ABC, GCB and Unclassified DLBCL Based on the ABC/GCB predictor score



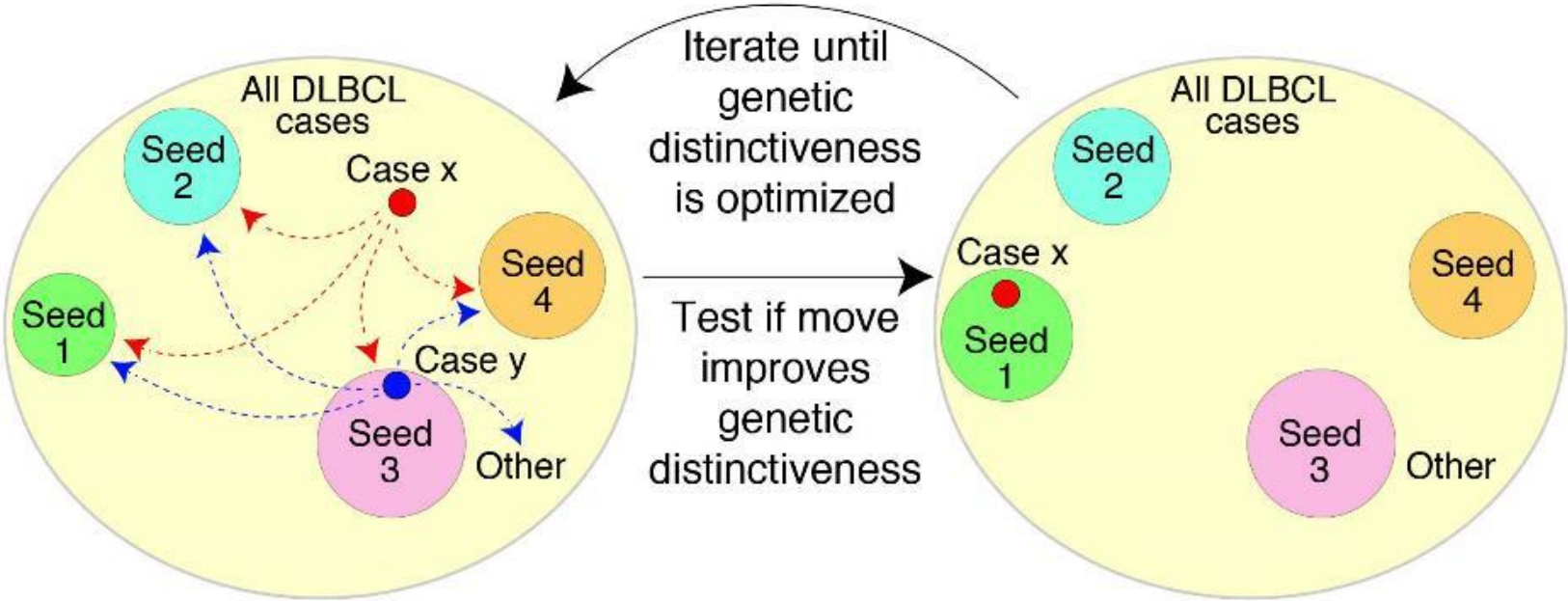
Schmitz et al. NEJM 2018

Heterogeneity of Genetic Aberrations Within DLBCL Gene Expression Subgroups



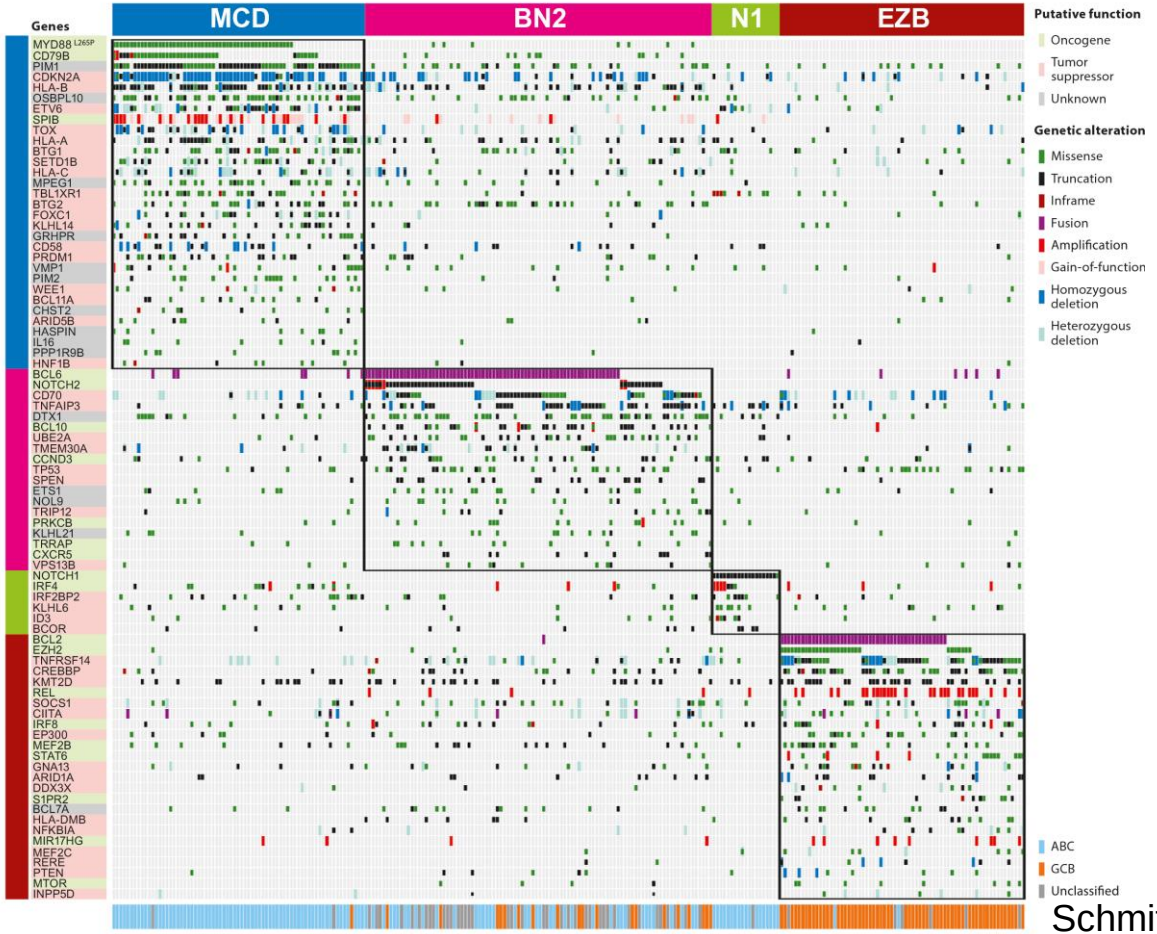
Schmitz et al. NEJM 2018

Building a Genetic Classification of DLBCL



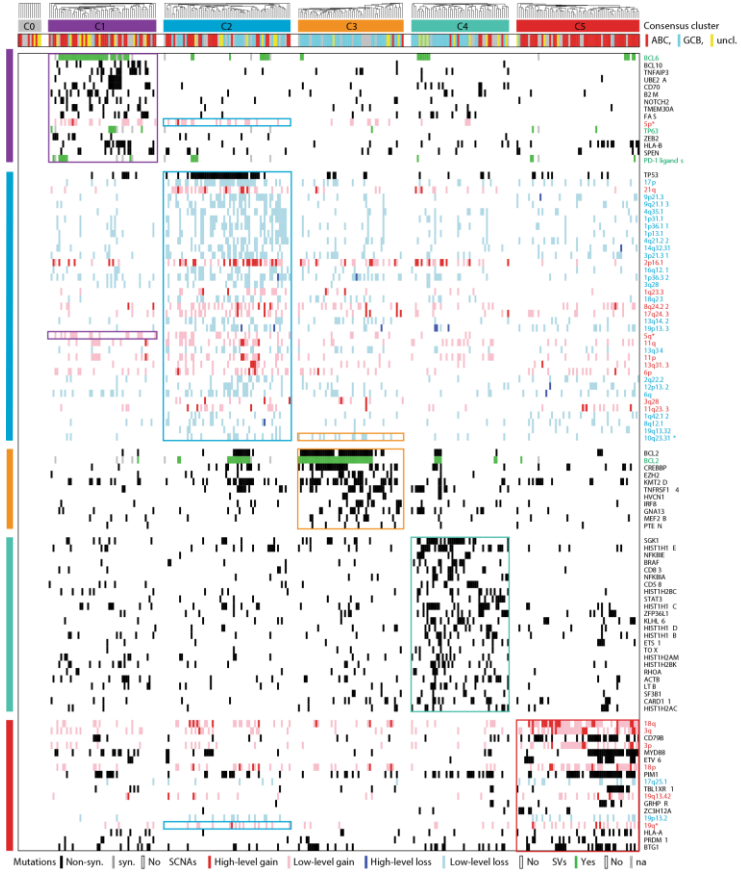
Schmitz et al. NEJM 2018

