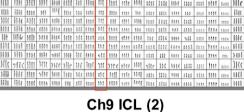
Expanded View Figures

Figure EV1. Comprehensive karyotypic characterization of the late passage ICL lines.

A–D Karyotypic analysis of later passage, control and ICL of a replicate (#2) of Ch12 (A), Ch10 (B), Ch14 (C) and Ch9 (D) lines. All chromosomes are shown for 20 metaphases. Target chromosomes are boxed in red.

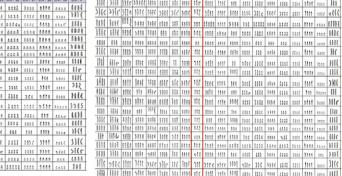
© 2017 The Authors

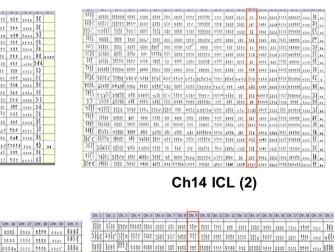




Chr. 1	Chr. 2	Chr. 3	Chr. 4	Chr. 5	Chr. 6	Chr. 7	Chr. 8	Chr. 9	Chr. 10	Chr. 11	Chr. 12	Chr. 13	Chr. 14	Chr. 15	Chr. 16	Chr. 17	Chr. 18	Chr. 19	Chr. X
111	8998	3184	\$831	1962	808	124	99At	\$\$\$\$	3885	4088	9999	204	1424	1224	6226	1011	\$850	64.4.6	
1111	3333	1116	1111	1111	1111	111	6698	1111	881	1111	0000	0000	1111	\$998	1038	0.014	1552	8684	11)(
1111	3363	1111	\$192	9998	8998	111	1461	5262	1111	0.000	8696	2234	11111			85.65	8655	4555	1111
8888	8686	8888	888	****	8888	888		0000	0000	0000	8898	8080	8660	0100	6666	0000	8688	8000	8889
3111	1988	88.88	1108	1686	8888				2325			5010		2000	4454	0000	8445	4844	8888
Rage	8888	8825	2262		0000		8690		0000						4444		6468		2898
2011	8888	88.00	8888	888	8998	868			1111			8268		6666	0200		6888		8868
		3141	3316	8668	3111	311	1111		10000	1778	2111	0000	0000	883.8	2615	3845	1111	1111	1111
>116	3310	2024	5142	3968	3441	111			33311		3365	1144	828	6688	1484	1111	1116	\$696	115
1111	1111	\$160	HII	1111	3894	211		2111	2882	2000	264	3886	1414	2655	4516	3116	160	5555	111(
1111	(())	10	1(1)	2115	1111	110	1445	111	1111	1111	2116	11(5	1111	310	2222	3350	3316	1111	>15
2114)111	3][6	Hic	3)16	111<	yie	2115	MIC	>}}8	1114	>111	2222	9191	3438	1111	388	1111	6688	1114
3115	1131	1114	5111	3988	1984	he	5864	3111	lite	1610	1110	2410	8868	1314	1	1000	3680	12265	1215
file	8691	5885	111	3115	1111	688	1200	35fe	3368	115 5	194	311	111<	0.000	6003	3881	111	44.40	113
3962	3388	3634	3111	3999	9989	886		-128	0000	1111	8496	1005	3328	4455	2004	5050	6825	4448	8668
)))((111	1111	3113	1111	1111	11	2999	1111	3131	5112	\$\$£*	1111	2111	1111	111	315	(1))	\$1.04)((
))(r	22/1	111)))(1112	5/16	111	MI	itte	ille	(11)	1)(1	1011	101)111	1111	143 (3711	1411	531(
1115	2110	2110	2115	1112	1110	36)))r	1114	1111	1158	1141	1115	1111	me	1111	2000	2115	\$144	2)(5
8888	8888	ABAR	400	8888	8989	285		0090	9886	\$8.8.8		0.0.0	1000		6004	0000	8888	444	6888

Ch9 Control (2)



