SnapShot: Acute Myeloid Leukemia

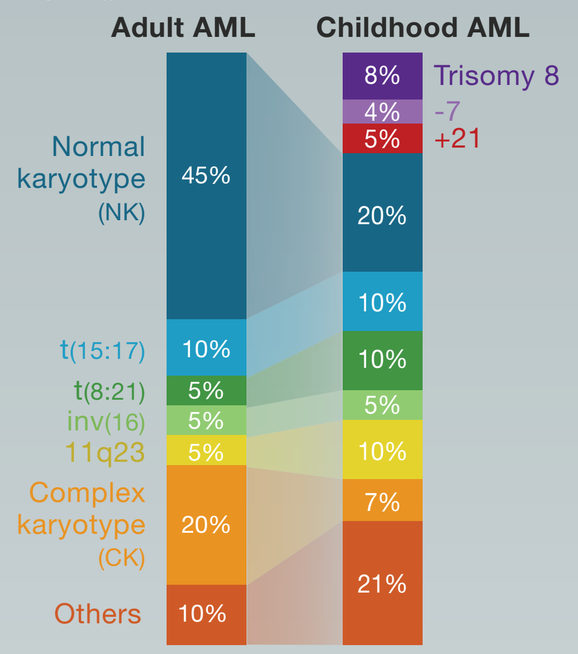
Bernd B. Zeisig, Austin G. Kulasekararaj, Ghulam J. Mufti, and Chi Wai Eric So
Department of Haematological Medicine, King's College London, London SE5 9NU, UK

Cancer Cell

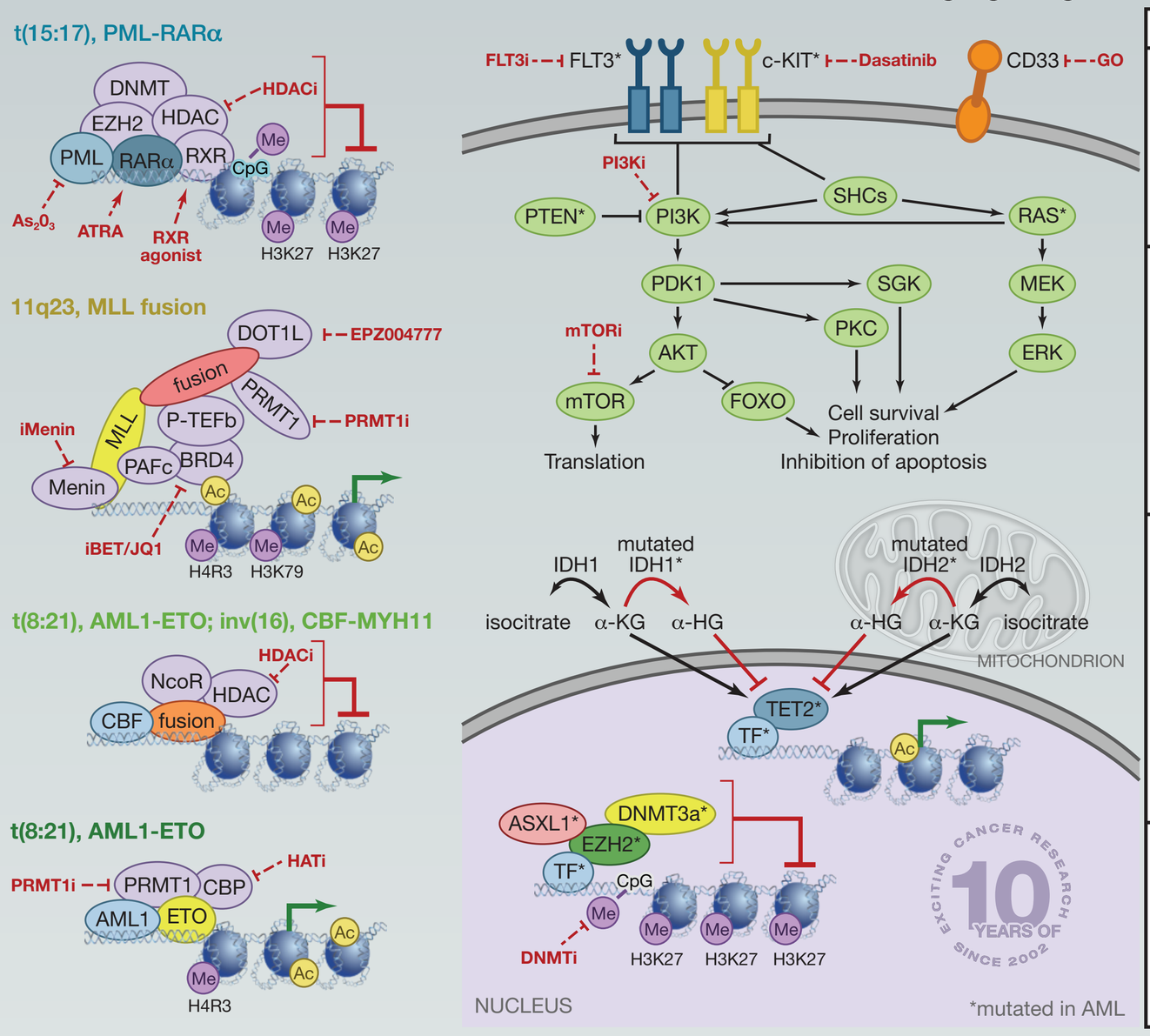
Clinical Features and Risk Stratification of AML