Genetic Subtypes of Diffuse Large B cell Lymphoma

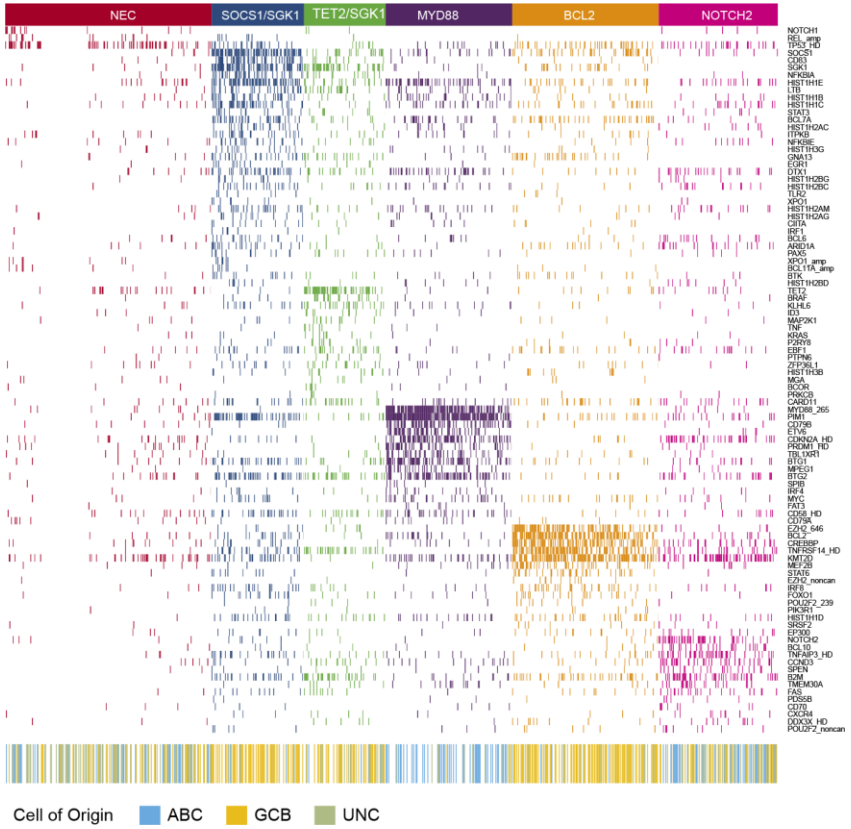


Schmitz et al. NEJM 2018

Genetic Subtypes of Diffuse Large B cell Lymphoma

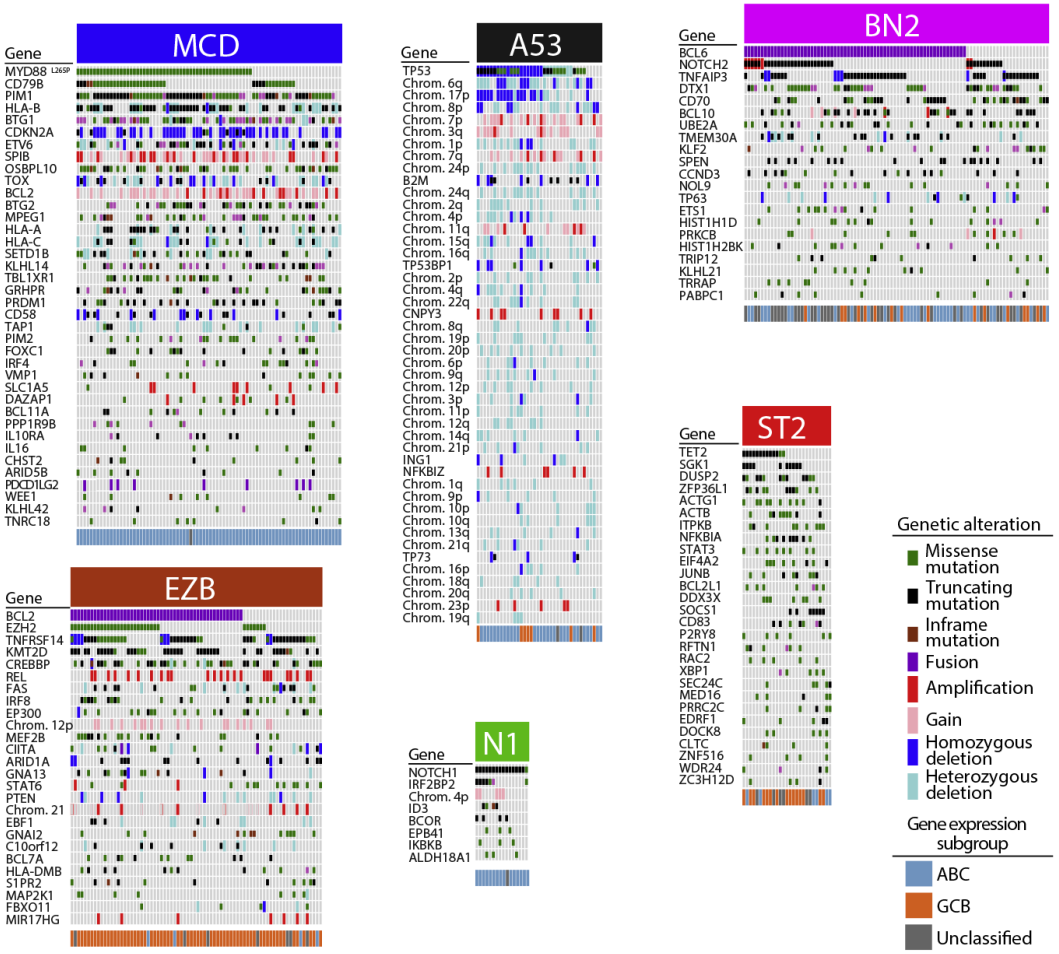


Chapuy et al. Nat. Med. 2018



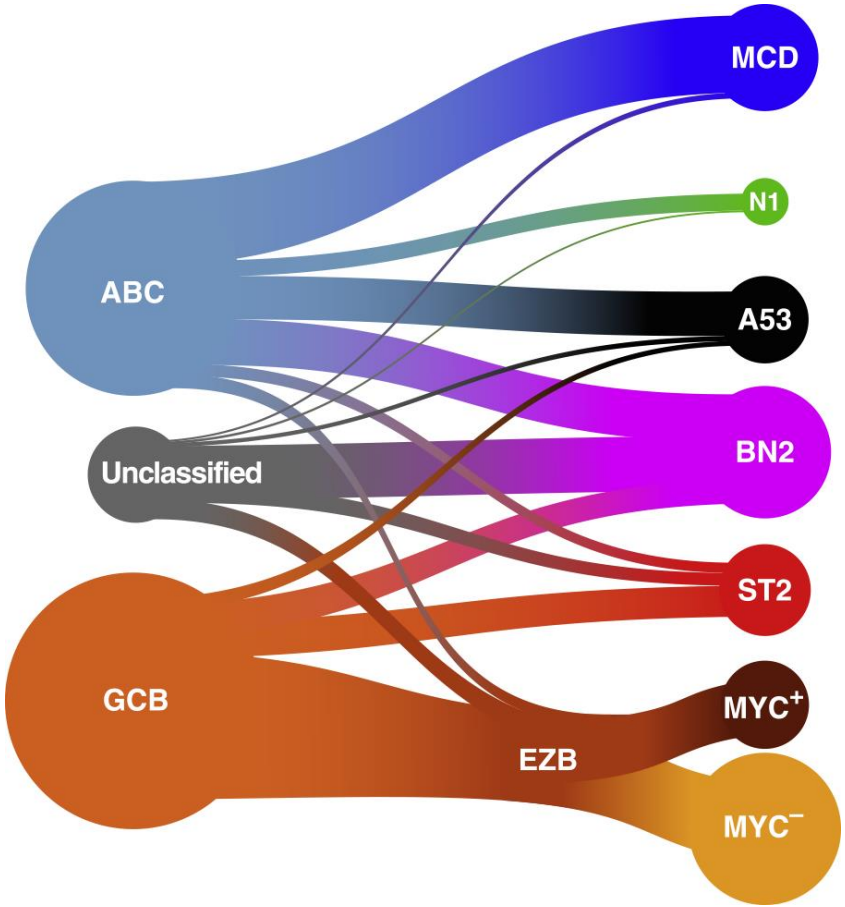
Lacy et al. Blood 2020

Genetic Subtypes of Diffuse Large B cell Lymphoma



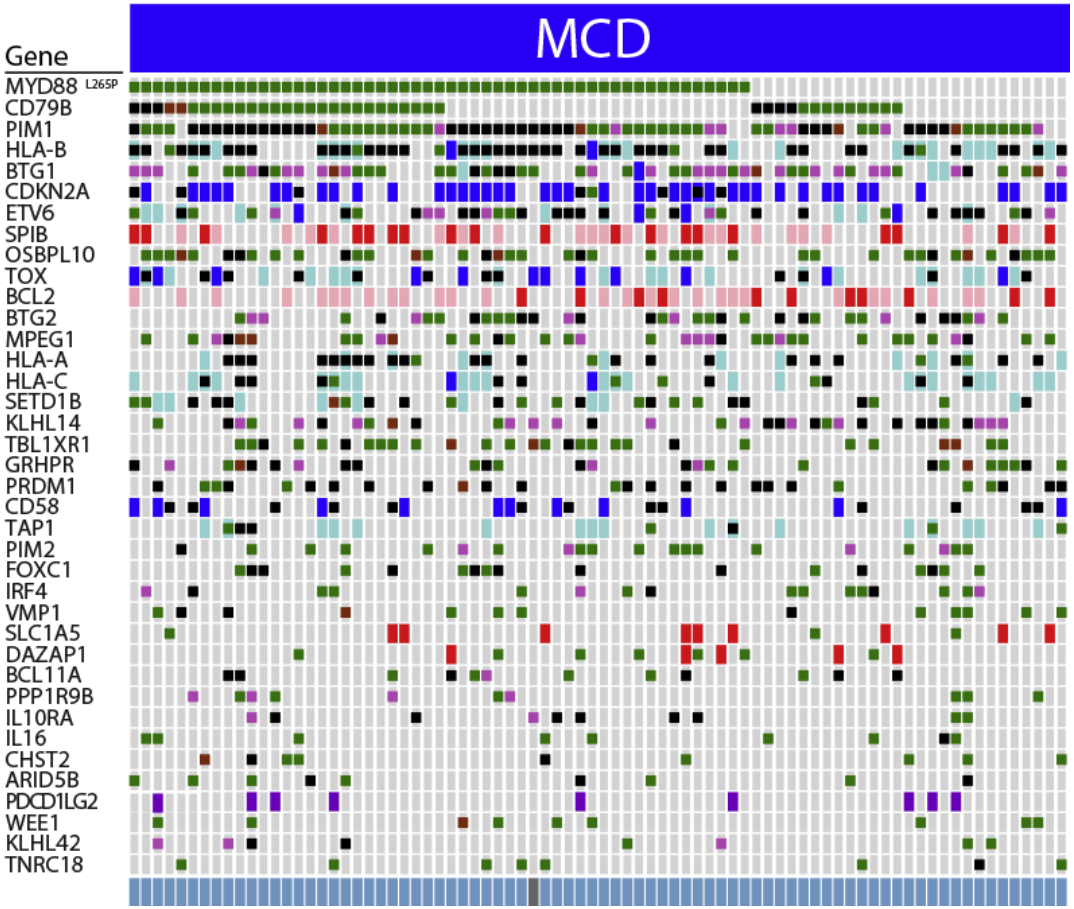
Wright et al. Cancer Cell 2020