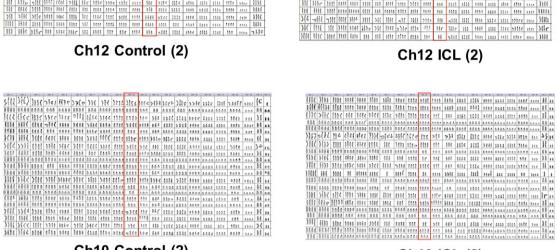


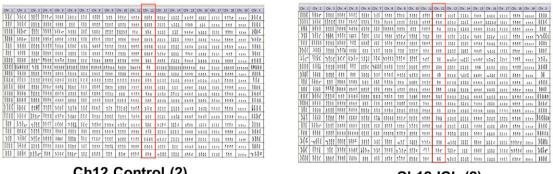
0+.1	Ov. 2	04.3	Ov. 4	Ov. 5	Ov. 6	04.7	Ov.8	Ov.9	City, 10	Ov. 11	Ov. 12	0+.13	Ov. 14	Ov. 15	Ov. 16	Ov. 17	Ov. 18	Cr. 19	OV X	O.
110	7117	1576	1150	1100	1010	({{	31114	1110	sile	311	£ 6 §	alat	1:33	1116	1564		316	3356	11	
110	life	>>1<<	1110	186	1114	111	115%	3110	lete	630	563	• 2 2 e	101	60.04	11>5	1111	334	4445	1(
(11)	1111	1111	3144	1111	100	248	(1)))	4172	1111	2.63	689	1000	1724	6304	340 A	105e	211	7 A & &	21	
Mr	99866	1111	8888	9988	848	\$84		1111	0000	101	684	1140	0.8		0404	0045	38.6	****	11	
110	1111	1600	53.8	8919	lite	111	11111	6113	11:11	511	889	2050	0010	5461	1004	5 0 5 C	4.5.5		11	
117	195	2111	111	334	110	01	11711	111	1111	2315	414	210	\$2	1111	\$895	101	111	44.5)(
115	sil<	-110	111	1376	1)]<	236	(()())	\$211	1105	110		1221	1611	3360	1111	3338	111	\$155){(
))((>(1(11(1	HIC	3111	3){{	111	fffce.	3111	1111	141	1951	1711	{[>	Ille	6111	911	101	:110	1)	
111	1111	111<	1111	3386	3486	120	3862e	3250	\$) et	100	346	111	0152	6133	4495	6830	315	4445	11	
)){	2016	3386	3131	8866	1114	111	68888	1111	224	111	144	\$248	1244		\$448	3.3 3 0	814	0303	11	
110	39888	8888	1100	3868	3111	111	8694	\$552	3352	2.6.2	888	2000	1ca1		42aa	1111	346	4444	11	
36	2110	1){{	2)15	1110	1114	540	11441	>1<	1115	3900	168	5410	211c	3536	1000	3455	335	4554	>>	
)[]	(1))(2110	3484	5992	1){c	243	39994	0000	2243	111	He	3249	310	3866	0000	0000	111	5885	38	
11>	>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>	211	3111	111	1114	110	10164	1000	1133	101	11	2225	1114	\$\$336	1010	1112	105		11	
111	8665	3998	488	****	8493	\$55	a319a	3003	aste	355	868	0.0.0	000		1000		224		н	
)11	444	1165	:111	101	3313	117	stile	secc	\$ [[e	577	111	11(1	1114	104	021	1141	110		11	
111	11165	1114	1341	3138	1111	134	28191	1100	648	14.5	386	e11	1111	steet	1220	1041	0.st		11	
a(c))(jv	5)()	\$16	101	10}	1)(1115	() c	34<	301	>>1	101	311	etste	141	(1) ((21) (154	1)	
\$16	fles	1111	6999	135C	8883	144	>398c	1111	4919	111	666	9110	1225	3 695	6485	c0 4 2	6.68	0344	11	
11()))))	1510	3888	9498	81136	\$60	000.	11.00	11111	111	111		1114	6455	\$5.00		111		11	
/15	7551	8102	9991	11018				4 C								2450	544	0000	9.5	

Ch12 Control (2)

