

# Eppur si muove...

## La terapia nel MONDO LINFOMI

*Linfoma diffuso a grandi  
cellule B: ottimizzazione  
diagnostica*

*Stefano A. Pileri*



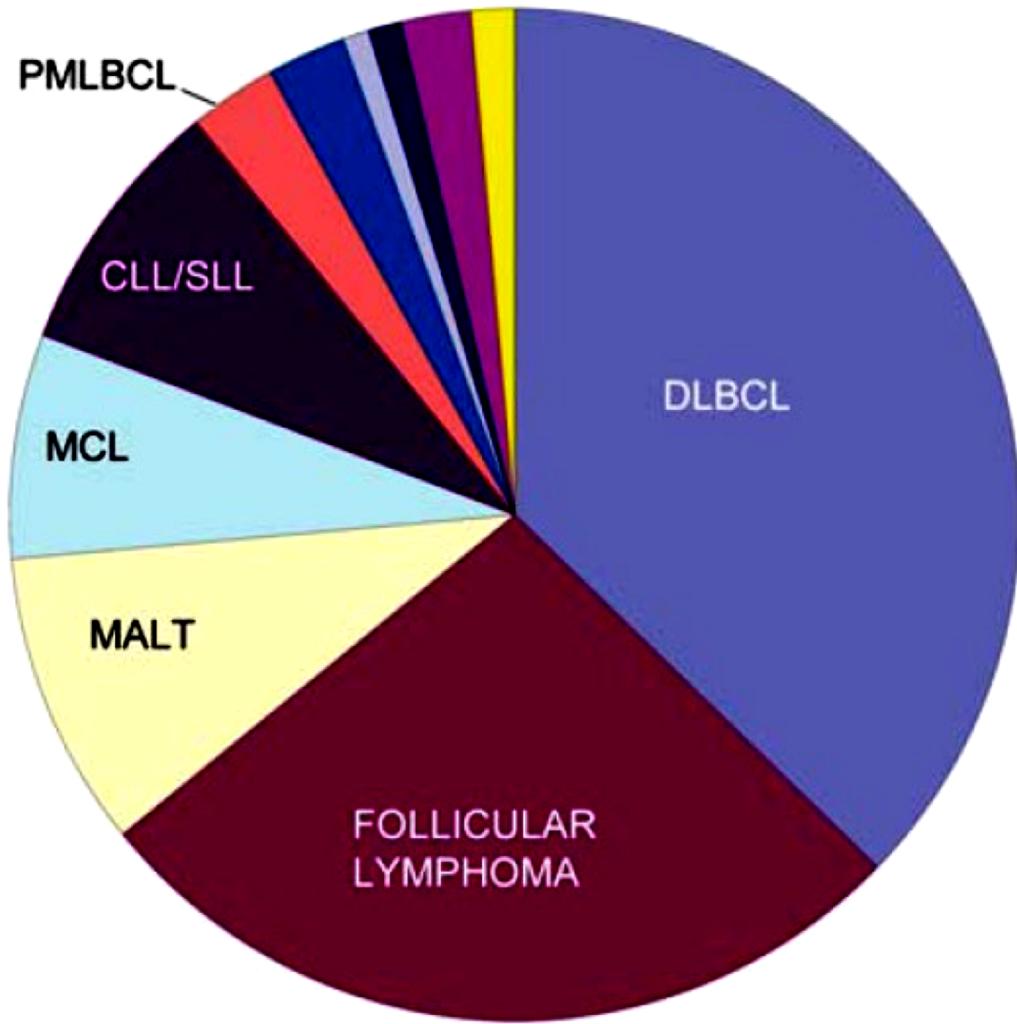
Istituto  
Europeo  
di Oncologia



MILANO, 4 APRILE 2022

## Disclosures of Stefano A. Pileri

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BeiGene						x	
Takeda						x	
Roche					x		
Diatech						x	



Diffuse large B-cell 37%

Follicular 29%

MALT lymphoma 9%

Mantle cell lymphoma 7%

CLL/SLL 12%

Primary med large B-cell 3%

High Grade B, NOS 2.5%

Burkitt 0.8%

Splenic marginal zone 0.9%

Nodal marginal zone 2%

Lymphoplasmacytic 1.4%

## Diffuse large B-cell lymphoma: variants, subgroups and subtypes/entities

### **Diffuse large B-cell lymphoma, not otherwise specified (NOS)**

Common morphologic variants

Centroblastic

Immunoblastic

Anaplastic

Other rare variants

Molecular subgroups

Germinal centre B-cell-like (GCB)

Activated B-cell-like (ABC)

### **Diffuse large B-cell lymphoma subtypes**

T-cell/histiocyte-rich large B-cell lymphoma

Primary DLBCL of the CNS

Primary cutaneous DLBCL, leg type

EBV-positive DLBCL, NOS

*Large B-cell lymphoma with IRF4 rearrangements\**

### **Other lymphomas of large B-cells**

Primary mediastinal (thymic) large B-cell lymphoma

Intravascular large B-cell lymphoma

DLBCL associated with chronic inflammation

Lymphomatoid granulomatosis

ALK-positive large B-cell lymphoma

Plasmablastic lymphoma

HHV-8-positive DLBCL, NOS

Primary effusion lymphoma

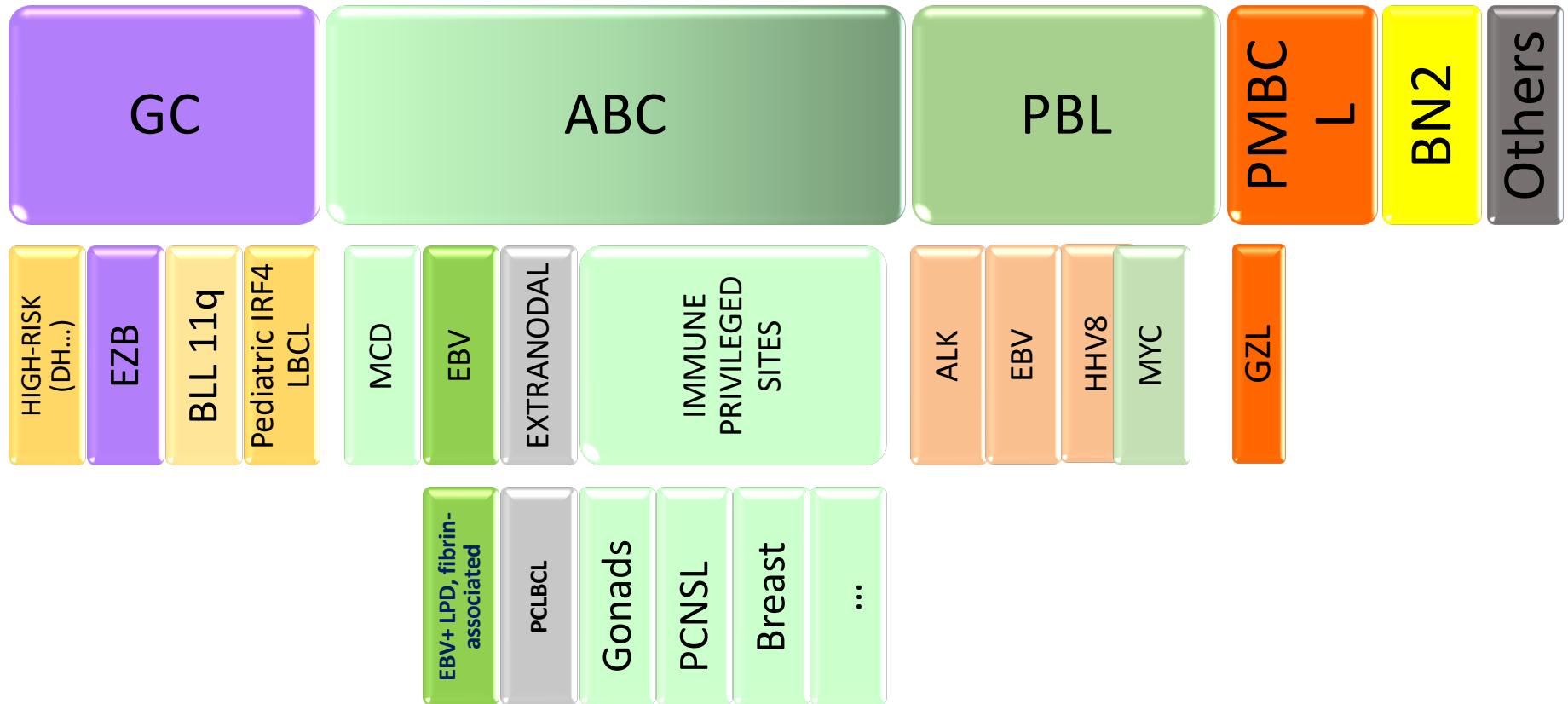
### **New provisional categories**

High grade B-cell lymphoma

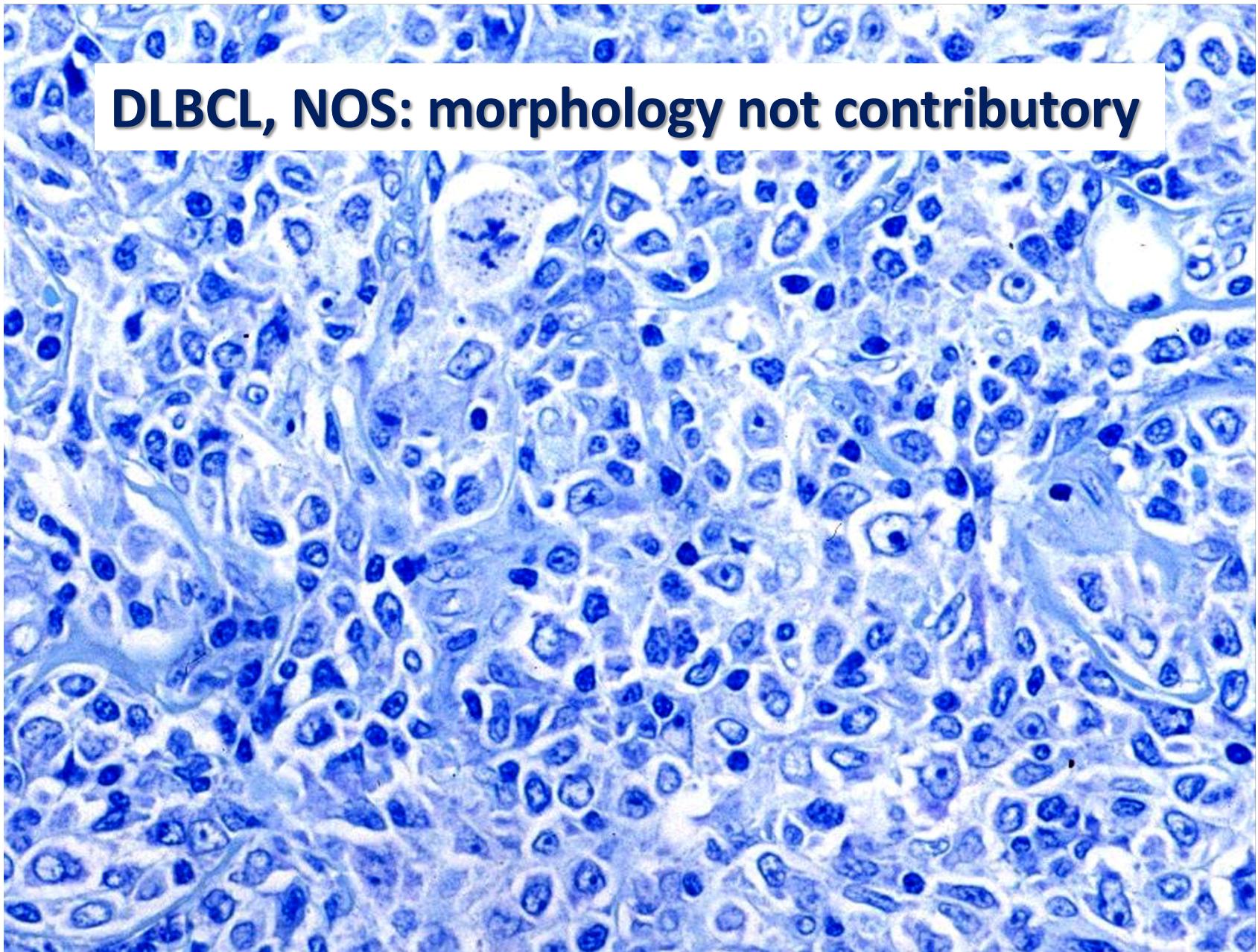
High grade B-cell lymphoma, with *BCL2* and/or *BCL6* and *MYC* rearrangements

High grade B-cell lymphoma, NOS

## Large B-Cell Lymphoma



**DLBCL, NOS: morphology not contributory**

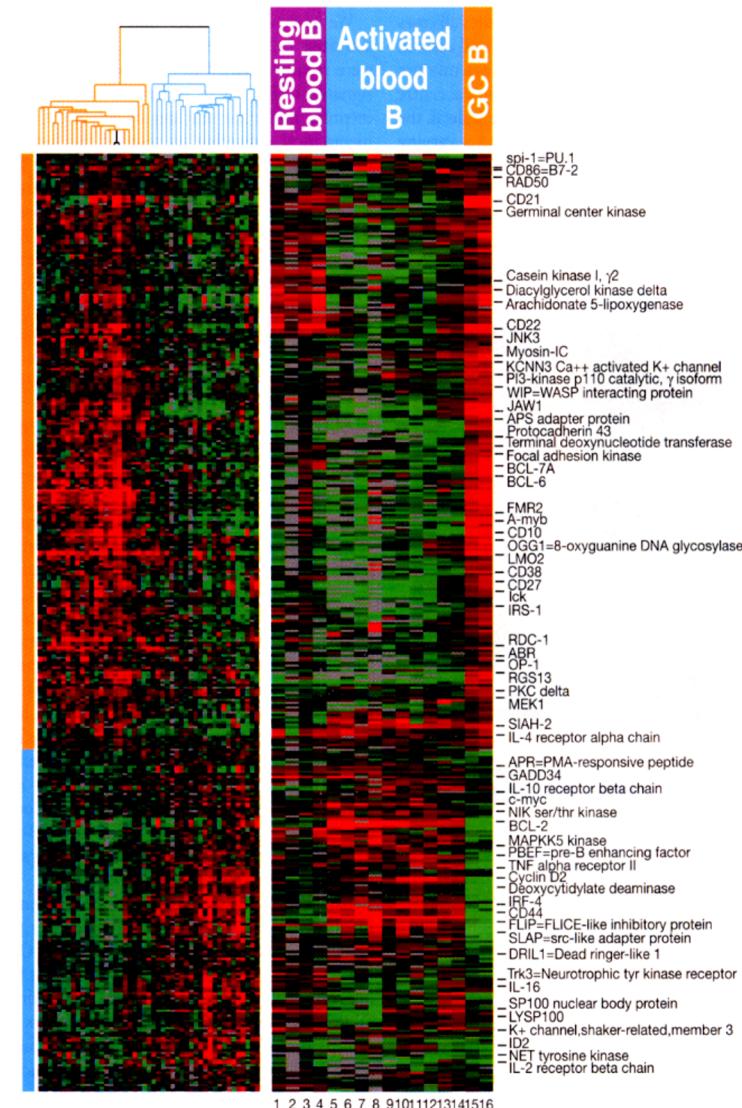
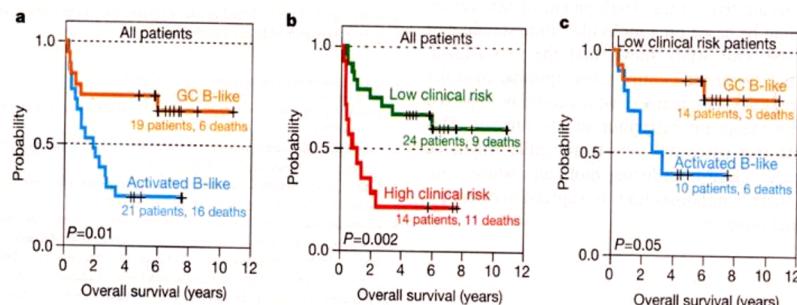


# Front-MIND

# Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling

Alizadeh AA et al.

Nature 2000, 403: 503-11



**Original limitation:  
need for fresh or frozen tissue, available  
in only a few patients!**

**Ideally, tool to apply to FFPE samples!**

# Gene-expression profiling and not immunophenotypic algorithms predicts prognosis in patients with diffuse large B-cell lymphoma treated with immunochemotherapy

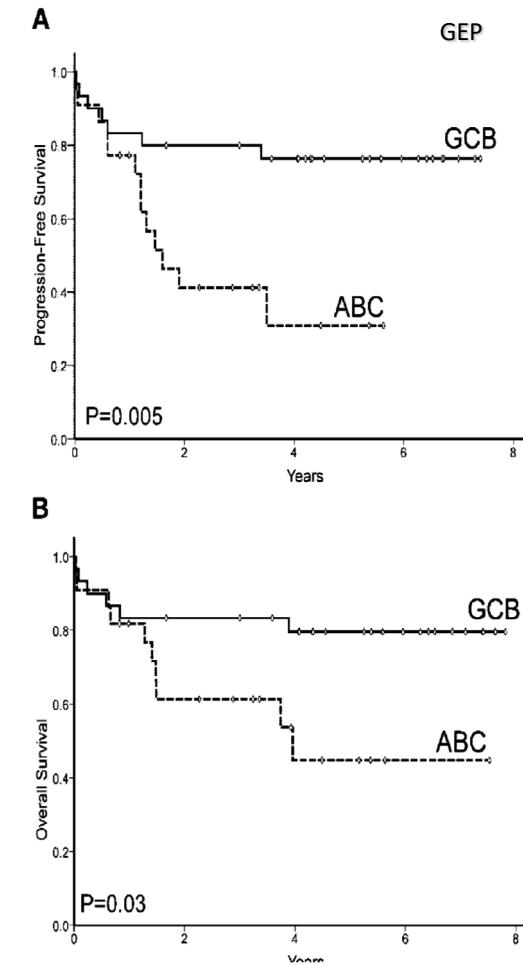
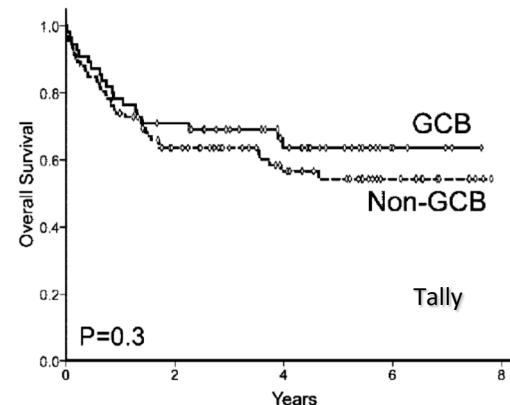
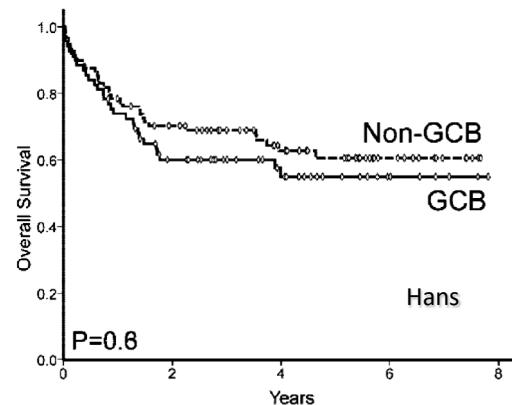
\*Gonzalo Gutiérrez-García,<sup>1</sup> \*Teresa Cardesa-Salzmann,<sup>1</sup> Fina Climent,<sup>2</sup> Eva González-Barca,<sup>2</sup> Santiago Mercadal,<sup>2</sup> José L. Mate,<sup>3</sup> Juan M. Sancho,<sup>3</sup> Leonor Arenillas,<sup>4</sup> Sergi Serrano,<sup>4</sup> Lourdes Escoda,<sup>5</sup> Salomé Martínez,<sup>5</sup> Alexandra Valera,<sup>1</sup> Antonio Martínez,<sup>1</sup> Pedro Jares,<sup>1</sup> Magdalena Pinyol,<sup>1</sup> Adriana García-Herrera,<sup>1</sup> Alejandra Martínez-Trillos,<sup>1</sup> Eva Giné,<sup>1</sup> Neus Villamor,<sup>1</sup> Elías Campo,<sup>1</sup> Luis Colomo,<sup>1</sup> and Armando López-Guillermo,<sup>1</sup> for the Grup per l'Estudi dels Limfomes de Catalunya i Balears (GELCAB)