Relationship between DLBCL COO Subgroups and Genetic Subtypes

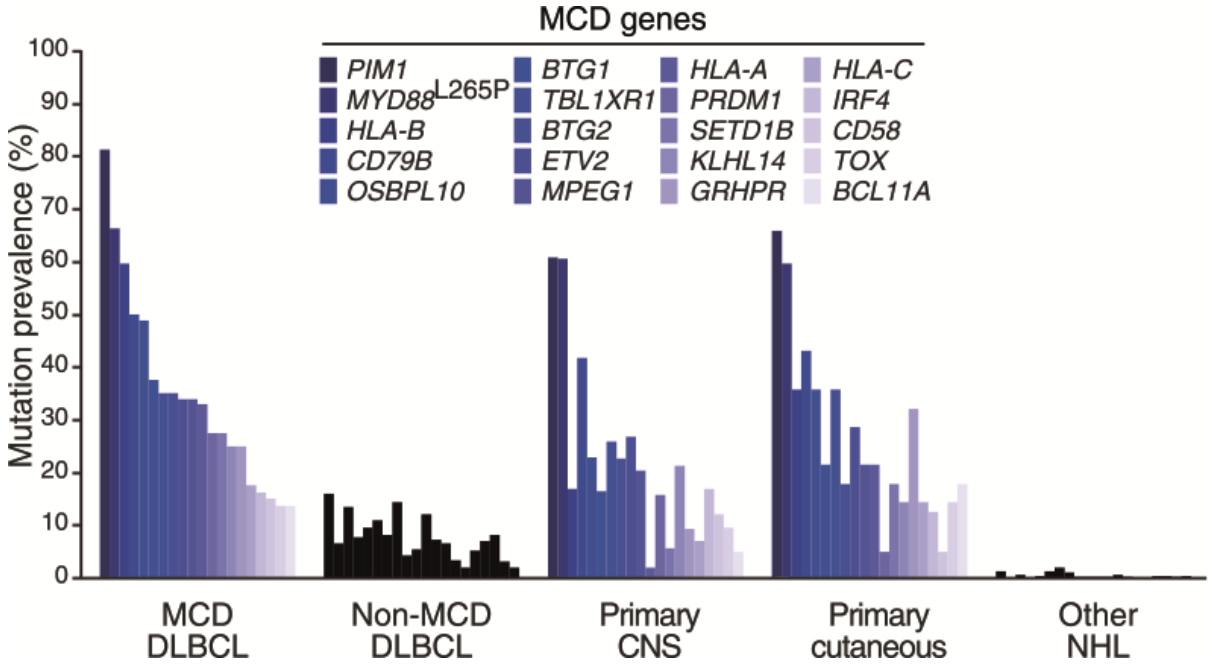


Wright et al. Cancer Cell 2020

The MCD Genetic Subtype of DLBCL

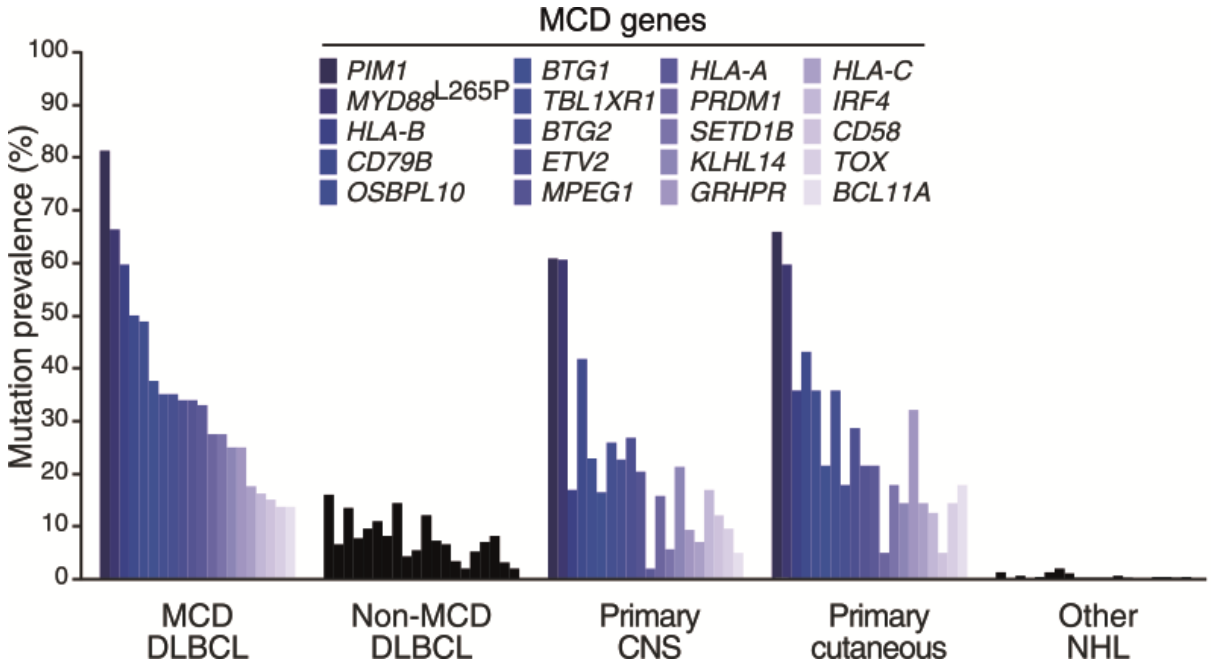


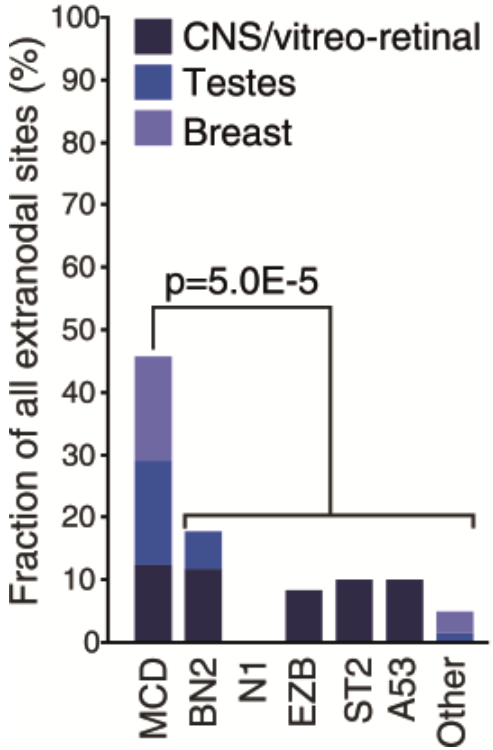
Similarities of MCD DLBCL to Extranodal DLBCL



Wright et al. Cancer Cell 2020

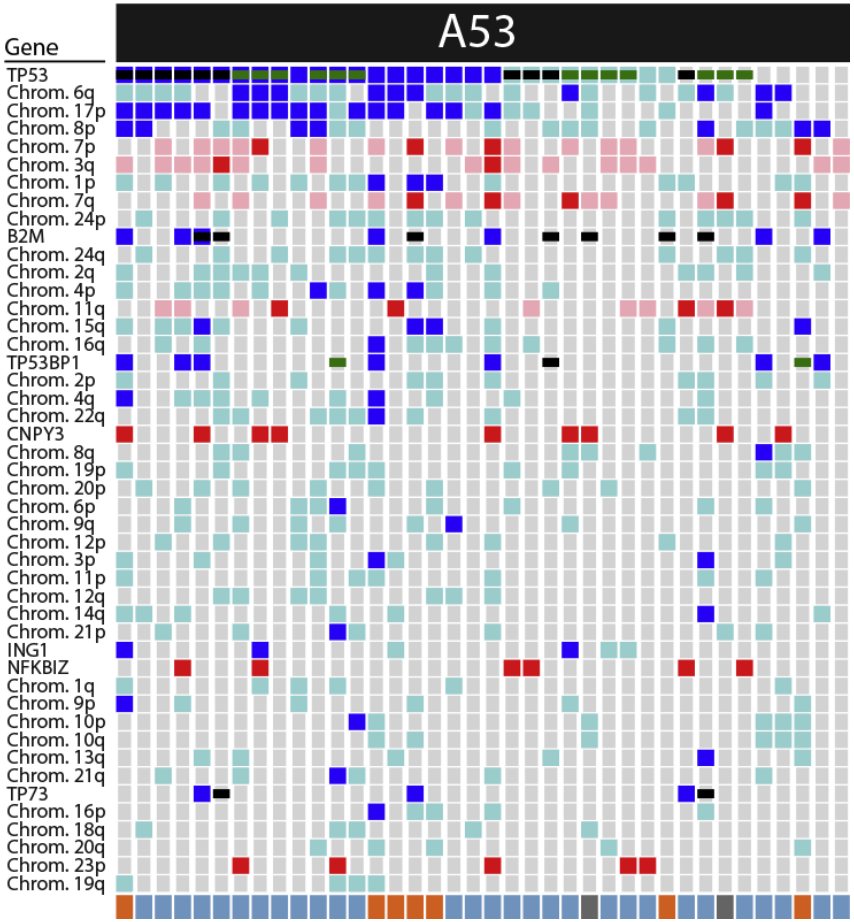
Similarities of MCD DLBCL to Extranodal DLBCL