			С	h	10	C	on	tre	ol	(2	2)								
*.3	Ov. 4	04.3	04.6	0+.7	Ov. 8	Ov. 5	Ow. 10	Ov. 11	Ow. 12	0= 11	Ov. 14	Or. 15	Ov. 16	Ov. 17	Ow. 18	Ov. 19	OV X	Ow.Y	
>(1454	3340		111))/)†	1114	3880 3886 1888	211	£111		1033	3833 6886	1004		386	3356 1115	11 1())		
100	8888	8988	1110	121	07598 00000 00000	1111	1000 1000 1000	243	888 888	2000	08	5050 5050	2404 2424	0000 0000	384	7466 8888 8088	11		
11	111 311 111 C	334 3376 3467	11c		1111	5211	1111	>>><	998	1111	82 1693	8944 335c	3114	3338	111	53.5 5165){{		
11	1111	2386	5711 588C 1884	225 225	18868 e 1888 e	3111 3252 3133	1993 1993 1994	141	844 385. 385	1751 130 1344	23> 0134 0144	111c 111c	6888 6488 8488	2010 2010 2010	344	233C 6365 0365	1) 7(1(_	
100	1100 73ec	8988 8986	3191 >111	318 5{c		2002 >1<	8888 9369	111 2]+6	888 168	2000	1030 2514	3586	4244 200 C	0000 3499	300	4484 4686	>>		
10	3484 3848 488	9992 8892	3380	316	39999e 3986e 9389e	1000 3460	2243	111	110	20112	31c 1544	5888 55356	0068 1088	111	111	5885 8888 8888	11		
111	658	11036	1.6483	1932	22125	3003	aste	355	869	888	101	1214	3000	8555	211	5565	11		







Α

В

A Chr. 1	Chr. 2	Chr. 3	Chr. 4	Chr. 5	Chr. 6	Chr. 7	Chr. 8	Chr. 9	Chr. 10	Chr. 11	Chr. 12	Chr. 13	Chr. 14	Chr. 15	Chr. 16	Chr. 17	Chr. 18	Chr. 19	Chr. X	Chr. 1	Chr. 2	Chr. 3	Chr. 4	Chr. 5	Chr. 6	Chr. 7	Chr. 8	Chr. 9	Chr. 10	Chr. 11	Chr. 12	Chr. 13	Chr. 14	Chr. 15	Chr. 16	Chr. 17	Chr. 18	Chr. 19	Chr. X
392	331	5338	215	3))((3))(10	1111	512	1341	151	XC	110.	\$115	1111	(1)	110	Itre	:0))(18888	838	8888	888	11		0.0.0	888	0.8.0	480*	****	6088		646	888	86	6000	622
1)1	111	3111	111	1111	())()	111	1111	1111	288¢	5 (31	m	110*	11010	4111	101	114	1111	me	11	15	3)	1996	10	5851	31	4	2136	31	31	110	88	800	2	1111	80	1159	558	300	11
111	IUSI	1111	1110	1020	11154	10	11111	2411	000	3114	1115	1119	3111	111111	111	11111	11111	mit	11	88	18	0.000	999	388	RA	88	1965	88	88	28	86	010	11	8008	86	9988	84	888	88
110	1)11	1110		1161									2221					3	31	21	and the	1000	21	9.0	0.00	11		t.,	89	110	98	81	2)	1011	- 11	1111	111	010	68
111)11	11		1111			1111			*****			111						1	<u>)</u>	38	118	33	58	38	11	3155,	310	684	****	9.9	00	<u>1</u> °	5111	0.0	644	366	484	91
111	(1)(1111		112		21	1111	2()	1110	14	116		1)10						+		88	898€*	11	88.e	98	86	erg	11	89	981	88	000	\$1	8988	8.6	888	966*	545	88
111	110			stu		11	1631	hil	1105	6143	689"		1111						11	58	898	0186 1225	886	1000	888	69 88	9998 99986	88 60	848	384	1999. 1999.	8584	8886	8998	6225	106	108	356	8888 8888
1(1	1111	1110	111	1111	111			0201					100						11	11	888	6030		8888		50	10100	20	480	88 888	999.	000°	0000	8888		888 888	686		****
)((311)()(15			1(12			31][11						111
331	1111	\$111	111	1115	щ	11	1111						1111								31	710						1		3)]{(111	'	2100	10	715	111	411	386
333	2111	1111	111	1111	111	11	1111	11	1111	3111	111	111.	1111	****	in	1111	111)	11			84866	285	3398	388	ic.	1998		699	991	166.	698*	9381		44.0	108	688	3666	188
((()(c	111((1111			1111	1211	1111	110	01	13'	1112	1111	Itte	\$111	1111	mel	()	121	15	2114)[13	15	12	2.13	25	1	111	74	12	01	111	11	11	H.	198	Х
11))(1111			XIII	211	1)11	1111	1)**	100.	000	MM	111	1111	1111	113	11	17	23	39381	H	10	23	10	1111	\$4	8	9958	34	198	21	4948	2.5	000	251	11	8
De	1)(1412									3714						11	11	186	1111	110	2121	ne	38	()))	11	216	811	\$\$6°	2110	111	6445	210	848	181	111	1168
141	1111	111((1)1	3111	1111	111	171((11)	1111	11118	101	1111	111	(1)))	m	1111	nit	m	1(1	888	19101	111	1111	1111	88	11116	11	6999	102	461	1111	1111	8988	111	116	655	48	1861
111	111	(11)					IH	1110	()))	sitt	()).	14	1111	*****	115	1111	1111	sol.	11	83	888	88988	8688	8888	888	86	8889	65	88	6008	888'	0000*	000		484	866	455	858	888
611	111	883338	111	1691	1111	88	111	11	6868	2431	949.	1001	63.63	10050	111	1111	6888	2445	11	11	160	Slife	311	1111	den la compañía de la	21	1111	111	996	189	1999.	11	1111	1111	211	196	110	2005	\$61