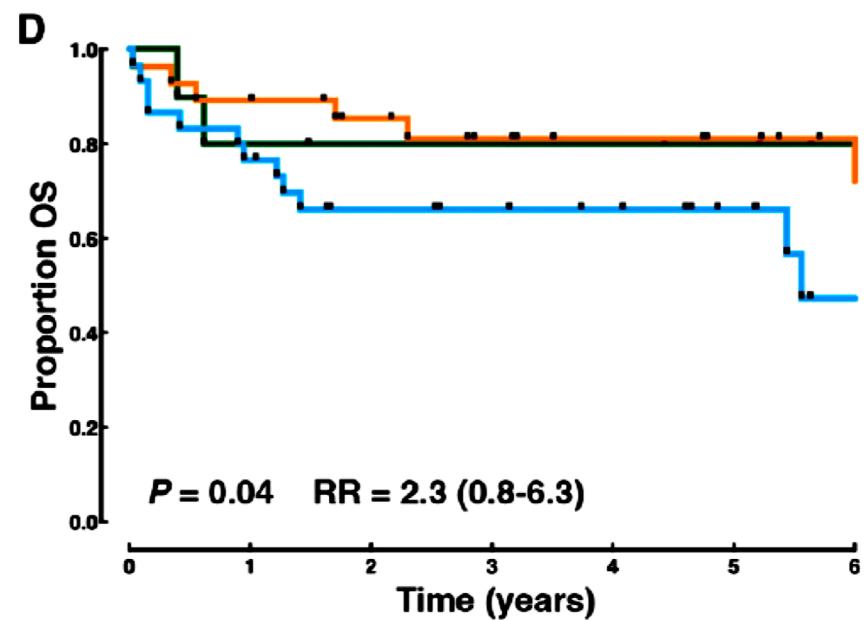
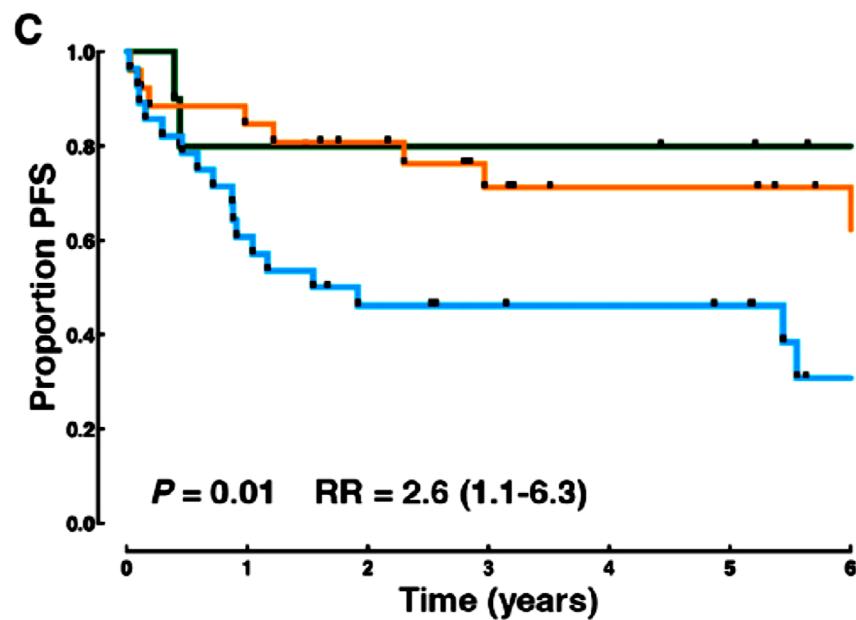
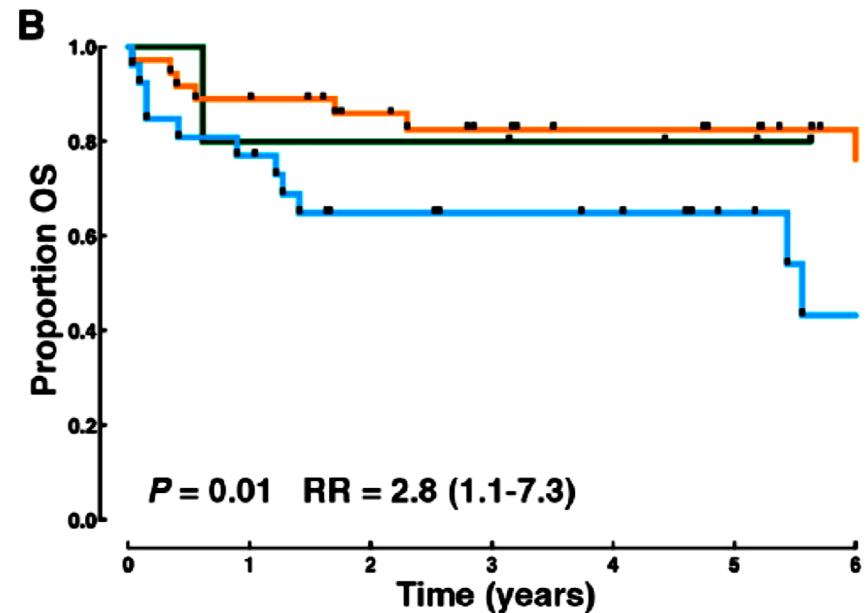
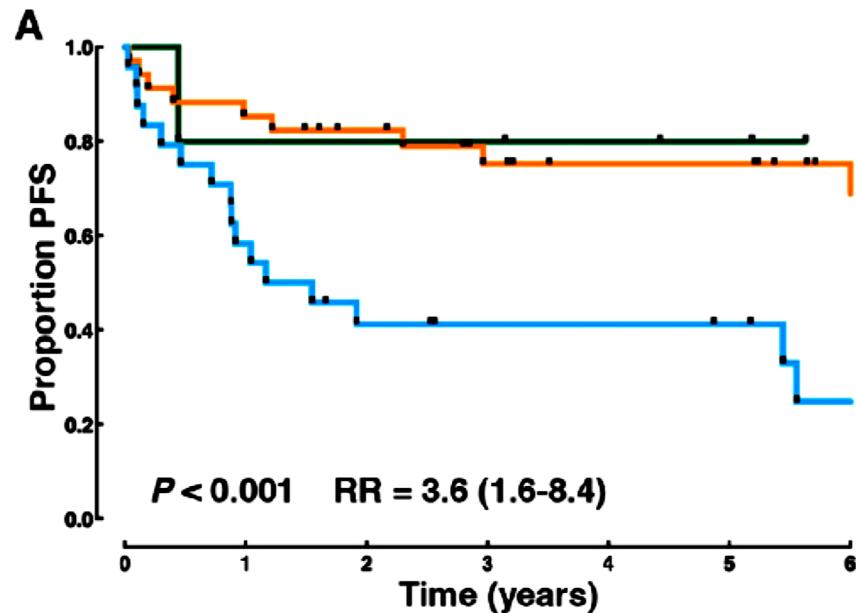
<sup>1</sup>Departments of Hematology and Pathology, Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; <sup>2</sup>Hospital Duran i Reynals, Hospital de Llobregat, Spain; <sup>3</sup>Hospital Germans Trias i Pujol, Badalona, Spain; <sup>4</sup>Hospital del Mar, Barcelona, Spain; and <sup>5</sup>Hospital Joan XXIII, Tarragona, Spain

Diffuse large B-cell lymphomas (DLBCLs) can be divided into germinal-center B cell-like (GCB) and activated-B cell-like (ABC) subtypes by gene-expression profiling (GEP), with the latter showing a poorer outcome. Although this classification can be mimicked by different immunostaining algorithms, their reliability is the object of controversy. We constructed tissue microarrays with samples of 157 DLBCL patients homogeneously treated with immunochemotherapy to apply the following algorithms:

Colomo (MUM1/IRF4, CD10, and BCL6 antigens), Hans (CD10, BCL6, and MUM1/IRF4), Muris (CD10 and MUM1/IRF4 plus BCL2), Choi (GCET1, MUM1/IRF4, CD10, FOXP1, and BCL6), and Tally (CD10, GCET1, MUM1/IRF4, FOXP1, and LMO2). GEP information was available in 62 cases. The proportion of misclassified cases by immunohistochemistry compared with GEP was higher when defining the GCB subset: 41%, 48%, 30%, 60%, and 40% for Colomo, Hans, Muris, Choi,

and Tally, respectively. Whereas the GEP groups showed significantly different 5-year progression-free survival (76% vs 31% for GCB and activated DLBCL) and overall survival (80% vs 45%), none of the immunostaining algorithms was able to retain the prognostic impact of the groups (GCB vs non-GCB). In conclusion, stratification based on immunostaining algorithms should be used with caution in guiding therapy, even in clinical trials. (*Blood*. 2011;117(18):4836-4843)





■ Germinal-Center B-cell-like DLBCL

■ Unclassified DLBCL

■ Activated B-cell-like DLBCL



## Targeted Digital Gene Expression Profiling

RefSeq NCBI	Gene	Length NCBI	Protein aa
NM_002467.4	MYC	2379	454
NM_000633.2	BCL2	6492	239
NM_012452.2	TNFRSF13B	1377	293
NM_014240.2	LIMD1	6284	676
NM_001195286.1	IRF4	5329	451*
NM_194071.3	CREB3L2	7471	520*
NM_006875.3	PIM2	2234	311
NM_001302826.1	CYB5R	1713	276
NM_003929.2	RAB7L1	3324	203
NM_174908.3	CCDC50	8421	306
NM_015361.3	R3HDM1	4722	1099
NM_017706.4	WDR55	2580	383
NM_020701.3	ISY1	3778	285
NM_014607.3	UBXN4	4018	508
NM_030961.2	TRIM56	4723	755
NM_000902.3	MME	5643	750
NM_001284275.1	SERPINA9	1661	435*
NM_024701.3	ASB13	2736	278
NM_018717.4	MAML3	7086	1138
NM_002221.3	ITPKB	6162	946
NM_001080416.3	MYBL1	5192	752
NM_004230.3	S1PR2	3589	353
NM_020529.2	NFKBIA	1579	371
NM_139276.2	STAT3	4978	770
NM_000314.6	PTEN	8718	403*
NM_006218.2	PKI3CA	3724	1068

26-gene-panel for  
COO & key-genes  
Haematologica, 2020

50-gene-panel for  
microenvironment  
Ann Oncol, 2018

MF-related genes

DC-related genes

CD4+ T cell-related genes

ACTA2	Actin, alpha 2, smooth muscle
AEBP1	AE binding protein 1
BGN	Biglycan
COL1A1	Collagen type I alpha 1
COL1A2	Collagen type I alpha 2
COL3A1	Collagen type III alpha 1
COL4A1	Collagen type IV alpha 1
COL5A2	Collagen type V alpha 2
COL6A3	Collagen type VI alpha 3
CTHRC1	Collagen triple helix repeat containing 1
CTSK	Cathepsin K
EGR1	Early growth response 1
FN1	Fibronectin 1
FSTL1	Follistatin like 1
GPNMB	Glycoprotein nmb
LAMB1	Laminin subunit beta 1
LUM	Lumican
MFAP2	Microfibrillar associated protein 2
MMMP2	Matrix metalloproteinase 2
MRC2	Mannose receptor, C type 2
MXIRAS5	Matrix-Remodelling Associated 5
PCOLCE	Procollagen C-endopeptidase enhancer
PLOD2	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2
POSTN	Periostin, osteoblast specific factor
SPARC	Secreted protein acidic and cysteine rich
SULF1	Sulfatase 1
TGFB1	Transforming growth factor beta induced
ALCAM	Activated leukocyte cell adhesion molecule
AMICA1	Adhesion molecule, interacts with CXADR antigen 1
CD300LF	CD300 molecule-like family member F
COL4A2	Collagen, type IV, alpha 2
IGSF6	Immunoglobulin superfamily, member 6
MDFIC	MyoD Family Inhibitor Domain Containing
P2RY14	Purinergic receptor P2Y, G-protein coupled, 14
SLC29A3	Solute carrier family 29 (nucleoside transporters), member 3;
SLC2A3	Solute carrier family 2 (facilitated glucose transporter), member 3
CTSZ	Cathepsin Z
HS3ST3A1	Heparan Sulfate-Glucosamine 3-Sulfotransferase 3A1
PMPCB	Peptidase, Mitochondrial Processing Beta Subunit
RAB27A	RAB27A, Member RAS Oncogene Family
SMAD1	SMAD Family Member 1

STROMAL GENES

IMMUNE GENES

# **A 3-gene signature based on MYC, BCL-2 and NFKBIA improves risk stratification in diffuse large B-cell lymphoma**

by Enrico Derenzini, Saveria Mazzara, Federica Melle, Giovanna Motta, Marco Fabbri, Riccardo Bruna, Claudio Agostinelli, Alessandra Cesano, Chiara Antonia Corsini, Ning Chen, Simona Righi, Elena Sabattini, Annalisa Chiappella, Angelica Calleri, Stefano Fiori, Valentina Tabanelli, Antonello Cabras, Giancarlo Pruneri, Umberto Vitolo, Alessandro Massimo Gianni, Alessandro Rambaldi, Paolo Corradini, Pier Luigi Zinzani, Corrado Tarella, and Stefano Pileri

Haematologica 2020 [Epub ahead of print]

224 DLBCL patients  
FFPE specimens

DLCL04 (n = 130)  
R-HDS (n = 94)

NanoString  
insufficient mRNA n = 17

207 DLBCL patients

IHC  
non-NOS n = 21

186 DLBCL patients

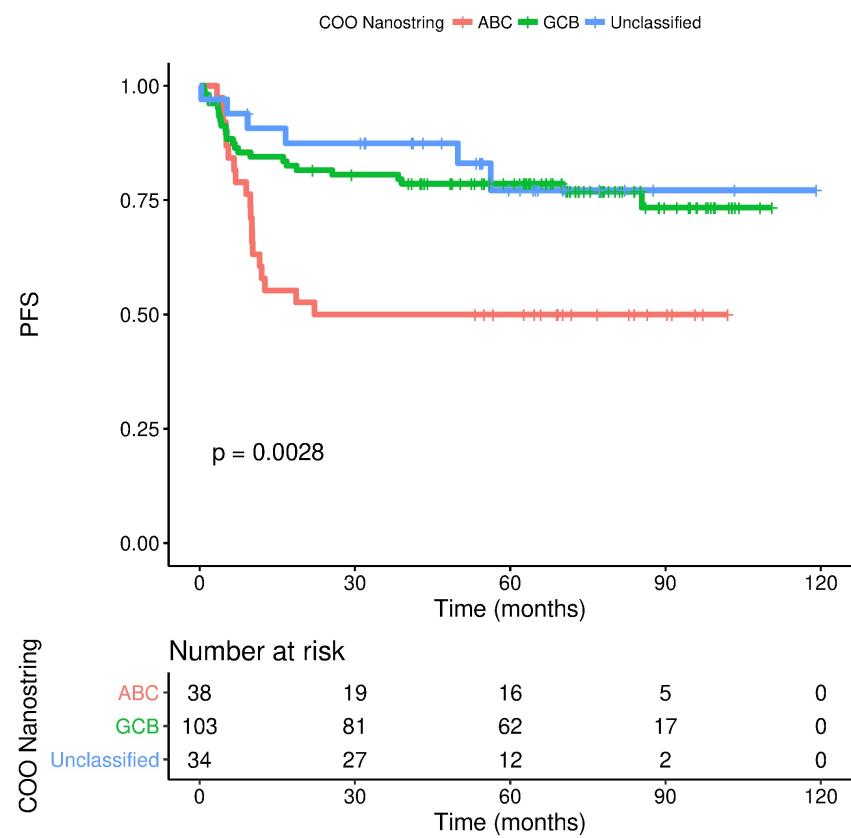
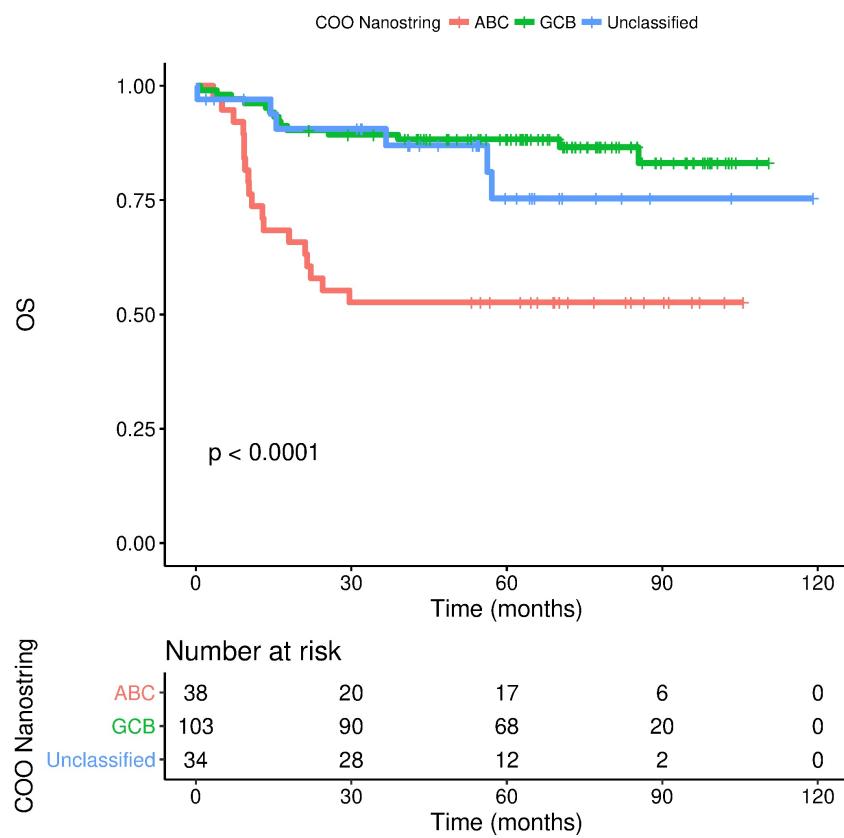
DLCL04 (n = 99)  
R-HDS (n = 87)

**In both trials, only patients staged III-IV were enrolled, all treated with R-CHOP or R-CHOP-like therapies followed or not by Auto-SCT.**