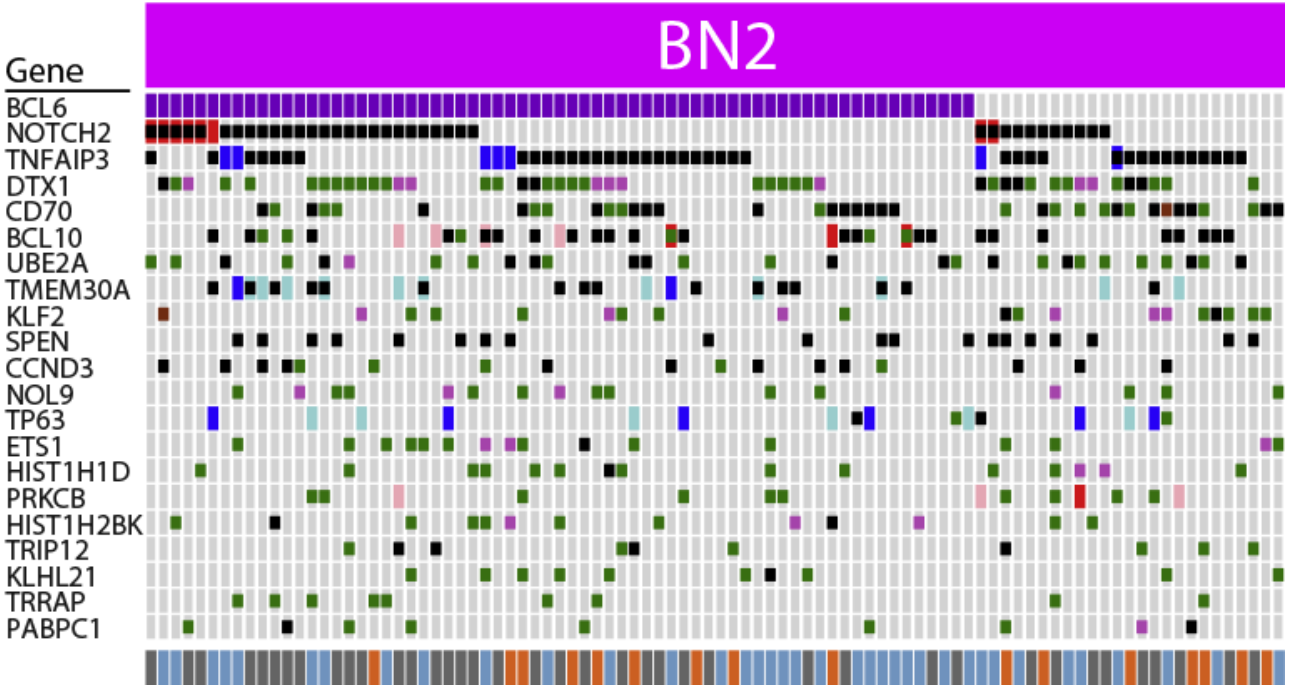


Wright et al. Cancer Cell 2020

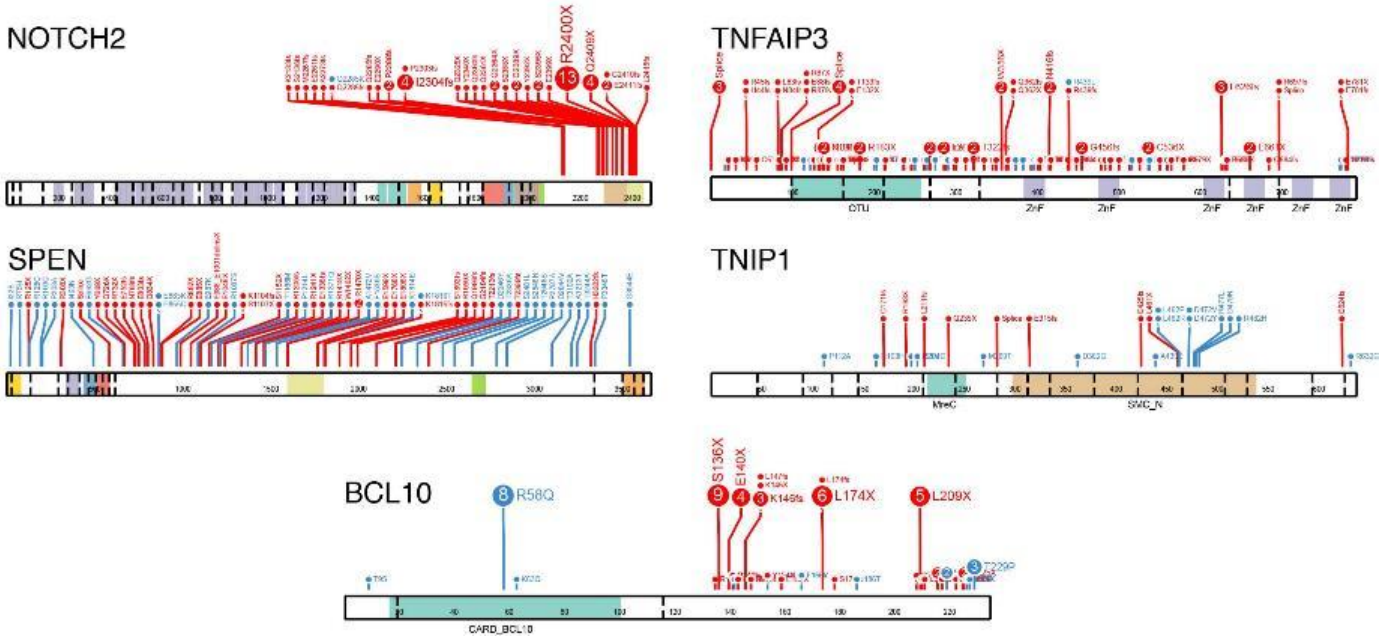
The A53 Genetic Subtype of DLBCL



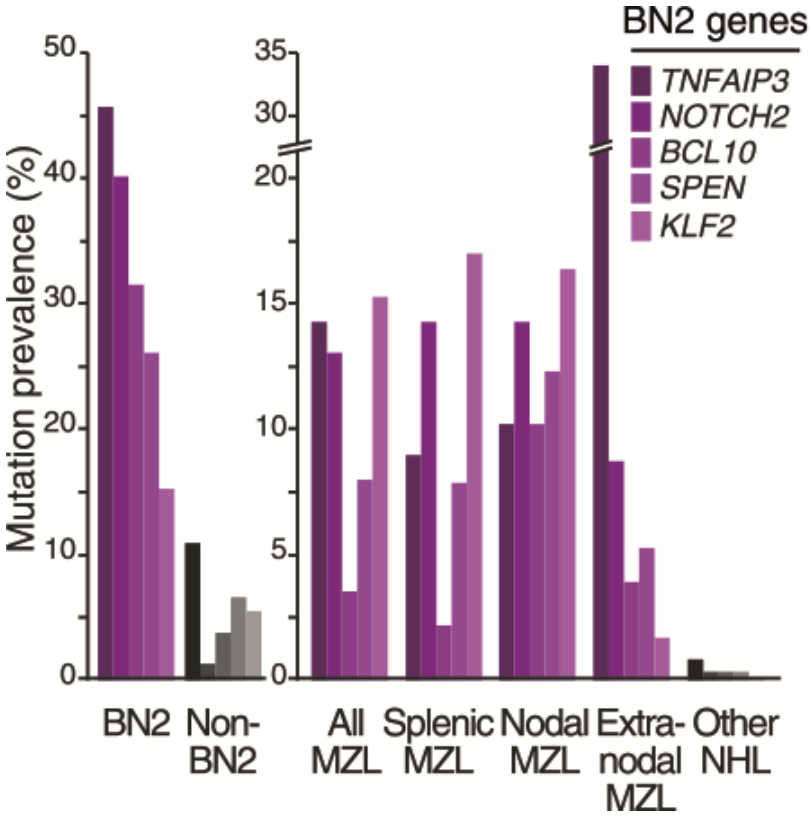
The BN2 Genetic Subtype of DLBCL



Genetic Relationship Between BN2 DLBCL and Marginal Zone Lymphomas

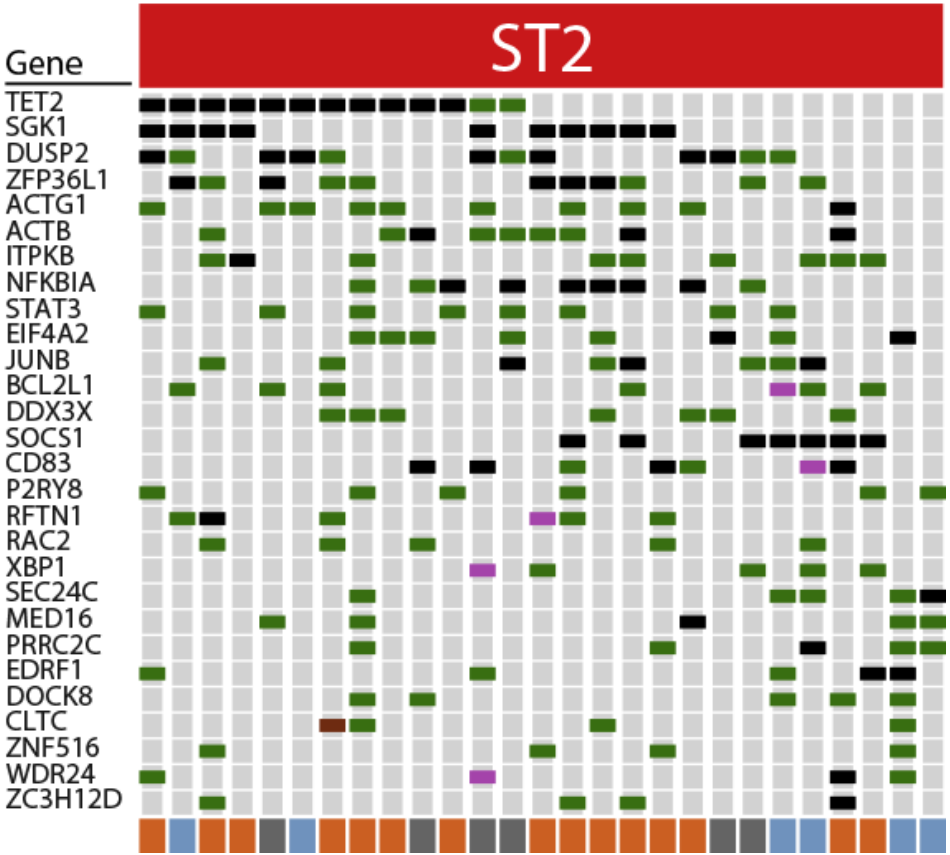


Genetic Relationship Between BN2 DLBCL and Marginal Zone Lymphomas

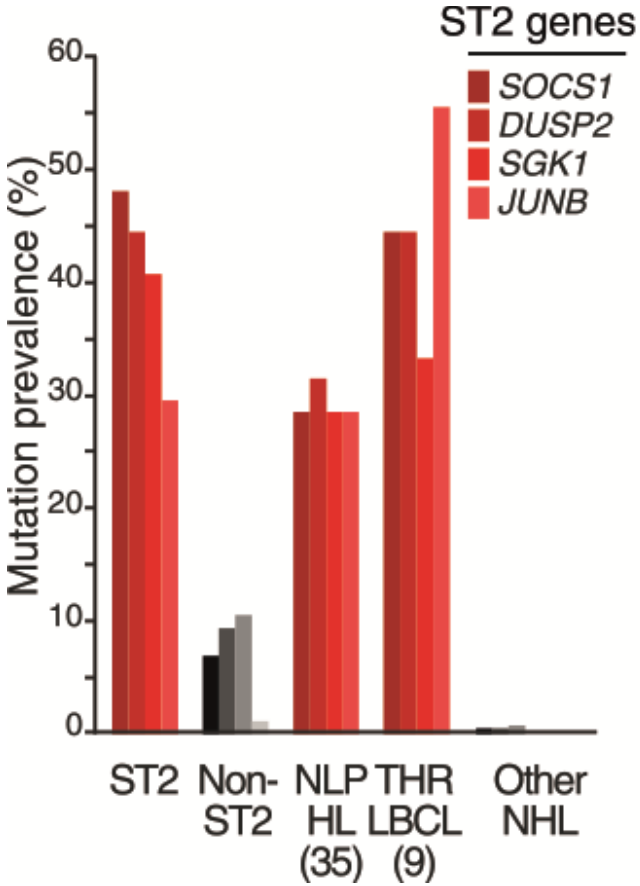


Wright et al. Cancer Cell 2020

The ST2 Genetic Subtype of DLBCL

