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Conventional Cytogenetic Analysis of Hematologic Neoplasms

A 20-Year Review of Proficiency Test Results From the College of American Pathologists/American College of Medical Genetics and Genomics Cytogenetics Committee

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• ***Context.***—**One goal of the joint College of American Pathologists/American College of Medical Genetics and Genomics Cytogenetics Committee is to ensure the accurate detection and description of chromosomal abnormalities in both constitutional and neoplastic specimens, including hematologic neoplasms.**

Objective.—**To report a 20-year performance summary (1999–2018) of conventional chromosome challenges focusing on hematologic neoplasms.**

Design.—**A retrospective review was performed from 1999 through 2018 to identify karyotype challenges specifically addressing hematologic neoplasms. The overall performance of participants was examined to identify potential recurring errors of clinical significance.**

Results.—**Of 288 total conventional chromosome challenges from 1999–2018, 87 (30.2%) were presented in the context of a hematologic neoplasm, based on the provided clinical history, specimen type, and/or chromosomal abnormalities. For these 87 hematologic neoplasm challenges, 91 individual cases were provided and graded on the basis of abnormality recognition and karyotype nomenclature (ISCN, International System for Human Cytogenomic [previously Cytogenetic] Nomenclature). Of the 91 cases, 89 (97.8%) and 87 (95.6%) exceeded the required 80% consensus for grading of abnormality recognition and correct karyotype nomenclature, respectively. The 2 cases (2 of 91; 2.2%) that failed to meet the 80% consensus for abnormality recognition had complex karyotypes. The 4 cases (4 of 91; 4.4%) that failed to meet the 80% consensus for correct karyotype nomenclature were the result of incorrect abnormality recognition (2 cases), missing brackets in the karyotype (1 case), and incorrect breakpoint designation (1 case).**

Conclusions.—**This 20-year review demonstrates clinical cytogenetics laboratories have been and continue to be highly proficient in the detection and description of chromosomal abnormalities associated with hematologic neoplasms.**

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The accurate identification and description of chromosomal abnormalities observed by conventional G-banded chromosome studies in hematologic neoplasms is critical for patient management, including diagnosis, prognosis, disease classification, and/or therapy-related decisions.[1,2] For example, the detection of t(9;22)(q34;q11.2) (*BCR/ABL1* gene fusion) and t(15;17)(q24;q21) (*PML/RARA* gene fusion) are required for the diagnoses of chronic

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myeloid leukemia and acute promyelocytic leukemia, respectively, and both are amenable to targeted therapy.[3,4] The prognosis of other hematologic neoplasms, such as myelodysplastic syndromes (MDS) and primary myelofibrosis, rely on the accurate detection and inclusion of specific chromosomal abnormalities in prognostic scoring systems.[1,5] Furthermore, each update of the World Health Organization (WHO) classification of hematologic malignancies incorporates additional recurrent genetic abnormalities in the definition of specific disease subtypes, most notably acute myeloid leukemia (AML) and B-lymphoblastic leukemia/lymphoma (B-ALL/LBL).[1]

In addition to the accurate detection of chromosomal abnormalities, communicating the chromosome results in the form of a karyotype (nomenclature) to clinicians, pathologists, and other cytogeneticists is equally important. The karyotype is a universally adopted method of communicating the normal or abnormal, constitutional or acquired, chromosomal complement of an individual, tissue, or cell line, based on rules provided by the International System for Human Cytogenomic (previously Cytogenetic) Nomenclature (ISCN).[6] First published in 1978, the ISCN has undergone multiple revisions, each of which reflect our current understanding of the evolving complexity of the human genome in both hereditary and neoplastic disorders. Correct use of ISCN ensures that the abnormalities observed by G-banding, fluorescence in situ hybridization (FISH), or chromosomal microarray are concisely, accurately, and uniformly described. Accordingly, use of accurate ISCN nomenclature must be demonstrated as part of a cytogenetics laboratory's ongoing accreditation by the College of American Pathologists (CAP).

Cytogenetics and genomics laboratories use other methods to detect recurrent genetic abnormalities in hematologic neoplasms, including FISH, chromosomal microarray, and next-generation sequencing. However, conventional chromosome analysis remains the most practical and cost-efficient assay for whole-genome evaluation of individual neoplastic cells for the detection of both structural and numerical abnormalities, the emergence of related subclones, or new unrelated clones. Since 1986, the CAP and the American College of Genetics and Genomics joint Cytogenetics Committee (CyC) (formerly Cytogenetics Resource Committee) has been providing conventional chromosome studies as proficiency testing to cytogenetics laboratories to ensure the accurate detection and description of chromosomal abnormalities. The purpose of this retrospective study was to evaluate 20 years (1999–2018) of laboratory results from proficiency tests assessing hematologic neoplasms, and to provide a comprehensive summary of participant performance on the identification and characterization of chromosomal abnormalities. Review of these data is important to determine the success of the CyC by summarizing the overall accuracy of the proficiency testing program for the routine clinical results generated by cytogenetic laboratories.

METHODS

Case Selection

All conventional chromosome challenges (CY) from 1999 through 2018 were reviewed to identify those specifically addressing hematologic neoplasms. Three CY survey sets (A–C; 5 challenges per set, 15 total challenges per year) were provided annually from 1999 through 2014 (240 total challenges), and 2 CY survey sets (A and B; 6 challenges per set, 12 total challenges per year) were provided annually from 2015 through 2018 (48 total challenges). Of the 288 total CY challenges administered from 1999–2018, 87 challenges (30.2%) were presented in the context of a hematologic neoplasm, based on the provided clinical history, specimen type, and/or chromosomal abnormalities presented (Table). In addition, 2 of the 87 hematologic neoplasm challenges consisted of multiple cases (4 cases for 2005B-10; 2 cases for 2012B-10), resulting in 91 total cases. A designated number of metaphases (range, 3–6; median, 5) were provided per case (paper and/or electronic) to each enrolled cytogenetic laboratory (participants). Cases were chosen by the CyC to reflect chromosomal findings likely to be encountered during routine conventional chromosome analysis of hematologic neoplasms, including recurring cytogenetic abnormalities observed in hematologic neoplasms, constitutional abnormalities (eg, trisomy 21 in Down syndrome), and apparently "normal" chromosome studies.