Tumor Karyotype – Ch10 Control

Tumor Karyotype – Ch10 ICL

(hr 1	Chr. 2	Chr. 3	Chr. 4	Chr. 5	Chr. 6	Chy 7	Chr.8	Chy 9	Chr 10	Chy 11	Chr. 12	Chy 13	The 14	Chy 15	Chy 16	Chr 17	Chy 18	Chy 19	Chy. X	Chr. 1	Chr. 2	Chr.
111	000	1411	0000	000	101	411	0000	1010		100	664.0	0.0	000	0000		656	16.0	440.4	1111	1	1111	81
233	198	111	0090	1888	111	118	1111	1	8888	15.0	8444	1111	080	444	1111	01.0		4444	2868	215	1968	333
11	111	8868	8888	888	111	666	9998	0000	8888	0.0	8888	000	88	666	1411	200	3684	4444	1000	200	8880	110
Control of Control	199	1991	1111	688	1111	22	1000	111	498	111	1000	111	665	668	1000	220	0060	0.000	111)	888	2222	660
101	111	13 ((111	111	411	111	111	1010	1111	116	6138	1	116	141	11005	111	1111	****	1111	222	9888	688
111	(1)	1)((1776	(1)	101	115	1111	111	111	111		033	245	113	1111	686	110		()()	888	8088	0.8.0
111	(li	11(2	1110	111(7	10	111	the	10	110	111	(())	11	61	ter	1112	102	inc	*****	1();	41	3888	111
111	888	3996	8888	6.8.8	8828	111	888	008	668	000		081	880	0.0.0	8448	888	0.000	44.65	111	808	180	228
618	111	1111	1111	58	111	111	1010	1	000	111	1100		858	44.5	4414	105	1000		1161	9.8.8	9194	091
611	111	3888	6968	888	688	886	9999	10	0008	111		000	120	100	4335	885	10.66	45.8.6	00000	311	iie.	11)
11(711	1016	(11)	311	3111	331	6333	111	813	111	1111	321	211	011	1111	888			111	880		8695
282	888	8888	8984	889	888	805	8008	8.6	0.0.0	888	6166	5556	000	65.6	440.4	0.00	665	0.000	****			
111	111	8888	8898	RRR	0.00	611	0080	44	584	11.0	ABBR	1010	255		04A§	A50	0.000		8818	996	2028	(1)
M)1	181	1111	185		610	88	14193	10	0000	44.0	9.0		000	0.00	0100	124	55.6		8888		ARRAR	000
111	-	9969	1125	642	919	860	1114	200	111	111	9200	4948	45.6	646	4644	646	60.68	4455	686			
115	311	011	1111	31	211	31	13100	110	ltte	11	1011	111	222	3312	51115	2201	atte	12110	111	Ren	889	626
				-	-	-		-		-				-	-					200	8888	681

