Genomic Integrity G-Banding for Cell & Gene Therapy Drug Products

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G-band karyotyping is utilized in clinical cytogenetics to detect chromosome abnormalities for the diagnosis of malignancies or congenital disorders, e.g., trisomy 21 (Down's syndrome). Such abnormalities are expected to occur at very high prevalence; therefore, analysis of 20 cells per sample is standard practice. When pools of cells are edited via CRISPR or other methods, the chromosomal rearrangements that may be generated are more randomized, and certainly at lower prevalence than a constitutive disorder. Based on an identified need from our customers for genomic integrity data to inform their gene and cell therapy treatment programs we reformatted the data output. The resulting analysis maintains the integrity of the method and whole genome de novo value of karyotype analysis, while focusing the data on differences from a reference and moving away from terms like "abnormal" and "clonal". The data are presented in a prevalence based report and there is no judgement placed on the result, only a statistical value of significance.

KromaTiD

Individual Karyotype Reports

Reference Sample

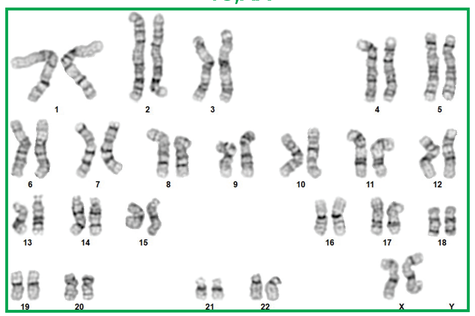
Karyotype	# Cells
45,X,-X	1
45,XX,-10	1
45,XX,-14	1
45,XX,-15,chtb(2)(q)	1
45,XX,-19	1
45,XX,-2,del(4)(p15)	1
45,XX,-20	1
45,XX,-22	1
45,XX,-3	1
45,XX,-6	1
45,XX,-8	1
46,X,del(X)(q22)	1
46,XX	77
46,XX,chrb(10)(p)	1
46,XX,chrb(6)(p)	1
46,XX,chtb(1)(p)	1
46,XX,chtb(16)(p)	1
46,XX,del(6)(q15)	1
46,XX,del(9)(p21)	1
46,XX,inv(2)(p11.2q31)	1
46,XX,t(5:11)(q31;q13)	1
47,XX,+11	1
47,XX,+M	1
47,XX,+X	18

Comparison → ?

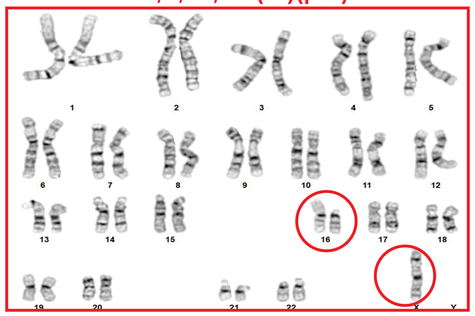
Treated Sample

Karyotype	# Cells
44,XX,-6,-11	1
44,XX,der(3;6)(p21.3;p21),-18	1
44,XX,dic(6;11)p25;p15),-9	1
45,X,-X	1
45,X,-X,del(16)(p12)	3
45,X,-X,t(15;16)q21;p13.3)	4
45,XX,-13	1
45,XX,-14	2
45,XX,-15	1
45,XX,-16	1
45,XX,-18	1
45,XX,-2	1
45,XX,-20	2
45,XX,-3,del(16)(p12)	1
45,XX,del(16)(p12),-19	1
45,XX,-4	1
45,XX,-3,del(16)(p12),-21	1
45,XX,del(3)(p10),der(14;16)p11.2;p13.2)	1
45,XX,der(14;16)(p11.2;p13.2)	3
45,XX,t(15;16)(q21;p13.2),-19	1
45,XX,t(15;16)(q21;p13.2),-21	1
46,X,-X,+M	3
46,XX	35
46,XX,+2,-16	1
46,XX,add(16)(p13.3)	1
46,XX,chrb(3)(p)	1
46,XX,chtb(10)(q)	1
46,XX,chtb(16)(q)	1
46,XX,chtb(4)(q)	1
46,XX,del(14)(q11.2)	1
46,XX,del(14)(q11.2),add(16)(p13.3)	1
46,XX,del(15)(q21),add(16)(p13.3)	1
46,XX,del(16)(p12)	5
46,XX,der(11)t(11;17)(p11.2;q21)	1
46,XX,dup(9)(q21q31),del(19)(p13.2)	1
46,XX,t(15;16)(q21;p13.3)	1
46,XX,t(3;11)(p24;p11.2)	1
46,XX,t(3;11)(p24;p11.2),add(16)(p13.3)	2
46,XX,t(3;11)(p24;p11.2),del16)(p13.2)	1
47,XX,+2	1
47,XX,+7	1
47,XX,+X	1
47,XX,+del(3)(p25),+M	1
70,XXX,del(14)(q11.2),del(16)(p13.2),+M	1
90,XX,-X,-X,del(16)(p12)x2	1
91,XX,-X,-X,-6,-11,-14,+4M	1
46,XX,del(14)(q11.2),t(15;16)(q21;p13.3)	2
46,XX,del(16)(p13.2)	1

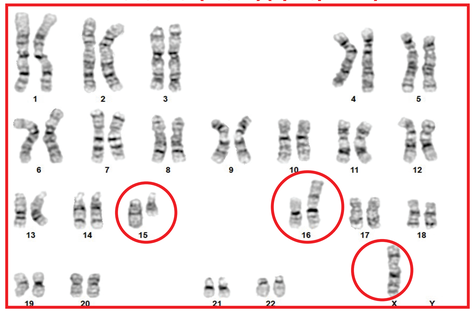
46,XX



46,X,−X,del(16)(p12)



