Clonal hematopoiesis in diffuse large B-cell lymphoma: clinical impact and genetic relatedness to lymphoma and therapy-related myeloid neoplasm

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Supplementary Figure 1: Distribution of CH, chemotherapy history and MN development of the cases included in the cohort.











Months

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TP53		
PIM1		
KMT2D		
CREBBP		
MYD88		
BCI 2		
TNERSE14		
B2M		
HLA-A		
SOCS1		
ARID1A		
CD79B		
HIST1H1E		
SETD1B		
CARD11		
TNFAIP3		
BTG1		
EZH2		
FAT1		
MYC		
EP300		
CD58		
IRF4		
IRF8		
IRF8 MEF2B		
IRF8 MEF2B TBL1XR1		
IRF8 MEF2B TBL1XR1 CCND3		
IRF8 MEF2B TBL1XR1 CCND3 DTX1		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB SGK1		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB SGK1 STAT3		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB SGK1 STAT3 TET2		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB SGK1 STAT3 TET2 MLL2		
IRF8 MEF2B TBL1XR1 CCND3 DTX1 ETV6 FOXO1 GNA13 PRDM1 FAS SPEN ROBO1 BCL10 LTB SGK1 STAT3 TET2 MLL2 NOTCH2		

Supplementary Figure 2. Characterization of CH mutations, swimmer plot of 54 CH+ patients and mutational profiles of DLBCL in CH- patients. 2A. Frequency of CH mutations in entire cohort. 2B. Number of CH mutations in individual patients of entire cohort. 2C. Distribution of CH mutations in entire cohort. 2D. Median and range of VAFs of CH mutations in entire cohort. 2E. Frequency of CH mutations detected in lymphoma tissue (core or excisional biopsies) and/or saliva in patients without paired PB/BM analysis. No significant difference for CH assignment (p=0.1) seen among sample types: core biopsy (2/85), excisional biopsy (1/24) and saliva (14/149). 2F. CH mutations detected in lymphoma tissue and saliva in patients without paired PB/BM analysis. 2G. Swimmer plot indicating the time points at which DLBCL chemotherapy was initiated, CH testing was performed, myeloid neoplasms were detected and occurrence of DLBCL relapse for the 54 CH+ patients. 2H: Mutational profiles of DLBCL of 331 CH- patients. Red: single mutation; Purple: double or multiple mutations.

	MN	CH clones				Lymphoma clones		Evidence of Clonal relatedness
		CH Mutations	VAF (CH)	VAF (MN)	VAF (lymphoma)	Lymphoma Mutations	VAF	
СН-	t-MDS	TP53 p.R248Q	< 0.005	0.97	< 0.005	KMT2D, ATM, SH2B3, SETD1A, WHSC1	0.41-0.83	None
CH+	t-MDS	TP53 p.H179D	0.01	0.35	<0.005	MYD88, PIM1, CD79B, ARID5B, MSH6, HIST1H1E, SP140, TBL1XR1	0.27-0.35	None
	t-MDS	TET2 p.S1284F	0.02	0.31	0	KMT2D, BCL6, CDNK2A, CTCF, P2RY8	0.11-0.46	None
		KMD5C p.S1215L	0.03	0.07	0			
		TET2 p.K1094*	0.02	0.03	0			
		SF3B1 p.K666N	0.01	0.03	0			
	t-MDS	DNMT3A p.R326C	0.02	0.46	<0.005	KMT2D, SOCS1, DTX1, FOXO1, CYLD, STAT5A, ACTG1, TYK2, HIST1H1E, HIST1H1C	0.16-0.47	None
	t-AML	TP53 p.C141Y	0.01	0.03	< 0.005	CDKN1B, MYD88, CD79B, PIM, IRF8	0.11-0.24	None

Supplementary Table 1. Mutational profiles and VAF of CH and lymphoma clones

	CML	TET2 p.P1419H	0.03	0.51	< 0.005	BCL6, MYC, PIM1, NOTCH2, SRSF2, EGFR, MDM2, DTX1, GNA13, PLCG2, FANCA	0.35-0.41	None
		TET2 p.A1341Gfs*3	0.02	0.45	< 0.005			
		SF3B1 p.W658G	0.03	0.48	0			
	MPN	JAK2 p.V617F	0.06	0.48	0	TET2	0.44	None
		SF3B1 p.K666N	0.08	0.47	< 0.005			