Grading

From 1999 through 2008, four grading components existed for each challenge, including modal chromosome number (M), sex chromosome designation (S), recognition of abnormalities (A), and nomenclature (N) (Table). In 2009, the grading components were consolidated to include the modal chromosome number, sex chromosome designation, and abnormalities under "recognition of abnormalities," while maintaining "nomenclature" as a separate grading component (Table). All grading was performed by using the most current ISCN designated in the kit instructions for each challenge. The most common response provided by "referees" (randomly selected laboratories from a pool of anonymized laboratories with 100% performance on the CY survey for the previous 3 mailing periods) was determined to be the "modal karyotype" against which all participant responses were graded. If at least 80% of participants responded with the modal karyotype, the CyC formally graded the challenge; challenges that did not meet 80% consensus were not graded. However, multiple karyotypes were accepted by the CyC for 12 challenges, based on the subjective morphologic interpretation of certain chromosomal abnormalities and/or various acceptable forms of ISCN designation. All of the participant data, as well as educational write-ups by members of the CyC, were provided to participants in a printed document, the Participant Summary Report.

RESULTS

Number of Participants

From 1999–2018 a total of 87 challenges (30.2% of all CY challenges, n = 288) were presented in the context of a hematologic neoplasm. The number of participants demonstrated an upward trend during this 20-year period and ranged from a low of 212 in 2004 to a high of 362 in 2018. The upward trend from 2011 through 2018 is mainly attributable to international participation (countries outside of the United States and Canada). Fifteen referee laboratories were used per challenge, with the exception of 1999A-3 (14 referees). The number of participants per challenge can be viewed in Figure 1.

Specimen Types and Clinical Histories

For each of the 91 cases, the specimen source of the metaphases (eg, bone marrow aspirate), in addition to a brief clinical case history, was provided (Table). Of the 91 cases, 85 (93.4%) were bone marrow aspirates, 3 (3.3%) were lymph nodes, 2 (2.2%) were peripheral blood samples, and 1 (1.1%) was tissue from a jaw mass. General (eg, acute leukemia, lymphoma) or specific (eg, AML, MDS) diagnoses were provided for 57 of 91 cases (62.6%), while 34 of 91 cases (37.4%) indicated laboratory and/or clinical findings (eg, pancytopenia, leukocytosis, bruising, fatigue). When

Performance Summary of a 20-Year Retrospective Review (1999–2018) of Karyotype Challenges Specifically Addressing Hematologic Neoplasms