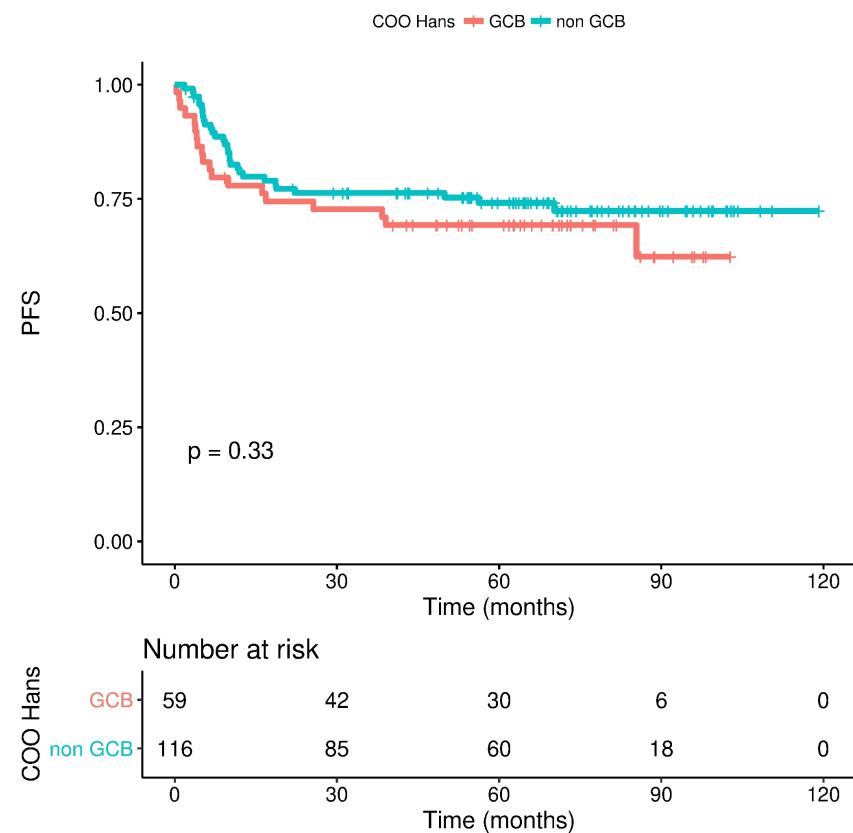
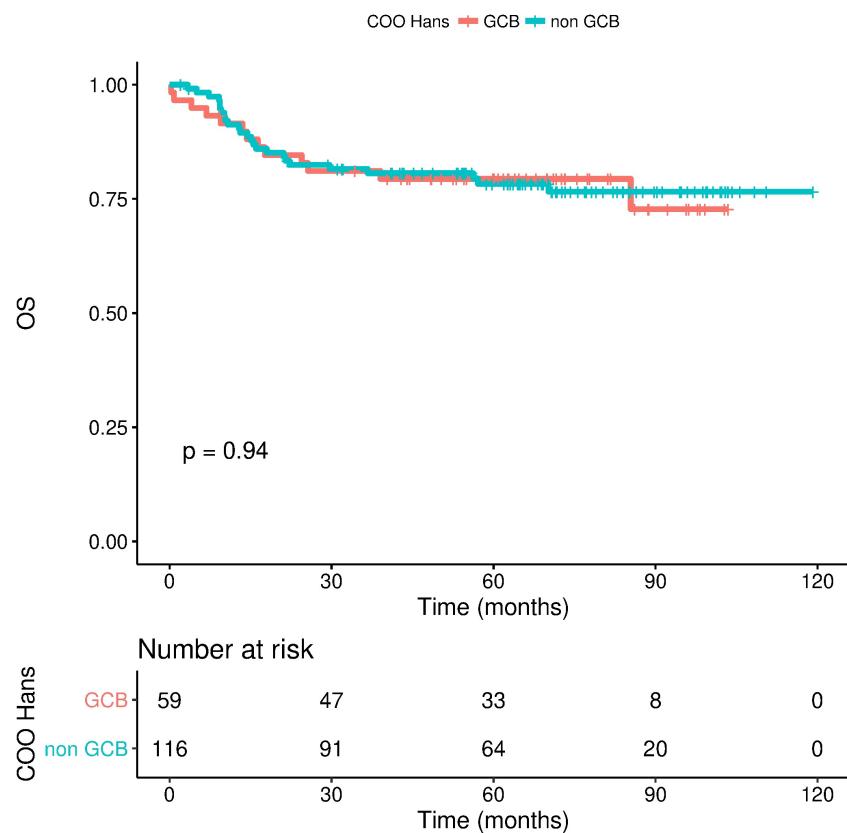
**The mean age was 52 yr.s (18 – 65)**

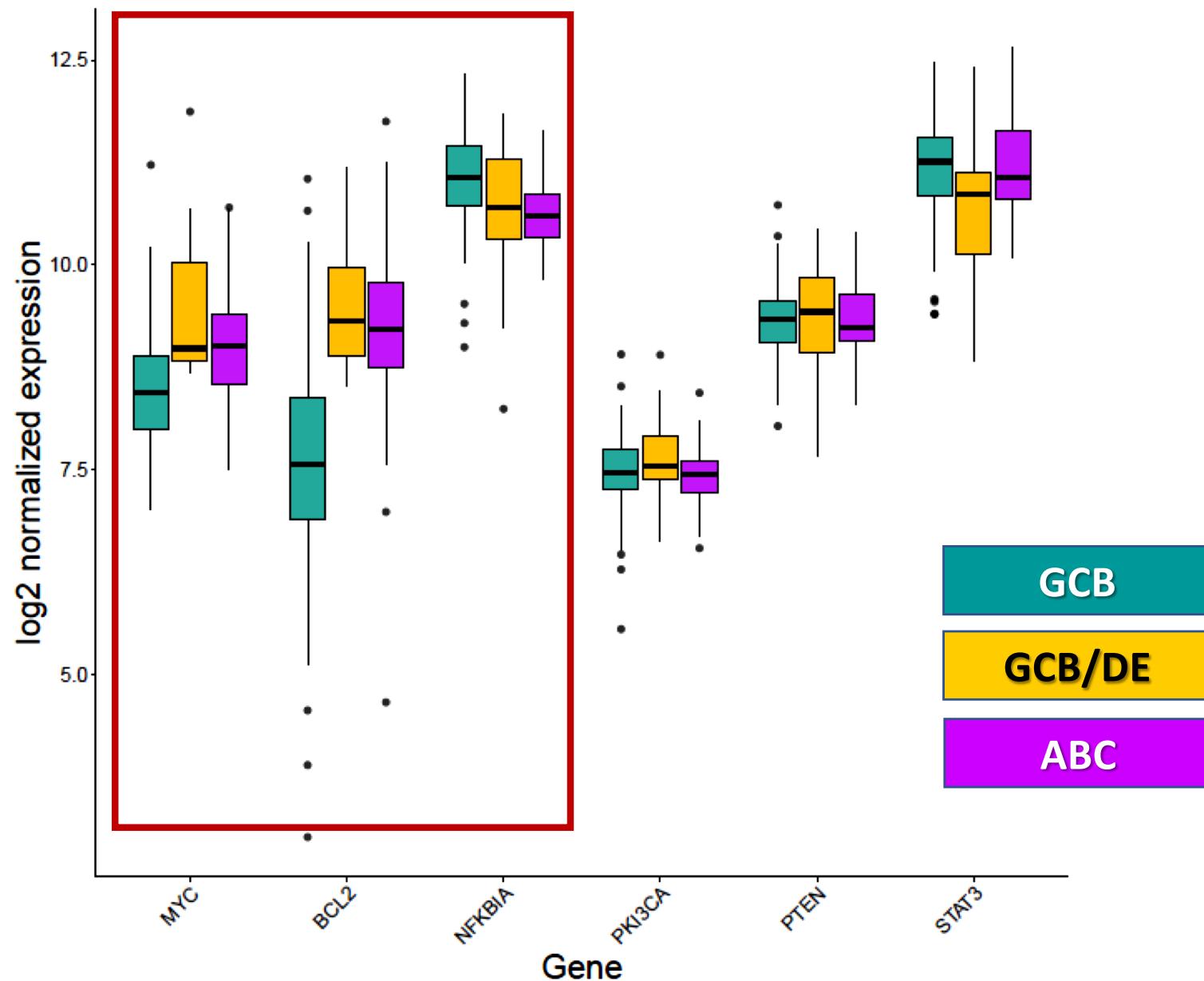
**All the cases were studied by immunohistochemistry, targeted GEP and FISH (*BCL2*, *MYC* and *BCL6*).**

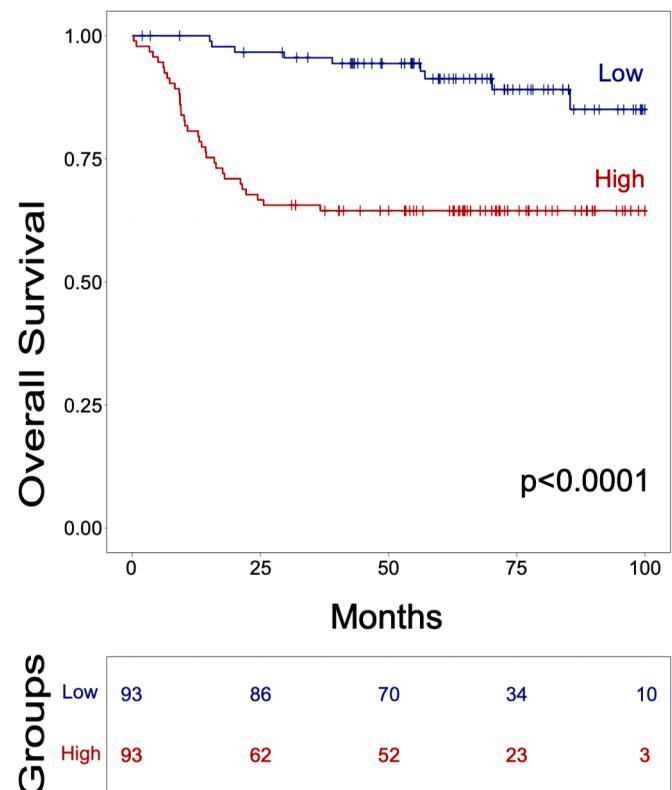
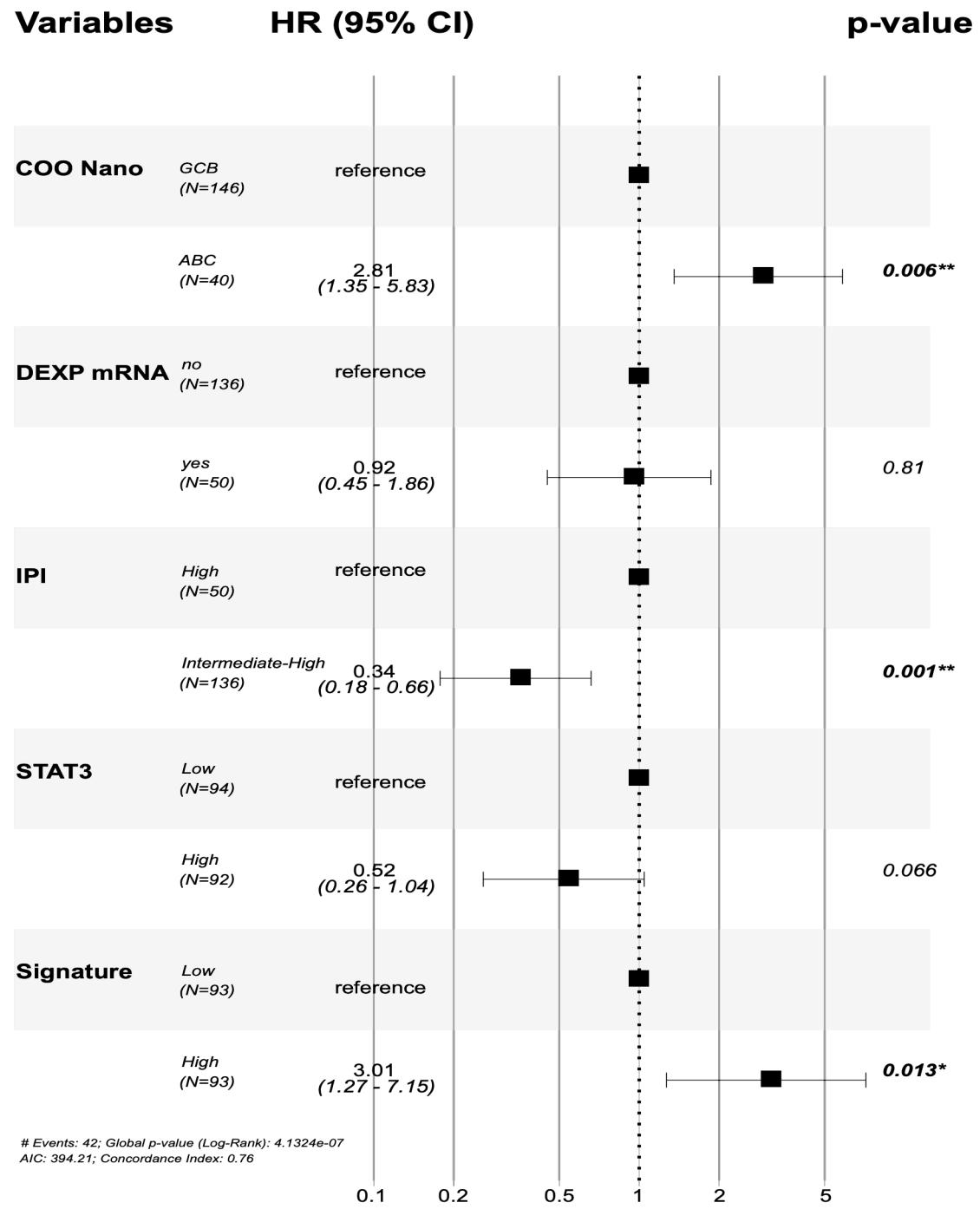
# COO according to targeted GEP

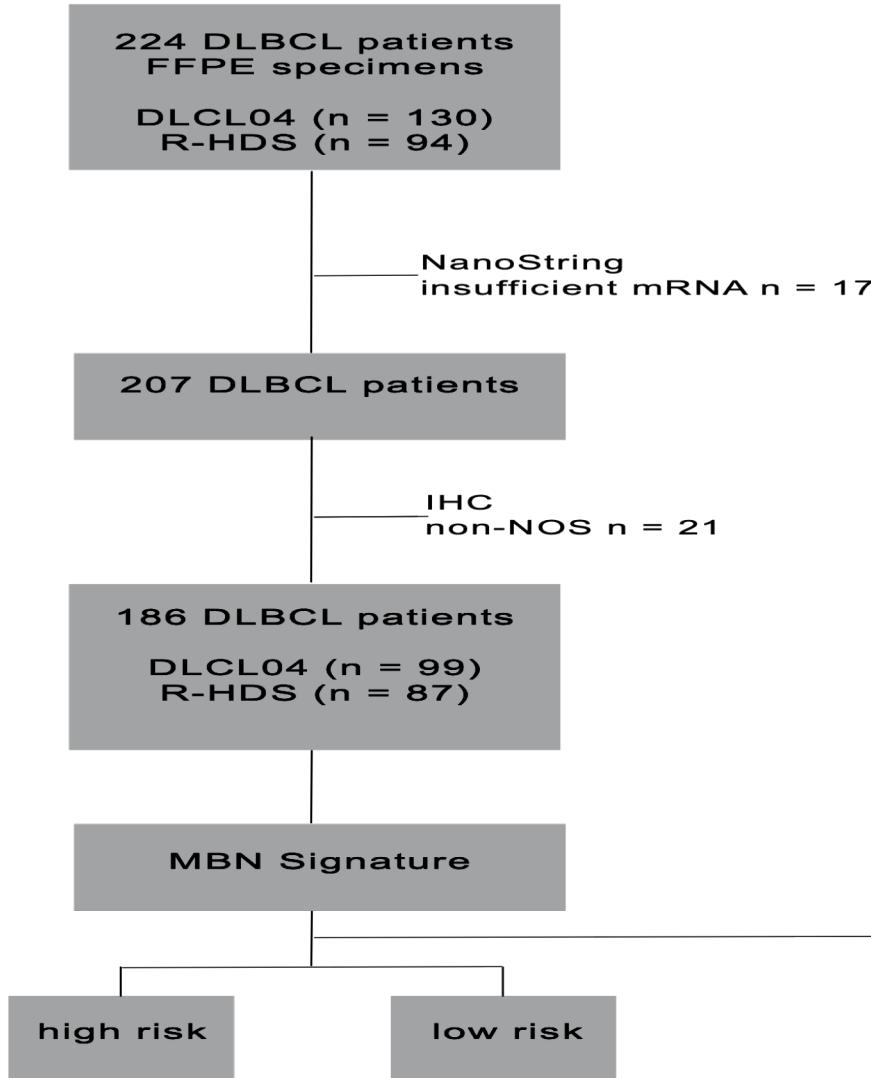


# COO according to Hans' classifier





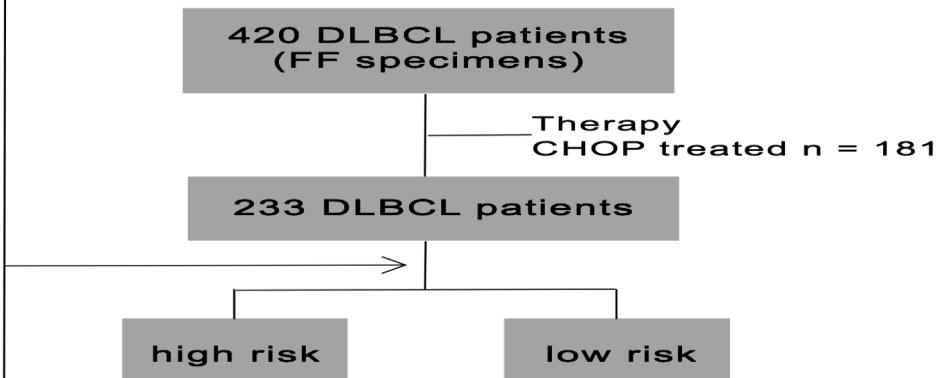




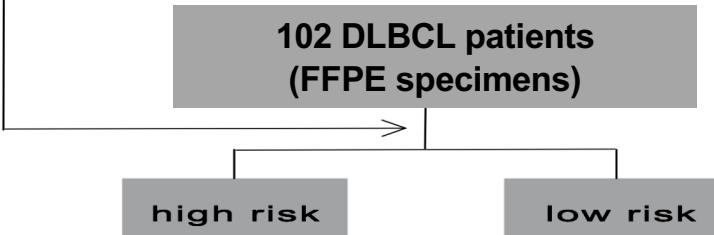
## Molecular High-Grade B-Cell Lymphoma: Defining a Poor-Risk Group That Requires Different Approaches to Therapy

Chulin Sha, PhD<sup>1</sup>; Sharon Barrans, PhD<sup>2</sup>; Francesco Cucco, PhD<sup>3</sup>; Michael A. Bentley, DPhil<sup>1</sup>; Matthew A. Care, PhD<sup>1</sup>; Thomas Cummin, MD<sup>4</sup>; Hannah Kennedy, PhD<sup>3</sup>; Joe S. Thompson, MPhil<sup>3</sup>; Rahman Uddin, MSc<sup>1</sup>; Lisa Worrillor, PhD<sup>2</sup>; Rebecca Chalkley, MPhil<sup>2</sup>; Moniek van Hoppe, MSc<sup>2</sup>; Sophia Ahmed, PhD<sup>1</sup>; Tom Maishman, PhD<sup>4</sup>; Josh Caddy, BSc<sup>4</sup>; Anna Schuh, MD<sup>5</sup>; Christoph Mamot, MD<sup>6</sup>; Catherine Burton, MD<sup>2</sup>; Reuben Tooze, PhD<sup>1</sup>; Andrew Davies, PhD<sup>4</sup>; Ming-Qing Du, PhD<sup>3</sup>; Peter W.M. Johnson, MD<sup>4</sup>; and David R. Westhead, DPhil<sup>1</sup>