46,X,−X,t(15;16)(q21;p13.3)



Genomic Integrity Comparison Report

Variant Frequency - Reference Sample

Karyotype	Category	# Events	# Cells	% of Cells
chtb(1)(p)	chromatid_break	1	1	1
chtb(16)(q)	chromatid_break	1	1	1
chtb(2)(q)	chromatid_break	1	1	1
chrb(10)(p)	chromosome_break	1	1	1
chrb(6)(p)	chromosome_break	1	1	1
del(4)(p15)	deletion	1	1	1
del(6)(q15)	deletion	1	1	1
del(9)(p21)	deletion	1	1	1
del(X)(q22)	deletion	1	1	1
11	gain	1	1	1
+X	gain	1	1	1
inv(2)(p11.2q31)	inversion	1	1	1
-2	loss	1	1	1
-3	loss	1	1	1
-6	loss	1	1	1
-8	loss	1	1	1
-10	loss	1	1	1
-14	loss	1	1	1
-15	loss	1	1	1
-19	loss	1	1	1
-20	loss	1	1	1
-22	loss	1	1	1
-X	loss	1	1	1
+M	marker_chromosome	1	1	1
t(5;11)(q31;q13)	translocation	1	1	1

Ploidy Comparison

Category	Reference # Cells	Treated # Cells	Fisher's Exact p.value	p-value significant < .05
Haploid	0	0	1	N/A
Diploid	100	97	0.246	No
Triploid	0	1	1	No
Tetraploid	0	2	0.497	No
Polyploid	0	0	1	N/A

Variant Frequency - Treated Sample

Karyotype	Category	# Events	# Cells	% of Cells
add(16)(p13.3)	additional_material_unkown_origin	5	5	5
chtb(1)(p)	chromatid_break	1	1	1
chtb(10)(q)	chromatid_break	1	1	1
chtb(16)(q)	chromatid_break	1	1	1
chtb(4)(q)	chromatid_break	1	1	1
chrb(3)(p)	chromosome_break	1	1	1
del(14)(q11.2)	deletion	5	5	5
del(15)(q21)	deletion	1	1	1
del(16)(p12)	deletion	12	12	12
del(16)(p12)x2	deletion	2	1	1
del(16)(p13.2)	deletion	3	3	3
del(19)(p13.2)	deletion	1	1	1
del(3)(p10)	deletion	1	1	1
del(3)(p25)	deletion	1	1	1
der(11)t(11;17)(p11.2;q21)	derivative_chromosome	1	1	1
der(14;16)(p11.2;p13.2)	derivative_chromosome	4	4	4
der(3;6)(p21.3;p21)	derivative_chromosome	1	1	1
dic(6;11)(p25;p15)	dicentric	1	1	1
dup(9)(q21q31)	duplication	1	1	1
2	gain	2	2	2
7	gain	1	1	1
+X	gain	1	1	1
-2	loss	1	1	1
-3	loss	1	1	1
-4	loss	1	1	1
-6	loss	2	2	2
-9	loss	1	1	1
-11	loss	2	2	2
-13	loss	1	1	1
-14	loss	3	3	3
-15	loss	1	1	1
-16	loss	2	2	2
-18	loss	2	2	2
-19	loss	2	2	2
-20	loss	2	2	2
-21	loss	2	2	2
-X	loss	15	13	13
+2M	marker_chromosome	4	1	1
+M	marker_chromosome	5	5	5
t(15;16)(q21;p13.3)	translocation	9	9	9
t(3;11)(p24;p11.2)	translocation	4	4	4

Variant Category Comparison

Category	Reference # Cells	Treated # Cells	Fisher's Exact p.value	p-value significant < .05
No Events	77	35	< 0.0001	Yes
Anueploidy *(Loss + Gain)	13	35	0.0004	Yes
Loss	11	32	0.0004	Yes
Gain	2	4	0.683	No
Acentric Fragment	0	0	1.0	N/A
Additional Material *(Unknown Origin)	0	5	0.59	No
Constitutional Anamoly	0	0	1	N/A
Chromosome Break	2	1	1	No
Chromatid Break	3	4	1	No
Chromothripsis	0	0	1	N/A
Deletion	4	24	0	Yes
Derivative Chromosome	0	6	0.029	Yes
Dicentric	0	1	1	No
Double minute	0	0	1	N/A
Duplication	0	1	1	No
Endoreduplication	0	0	1	N/A
Fragile Site	0	0	1	N/A
Heterochromatin (constitutive)	0	0	1	N/A
Homogenously Staining Region	0	0	1	N/A
Isochromosome	0	0	1	N/A
Isodicentric	0	0	1	N/A
Insertion	0	0	1	N/A
Inversion	1	0	1	No
Marker Chromosome	1	6	0.118	No
Quadriradial	0	0	1	N/A
Ring Chromosome	0	0	1	N/A
Translocation	1	14	0.001	Yes
Triradial	0	0	1	N/A

Specific Variant Comparison

Category	Reference # Cells	Treated # Cells	Fisher's Exact p.value	p-value significant < .05
del(16)(p12)	0	12	0.0003	Yes
-X	1	13	0.001	Yes
t(15;16)(q21;p13.3)	0	9	0.003	Yes
del(14)(q11.2)	0	5	0.059	No
add(16)(p13.3)	0	5	0.059	No
t(3;11)(p24;p11.2)	0	4	0.121	No
der(14;16)(p11.2;p13.2)	0	4	0.121	No
+M	1	8	0.212	No
del(16)(p13.2)	0	3	0.246	No
-18	0	2	0.497	No
-21	0	2	0.497	No
-11	0	2	0.497	No
2	0	2	0.497	No
-16	0	2	0.497	No
-14	1	3	0.621	No