Cytogenetics in the management of hematological malignancies: an overview of alternative technologies for cytogenetic characterization

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Table 1: Characteristics of alternative technology and the spectrum of detectable/non-detectable chromosomal abnormalities

	CBA	FISH	CMA	MLPA	OGM	LD-RTPCR	Chromatin conformation analysis	LR-WGS	RNA-seq
Technical considerations									
Matrix	Chromosomes in dividing cells	DNA in interphase nuclei and metaphase	DNA	DNA	DNA	RNA	DNA	DNA	RNA
Prior cell culture	☑	possible	possible	☑	possible	☑	☑	possible	☑
Cytogenetic pellet extraction	NA	NA	☑	☑	under development	NA	NA	under development	NA
DNA quality	NA	NA	high quality	high quality	UHMW (> 150kb)	NA	all (FFPE included)	high quality	NA
Coverage	whole	targeted	whole	targeted	whole	targeted	whole (Hi-C) and targeted (FFPE-TLC)	whole	whole or targeted
Resolution	5-10 Mb	150 kb	30 kb	1b to 80 Mb	> 500pb or > 5kb depending on pipeline	100-1000 bp	up to 35kb in Hi-C	SNV	gene level
Sensibility	1-3 out of 20 metaphases	1-5%	25-30%	25-30%	5~10% SV / 20% CNA	20%	up to 5%	20-30%	5-10%
Sub-clone detection	1-3 out of 20 metaphases	1-5%	> 30%	> 30%	5~10% SV / 20% CNA	No	if more than 5%	20-30%	5-10%

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					SV detection				
Balanced translocation with fusion gene	☑	☑	No	No	☑	☑	☑	☑	☑
Unbalanced translocation with fusion gene	☑	☑	☑	No	☑	☑	☑	☑	☑
Balanced translocation with gene overexpression	☑	☑	No	No	☑	No	☑	☑	☑
Unbalanced translocation with gene overexpression	☑	☑	☑	No	☑	No	☑	☑	☑
Whole-arm translocation (Robertsonian type)	☑	☑	No	No	No	No	☑	No	No
Inversion (para- and pericentric)	☑	☑	No	No	☑	☑ if transcript	☑	☑	☑
Chromoanagenesis	possible	☑	☑ [1]	No	☑	No	☑	☑	☑

[1] Chromoanagenesis may be suspected on highly variable CNA profile

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CNA detection									
CNA size	5-10 Mb	150 kb	30 kb	1 kb	500 kb	No	up to 35 kb in Hi-C	SNV	challenging
Haploidy, triploidy, tetraploidy,	☑	☑	aSNP	☑	☑+/- [2]	No	☑+/- [3]	☑	☑+/- [4]
Nullosomy, monosomy, trisomy, tetrasomy, etc.	☑	☑	☑	☑	☑	No	☑	☑	☑
Intra-chromosomal CNA	☑	☑	☑	☑	☑	No	☑	☑	☑
Other abnormality detection									
SNV	No	No	No	No	No	No	☑	☑	☑
CN-LOH	No	No	aSNP	No	☑	No	☑	No	No
Routine implementation									
Cost	low	low	low	low	high	low	high	high	high
Turnaround time	2 d	4 h to 2 d	3 d	1-2 d	3-4 d	3 d	3-4 d	15-21 d	15-21 d
Bioinformatic software availability	NA	NA	commercially available	commercially available	included with hardware	local development	local development	local development	local development

[2] Theoretically not detectable but indirect detection possible for haploidies via the loss of heterozygosity detection tool. [3] Indirect detection possible by bioinformatic tool studying allele frequencies of inherited variants. [4] Depending on the bioinformatics tools used

Figure 1: Chart illustrating the detection capabilities of technology by type of chromosomal abnormality