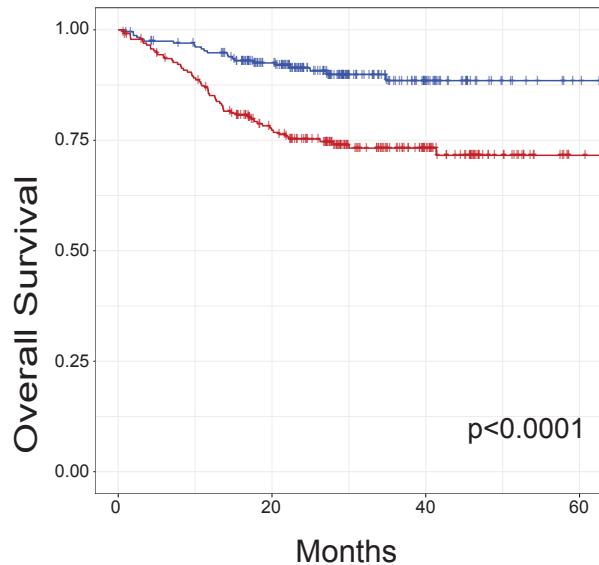
### Validation Cohort (Lenz et al)



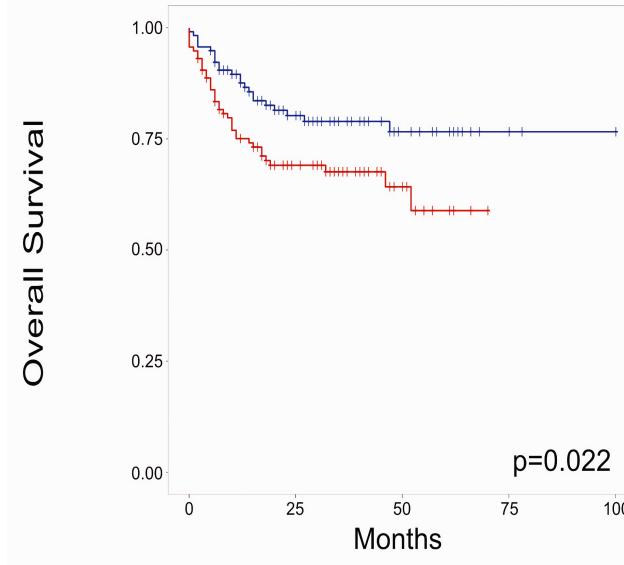
### Validation Cohort (Real-life patients)



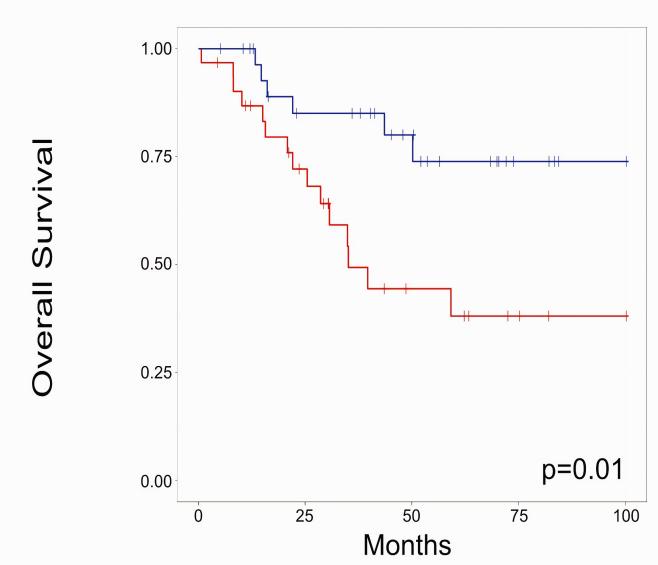
## Sha's



## Lenz's

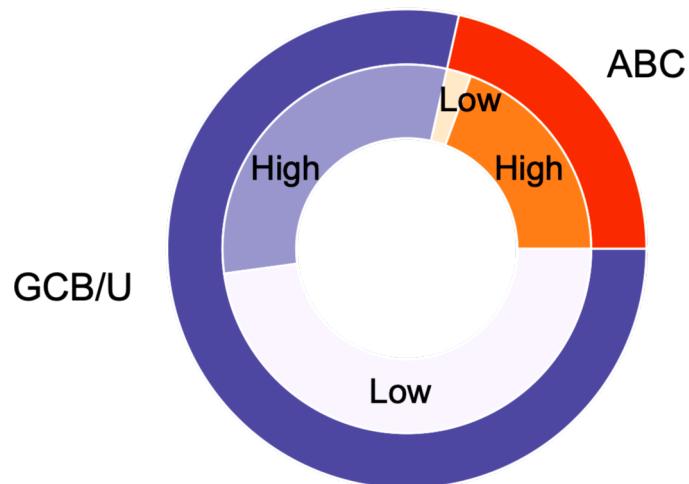


## Real-life

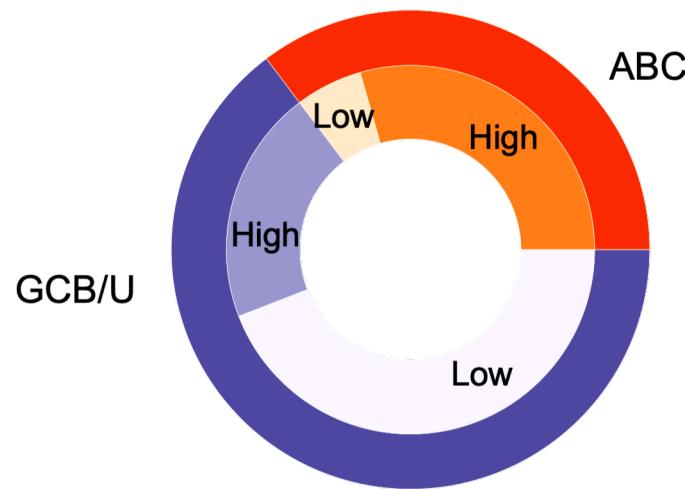


# R-CHOP

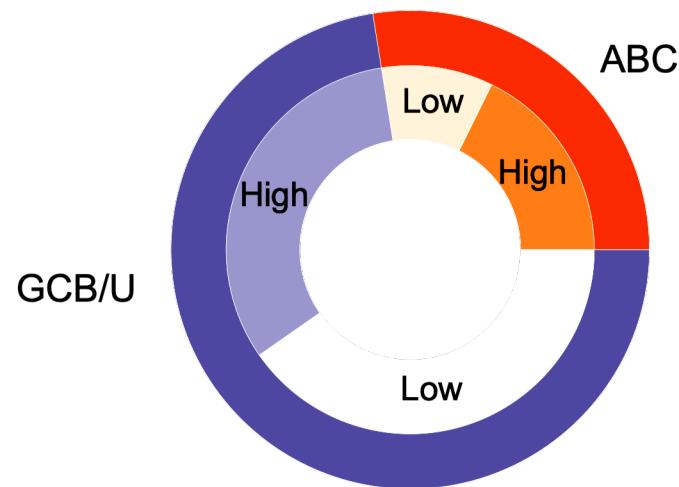
TRIALS n = 186

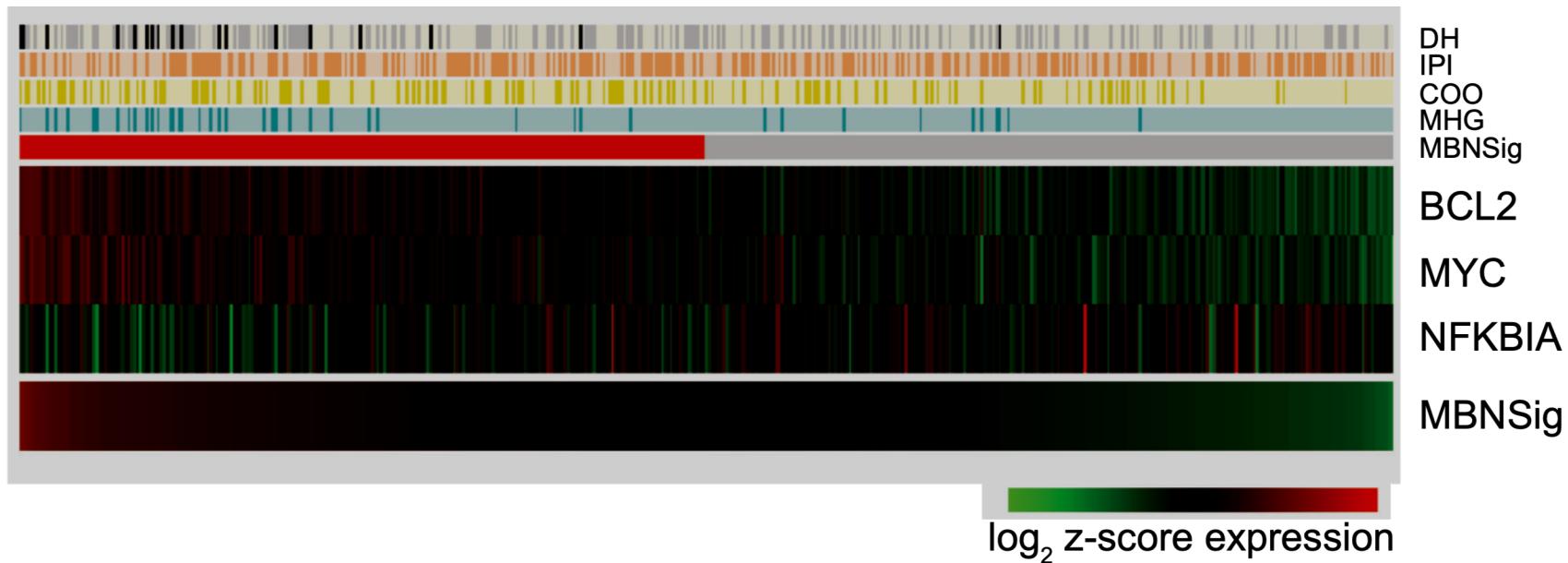


REAL-LIFE n = 102



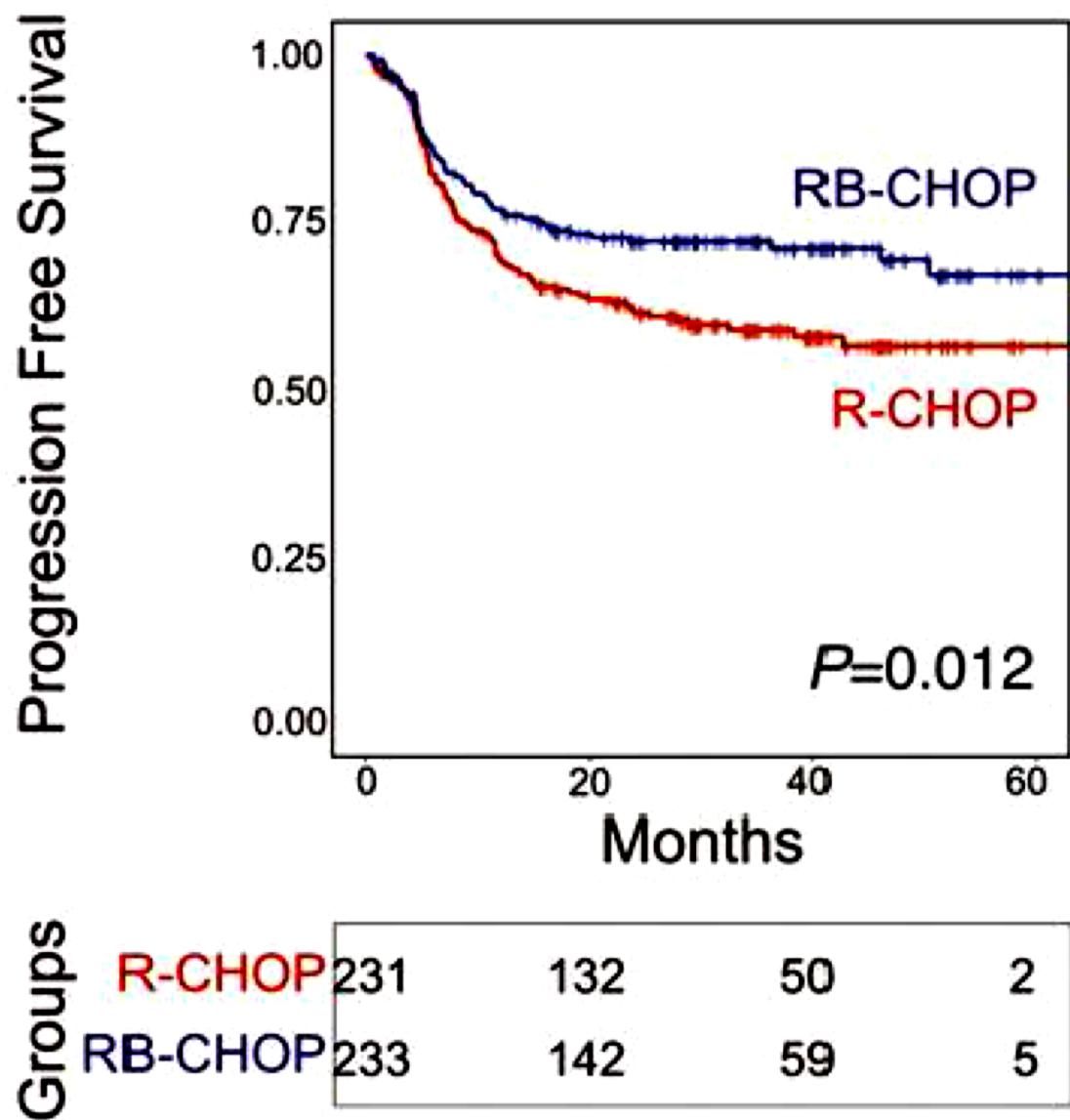
SHA COHORT n = 469





MBNSig	■ Positive	■ Negative	
MHG	■ MHG	■ Not MHG	
COO	■ ABC	■ Not ABC	
IPI	■ High	■ Low	
DH	■ Positive	■ Negative	■ NA

## Patients from Sha's series with high MBN



# **Conclusions**

- The MBN signature does implement the cell of origin (COO) determination.
- A higher risk group (enriched in genetic aberrations) can be identified among GCB/U and ABC DLBCLs.
- Potential therapeutic implications.
- Applicable to all patients at low cost!!!

# *The* NEW ENGLAND JOURNAL *of* MEDICINE

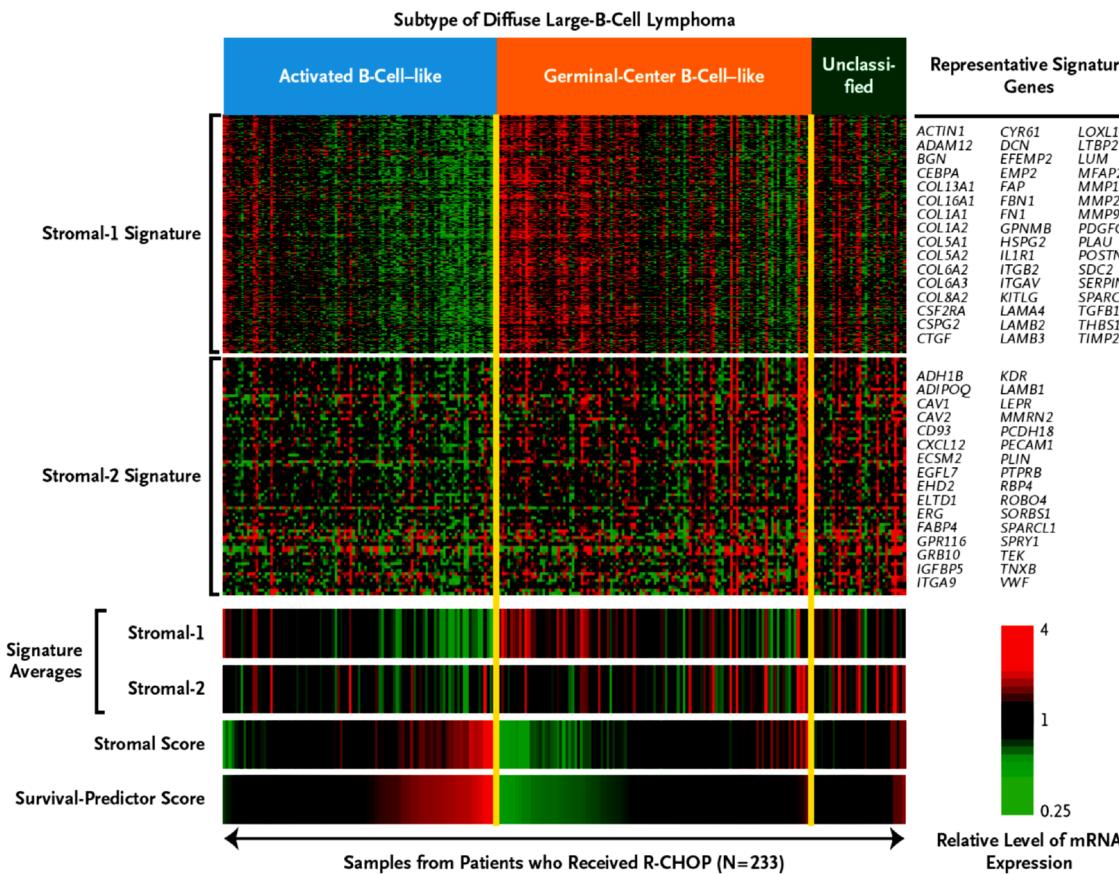
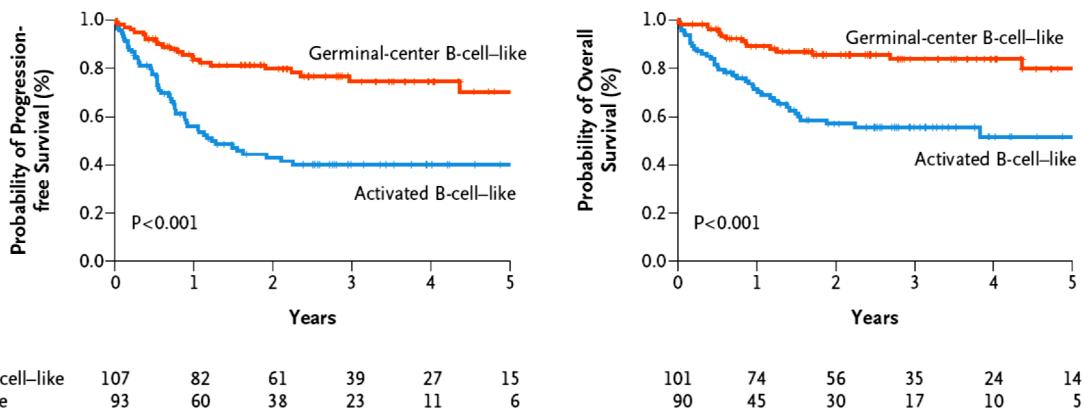
ESTABLISHED IN 1812