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
1999	A	3	BM	AIDS, pancytopenia	46,XY,t(3;21)(q26.2;q22)[5]	t(3;21) in myeloid neoplasms, and use of brackets in neoplastic karyotypes	14	13 (92.9)	**9 (64.3)[a]**	227	195 (85.9)	**147 (64.8)[a]**
	B	7	BM	Amyloidosis, suspect PCM	46,XY[5]	Normal male karyotype	15	15 (100)	15 (100)	229	205 (89.5)	200 (87.3)
2000	A	3	BM	Anemia, thrombocytopenia and blasts in PB	46,XY,t(9;11)(p22;q23)[2]/47,idem,+8[3] 46,XY,t(9;11)(p22;q23)[2]/47,XY,+8,t(9;11)(p22;q23)[3]	*KMT2A* (*MLL*) rearrangements in hematologic neoplasms	15	13 (86.7)	13 (86.7)	252	**197 (78.2)[a]**	**179 (71)[a]**
	B	7	BM	MDS, history of breast cancer	47,XX,+8[2]/47,XX,+8,del(12)(p11.2)[3] 47,XX,+8[2]/47,idem,del(12)(p11.2)[3] 47,XX,+8[2]/47,XX,+8,del(12)(p11.2p13)[3] 47,XX,+8[2]/47,idem,del(12)(p11.2p13)[3]	MDS	15	15 (100)	15 (100)	255	241 (94.5)	231 (90.6)
	C	13	BM	PCM	52,X,-X,+5,+9,+11,+11,+15,+19,+19[2]/52,idem,del(6)(q13q23)[2]	Myeloma	15	13 (86.7)	13 (86.7)	255	**188 (73.7)[a]**	**170 (66.7)[a]**
		14	BM	Pancytopenia, 18 y/o	45,XX,der(13;22)(q10;q10)[4]	Acquired versus inherited Robertsonian translocation	15	15 (100)	13 (86.7)	254	241 (94.9)	**191 (75.2)[a]**
2001	A	2	BM	AML, 34 y/o	46,XX,inv(16)(p13.1q22)[4]	AML	15	15 (100)	14 (93.3)	241	229 (95)	**168 (69.7)[a]**
		4	BM	MPN, possible ET	46,XY,+1,der(1;14)(q10;q10)[4] 46,XY,der(14)t(1;14)(q12;p11.2)[4]	Balanced whole arm versus unbalanced whole arm translocation nomenclature	15	15 (100)	15 (100)	241	200 (83)	**181 (75.1)[a]**
	B	9	BM	Acute leukemia, 24 y/o	47,XY,t(11;17)(q23;q21),+19[5]	*KMT2A* (*MLL*) rearrangement versus *ZBTB16/RARA* fusion [t(11;17)] in APL	15	15 (100)	15 (100)	223	209 (93.7)	186 (83.4)
	C	12	BM	Leukemia, 72 y/o	46,XY,t(9;11)(p22q23),t(9;22)(q34)(q34;q11.2)[5]	*KMT2A* (*MLL*) rearrangement as secondary abnormality in CML blast phase	15	15 (100)	15 (100)	227	213 (93.8)	199 (87.7)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2002	A	1	BM	Leukemia, 55 y/o	48,XX,+8,t(9;22)(q34;q11.2),inv(16)(p13.1q22),+21[5]	Clonal evolution in CML blast phase	15	15 (100)	14 (93.3)	234	228 (97.4)	188 (80.3)
	B	6	BM	Leukocytosis, 36 y/o	46,XX,inv(3)(q21q26.2),t(9;22)(q34;q11.2)[5]	Clonal evolution in CML blast phase	15	14 (93.3)	12 (80)	249	222 (89.2)	**180 (72.3)[a]**
2003	B	9	BM	Anemia, rheumatoid arthritis, 66 y/o	46,XX[5]	Normal female karyotype	15	13 (86.7)	12 (80)	241	222 (92.1)	199 (82.6)
	C	12	BM	Leukemia, 5 y/o	47,XY,+8,t(16;21)(q24;q22.1)[5]	Therapy-related and de novo AML	15	15 (100)	15 (100)	235	219 (93.2)	211 (89.8)
2004	A	1	BM	Lymphoma, anemia, 35 y/o	46,XY,t(8;22)(q24.1;q11.2)[5]	Burkitt lymphoma with variant *MYC* rearrangement	15	15 (100)	15 (100)	212	210 (99.1)	190 (89.6)
	B	**6**	**BM**	**Lymphoma**	**47,X,-Y,dup(1)(q21q25),+7,t(8;14)(q24.1;q32),+13[3]**	**Burkitt lymphoma chromosome abnormalities**	**15**	**9 (60)[a]**	**9 (60)[a]**	**212**	**78 (36.8)[a]**	**68 (32.1)[a]**
	C	14	BM	Chronic myeloid disorder, 73 y/o	46,XY,+i(1)(q10),-18[5]	Isochromosome 1q observed in various hematologic neoplasms	15	15 (100)	15 (100)	236	227 (96.2)	220 (93.2)
2005	A	1	Tissue	Jaw mass, 25 y/o	46,XX,t(8;21)(q22;q22)[5]	Myeloid sarcoma with t(8;21)	15	15 (100)	15 (100)	235	234 (99.6)	228 (97)
		2	BM	Anemia, 80 y/o	46,XX,del(5)(q13q33)[5]	5q- syndrome	15	15 (100)	15 (100)	234	234 (100)	226 (96.6)
	B	6	BM	Rule out hematologic neoplasm, 48 y/o	45,XY,inv(3)(q21q26.2),-7[5]	Poor prognosis of inv(3)/t(3;3) in myeloid neoplasms	15	15 (100)	**11 (73.3)[a]**	247	226 (91.5)	**179 (72.5)[a]**
		10a	BM	Anemia, 52 y/o	46,XX[4]	Normal female karyotype	15	15 (100)	15 (100)	247	244 (98.8)	244 (98.8)
		10b	BM	Bruising, 6 y/o	46,XX,inv(16)(p13.1q22)[4]	Recurrent rearrangement in AML	15	15 (100)	14 (93.3)	247	245 (99.2)	211 (85.4)
		10c	BM	Eosinophilia, 26 y/o	46,XX,t(16;16)(p13.1;q22)[4]	Recurrent rearrangement in AML	15	15 (100)	14 (93.3)	247	237 (96)	203 (82.2)
		10d	BM	Leukocytosis, 46 y/o	46,XX,del(16)(q22)[4] 46,XX,del(16)(q13q22)[4]	del(16q) is not equivalent to inv(16)/t(16;16) in AML	15	15 (100)	14 (93.3)	247	247 (100)	245 (99.2)
	C	12	BM	Weight loss, leg pain, 12 y/o	46,XY,t(9;22)(q34;q11.2)[2]/51,idem,+7,+8,+10,+19,+der(22)t(9;22)[2]	*BCR/ABL1* fusion and secondary abnormalities in B-ALL	15	13 (86.7)	13 (86.7)	265	250 (94.3)	236 (89.1)
		13	BM	Anemia, 73 y/o	46,XX[5]	Normal female karyotype	15	14 (93.3)	14 (93.3)	260	246 (94.6)	237 (91.2)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2006	A	3	BM	AML, Down syndrome, 18 m/o	49,XY,+8,+21c,+21[5]	AML in patients with Down syndrome	15	15 (100)	15 (100)	219	215 (98.2)	205 (93.6)
		4	BM	Leukocytosis, 75 y/o	47,XY,+12[5]	CLL	15	15 (100)	15 (100)	219	218 (99.5)	217 (99.1)
	B	7	BM	Acute leukemia, 74 y/o	47,XY,+8[3]/48,idem, +19[2]	Trisomy 8 in myeloid neoplasms	15	15 (100)	13 (86.7)	214	213 (99.5)	208 (97.2)
	C	13	BM	Leukocytosis, 22 y/o	46,XX,t(9;11)(p22;q23)[5]	*MLLT3/KMT2A* (*MLL*) fusion [t(9;11)] in AML	15	14 (93.3)	14 (93.3)	229	226 (98.7)	222 (96.9)
		14	BM	MDS, 59 y/o	46,XY,del(13)(q12q14)[5]	MDS with del(13q)	15	15 (100)	15 (100)	229	228 (99.6)	222 (96.9)
2007	A	1	BM	Thrombocytopenia, 59 y/o	46,XX,t(15;17)(q22;q21)[5]	*PML/RARA* fusion and *RARA* variants in APL	15	15 (100)	15 (100)	223	222 (99.6)	220 (98.7)
		3	BM	Myelofibrosis, 79 y/o	46,XY,dup(12)(q13q22)[3]/ 46,XY[2]	Association between chromosome 12 abnormalities and myelofibrosis	15	15 (100)	15 (100)	222	215 (96.8)	211 (95)
	B	6	BM	Leukocytosis, 38 y/o	46,XY,t(9;22)(q34;q11.2) [3]/47,idem,-Y,+8, +der(22)t(9;22)[3]	Clonal evolution in CML accelerated or blast phase	15	15 (100)	15 (100)	226	220 (97.3)	206 (91.2)
		9	BM	Lymphoma, 3 y/o	47,XY,t(2;5)(p23;q35),+7[5]	*ALK* rearrangements in ALCL	15	15 (100)	15 (100)	225	219 (97.3)	219 (97.3)
	C	14	BM	Rule out leukemia, 11 y/o	45,X,-Y,t(8;21)(q22;q22)[3]/ 45,idem,del(9)(q22q34) [2] 45,X,-Y,t(8;21)(q22;q22)[3]/ 45,idem,del(9)(q13q22) [2]	t(8;21) in AML	15	14 (93.3)	14 (93.3)	242	236 (97.5)	223 (92.1)
2008	A	3	BM	Acute leukemia, 58 y/o	46,XX,t(6;9)(p23;q34)[5]	Recurrent rearrangement in AML	15	15 (100)	15 (100)	226	225 (99.6)	223 (98.7)
	B	7	BM	AML, 65 y/o	47,XY,t(6;11)(q27;q23), +8[5]	*AFDN/KMT2A* (*MLL*) fusion [t(6;11)] in AML	15	13 (86.7)	13 (86.7)	253	240 (94.9)	235 (92.9)
		8	BM	Leukemia, 55 y/o	48,XX,+8,t(9;22) (q34;q11.2),inv(16) (p13.1q22),+21[5]	Coexistence of inv(16) and t(9;22) in CML	15	15 (100)	13 (86.7)	252	247 (98)	211 (83.7)
	C	12	BM	AML, pancytopenia, 58 y/o	47,XX,+X,t(4;11)(q21;q23) [5]	*AFF1/KMT2A* (*MLL*) fusion [t(4;11)] in acute leukemia	15	15 (100)	15 (100)	236	236 (100)	234 (99.2)
		13	BM	AML, 22 y/o	46,XX,t(16;16)(p13.1;q22) [5]	Recurrent rearrangement in AML	15	15 (100)	14 (93.3)	236	199 (84.3)	**172 (72.9)**[a]