Tumor Karyotype – Ch14 Control

Chr. 3	Chr. 4	Chr. 5	Chr. 6	Chr. 7	Chr. 8	Chr. 9	Chr. 10	Chr. 11	Chr. 12	Chr. 13	Chr. 14	Chr. 15	Chr. 16	Chr. 17	Chr. 18	Chr. 19	Chr. X
510	8888	88888	60				111	111	2.0	661	808	030	****				11110
1166	(()	886	996	225	0000		100	100	1111	10	100	162	11114	0000	260	****	133(1
8888	180	8888	88	111	10000	88	988	644	860	000	10	855	0000	0.0	888	8.8	11111

813	8880	2026	164	8868	1.1	888	16698	88	988	0.0.0	860	838	- 6.2	800	1000	0.0	000	6.5	8382K
888	9998	66018	4545	8888	611	8868		0.0	\$0.8	000	888	1000	ee ĝ	44	0000		000		88888
222	9888	00000	1111	888	888	888	8898	000	0000	000	8666	0.5.0	008	666	2240	008	6.8	4646	88888
888	8998	aabâf.	888	888	888	688		0.0	88.8	000	8666	0000	0.0		4460	8000	0.0	A 8 8	38898
1	8888	1111	\$\$85	8.8	1011	111	89968	181	010	666	1888	88	40 C R	100	22.03	8898	808	85.55	11116
自由意	989			688	888	286		680	000	100		000	408	465	6666	000	0.0	0500	2695
988	9099	0986	4994		888	828	49.804	01	1966	nAn.	688	685	808	444	0000	44493	6.66	4888	88888
3][110	11)16	511	seletes	11	111	10100	111	55.5	355	1116	111	88	62.0	111	611.8	0.00		3211
880	80.08		0000	888	888	000		600	0.0	888	666	0.00	osg	0.00	0000	0008	010		28682
)](1111	endle	2210	6101)	100	10	5463	1111	1011	211	124	60	44	1 6 5 5	140		10.04		20(3)
988	6889	0000	0000	888	8686	000	6606	80	\$0.5	000	4898	000	aag	0000	8668	0000	0.00	0100	28995
888	88888	8888	0000	686	080	666	88888	2020	66	655	0000	88	0.08	0.0.0	0000	00400	0.5	4666	£863.
111	889	83866	0000	988	11	888		0010	494	180	8968	0.5	810	455	1054	8888	600	45364	11166
hit	8888	6898	8868	88	11	181	10010	0000	888	68	80	20	642	68.5	100	8888	815		1111

Tumor Karyotype – Ch14 ICL

OV. 1	Ov.2	OV. 3	QV.4	Qv. 1	OY.6	QY.7	07.8	QY.9	CW. 30	QV. 11	Ov. 12	QW. 13	Qy. 14	Oy. 15	Qv. 26	Ov. 17	Or. 18	Qv. 19	QY.X	Ov. Y
>){	1100)]]{	1111	31111	1984	17	111	11	386	111	1116	2000	31	3885	1:11	1114	10		11	
\$88	111	1111	4888	\$ 6 8 9 8	8368	11	6886	11	226	1111	*****	0.0.0	000	6868	000	60.0	888	0535	111	
388	888	1000		8888	3888	88		11	0000				83		45.8	8888			88	1
818	811	3863	\$ \$ \$ \$	8888	899.6	66	0000	88	8885	stee	888	0000	99	6960	636	1111	0110	0000	11	
311	λ(¢	ШK	\$\$\$\$(3388	1011	31	\$118	31	265	>>=>	111	1111	11	4344	144	() (°	11	1016	11	
1191	828	8688				98	2000	80	0.0.0	1015	9996	0.0	0.0		5 6 8 F	1010		60.00	58	11
89.9	886	8118	0086	8888	9889	88		8.6	698	1000	0808	8298	0.0		00	000	6666	6464	18	
1)5	214	HR	1110	2)()(31115	11	1115	30	2114	3116	310	1010	11	2634	1111	1111	115	1560	11	
111	888	11111	30	21116	111	15	843	11		4414	1011	(111)	2.5		642.6	0111	\$28		11	
218	116	1111	2386	3(115)	23388	56	\$\$\$20	20	314	3110	396		88		220	1111	535	2000	38	
111	110	11110	me	805685	51111	58	1911	55	2396	0101	9695	100	00	8636	330	0000	1016		11	
111	111	1111	3890	11111	1111	21	1110	11	11111	3110	1666	1111		1111	\$232	1111	1111		14	
000	111	1111	1692	10100	1996	\$1	69.0	11	1111	322	833	111	68	4468	415	3526	000	\$556	11	
110	886	1000	1988	3838	8988	88		11	8888	1111	806.6		¢٢	****	\$ 6.6	3 5 5 5	24		\$8)
111	1111	()))	3334	\$1166	111116	111	1000	11	811	111(1)	1111	10000	11		414	1116	111		11	
11	lle	1111	2110	3992	3115	11	1501	11	1115	3998	111	164	11	6984	110	1000		3650		
111	886	1111	3698	94494	8988	68	6886	11	888	1111	9693	0034	88		865	010				
)11	1111	1999 (1111	1074	1111	58	1111	11	0005	1662	3884	111	11	8.6	tte	355¢	1111		51	
211	HC.	1111	311	33106	1116	22	\$ (11	IJ	1111	1112	1111	111	6	6434	111	1115.				(
111	11(1114	1111	1111	()))	11	111	10	111	1111	111	1111	=	****	114	111	111		11	