NOVEMBER 27, 2008

VOL. 359 NO. 22

## Stromal Gene Signatures in Large-B-Cell Lymphomas

G. Lenz, M.D., G. Wright, Ph.D., S.S. Dave, M.D., W. Xiao, Ph.D., J. Powell, M.S., H. Zhao, M.S., W. Xu, M.S.,  
B. Tan, M.D., N. Goldschmidt, M.D., J. Iqbal, Ph.D., J. Vose, M.D., M. Bast, B.S., K. Fu, M.D., Ph.D.,  
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A. Lopez-Guillermo, M.D., E. Montserrat, M.D., E. Campo, M.D., R.M. Braziel, M.D., T.P. Miller, M.D.,  
L.M. Rimsza, M.D., J.R. Cook, M.D., B. Pohlman, M.D., J. Sweetenham, M.D., R.R. Tubbs, M.D., R.I. Fisher, M.D.,  
E. Hartmann, M.D., A. Rosenwald, M.D., G. Ott, M.D., H.-K. Muller-Hermelink, M.D., D. Wrench, M.D.,  
T.A. Lister, M.D., E.S. Jaffe, M.D., W.H. Wilson, M.D., Ph.D., W.C. Chan, M.D., and L.M. Staudt, M.D., Ph.D.,  
for the Lymphoma/Leukemia Molecular Profiling Project

**A**

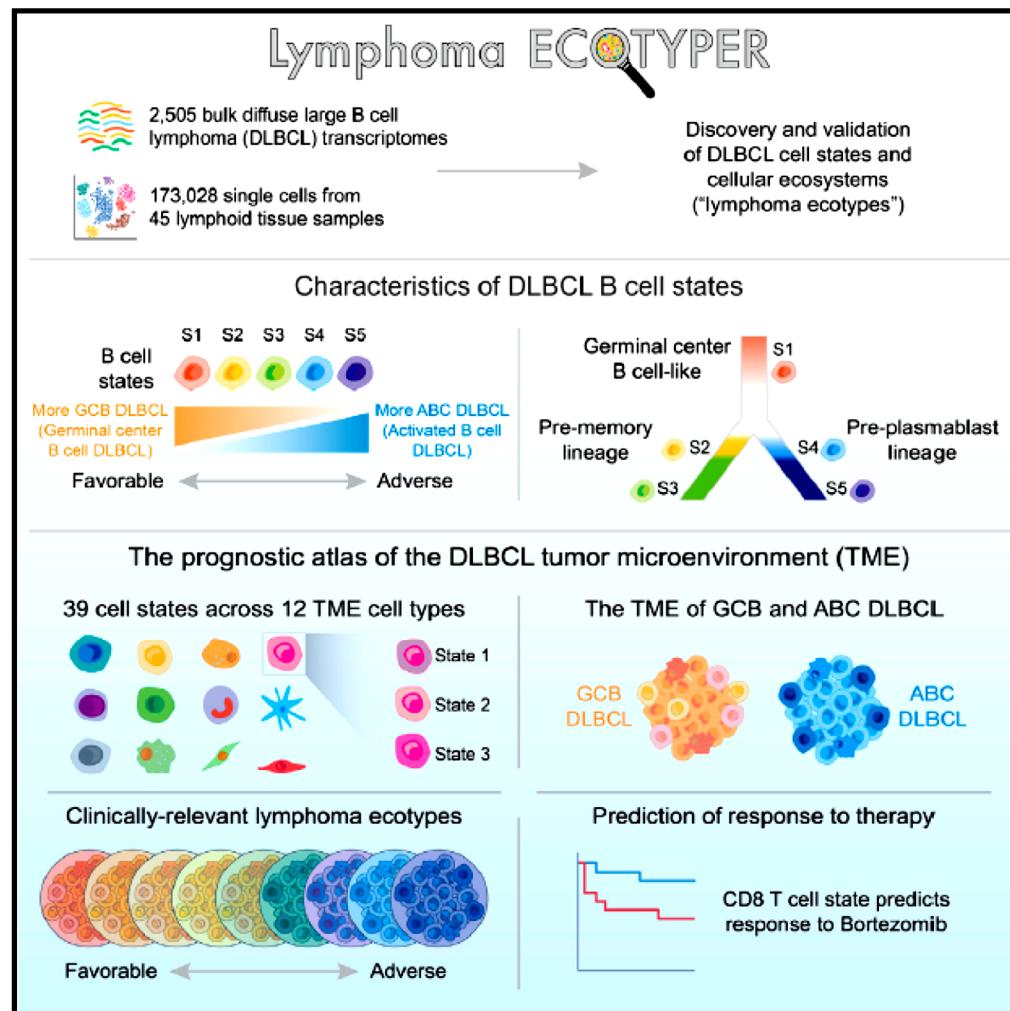
**Stromal-1:**  
**Extra-cellular matrix deposition + Macrophage infiltration**

**Stromal-2:**  
**Angiogenic genes → Micro-vessel density**

# Cancer Cell

## The landscape of tumor cell states and ecosystems in diffuse large B cell lymphoma

### Graphical abstract



### Authors

Chloé B. Steen, Bogdan A. Luca,  
Mohammad S. Esfahani, ...,  
Andrew J. Gentles, Aaron M. Newman,  
Ash A. Alizadeh

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### In brief

Steen et al. implement EcoTyper, a machine-learning approach for dissecting cellular heterogeneity in the most common blood cancer, diffuse large B cell lymphoma (DLBCL). Forty-four cell states spanning malignant cells and the microenvironment are defined, uncovering a rich landscape of cellular ecosystems that extend beyond traditional DLBCL classifications, revealing new opportunities for therapy selection.

ACCEPTED MANUSCRIPT

# Dissection of DLBCL Microenvironment Provides a Gene Expression-Based Predictor of Survival Applicable to Formalin-Fixed Paraffin-Embedded Tissue

S Ciavarella, M C Vegliante, M Fabbri, S De Summa, F Melle, G Motta, V De Iuliis, G Opinto, A Enjuanes, S Rega, A Gulino, C Agostinelli, A Scattone, S Tommasi, A Mangia, F Mele, G Simone, A F Zito, G Ingravallo, U Vitolo, A Chiappella, C Tarella, A M Gianni, A Rambaldi, P L Zinzani, B Casadei, E Derenzini, G Loseto, A Pileri, V Tabanelli, S Fiori, A Rivas-Delgado, A López-Guillermo, T Venesio, A Sapino, E Campo, C Tripodo, A Guarini, S A Pileri ✉

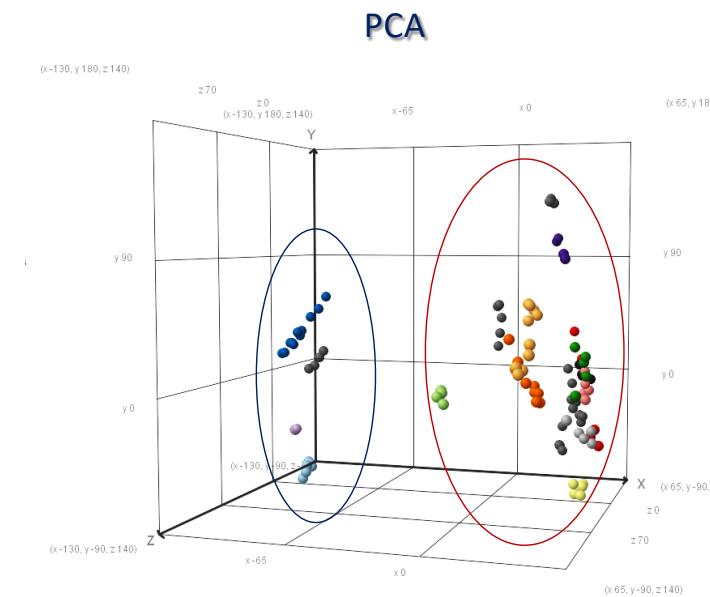
*Annals of Oncology*, mdy450, <https://doi.org/10.1093/annonc/mdy450>

**Published:** 11 October 2018

# CIBERSORT analysis and selection of prognostic genes

A customized signature including 1,028 genes was generated to distinguish 17 cell types of both **stromal** and **immune** origin.

- Adipocytes
- CD4-T cells
- CD8-T cells
- Dendritic cells
- Eosinophils
- Lymphatic endothelial cells
- Macrophages M2
- Memory\_B cells
- Monocytes
- Myofibroblasts
- NK\_activiated
- NK\_resting
- Naive\_B
- Neutrophils
- Pericytes
- Plasmacells
- Tgamma-delta

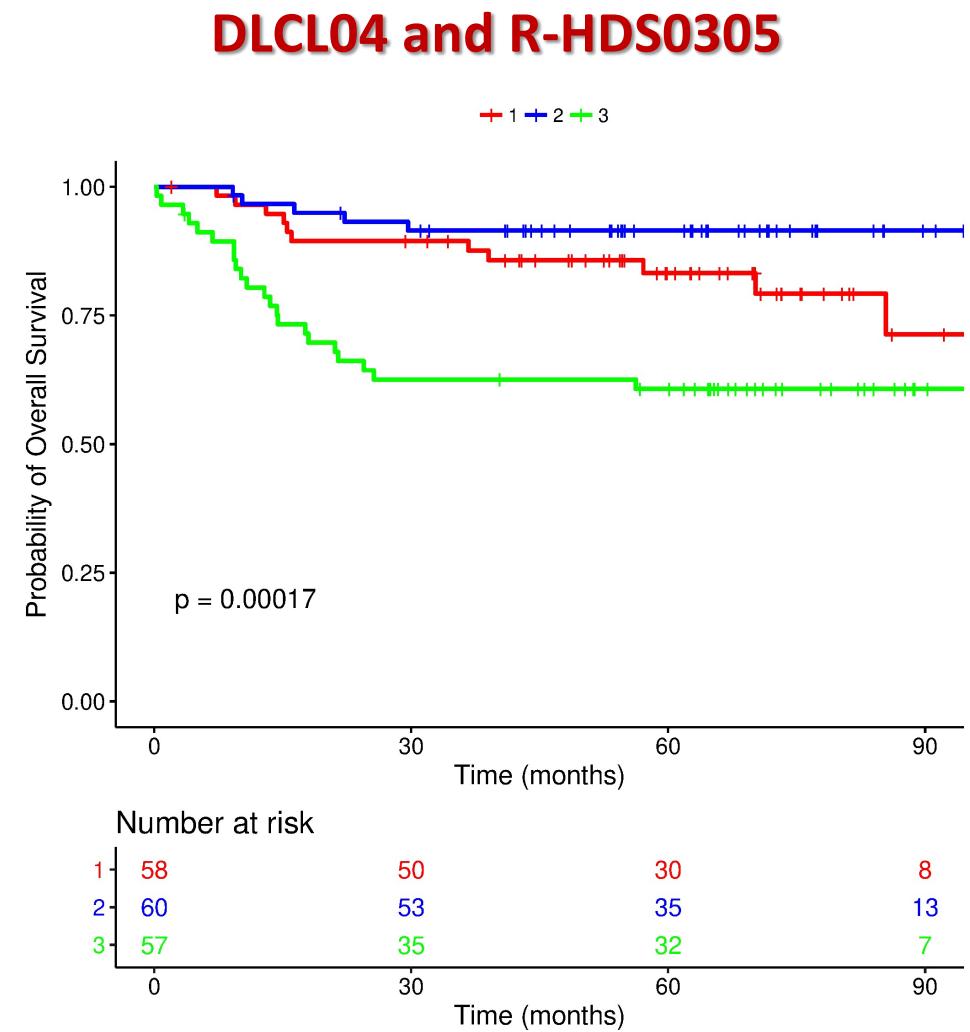
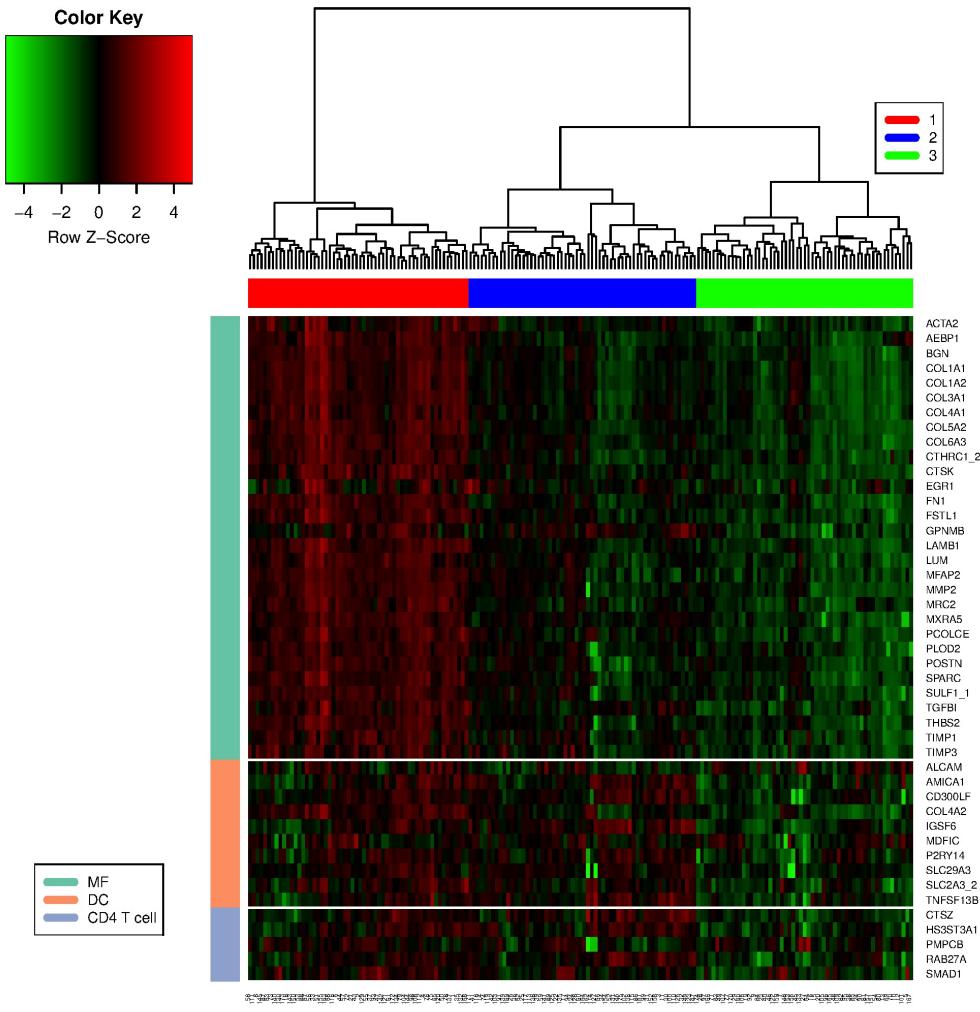


MF-related genes

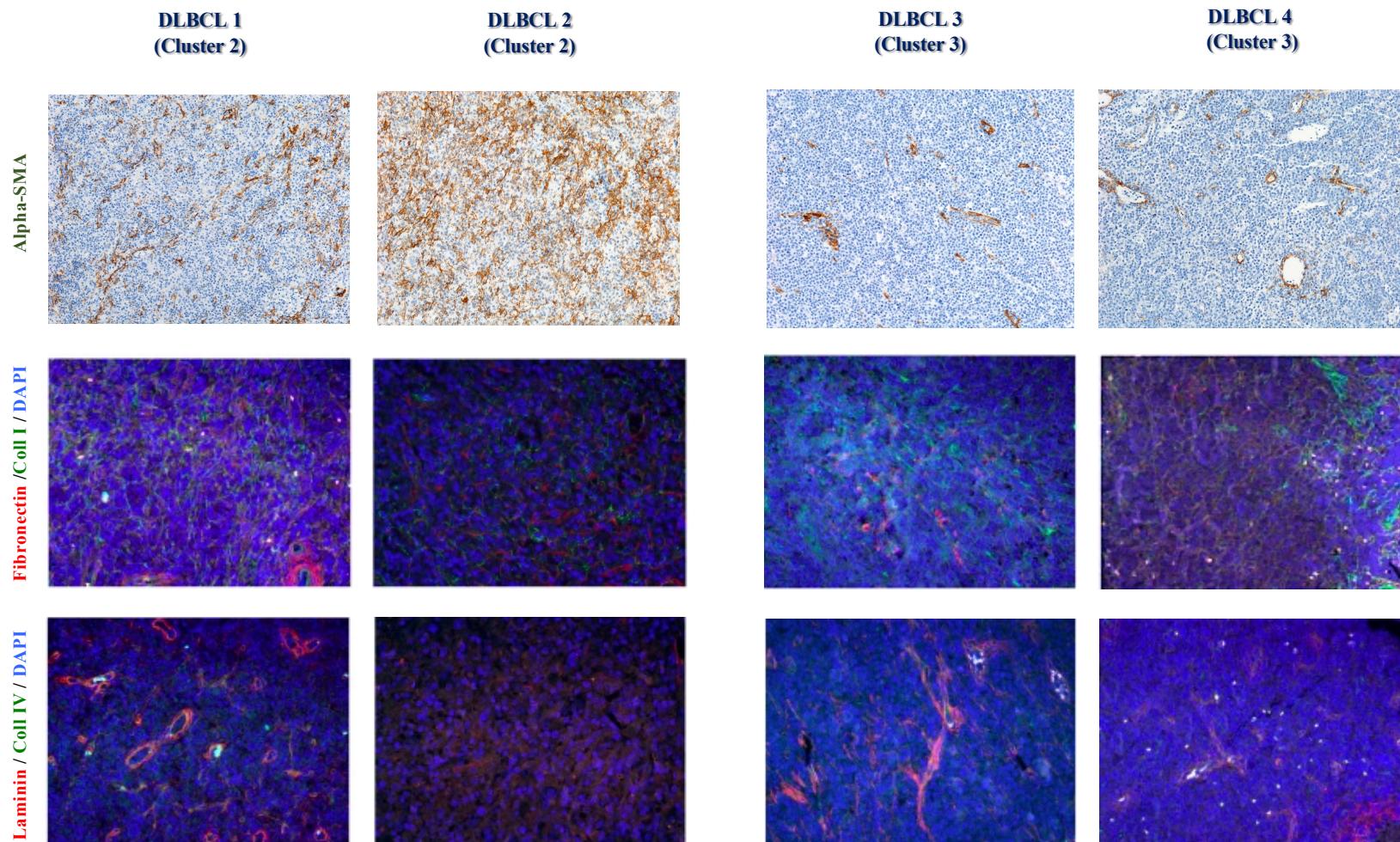
<i>ACTA2</i>	Actin, alpha 2, smooth muscle
<i>AEBP1</i>	AE binding protein 1
<i>BGN</i>	Biglycan
<i>COL1A1</i>	Collagen type I alpha 1
<i>COL1A2</i>	Collagen type I alpha 2
<i>COL3A1</i>	Collagen type III alpha 1
<i>COL4A1</i>	Collagen type IV alpha 1
<i>COL5A2</i>	Collagen type V alpha 2
<i>COL6A3</i>	Collagen type VI alpha 3
<i>CTHRC1</i>	Collagen triple helix repeat containing 1
<i>CTSK</i>	Cathepsin K
<i>EGR1</i>	Early growth response 1
<i>FN1</i>	Fibronectin 1
<i>FSTL1</i>	Follistatin like 1
<i>GPNMB</i>	Glycoprotein nmb
<i>LAMB1</i>	Laminin subunit beta 1
<i>LUM</i>	Lumican
<i>MFAF2</i>	Microfibrillar associated protein 2
<i>MMP2</i>	Matrix metallopeptidase 2
<i>MRC2</i>	Mannose receptor, C type 2
<i>MXRA5</i>	Matrix-Remodelling Associated 5
<i>PCOLCE</i>	Procollagen C-endopeptidase enhancer
<i>PLOD2</i>	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2
<i>POSTN</i>	Periostin, osteoblast specific factor
<i>SPARC</i>	Secreted protein acidic and cysteine rich
<i>SULF1</i>	Sulfatase 1
<i>TGFBI</i>	Transforming growth factor beta induced
<i>ALCAM</i>	Activated leukocyte cell adhesion molecule
<i>AMICA1</i>	Adhesion molecule, interacts with CXADR antigen 1
<i>CD300LF</i>	CD300 molecule-like family member F
<i>COL4A2</i>	Collagen, type IV, alpha 2
<i>IGSF6</i>	Immunoglobulin superfamily, member 6
<i>MDFIC</i>	MyoD Family Inhibitor Domain Containing
<i>P2RY14</i>	Purinergic receptor P2Y, G-protein coupled, 14
<i>SLC29A3</i>	Solute carrier family 29 (nucleoside transporters), member 3;
<i>SLC2A3</i>	Solute carrier family 2 (facilitated glucose transporter),
<i>CTS2</i>	Cathepsin Z
<i>HS3ST3A1</i>	Heparan Sulphate-Glucosamine 3-Sulfotransferase 3A1
<i>PMPCB</i>	Peptidase, Mitochondrial Processing Beta Subunit
<i>RAB27A</i>	RAB27A, Member RAS Oncogene Family
<i>SMAD1</i>	SMAD Family Member 1