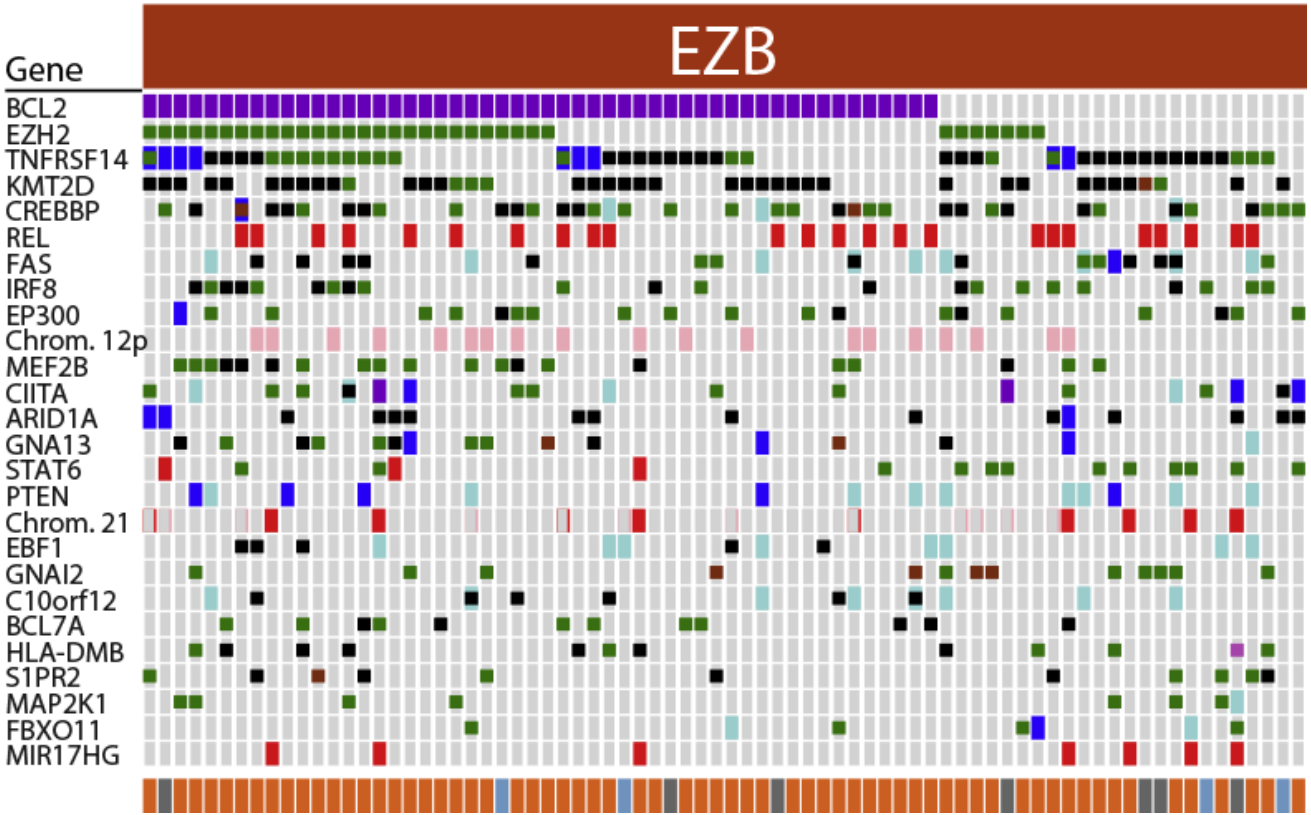


Genetic Relationship Between ST2 DLBCL and T cell/histiocyte-rich large B cell lymphoma / Hodgkin Lymphoma

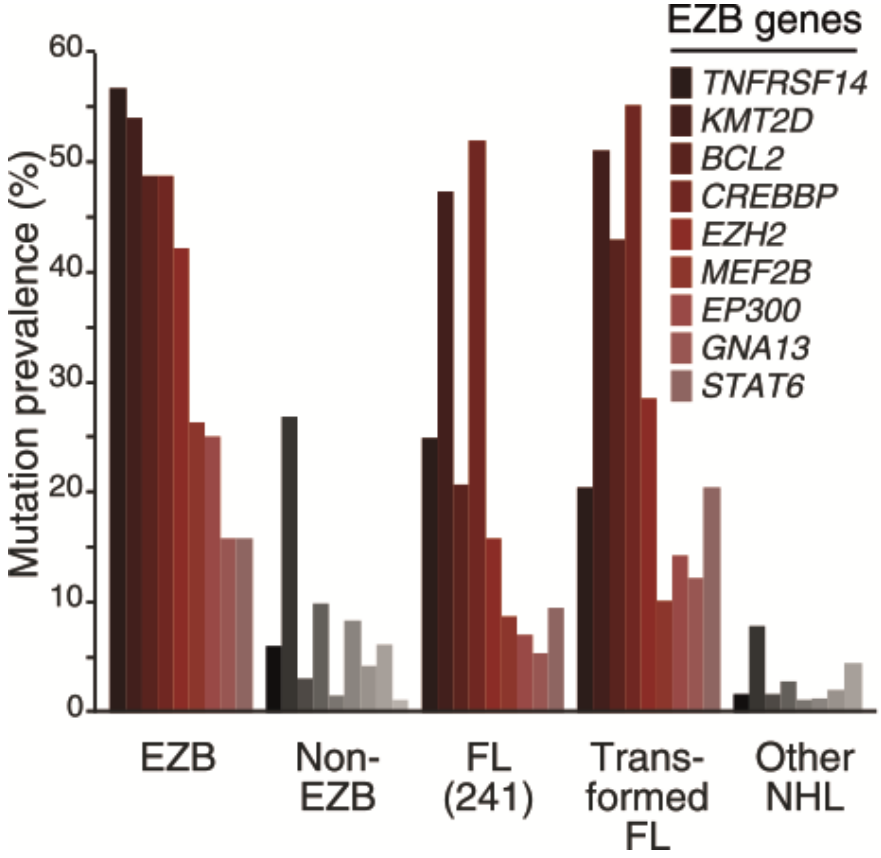


Wright et al. Cancer Cell 2020

The EZB Genetic Subtype of DLBCL

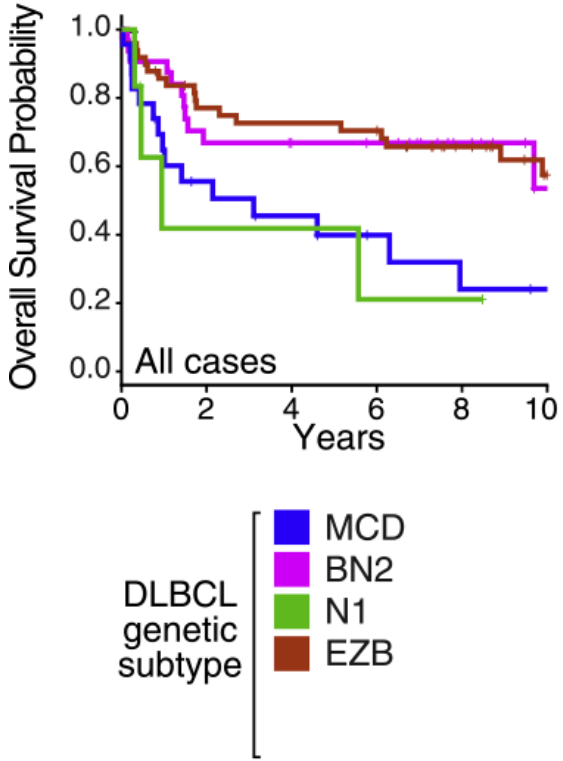


Genetic Relationship Between EZB DLBCL and Follicular Lymphomas



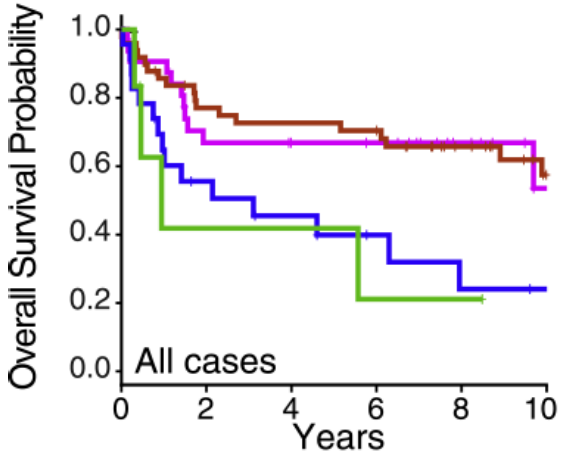
Wright et al. Cancer Cell 2020

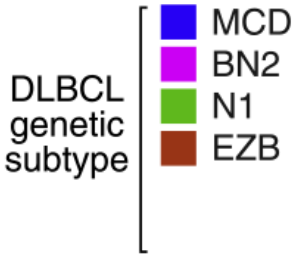
DLBCL Genetic Subtype Predict Survival Following R-CHOP