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2009	A	2	BM	MDS, 87 y/o	46,XX,del(20)(q11.2q13.1)[5]	Deletion 20q in myeloid neoplasms	15	15 (100)	15 (100)	243	239 (98.4)	233 (95.9)
		5	BM	Thrombocytopenia, 31 y/o	46,XY,t(3;12)(q26.2;p13)[5]	Recurrent rearrangement in myeloid leukemia subtypes	15	15 (100)	13 (86.7)	242	228 (94.2)	**174 (71.9)**[a]
	B	8	BM	ALL, 17 y/o	37,XY,-2,-3,-4,-7,-12,-13,-15,-16,-17[3]/46,XY[2]	Importance of analyzing hypodiploid cells, and cells with poor chromosome morphology in pediatric ALL	15	15 (100)	14 (93.3)	244	244 (100)	207 (84.8)
	C	12	BM	Anemia, thrombocytopenia, eosinophilia, 81 y/o	46,XX,i(17)(q10)[5]	Isochromosome 17q in myeloid neoplasms	15	15 (100)	15 (100)	250	249 (99.6)	242 (96.8)
		15	BM	AML, 83 y/o	47,XX,+9,t(9;11)(p22;q23)[3]/47,XX,t(9;11)(p22;q23),+21[2]	*MLLT3/KMT2A* (*MLL*) fusion [t(9;11)] in AML	15	14 (93.3)	13 (86.7)	249	226 (90.8)	210 (84.3)
2010	A	4	PB	Lymphadenopathy, fevers, fatigue, 14 y/o	46,XY,t(7;11)(q11.2;p15)[5]	*NUP98* rearrangements in myeloid neoplasms	15	15 (100)	15 (100)	263	261 (99.2)	250 (95.1)
	B	6	BM	Pancytopenia, 39 y/o	46,XY,t(11;19)(q23;p13.1)[5]	*ELL/KMT2A* (*MLL*) fusion [t(11;19)] in AML	15	15 (100)	14 (93.3)	294	280 (95.2)	272 (92.5)
	C	11	BM	MDS, 73 y/o	47,XX,+1,der(1;7)(q10;p10),+9,del(20)(q11.2)[5] 47,XX,+1,der(1;7)(q10;p10),+9,del(20)(q11.2q13.3)[5]	der(1;7)(q10;q10) in myeloid neoplasms	15	15 (100)	14 (93.3)	318	292 (91.8)	**226 (71.1)**[a]
		13	BM	AML, 62 y/o	46,XX,inv(3)(q21q26.2)[5]	inv(3)/t(3;3) in myeloid neoplasms	15	15 (100)	14 (93.3)	317	302 (95.3)	**226 (71.3)**[a]
		15	BM	Lymphoma, 64 y/o	46,XY,del(17)(p11.2)[3]/47,XY,+12[2]	Chromosome abnormalities observed in CLL/SLL	15	13 (86.7)	13 (86.7)	318	293 (92.1)	281 (88.4)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2011	A	2	BM	T-ALL, 4 y/o	46,XX,t(4;11)(q21;p15), del(6)(q–q–)[5]	Rare recurrent translocation in T-ALL	15	15 (100)	15 (100)	316	303 (95.9)	288 (91.1)
		5	LN	CLL, 70 y/o	47,XY,+i(1)(q10),t(8;14)(q24.1;q32)[5] 47,XY,+1,i(1)(q10),t(8;14)(q24.1;q32)[5]	*MYC* rearrangements in mature B-cell neoplasms	15	15 (100)	14 (93.3)	311	294 (94.5)	259 (83.3)
	B	6	BM	APL	46,XX,t(15;17)(q22;q21)[5]	*PML/RARA* fusion [t(15;17)] in APL and responsiveness to ATRA therapy	15	15 (100)	14 (93.3)	305	294 (96.4)	288 (94.4)
	C	12	BM	CLL	49,XY,+12,+18,+19[3]/46,XY[2]	Chromosome abnormalities observed in CLL	15	15 (100)	15 (100)	327	319 (97.6)	311 (95.1)
2012	A	1	BM	MDS/AML, 55 y/o	46,XY,t(6;9)(p23;q34), del(12)(p11.2p13)[5]	Recurrent rearrangement in AML	15	15 (100)	15 (100)	283	273 (96.5)	263 (92.9)
		5	BM	AML, 45 y/o	46,XY,t(8;21)(q22;q22)[2]/46,idem,t(4;12)(q27;p11.2)[3]	t(8;21) in AML	15	15 (100)	15 (100)	282	263 (93.3)	**221 (78.4)**[a]
	B	6	BM	AML	46,XY,del(7)(q32q36), inv(19)(p13.3q13.1)[3]/46,XY[2] 46,XY,del(7)(q32),inv(19)(p13.3q13.1)[3]/46,XY[2]	del(7q) in myeloid neoplasms	15	15 (100)	14 (93.3)	285	279 (97.9)	265 (93)
		10a	BM	MDS, 76 y/o	46,X,i(X)(p10)[4] 46,X,idic(X)(q13)[4]	Isodicentric X chromosome in myeloid neoplasms	15	15 (100)	15 (100)	289	280 (96.9)	**228 (78.9)**[a]
		10b	BM	MDS, 72 y/o	46,X,i(X)(q10)[4]	Isochromosome Xq is not a recurrent abnormality in myeloid neoplams	15	15 (100)	14 (93.3)	289	280 (96.9)	**228 (78.9)**[a]
	C	12	BM	Leukocytosis, 63 y/o	46,XY,t(3;21)(p21;q22), t(9;22)(q34;q11.2) [3]/46,XY[2]	t(3;21) in therapy-related myeloid neoplasms	15	15 (100)	15 (100)	275	272 (98.9)	266 (96.7)
		14	BM	Plasmacytoma, 55 y/o	48,XX,+9,+15[5]	Prognostic significance of hypodiploidy versus hyperdiploidy in PCM	15	15 (100)	15 (100)	273	272 (99.6)	266 (97.4)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2013	A	1	BM	Therapy-related AML, 68 y/o	49,XX,del(1)(q32q42),+3, t(11;19)(q23;p13.3),+20, +21[5]	No discussion provided	15	15 (100)	15 (100)	299	288 (96.3)	274 (91.6)
		5	BM	AML, 27 y/o	45,XX,t(3;3)(q21;q26.2), -7[5]	No discussion provided	15	15 (100)	15 (100)	300	292 (97.3)	257 (85.7)
	B	6	BM	AML, 41 y/o	48,XY,+4,t(6;11)(q27;q23), +8[5]	*KMT2A* (*MLL*) rearrangements in hematologic neoplasms	15	13 (86.7)	12 (80)	303	271 (89.4)	261 (86.1)
	C	14	BM	AML, 47 y/o	46,XX,inv(16)(p13.1q22)[5]	Recurrent rearrangement in AML	15	15 (100)	14 (93.3)	307	290 (94.5)	262 (85.3)
2014	A	3	BM	Pancytopenia, 51 y/o	46,XY,t(5;12)(q33;p13)[5]	*PDGFRB* rearrangements in MPN and responsiveness to TKI therapy	15	14 (93.3)	14 (93.3)	335	327 (97.6)	321 (95.8)
	B	6	BM	AML, 19 y/o	46,XY,t(9;11)(p22;q23)[5]	*KMT2A* (*MLL*) rearrangements in acute leukemia	15	15 (100)	15 (100)	317	314 (99.1)	308 (97.2)
		7	BM	AML, 63 y/o	46,XX,t(4;12)(q12;p13)[5]	*PDGFRA* rearrangements in chronic eosinophilic leukemia and responsiveness to TKI therapy	15	15 (100)	15 (100)	316	312 (98.7)	307 (97.2)
		9	BM	Myeloma, 69 y/o	46,XX[5]	Normal female karyotype	15	15 (100)	15 (100)	313	294 (93.9)	286 (91.4)
	C	**11**	**BM**	**B-ALL, 8 w/o**	**46,XX,ins(11;5) (q23;q13q31)[3]/50, idem,+6,+9,+13,+19[2]**	***KMT2A* (*MLL*) rearrangements observed in infant ALL**	**15**	**10 (66.7)[a]**	**10 (66.7)[a]**	**296**	**189 (63.9)[a]**	**189 (63.9)[a]**