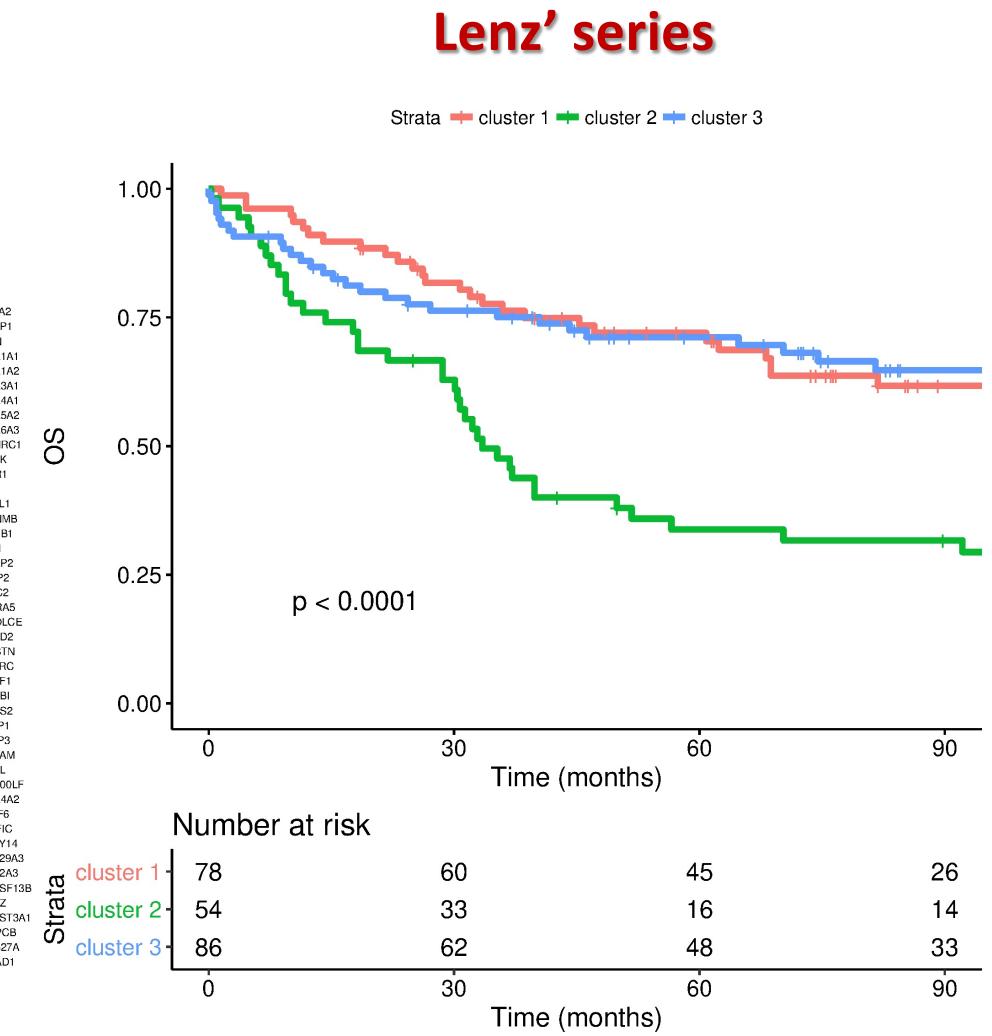
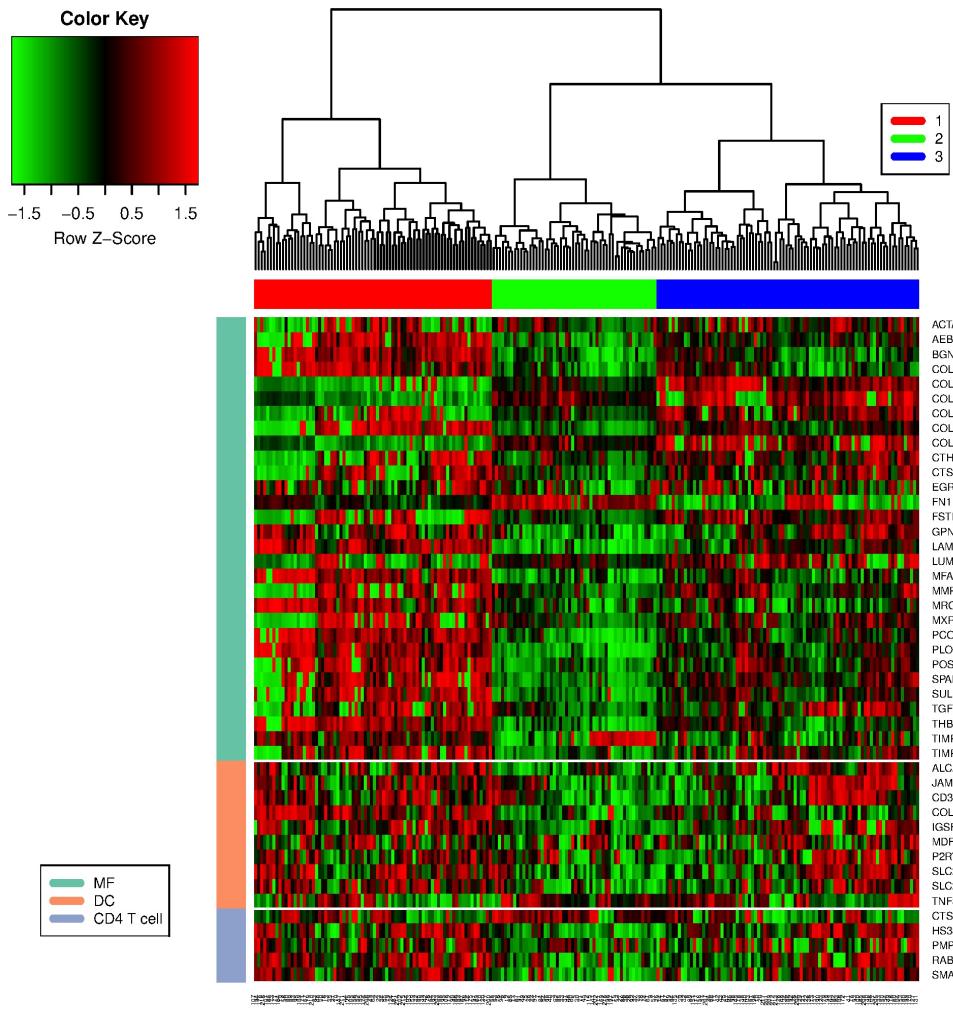
DC-related genes

CD4+ T cell-related genes

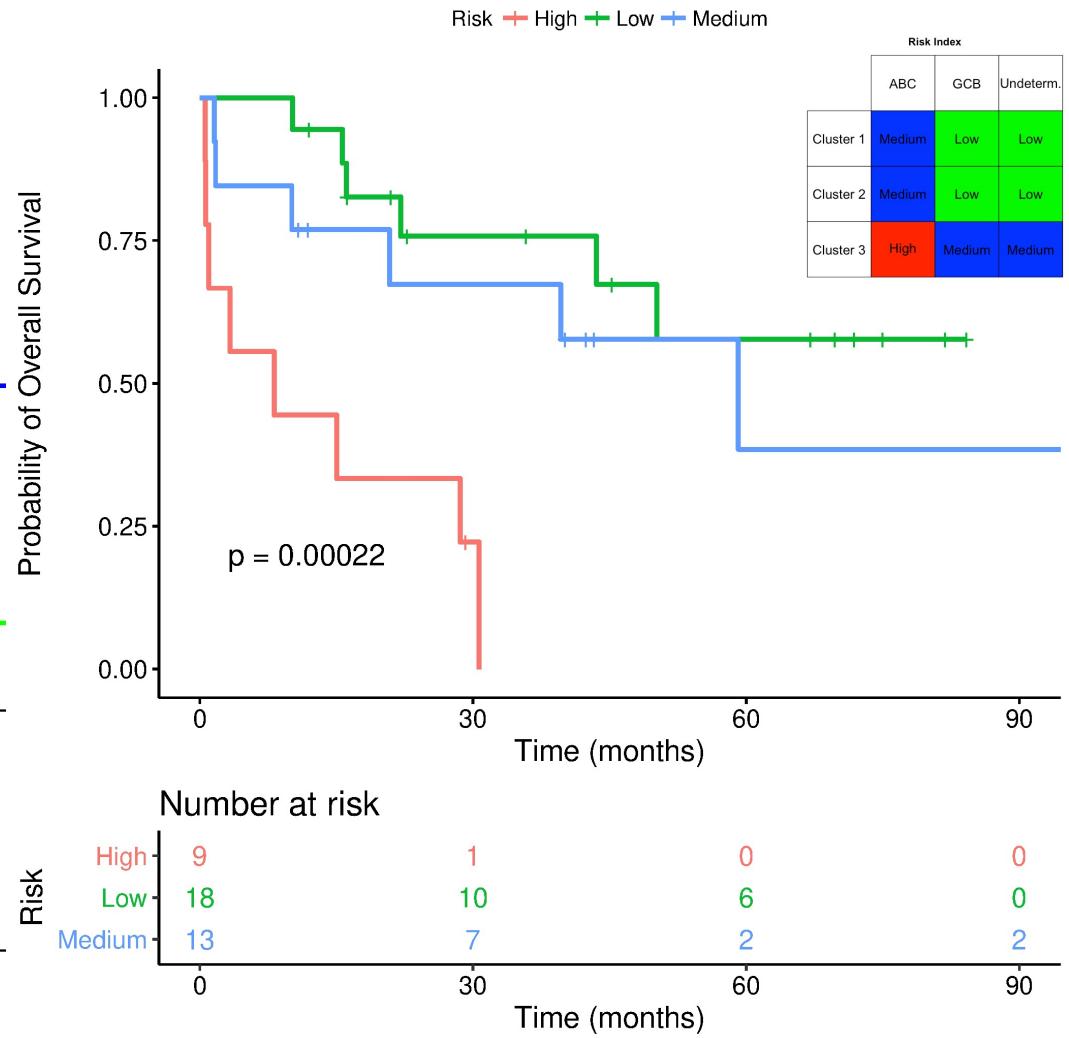
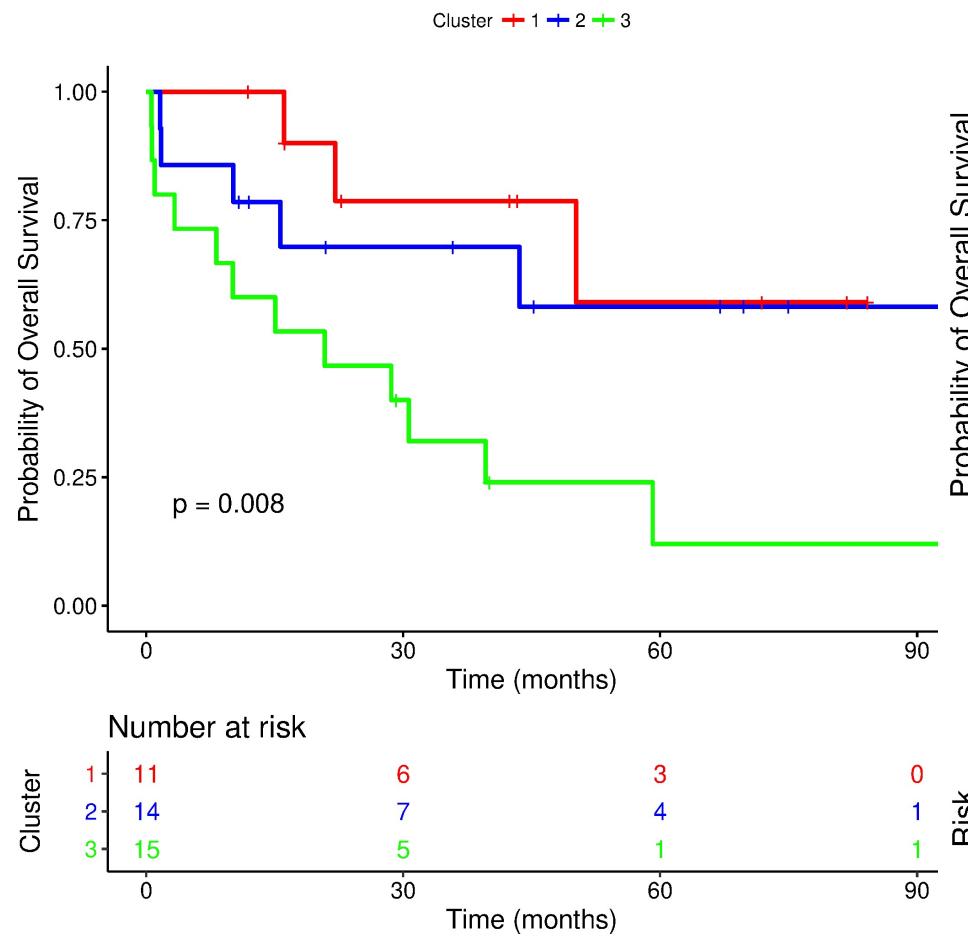


By *in situ* immunostaining we analyzed the expression of ECM proteins encoded by four of the fronting genes of the MF signature, namely Fibronectin, Collagen-I, Laminin, and Collagen-IV. However, the expression variability of these proteins does not support the use of immunohistochemistry as a reliable assay to provide insight on the prognostic gene expression patterns of DLBCL microenvironment determinants.





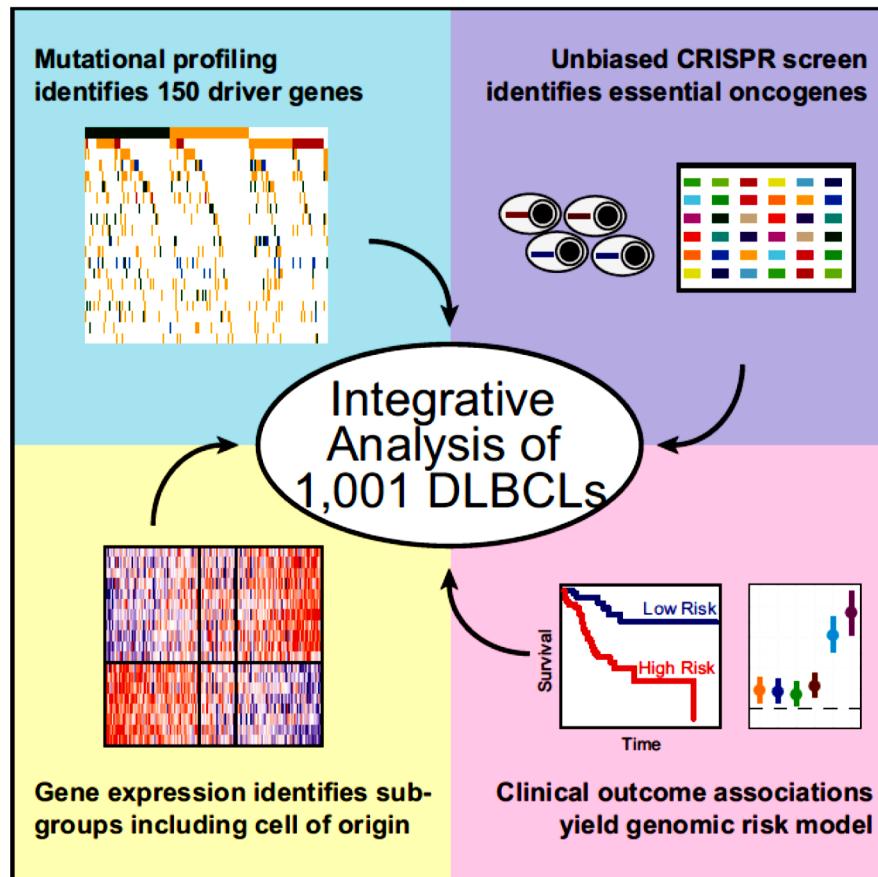
## Real-life



# **Next generation sequencing**

# Genetic and Functional Drivers of Diffuse Large B Cell Lymphoma

## Graphical Abstract



## Authors

Anupama Reddy, Jenny Zhang,  
Nicholas S. Davis, ..., Jyotishka Datta,  
David B. Dunson, Sandeep S. Dave