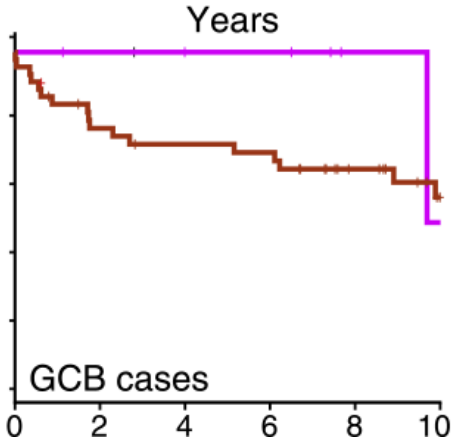


Wright et al. Cancer Cell 2020

DLBCL Genetic Subtype Predict Survival Following R-CHOP

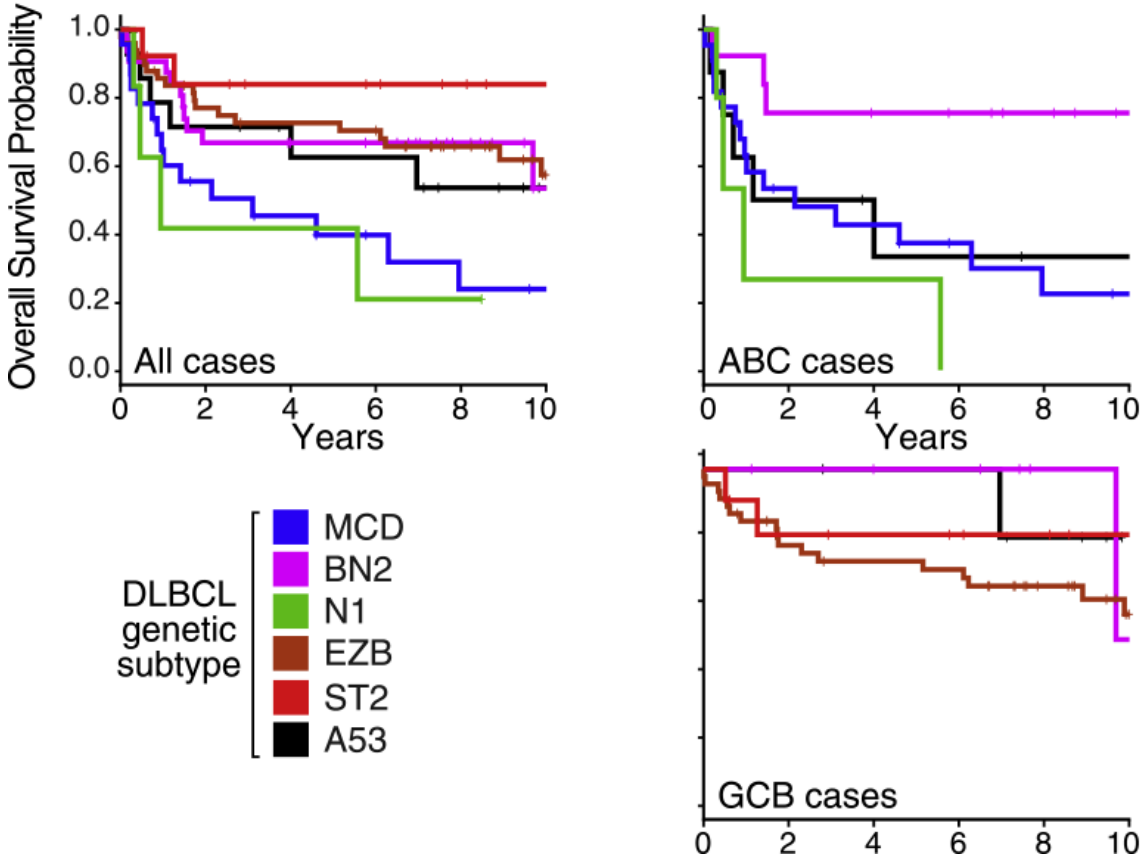






Wright et al. Cancer Cell 2020

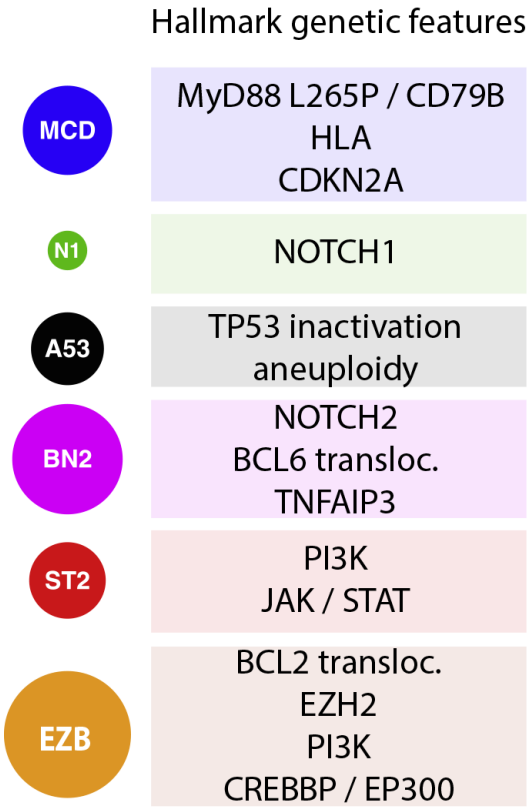
DLBCL Genetic Subtype Predict Survival Following R-CHOP



Wright et al. Cancer Cell 2020

Genetic Subgroups of Diffuse Large B cell Lymphoma

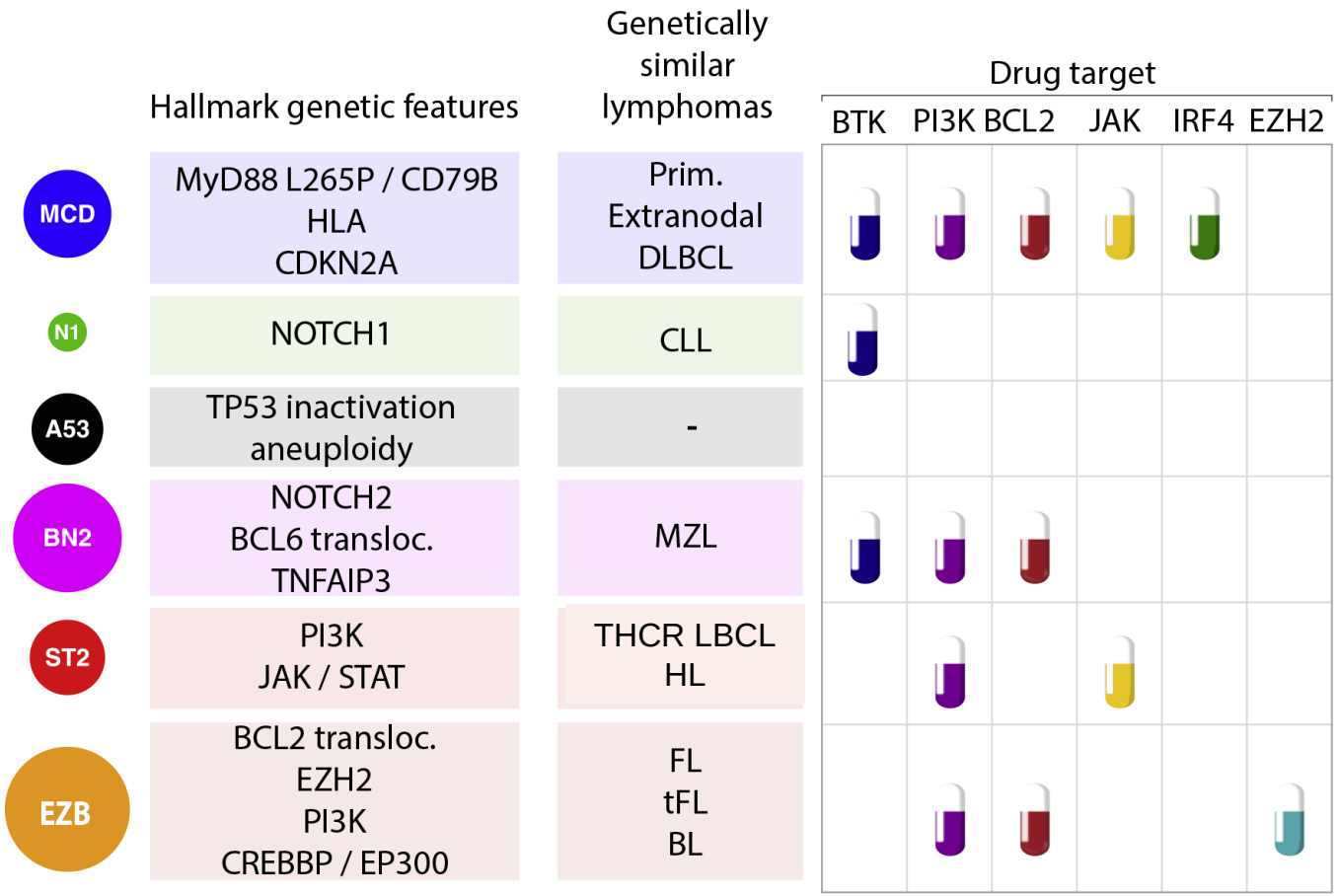
Genetic Subgroups of Diffuse Large B cell Lymphoma



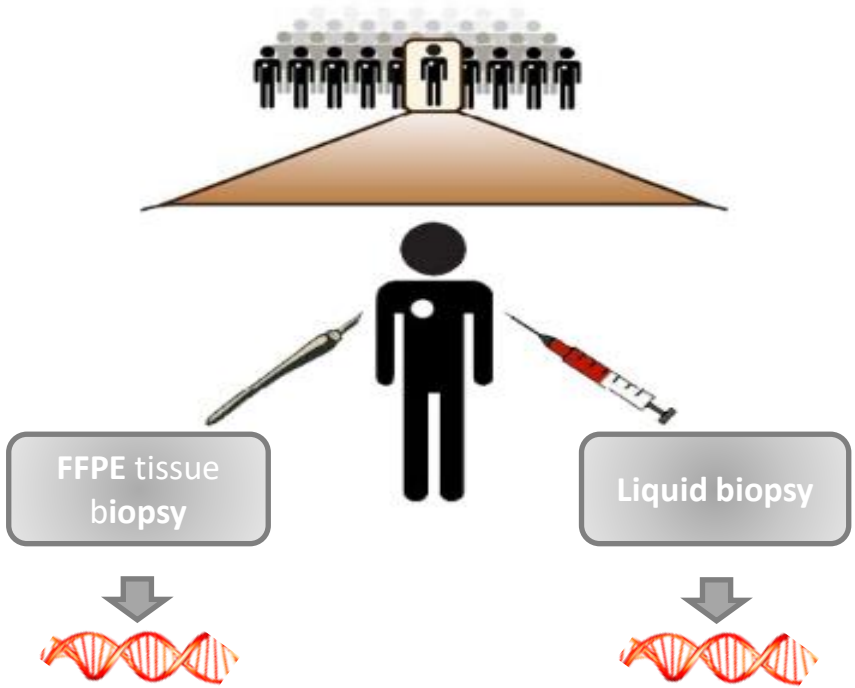
Genetic Subgroups of Diffuse Large B cell Lymphoma