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2015	A	4	BM	CML	46,XY,t(9;22)(q34;q11.2)[3]/47,idem,+der(22)t(9;22)[2]	No discussion provided	15	15 (100)	15 (100)	353	326 (92.4)	312 (88.4)
		5	BM	Acute leukemia, 38 y/o	46,XY,t(4;11)(q21;q23)[3]/47,idem,+X[2]	Nomenclature designation of acquired sex chromosome abnormalities	15	15 (100)	15 (100)	351	339 (96.6)	331 (94.3)
		6	BM	Anemia, thrombocytopenia, fatigue, 3 y/o	46,XY,inv(5)(q22q31)[5]	No discussion provided	15	14 (93.3)	14 (93.3)	348	309 (88.8)	**277 (79.6)**[a]
	B	10	BM	Anemia	47,XY,+8[3]/46,XY[2]	Nomenclature pertaining to number of cells observed for each clone	15	15 (100)	15 (100)	331	325 (98.2)	320 (96.7)
		11	BM	Leukocytosis, 40 y/o	46,XX,inv(9)(q13q34)[5]	Nomenclature pertaining to number of cells observed for each clone	15	15 (100)	15 (100)	329	318 (96.7)	303 (92.1)
2016	A	3	BM	Pancytopenia, history of DSRCT, 18 y/o	46,XX,dup(1)(q21q32)[5]	Duplication of 1q in hematologic neoplasms	15	15 (100)	15 (100)	339	336 (99.1)	322 (95)
	B	10	BM	MDS, 60 y/o	46,XY,del(5)(q15q33)[2]/46,idem,del(13)(q14q32)[3] 46,XY,del(5)(q15q33)[2]/46,sl,del(13)(q14q32)[3] 46,XY,del(5)(q15q33)[2]/46,XY,del(5)(q15q33),del(13)(q14q32)[3] 46,XY,del(5)(q15q33)[2]/46,idem,del(13)(q14)[3] 46,XY,del(5)(q15q33)[2]/46,sl,del(13)(q14)[3] 46,XY,del(5)(q15q33)[2]/46,XY,del(5)(q15q33),del(13)(q14)[3]	Deletion (5q) in MDS	15	15 (100)	14 (93.3)	326	316 (96.9)	297 (91.1)
		11	BM	AML, 44 y/o	47,XX,inv(16)(p13.1q22),+22[5]	Trisomy 22 associated with inv(16) in AML	15	14 (93.3)	14 (93.3)	324	313 (96.6)	267 (82.4)
		12	BM	Anemia, thrombocytopenia, 15 y/o	46,XX,t(6;9)(p23;q34)[5]	Recurrent rearrangement in AML	15	15 (100)	15 (100)	326	319 (97.9)	315 (96.6)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2017	A	4	BM	AML/MDS, 75 y/o	45,XX,inv(3)(q21q26.2), -7[5]	Recurrent rearrangement in MDS/AML	15	15 (100)	15 (100)	337	321 (95.3)	284 (84.3)
		5	BM	Pancytopenia, 77 y/o	55,XX,+1,del(5)(q22q35), +6,+8,+8,+9,+11,+19, +21,+22[5]	Hyperdiploidy in AML	15	14 (93.3)	13 (86.7)	337	314 (93.2)	289 (85.8)
		6	BM	Rule out CML	47,XY,+14[5]	Trisomy 14 observed in myeloid neoplasms	15	15 (100)	15 (100)	338	331 (97.9)	328 (97)
	B	10	BM	Leukocytosis, 10 m/o	47,XY,+8,t(11;19) (q23;p13.1)[5]	Difficulty distinguishing *KMT2A/ELL* from *KMT2A/MLLT1* fusions by conventional chromosome analysis	15	15 (100)	15 (100)	350	294 (84)	286 (81.7)
		11	LN	Suggestive of lymphoma, 62 y/o	46,XX,der(1)t(1;1) (p36.1;q21)[5]	Loss of 1p36 in a subtype of follicular lymphoma with diffuse-appearing growth pattern	15	15 (100)	14 (93.3)	331	299 (90.3)	272 (82.2)
		12	BM	B-LPD, CpG cultures, 63 y/o	46,XY,del(6)(q11q21), del(13)(q12q22)[5] 46,XY,del(6)(q12q21), del(13)(q12q22)[5]	Deletions of 6q and 13q are recurrent, nonspecific abnormalities in lymphoid neoplasms	15	14 (93.3)	13 (86.7)	342	330 (96.5)	274 (80.1)