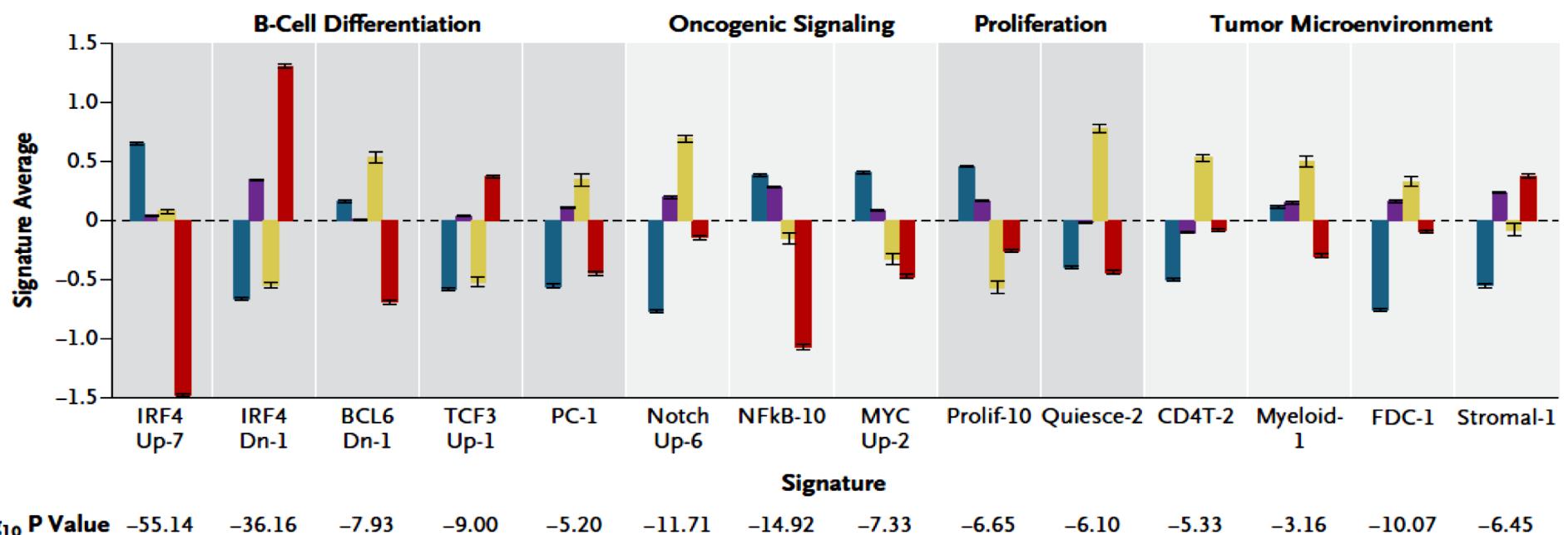
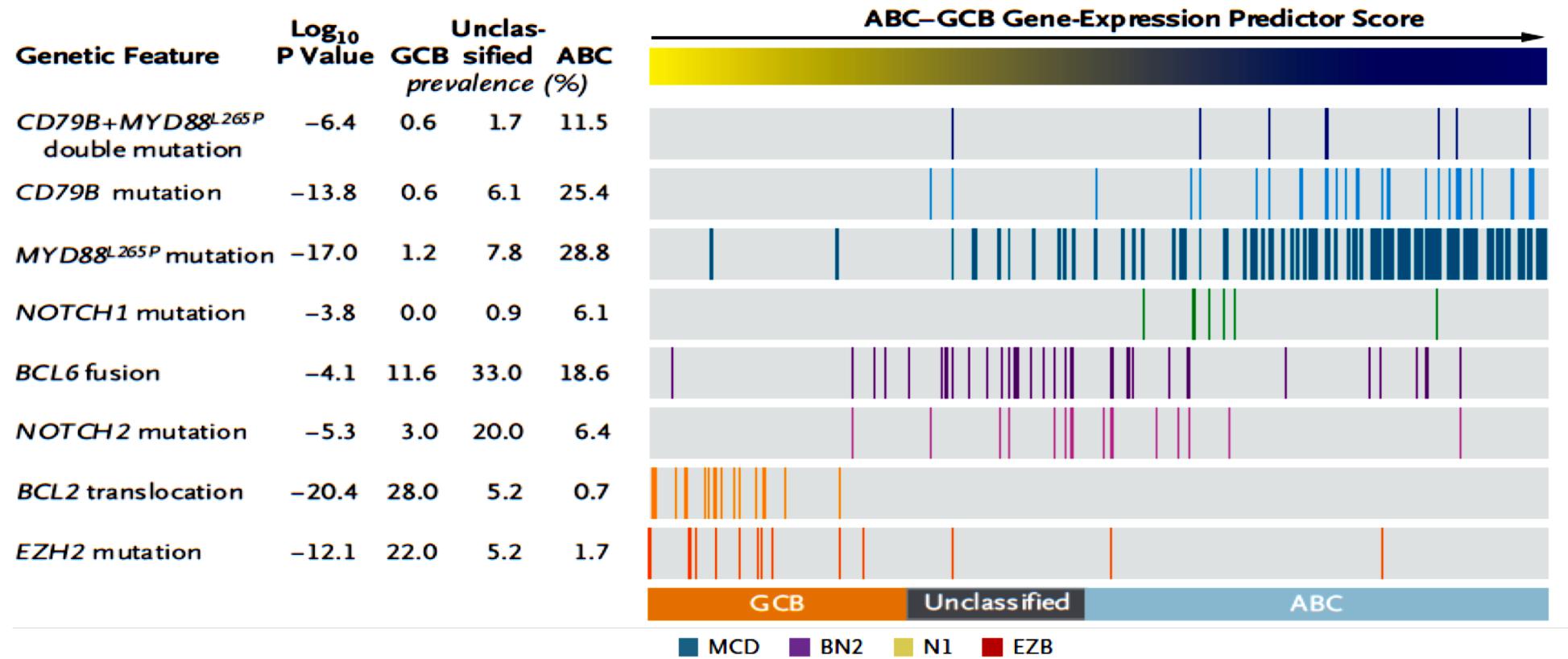
## Correspondence

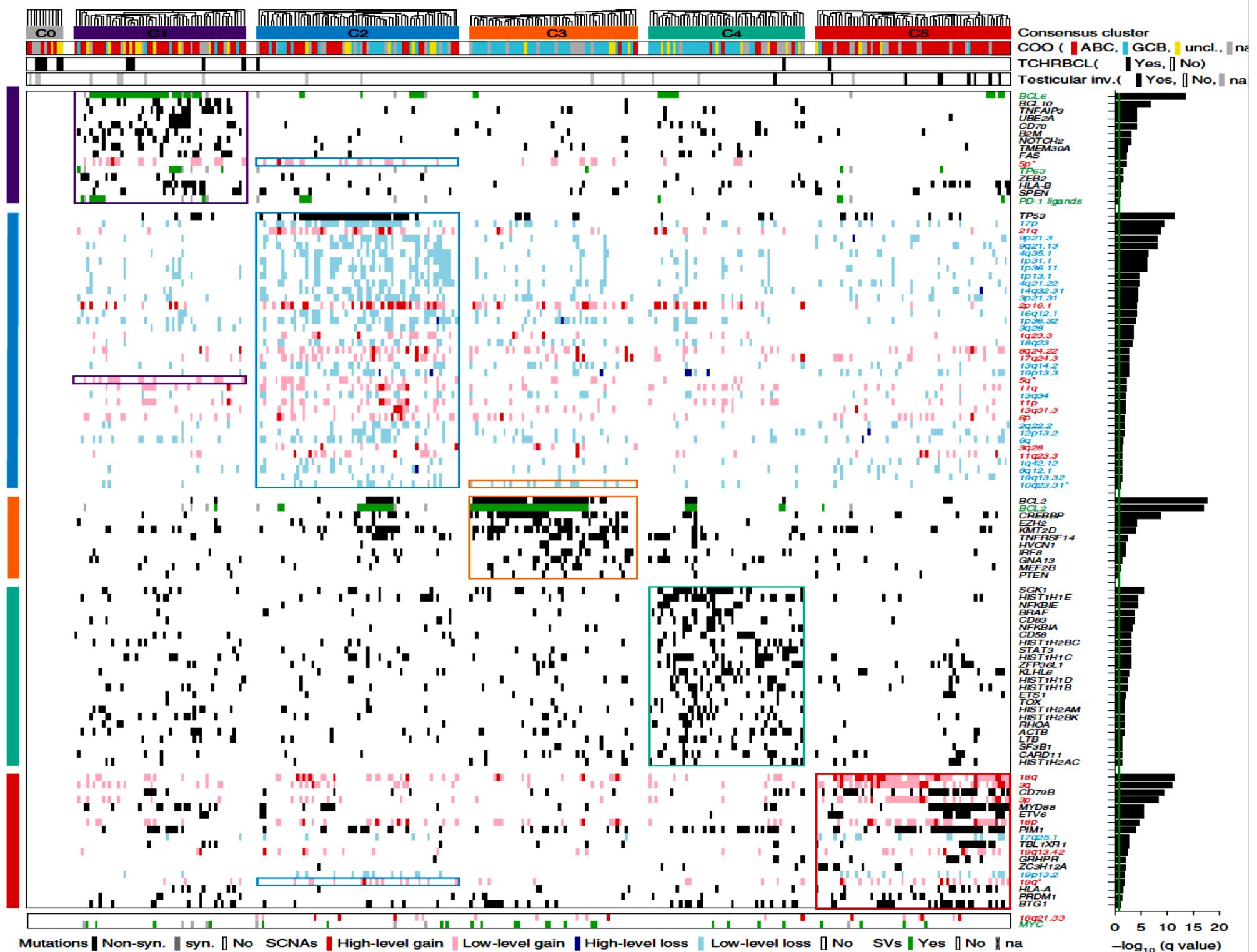
sandeep.dave@duke.edu

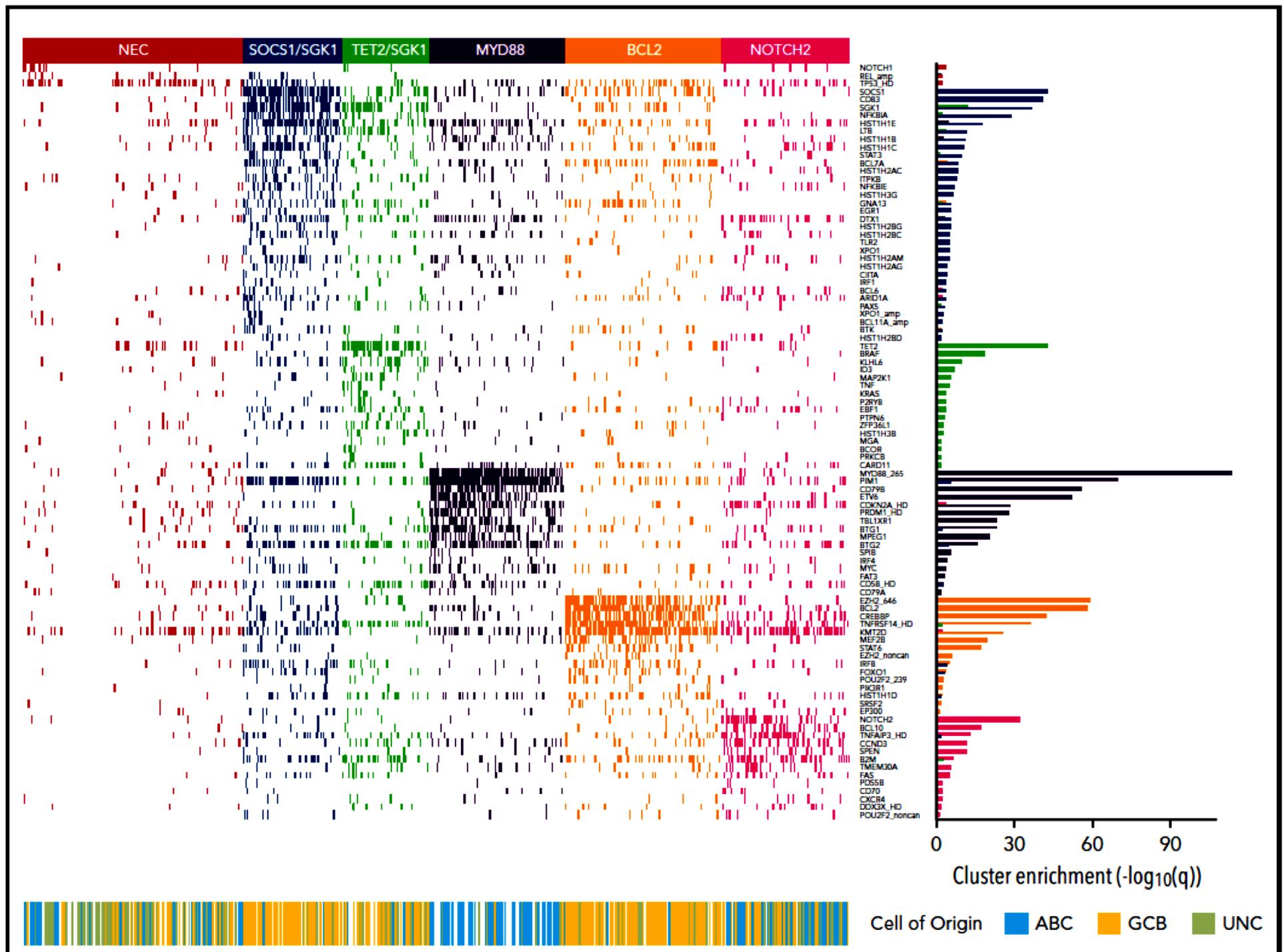
## In Brief

An integrative analysis in 1,001 newly diagnosed DLBCL patients identifies 150 genetic drivers with functional characterization using an unbiased CRISPR screen in DLBCL cell lines and connects with clinical outcome.

Cell 171, 481–494, October 5, 2017



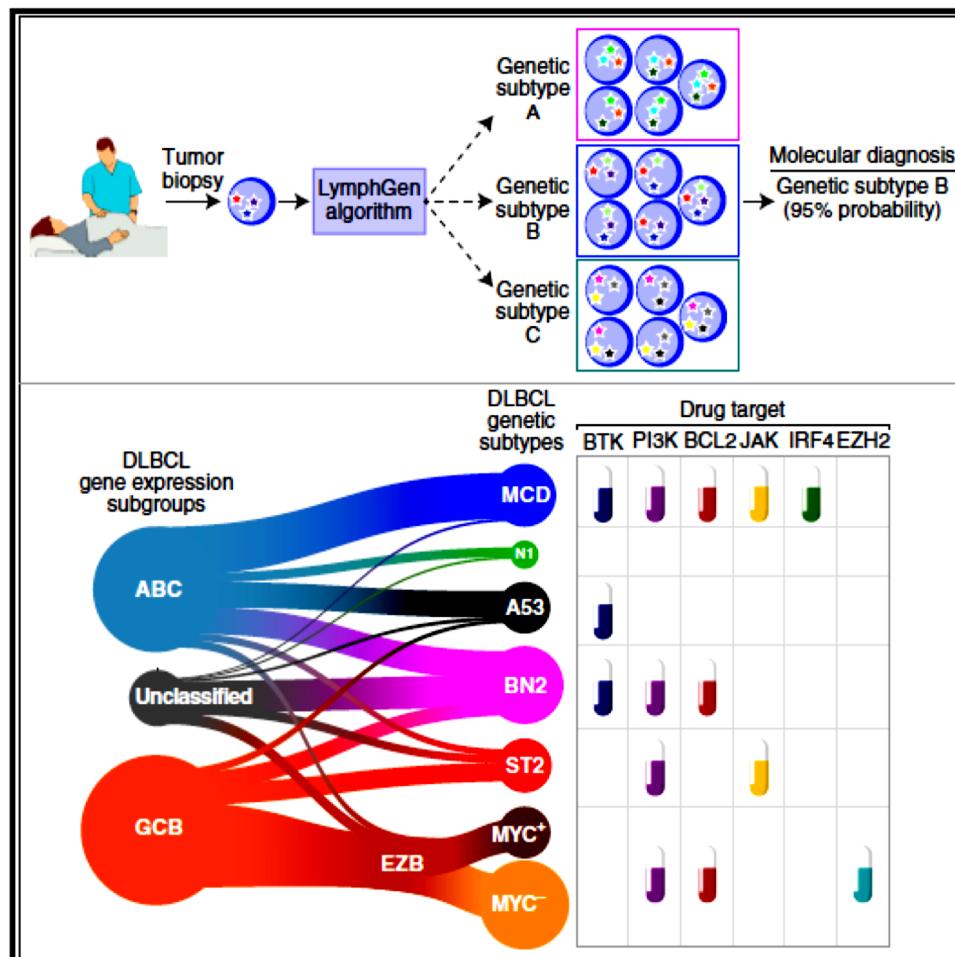




# Cancer Cell

## A Probabilistic Classification Tool for Genetic Subtypes of Diffuse Large B Cell Lymphoma with Therapeutic Implications

### Graphical Abstract



### Authors

George W. Wright, Da Wei Huang,  
James D. Phelan, ...,  
Wyndham H. Wilson, David W. Scott,  
Louis M. Staudt

Correspondence  
[Istaudt@mail.nih.gov](mailto:Istaudt@mail.nih.gov)

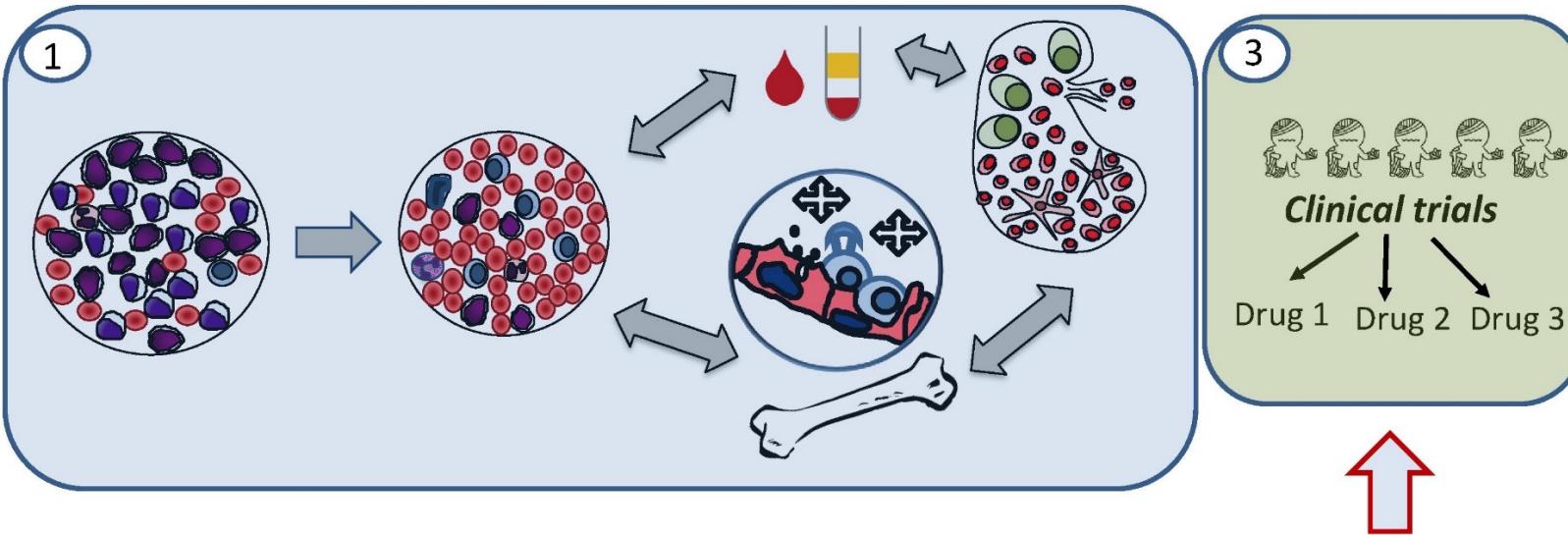
### In Brief

Wright et al. identify seven genetic subtypes of diffuse large B cell lymphoma (DLBCL) with distinct outcomes and therapeutic vulnerabilities. The LymphGen probabilistic classification tool that can classify a DLBCL biopsy into the genetic subtypes is developed, which could be used for precision medicine trials.

