Table A5.1. Commonly used methods for detection of genetically variant cells

Method	Types of Abberations Detected	Resolution	Sensitivity	Cost	Speed	Advantages	Disadvantages
Karyotyping	Aneuploidy Duplications/ deletions Balanced and unbalanced translocations	5-10Mb (depending on the level of banding and chromosomal region)	Depends on the number of metaphases analyzed, e.g., 20 metaphases analyzed can exclude 15% mosaicism	Moderate	Slow	Provides an overview of the entire chromosome complement in a cell in a single assay. Makes a distinction of individual clones. Can detect balanced translocations.	Requires testing proliferative cells. Has limited resolution. Requires specialist skills.
SNP/CGH arrays	Aneuploidy Duplications/ deletions Unbalanced translocations	10-100kb	Typically, 10-20%	Moderate	Moderate	Can be performed on non-proliferative cells. Provide higher resolution than karyotyping, allowing the detection of small copy number variants.	Cannot detect balanced translocations or inversions. Cannot detect very small copy number changes.

eSNP karyotyping	Aneuploidy Duplications/ deletions	5-10Mb	Depends on the sequencing depth	Moderate	Slow	Allows using existing RNAseq data to assess for presence of genetic changes and thereby both genetic integrity and expression analyses can be done on the same sample.	Limited resolution and sensitivity.
qPCR/ ddPCR	Single nucleotide variants Copy number variants Aneuploidy	>1bp	Depends on the type of abnormality analyzed; for SNVs the sensitivity can be <0.1%; for copy number changes it is typically around 10%	Low	Rapid	Accessible to any standard lab. Allows rapid turnover. Relatively cheap.	Targeted approach, i.e., only detects aberrations at predetermined loci.
FISH	Aneuploidy Copy number variations Gene fusions	100-1Mb	Depends on the number of cells examined and the type of an aberration assessed; e.g., for whole chromosome gains, screening of 100 cells typically yields 5% sensitivity	Moderate	Moderate	Can be performed on proliferative or non-proliferative cells. Can afford higher resolution and sensitivity compared to karyotyping. Makes a distinction of individual clones. Limited resolution and sensitivity.	Targeted approach, i.e., only detects aberrations at predetermined loci. Tandem duplications can be difficult to detect, because of the overlap in the signal.

Next generation low-pass sequencing	Aneuploidy Copy number variations	0.5-5Mb (depending on the sequencing depth)	Depends on the sequencing depth	Moderate	Moderate	Can be performed on proliferative or non-proliferative cells. High throughput.	
Next generation deep sequencing (whole genome (WGS) or whole exome (WES))	Sequence changes Indels Copy number variations	1bp	Depends on the sequencing depth	High	Slow	Nucleotide-level resolution allowing detection of single nucleotide variants. High throughput. May require ethics approval.	High demands for data storage and relatively long time for bioinformatics processing (both are reduced in WES, but WES only interrogates around 1% of the genome).

This table was adapted from McIntire et al., 2020.