Continued

Year	CY Survey	Specimen No.	Specimen Type	Case History	Accepted Karyotype(s)	Diagnosis and/or Discussion Point(s)	Referees			Participants		
							No.	A, Acceptable (%)	N, Acceptable (%)	No.	A, Acceptable (%)	N, Acceptable (%)
2018	A	5	BM	MDS, 75 y/o	46,XY,t(3;21)(q26.2;q22)[2]/49,idem,+8,+8,+9[3]	t(3;21) observed in therapy-related MDS	15	15 (100)	15 (100)	331	307 (92.7)	**257 (77.6)**[a]
		6	BM	AML, 79 y/o	46,XY,del(20)(q11.2q13.1)[5] 46,XY,del(20)(q11.2)[5]	In the absence of morphologic criteria, del(20q) is not diagnostic for a myeloid neoplasm	15	15 (100)	15 (100)	334	321 (96.1)	316 (94.6)
	B	10	BM	AML, 37 y/o	46,XX,t(9;11)(p22;q23)[5]	*MLLT3/KMT2A* (*MLL*) fusion [t(9;11)] in AML, in addition to a new band designation for *MLLT3* (9p21.3)	15	14 (93.3)	14 (93.3)	362	352 (97.2)	342 (94.5)
		11	LN	Lymphoma, 54 y/o	49,XY,+3,t(8;14)(q24.1;q32),+18,+18[3]/46,XY[2]	*MYC* rearrangements in mature B-cell neoplasms	15	15 (100)	15 (100)	345	334 (96.8)	**252 (73)**[a]
		12	PB	B-cell lymphoma, CpG cultures, 65 y/o	46,XX,t(11;14)(q13;q32)[3]/46,XX[2]	t(11;14) in mantle cell lymphoma and PCM	15	15 (100)	15 (100)	359	349 (97.2)	348 (96.9)

Abbreviations: A, abnormality recognition; AIDS, acquired immunodeficiency syndrome; ALCL, anaplastic large cell lymphoma; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; ATRA, all-trans retinoic acid; B-ALL, B-lymphoblastic leukemia; B-LPD, B-cell lymphoproliferative disorder; BM, bone marrow; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; CML, chronic myeloid leukemia; CY, cytogenetics; DSRCT, desmoplastic small round cell tumor; ET, essential thrombocythemia; LN, lymph node; M, modal chromosome number; MDS, myelodysplastic syndrome; m/o, months old; MPN, myeloproliferative neoplasm; N, karyotype nomenclature; PB, peripheral blood; PCM, plasma cell myeloma; S, sex chromosome designation; T-ALL, T-lymphoblastic leukemia; TKI, tyrosine kinase inhibitors; w/o, weeks old; y/o, years old.

[a] Bolded data indicate abnormality and/or nomenclature that did not meet 80% consensus for referee and/or participant groups.

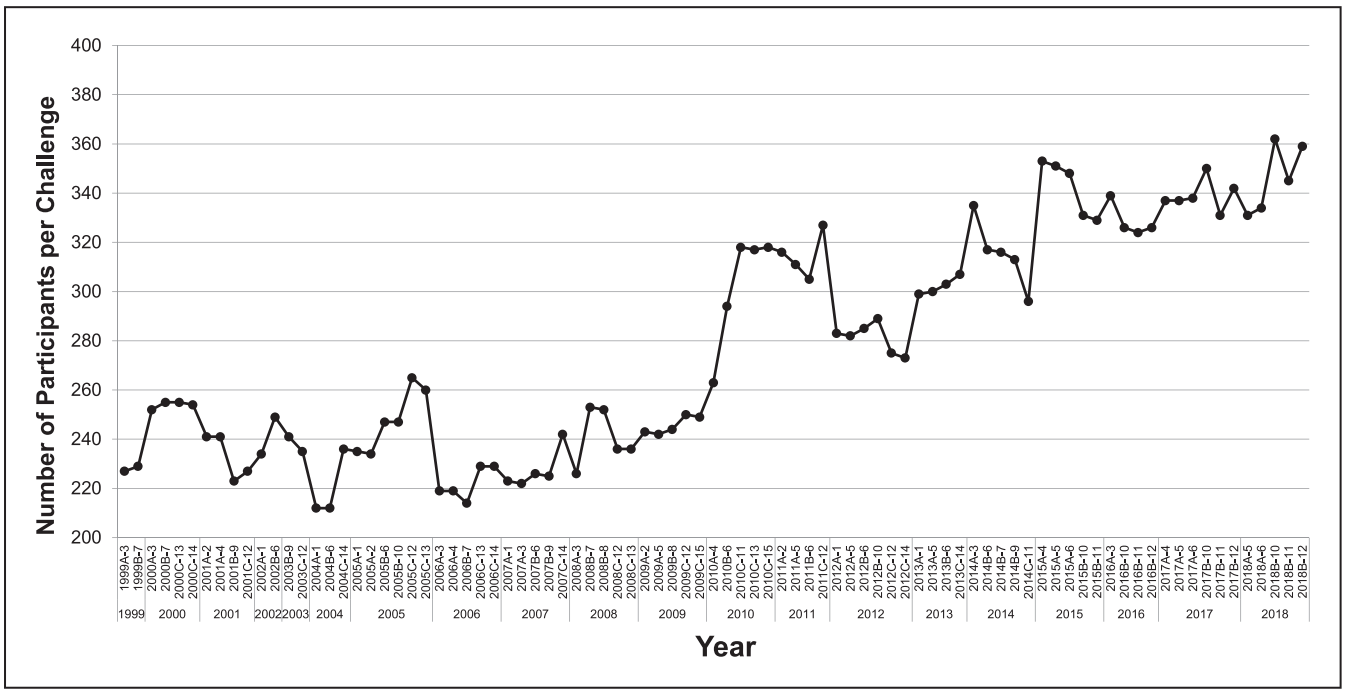

Figure 1. *Line chart demonstrating the number of participants for each of the 87 conventional chromosome challenges for hematologic neoplasms from 1999–2018. The range of participants, based on at least 80% of responses (threshold for survey grading), was 212 to 362.*

provided, the most commonly used specific diagnosis in the clinical history was AML or MDS (29 of 91 cases; 31.9%).