Prognostic category	Favorable risk (5 yr OS: 45%-80%)		Intermediate risk (5 yr OS: 20%-40%)		Adverse risk (5 yr OS: 5%-20%)	
	40%-45% of AML cases		25%-35% of AML cases		25%-30% of AML cases	
	Aberration	Frequency (%)	Aberration	Frequency (%)	Aberration	Frequency (%)
	• t(15:17)	7-12	• NK with *FLT3*-ITD	15-20	• 11q23,	3-5
	• t(8:21)	5-8	• NK with NPM^{WT} & no *FLT3*-ITD	10-17	• inv(3)/t(3;3)/*EVI-1*	~1
	• inv(16)	5-8	• t(9:11)	2-3	• t(6;9)/*DEK-NUP214*	~1
	• NK with NPM^{mut} & no *FLT3*-ITD	18-25	• Other cytogenetic abnormalities not included elsewhere	5-8	• -7/7q-	3-5
	• NK with biallelic $CEBPA^{mut}$	6-12			• -5/5q-	2-3
					• 17p deletions	~2
					• CK	10-12
Current therapies	Standard induction cytotoxic therapy ("3+7"), followed by postremission therapy with high dose cytarabine ATRA as a differentiating agent with anthracycline based chemotherapy in t(15;17)		Standard induction cytotoxic therapy ("3+7"), followed by postremission consolidation Allogeneic HSCT should be considered as main modality of consolidation, especially in patients with *FLT3*-ITD		Standard induction cytotoxic therapy ("3+7"), although dismal outcome with chemotherapy alone Allogeneic HSCT should be offered in clinical remission 1 Consider use of investigational and novel agents	