	Hallmark genetic features	Genetically similar lymphomas
MCD	MyD88 L265P / CD79B HLA CDKN2A	Prim. Extranodal DLBCL
N1	NOTCH1	CLL
A53	TP53 inactivation aneuploidy	-
BN2	NOTCH2 BCL6 transloc. TNFAIP3	MZL
ST2	PI3K JAK / STAT	THCR LBCL HL
EZB	BCL2 transloc. EZH2 PI3K CREBBP / EP300	FL tFL BL

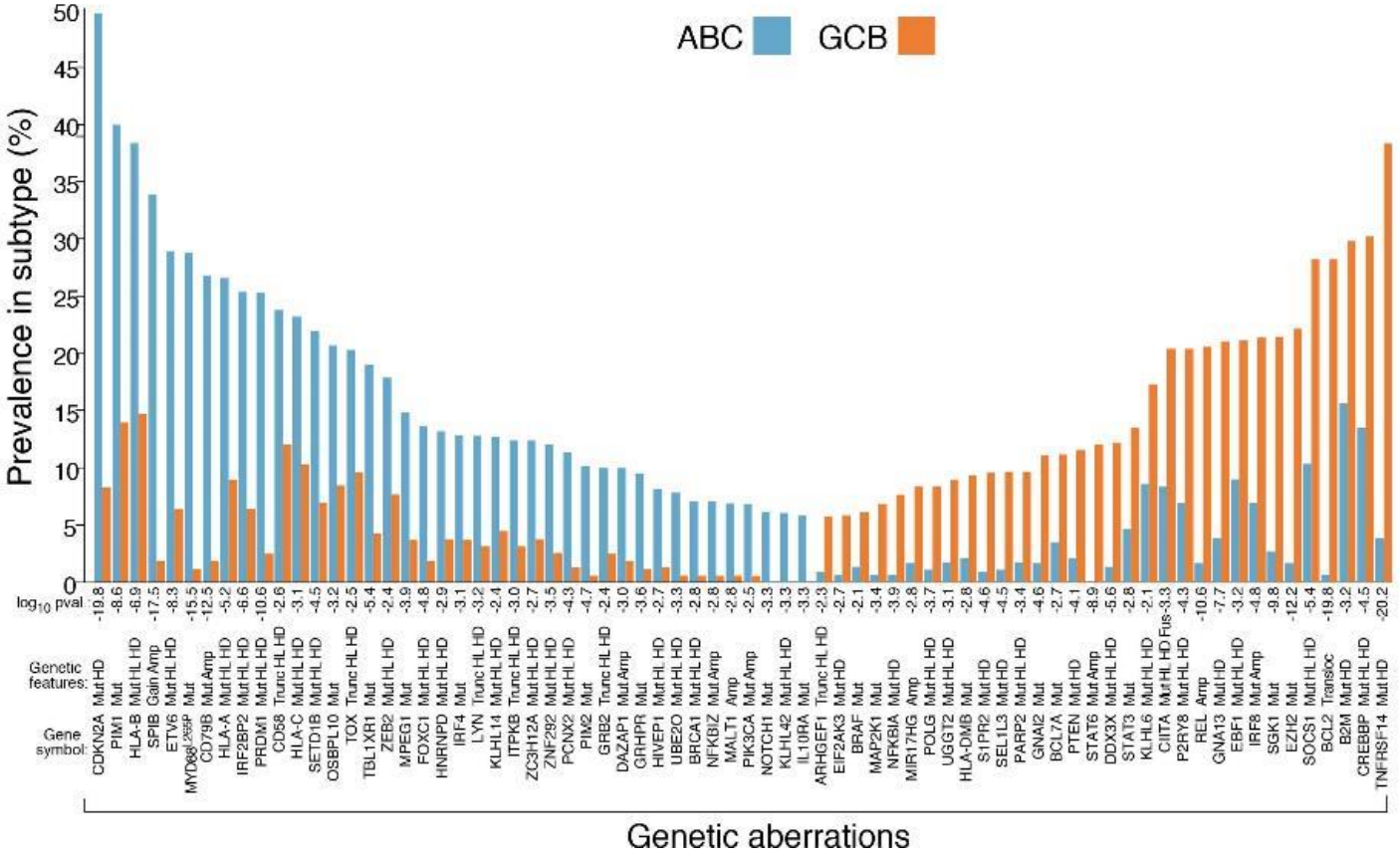
Genetic Subgroups of Diffuse Large B cell Lymphoma



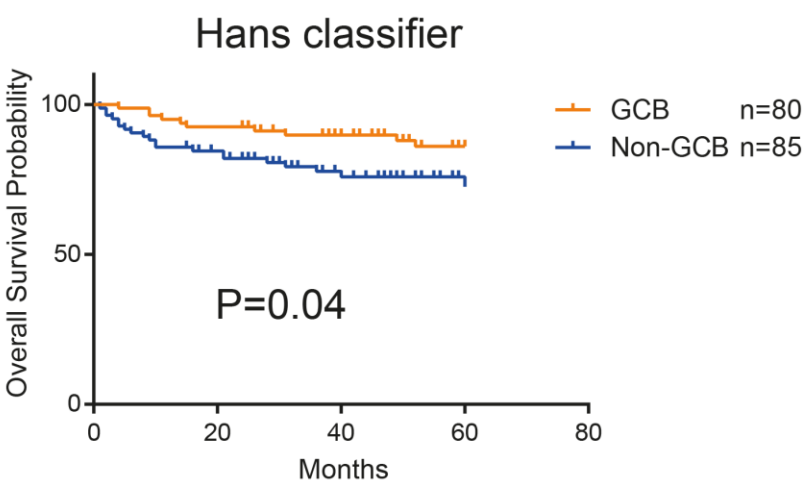
Genetic Subclassification in a “Real-World” Analysis

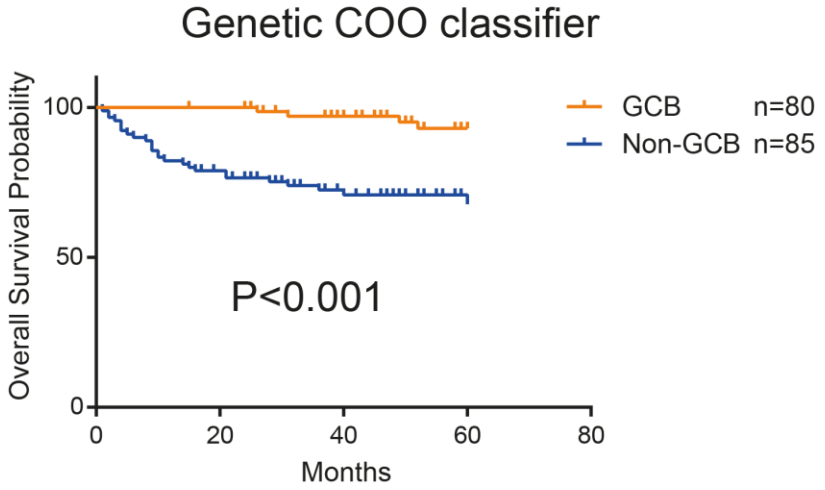


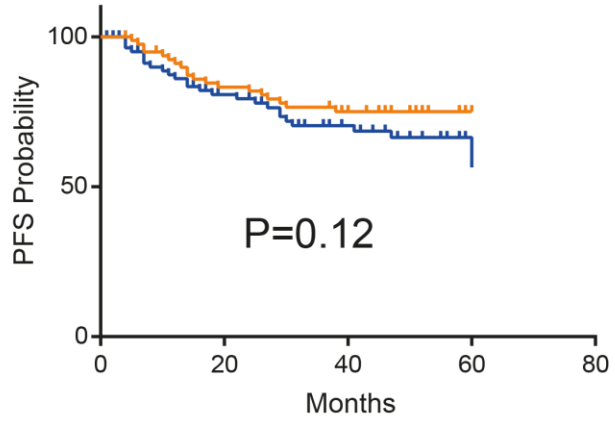
Cell of Origin Classification Using Mutation Profiling