Chromosomal Abnormalities

Of the 91 total cases, 5 (5.5%) had a normal karyotype (4 female, 1 male), 38 (41.8%) had a single abnormality, and 48 (52.7%) had multiple abnormalities within the stemline and/or the sideline. Of the 38 karyotypes with single abnormalities, there were 18 balanced translocations (excluding whole-arm rearrangements) (47.4%); 6 inversions (15.8%); 5 deletions (13.2%); 4 whole-arm rearrangements (10.5%); 3 trisomies (7.9%); and 2 duplications (5.3%). Karyotypes with more than 1 abnormality in the stemline and/or the sideline included multiple combinations of structural and/or numeric chromosomal abnormalities (eg, 2005C-12, 2016B-10). No more than 1 sideline was included in any of the provided cases.

Multiple recurring chromosomal abnormalities were included in the challenges from 1999–2018 (Table). The 5 most common abnormalities in decreasing order were *KMT2A* (*MLL*) rearrangements at 11q23 [15 total cases: 6 cases with t(9;11)(p22;q23); 2 cases each with t(4;11)(q21;q23), t(6;11)(q27;q23), and t(11;19)(q23;p13.1); and 1 case each with ins(11;5)(q23;q13q33), t(11;17)(q23;q21), and t(11;19)(q23;p13.3)]; polysomy 8 (14 total cases: 13 cases with trisomy 8; 1 case with tetrasomy 8); t(9;22)(q34;q11.2) (8 total cases, all of which had additional structural and/or numerical abnormalities); inv(16)(p13.1q22)/t(16;16)(p13.1;q22) (8 total cases); and inv(3)(q21q26.2)/t(3;3)(q21;q26.2) (4 total cases).

Participant and Referee Performance

From 1999–2008 the modal chromosome number (M) and sex chromosome designation (S) were independently graded for each challenge. None of the modal chromosome number or sex chromosome designation components (referee or participants) failed to meet the grading threshold of 80% or greater from 1999–2008 (data not shown).

Recognition of abnormalities (A) and nomenclature (N) components were graded independently from 1999–2018. However, starting in 2009 the modal chromosome number and sex chromosome designations were incorporated into recognition of abnormalities (see above). Of the 91 total cases, 2 failed to meet 80% consensus for abnormality identification (2004B-6 [Figure 2], 2014C-11 [stemline: Figure 3, A; sideline: Figure 3, B]). Both cases had complex karyotypes, each with 5 total abnormalities within the stemline and/or sideline. While the remaining 89 cases were graded (referees exceeded the 80% consensus for abnormality identification), 2 cases (2000A-3, 2000C-13) from the participant group were below 80% for both recognition of abnormalities (A) and nomenclature (N).

Of the 91 total cases, 4 failed to meet the 80% consensus for karyotype nomenclature by the referees (1999A-3, 2004B-6, 2005B-6, 2014C-11), which includes the 2 cases that also failed to meet 80% consensus for correct abnormality identification (see above). While these 4 cases were not graded because an 80% consensus for nomenclature was not achieved, the remaining 87 cases were graded (referees exceeded 80% consensus), although 16 total cases were below an 80% consensus from the participants (2000A-3, 2000C-13, 2000C-14, 2001A-2, 2001A-4, 2002B-6, 2008C-13, 2009A-5, 2010C-11, 2010C-13, 2012A-5, 2012B-10a, 2012B-10b, 2015A-6, 2018A-5, 2018B-11). Most of these 16 cases had a complex karyotype, a whole-arm rearrangement, an interstitial deletion, or a combination of these abnormalities (Table).

Of the 91 total cases, 79 (86.8%) had a single acceptable karyotype, while 12 (13.2%) had multiple karyotypes that were deemed acceptable by the CyC. Both terminal and distal interstitial deletions were accepted for 7 cases (2000B-7, 2005B-10d, 2007C-14, 2010C-11, 2012B-6, 2016B-10,

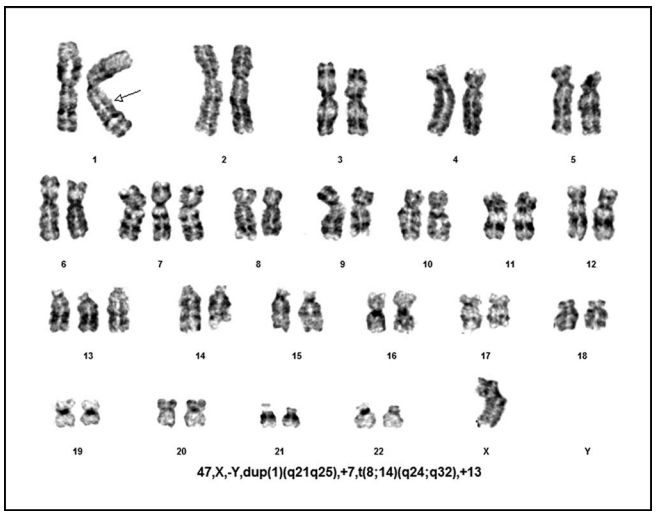

Figure 2. *Representative karyogram for case 2004B-6. Both abnormality and nomenclature components failed to reach the 80% grading consensus. Only 60% of referees and 36.8% of participants identified all the abnormalities. Failure to recognize the 1q duplication (arrow) was the primary reason this challenge failed.*

2018A-6), rewriting the stemline or use of "idem" or "sl" to describe a subclone was accepted in 3 cases (2000A-3, 2000B-7, 2016B-10), alternative ISCN for whole-arm rearrangements was accepted in 3 cases (2001A-4, 2011A-5, 2012B-10a), and varying interstitial deletion breakpoints (6q11 versus 6q12) were accepted in 1 case (2017B-12).