## *Diagnosis*

## *Resistance*

## *Dissemination*



2

### *WES/RNAseq*

## *Platforms*

### *cfDNAseq*

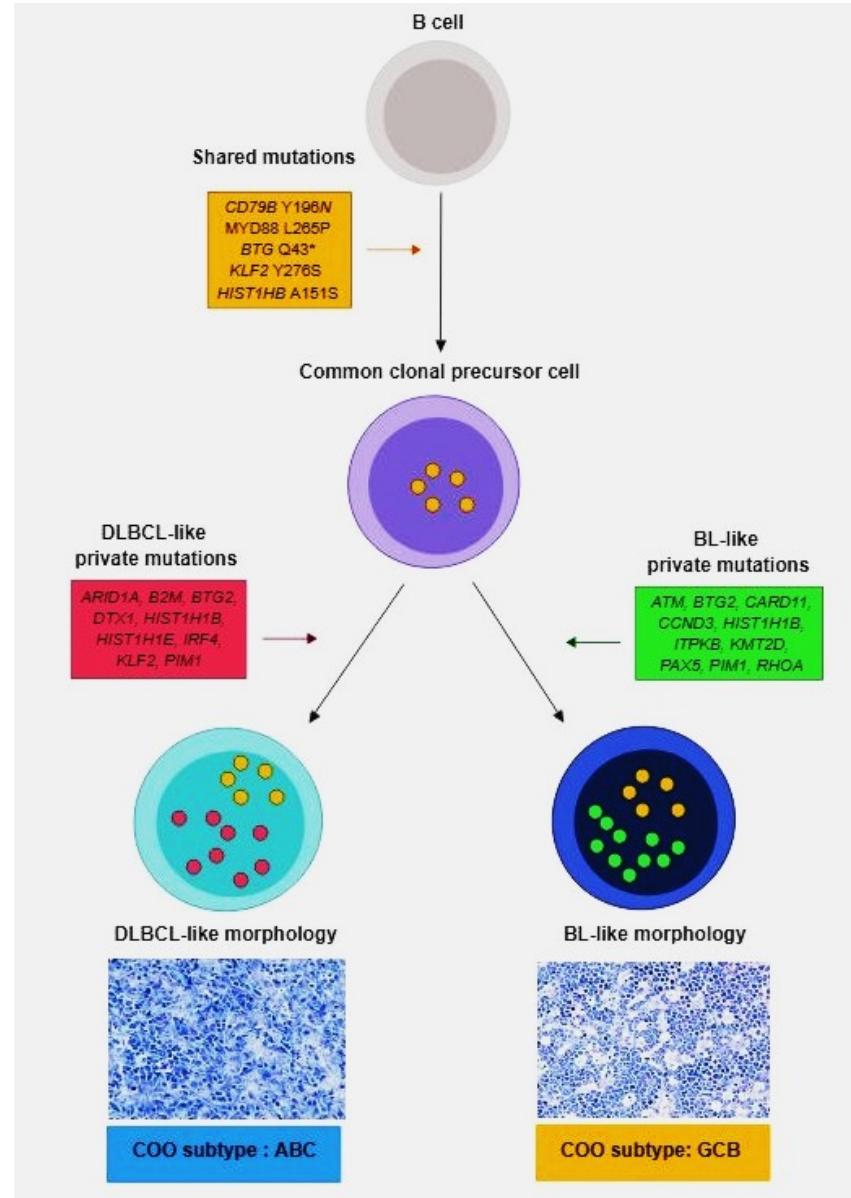
### *In vitro 2D/3D Models*

### *Mouse Models*

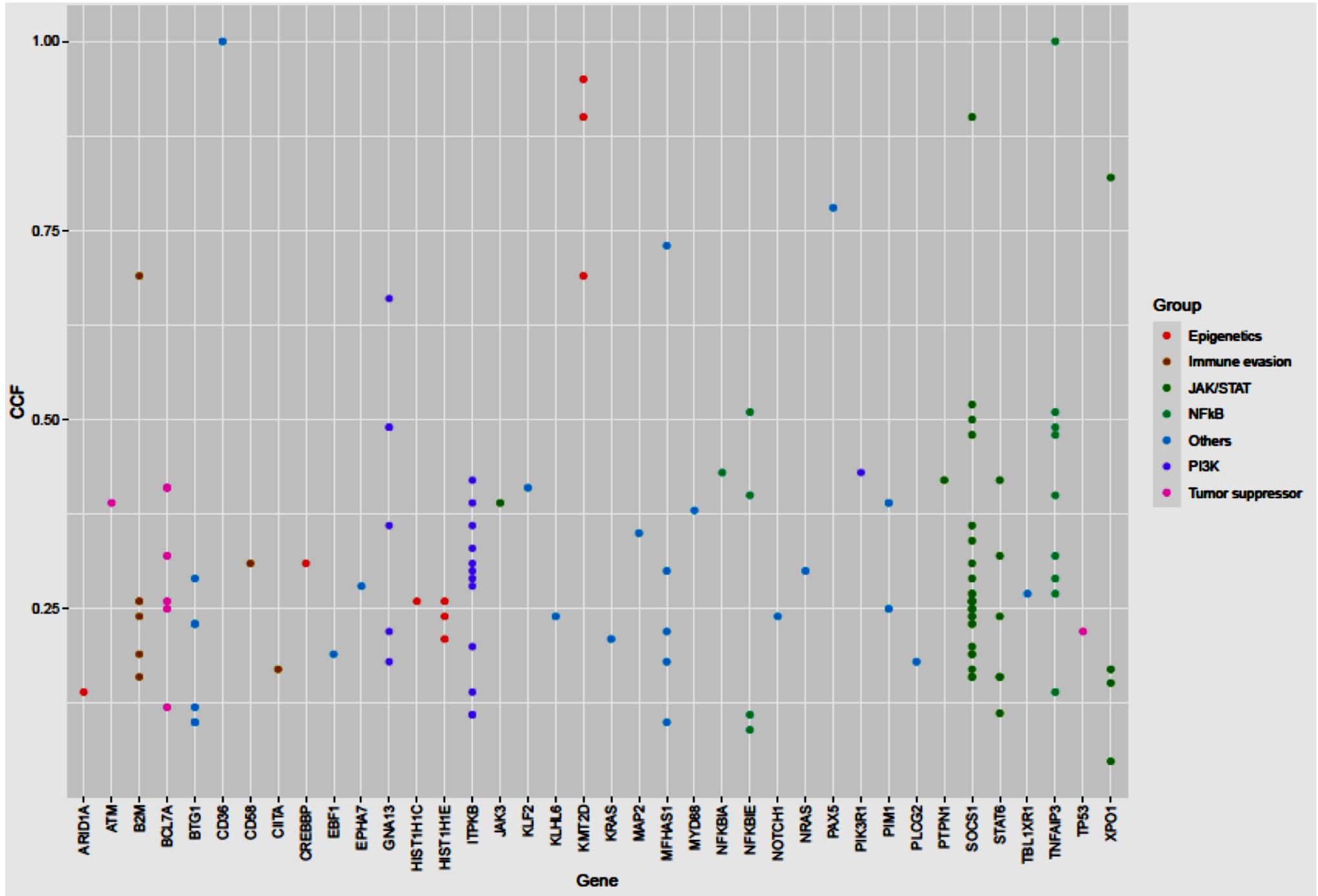
## Evolutionary crossroads: morphological heterogeneity reflects divergent intra-clonal evolution in a case of high-grade B-cell lymphoma

by Valentina Tabanelli, Federica Melle, Giovanna Motta, Saveria Mazzara, Marco Fabbri, Chiara Corsini, Elvira Gerbino, Angelica Calleri, Maria Rosaria Sapienza, Ignazio Abbene, Viviana Stufano, Massimo Barberis, and Stefano A. Pileri

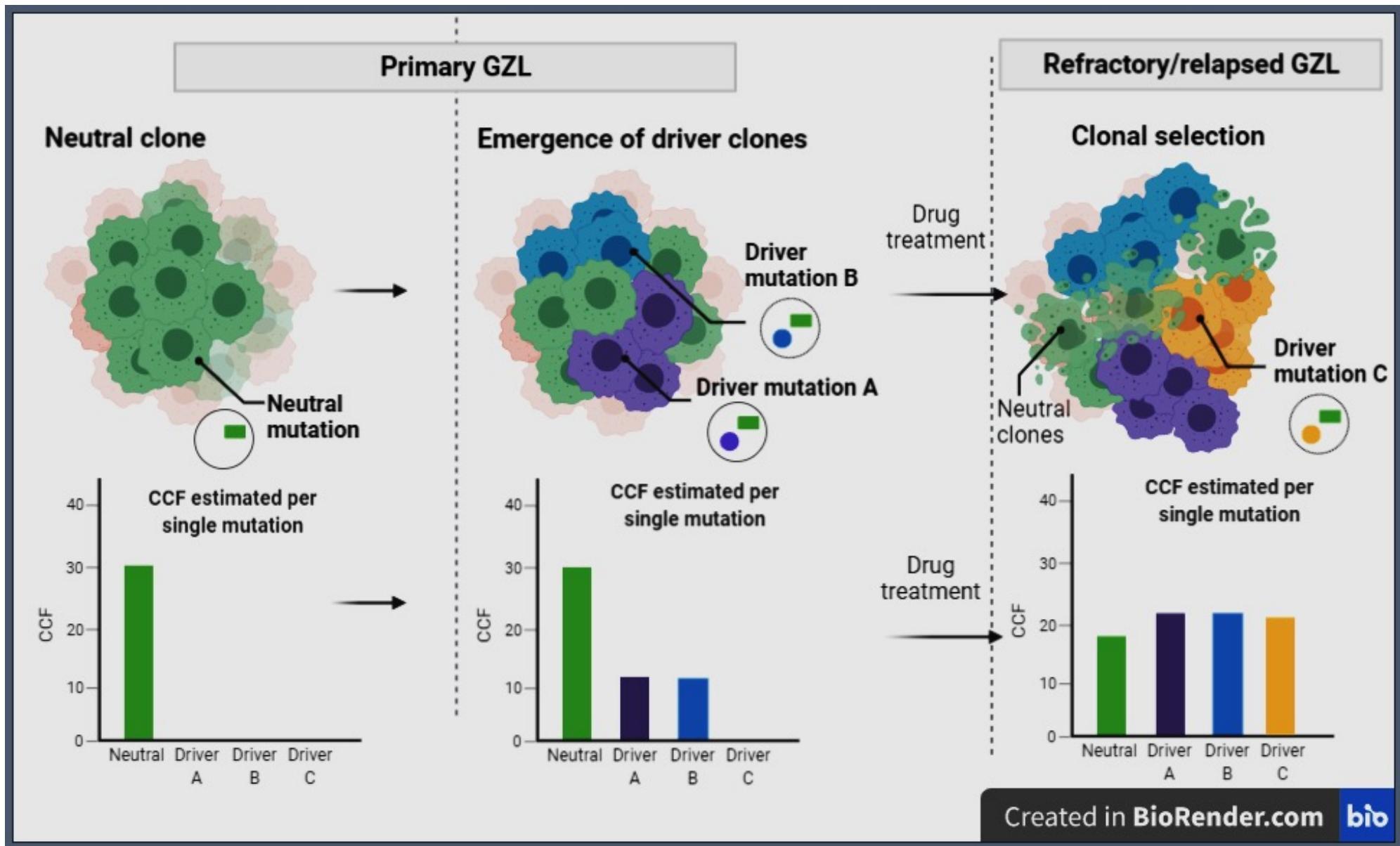
Haematologica 2020 [Epub ahead of print]

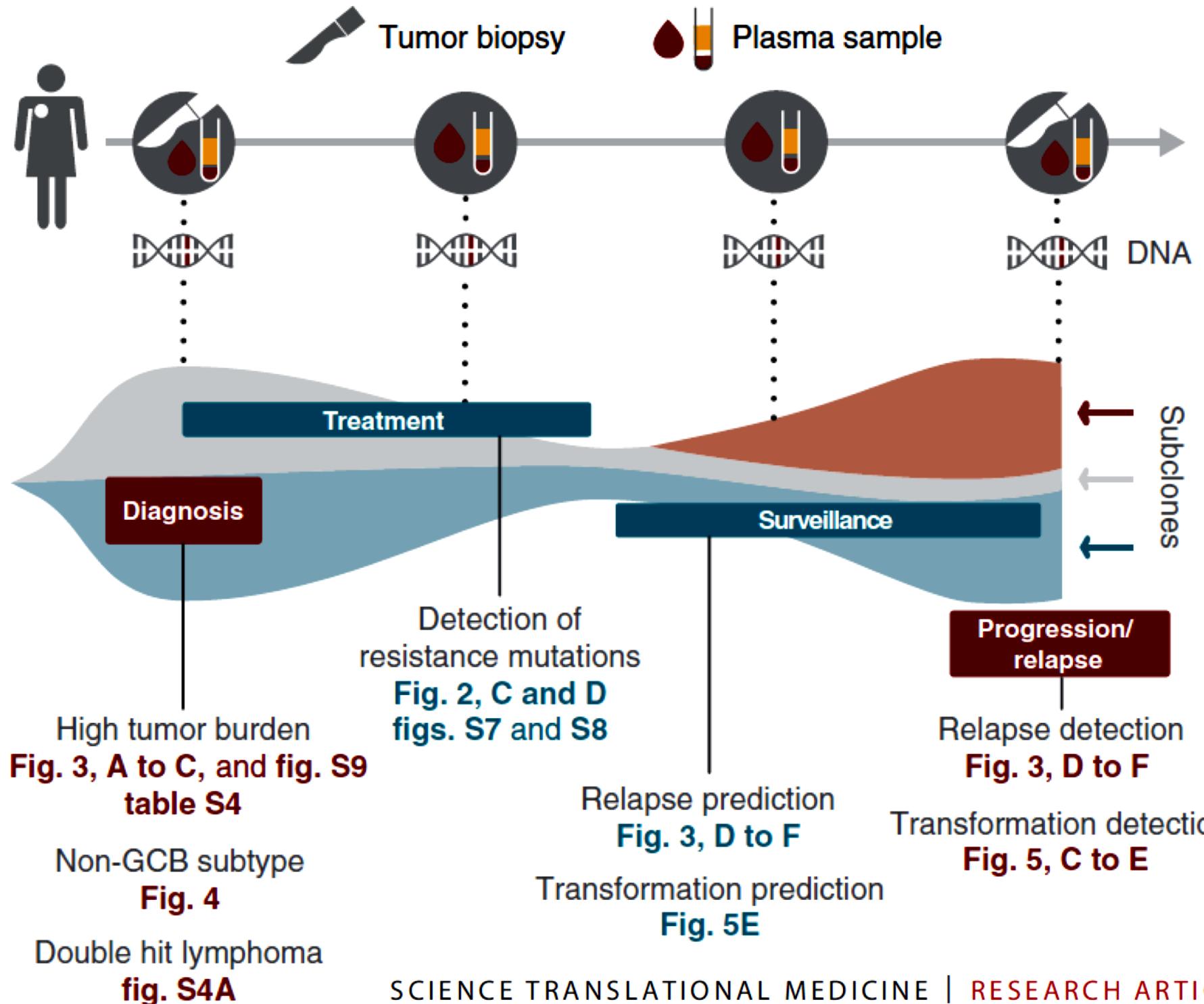


# 11 mediastinal GZLs (3 R/R) + 30 (EAHP Workshop)

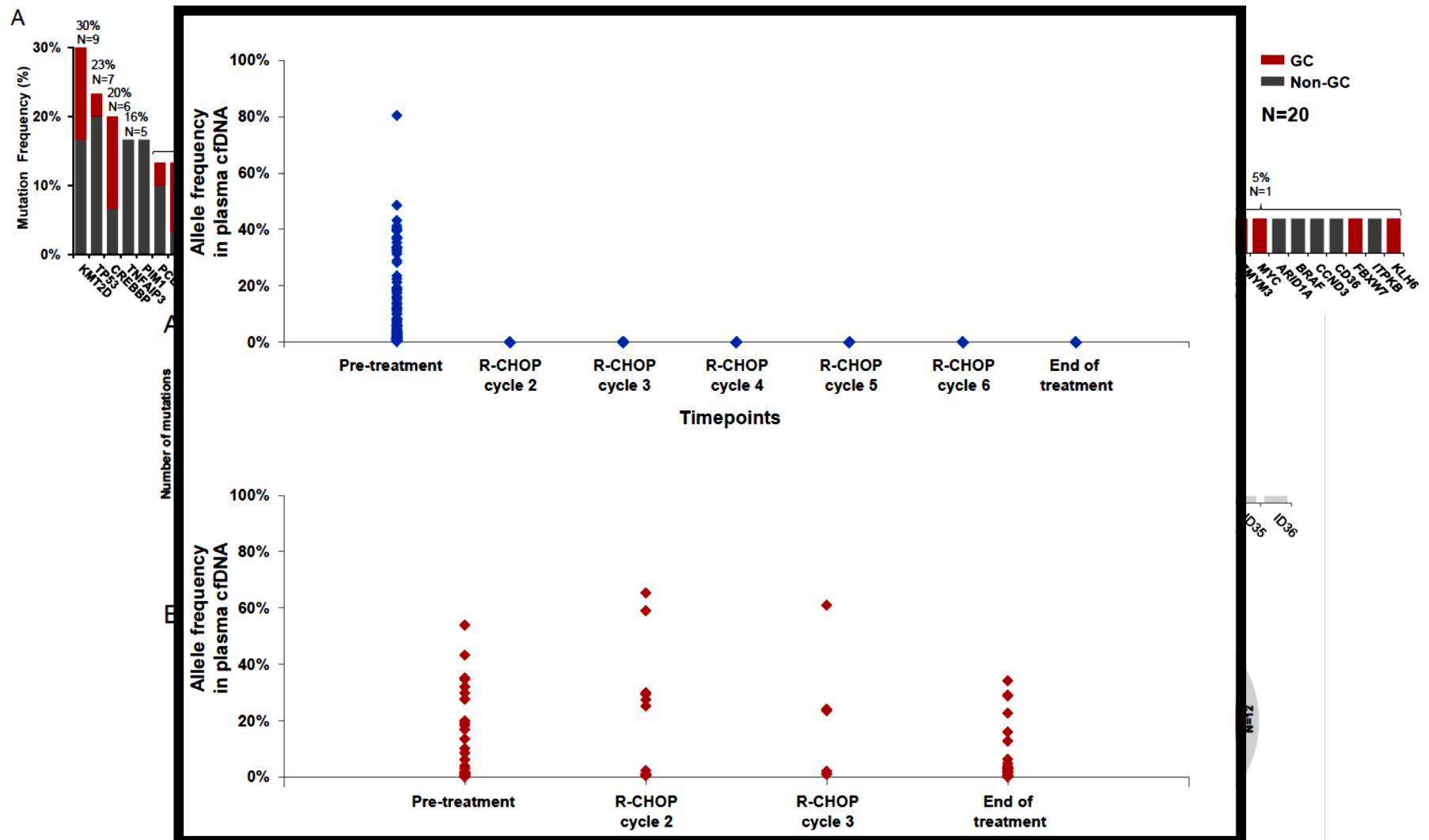


Relapses due to subclonal  
selection?





# DIFFUSE LARGE B-CELL LYMPHOMA GENOTYPING ON THE LIQUID BIOPSY



**thank you**

danke 謝謝  
спасибо faafelai lava  
спасибо dankie  
спасибо nandi  
спасибо bayarlaaa  
спасибо hvala  
спасибо mauruuru  
спасибо koszonam  
спасибо bedankt  
спасибо dziekuje  
спасибо obrigado  
спасибо sagoluun  
спасибо sukriya  
спасибо terima kasih  
спасибо 감사합니다  
спасибо xiexie  
спасибо рахмат  
спасибо mersi  
спасибо vinaka  
спасибо blagodaram  
спасибо kia ora  
спасибо barka  
спасибо welalim  
спасибо tack  
спасибо dank je  
спасибо misaotra  
спасибо matondo  
спасибо paldies  
спасибо grazzi  
спасибо ngiyabonga  
спасибо тәшеккүр едерим  
спасибо mahalo  
спасибо tapadħ leat  
спасибо хвала  
спасибо asante manana  
спасибо obrigada  
спасибо murakoze  
спасибо tenki  
спасибо djiere dieuf  
спасибо mochchakkeram  
спасибо go raibh maith agat  
спасибо arigatō  
спасибо takk  
спасибо dakujem  
спасибо trugarez  
спасибо shukriya  
спасибо мерси  
спасибо merci