Tumor Karyotype – Ch9 ICL



1

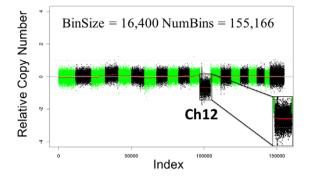
В

	No	Ch9	Control	Tumor
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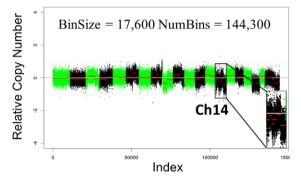
Figure EV2.	Comprehensive karyotypic characterization of the late passage ICL tumor explants.

A-C Karyotypic analysis of later passage, control, and ICL tumor explants derived from the injecting the late passage control and ICL cells of Ch10 (A), Ch14 (B), and Ch9 (C). All chromosomes are shown for 20 metaphases. Target chromosomes are boxed in red. No karyotypes are shown for the Ch9 controls, as they did not form tumors in nude mice.

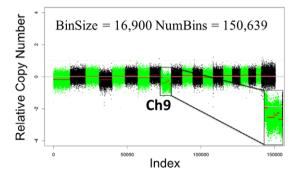
Late Passage – Ch12 ICL normalized to Ch12 Control



Late Passage – Ch14 ICL normalized to Ch14 Control



Late Passage – Ch9 ICL normalized to Ch9 Control



Late Passage – Ch10 ICL normalized to Ch10 Control

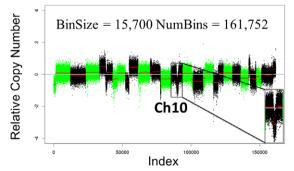


Figure EV3. Global copy number profiles of the late passage ICL MEFs.

A–C Shallow whole-genome sequencing (copy number profiles) of large T antigen immortalized, late passage MEFs after exposure to Cre recombinase and serially sorted for control (hCD2 Plus) and ICL (hCD2 Minus) cells for chromosomes 12, 14 and 9 and 10.

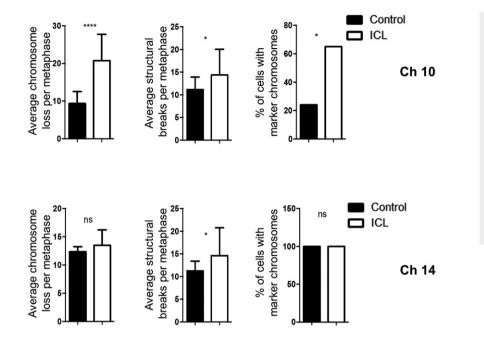


Figure EV4. Increased chromosomal instability in ICL tumors.

Chromosomal instability readouts, of tumor lines, assessed by average chromosomes loss per metaphase, average number of structural rearrangements per metaphase and percentage of metaphases with marker chromosomes (n = 20 for each data set and error bars denote SD, average chromosome loss: ****P < 0.001 for Ch10; average structural rearrangements: *P < 0.05 for Ch10 and Ch14; percentage of metaphases with marker chromosomes: *P < 0.05 for Ch10. Two-tailed unpaired *t*-test was used to determine statistical significance for average chromosome loss and structural breaks. Two-tailed *Z*-test was used to determine statistical significance for the percentage of cells with marker chromosomes.