Cytogenetic Aberrations in AML

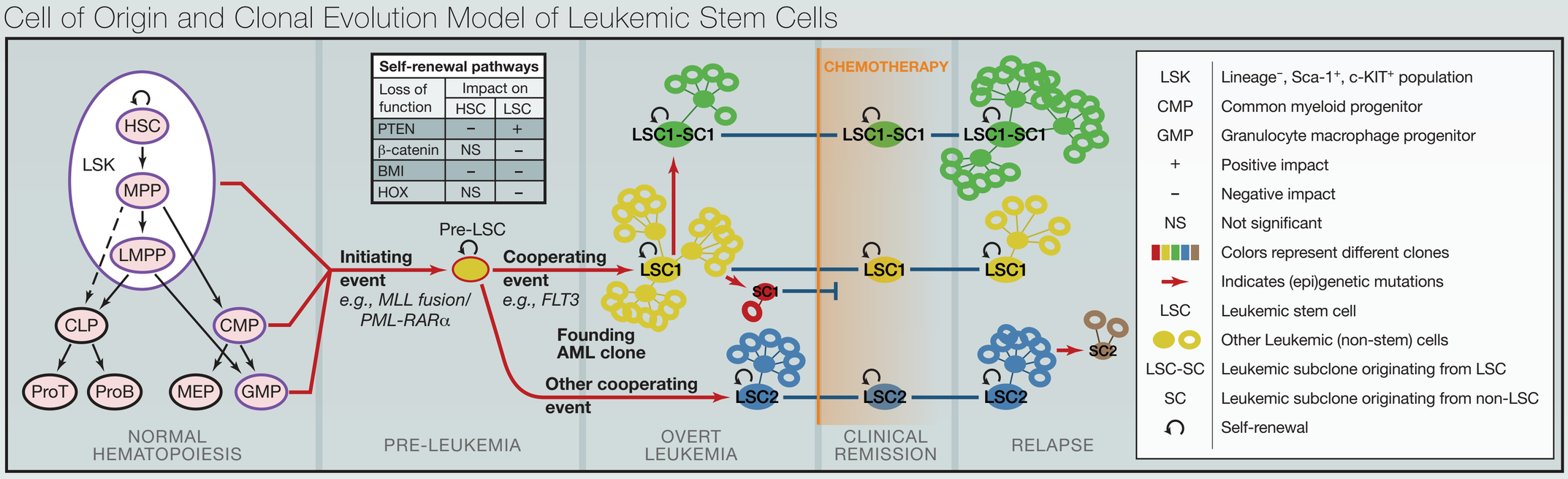


Molecular Mechanisms, Recurrent Gene Mutations, and Emerging Targeted Therapies in AML



	Gene	Frequency (in NK-AML) and comments
Signalling	*FLT3*-ITD	20%-25% (28%-35%); High blast count; Poor prognosis especially in cases with high mutant to WT allelic ratio
	FLT3-TKD	5%-7% (10%-14%); Prognostic impact remains controversial
	NRAS	10% (9%-14%); Enriched in CBF AML; Prognosis unknown
	C-KIT	<5% (<5%); 25-30% in CBF leukaemia
	PTEN	<2% (2%); Prognosis unknown
Transcription factors (TF)	*NPM1*	25%-30% (40%-65%); M4 blast morphology lacks CD34 expression; Hox gene upregulation; Favorable prognosis in the presence of $FLT3^{WT}$; Female preponderance
	CEBPA	5%-10% (10-19%); Favorable prognosis if biallelic mutation
	RUNX1	5%-13% (6-25%); Enriched in trisomy 13 and FAB M0; Poor prognosis
	WT1	10% (10%-13%); Associated with M0 FAB type; Poor prognosis
	TP53	2%-4% (<2%); Predominantly in CK-AML; Very poor prognosis
Epigenetic modifiers	*DNMT3A*	20%-25% (32%-35%); Heterozygous R882 mutations account for 40%-60% of mutations; Poor prognosis in NK-AML
	IDH1/IDH2	12%-22% (25%-30%); Mutant *IDH1 & 2* are mutually exclusive; *IDH1* mutations enriched in patients with $NPM1^{mut}$; IDH1 is localized in cytoplasm and peroxisomes
	TET2	7%-15% (15%-23%); Mutually exclusive to *IDH1/2* mutations; More prevalent in secondary AML especially MPN
	ASXL1	3% (3%-5%); Poor prognosis
	EZH2	<2% (<1%); Enriched in MDS/MPN; Prognosis unknown
	MLL-PTD	<2% (2%-5%); Enriched in trisomy 11
Overexpressed	*EVI-1*	Deregulated in inv(3)(q21q26); Poor prognosis
	MN1	Poor response to chemotherapy; Correlated with NPM^{WT} and high BAALC expression
	BAALC	High expression in NK and +8; Poor prognosis
	ERG	Poor prognosis in CK and NK AML
	miR-181	Increased in FAB M1/M2, $CEBPA^{mut}$; Favorable prognosis

Cell of Origin and Clonal Evolution Model of Leukemic Stem Cells



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