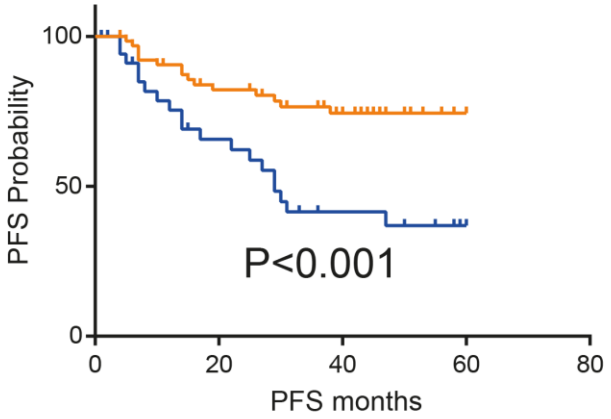


Cell of Origin Classification Using Mutation Profiling

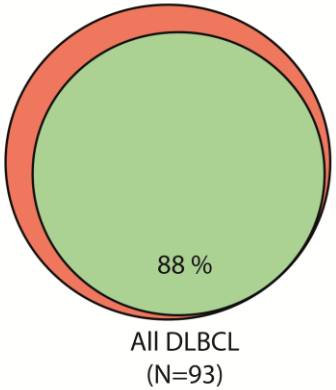


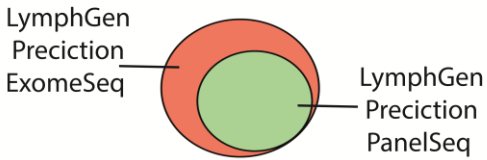




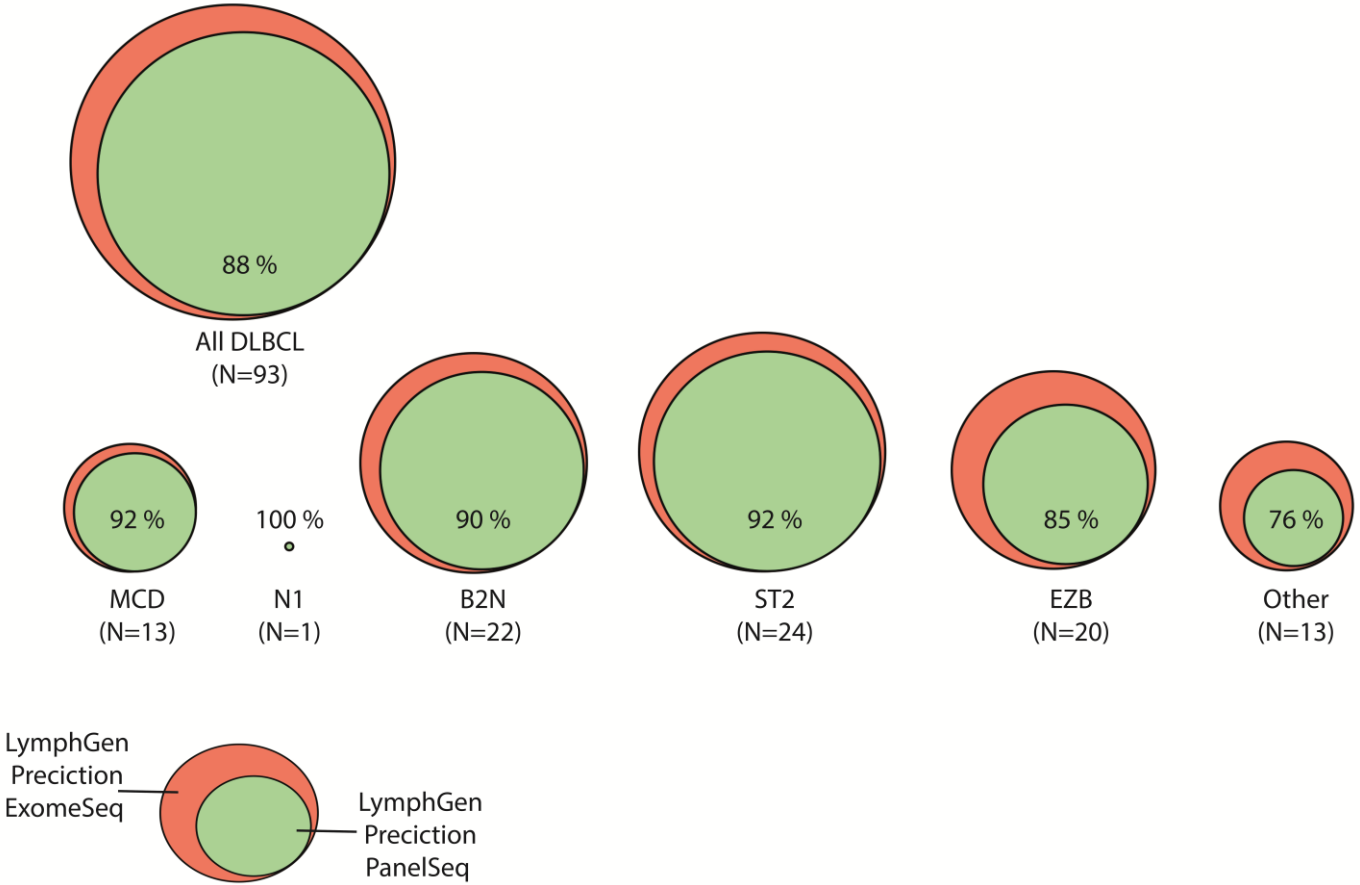


Genetic Subgroups using Whole Exome Seq and Panel Seq

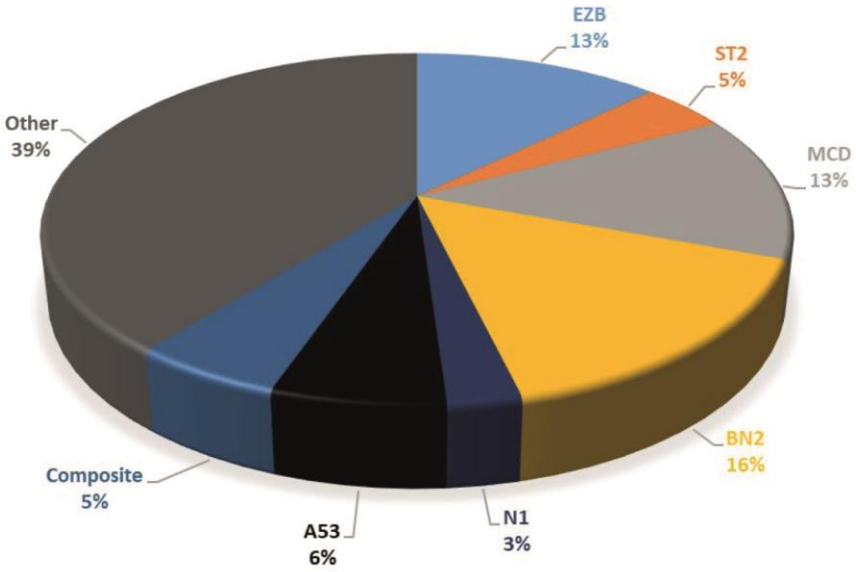




Genetic Subgroups using Whole Exome Seq and Panel Seq

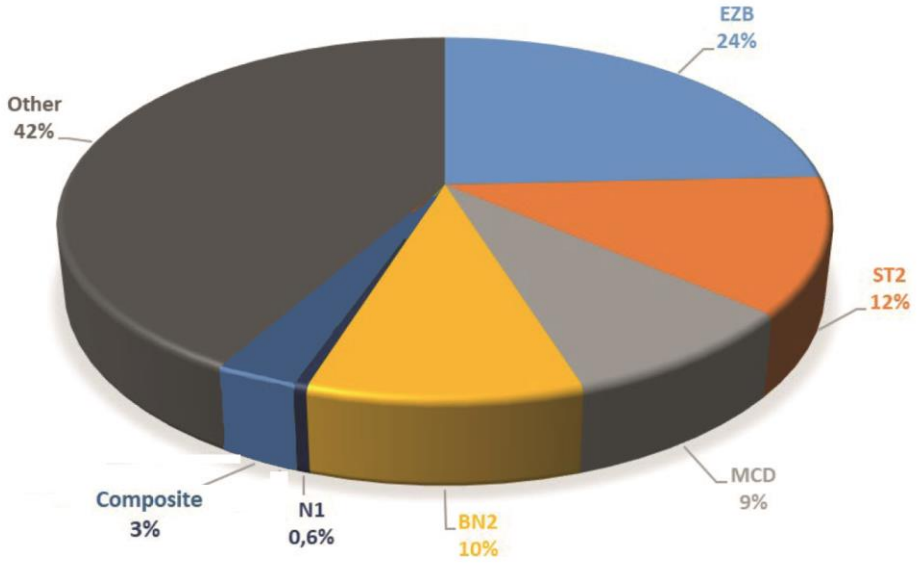


Similar Composition of DLBCL Cohorts



NCI cohort

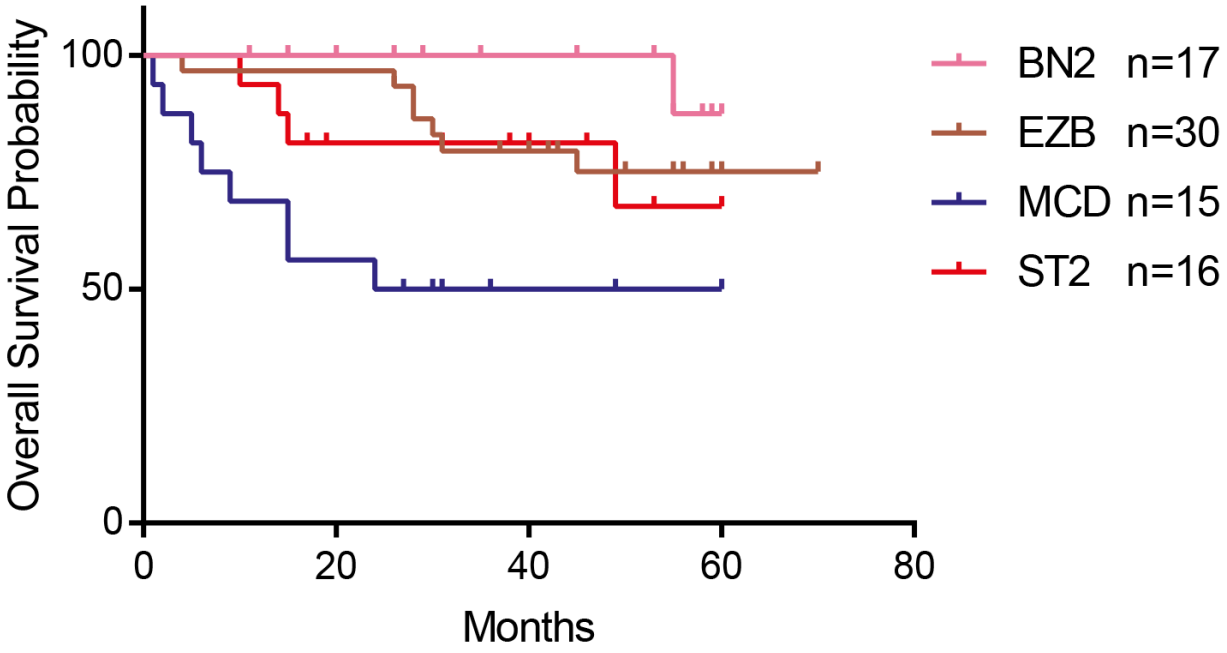
N=574



study cohort

N=206

DLBCL Genetic Subtype Predict Survival Following R-CHOP



Genetic Subgroups of Diffuse Large B cell Lymphoma

1. DLBCL is genetically very heterogeneous

2. Comprehensive, multi-platform genomic analysis reveals at least 6 genetic subtypes of DLBCL
3. DLBCL genetic subtypes reveal genetic relationships with other lymphoma types point towards an origin from occult indolent lymphomas
4. The response to R-CHOP therapy is influenced by the DLBCL genetic subtype distinction
5. Precision medicine approaches should take into account both the DLBCL genetic subtypes AND genetic aberrations in oncogenic pathways

Acknowledgements

National Cancer Institute

Da Wei Huang
George Wright
Calvin Johnson

Stefania Pittaluga
Lou Staudt

Members of the LLMPP Consortium

Alliance Cooperative Group
Nancy Bartlett
John Leonard
Andy Zelenetz

Department of Pathology
University of Giessen

Frederike Hagedorn
Hung Dang
Nicolai Fuhr

Andreas Bräuninger
Stefan Gattenlöhner

Hematology Department
University of Giessen

Tobias Arnold
Felix Schell

Mathias Rummel