DISCUSSION

The accurate detection and description of conventional chromosome results are critical for diagnosis, prognosis, disease classification, and/or clinical management for most hematologic neoplasms.[1,2] Indeed, most entities listed in the current *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue*[1] have included a "genetic profile" that describes genetic abnormalities of clinical importance, many of which are identified by conventional chromosome studies. The importance of conventional chromosome studies was also reaffirmed by the recently published European recommendations, particularly for chronic myeloid leukemia, MDS, and AML.[7] The gradual increase of hematologic neoplasm challenges per survey, in addition to the overall number of participants per survey (Figure 1), indicates the continued importance of conventional chromosome studies in hematologic neoplasms and the continued need to offer a high-quality proficiency testing program. In 1999, only 2 of 15 challenges (13%) from 3 surveys (survey C from 1999 did not include any hematologic neoplasm challenges) represented hematologic neoplasms: 1 with 227 participants and the other with 229 participants (Table). In 2018, five of 12 challenges (42%) from both surveys (A and B) represented hematologic neoplasms, with a range of 331 to 362 participants (Table).

The selection of chromosome challenges by the CyC aims to reflect the routine practice of a clinical cytogenetics laboratory that offers chromosome testing for hematologic neoplasms. As reflected in the challenges sent to survey participants, the overwhelming majority of specimens sent to a cytogenetics laboratory for hematologic evaluation are bone marrow aspirates submitted for an evaluation of a

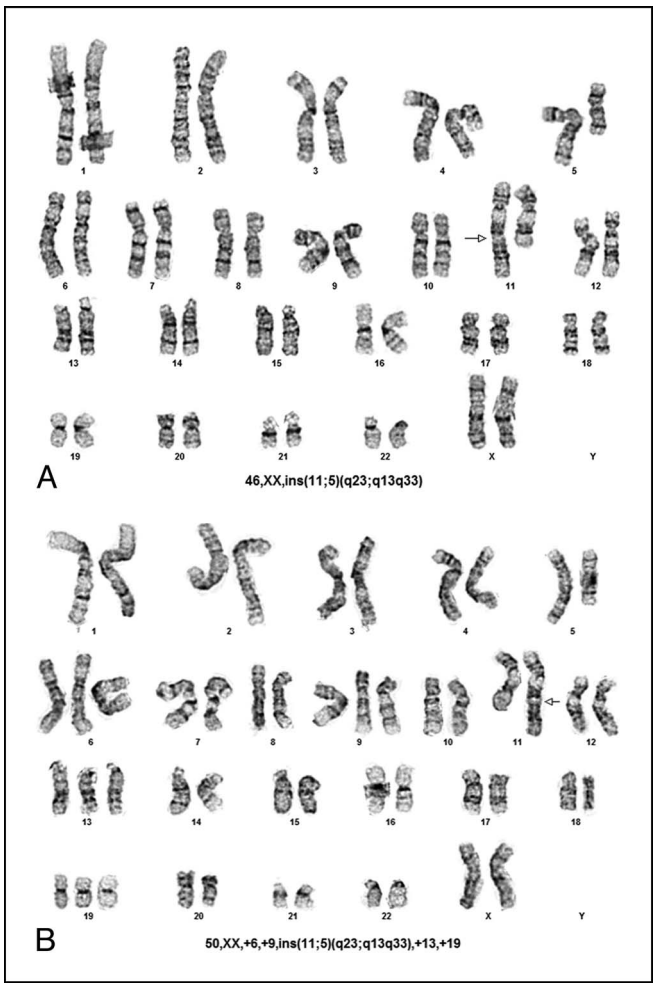

Figure 3. *Representative stemline (A) and sideline (B) karyograms for case 2014C-11. Both abnormality and nomenclature components failed to reach the 80% grading consensus. Only 66.7% of referees and 63.9% of participants identified all the abnormalities. The failure of this challenge was due to mischaracterization of ins(11;5)(q23;q13q31) (indicated by the arrow in each karyogram) as a 5q deletion and an unbalanced 11;12 translocation [der(11)t(11;12)(q23;q13)]. In addition, varying chromosome 5 breakpoints and incorrect insertion orientation contributed to the failure.*

myeloid neoplasm. The WHO subsections on all myeloid malignancies indicate conventional chromosome studies are recommended in the diagnostic evaluation of the myeloid clone.[1] In contrast to myeloid neoplasms, it is uncommon to encounter dividing lymphoid clones in unstimulated bone marrow aspirate specimens unless the clone is behaving in an aggressive fashion, that is, lymphoid clones seldom "outdivide" the normally rapidly dividing myeloid precursor cells. The rapidly dividing lymphoid neoplasms typically encountered in a cytogenetics laboratory include B-ALL/LBL or T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) or aggressive subtypes of mature B-cell lymphoma such as Burkitt lymphoma or "high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements." While these B-cell clones are less commonly encountered, the CyC has included a subset of chromosome challenges to evaluate for B-ALL, T-ALL, and Burkitt lymphoma.

Conventional chromosome studies are currently not recommended by the WHO for mature B- or T-cell neoplasms on unstimulated bone marrow aspirates or lymph node samples, including the most commonly encountered diagnoses of plasma cell myeloma (PCM) and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).[1] Although abnormal clones associated with PCM or CLL/SLL can be encountered in an unstimulated bone marrow chromosome evaluation, FISH testing is more informative than G-banding in the evaluation of both of these mature B-cell clones.[1] For neoplastic PCM cells, CD138-sorted cells are recommended for the evaluation of the prognostic genetic abnormalities in a diagnostic specimen. A FISH panel test may be more informative than chromosome studies, since several of the high-risk PCM abnormalities (ie, *TP53* deletion or *FGFR3/IGH* fusion) cannot be reliably identified by chromosome studies. Similarly, the standard prognostic markers used for evaluation in a CLL/SLL diagnostic evaluation are not identified by an unstimulated chromosome study and are typically evaluated by a FISH panel test. However, a CpG-stimulated chromosome study to evaluate chromosome complexity of the CLL/SLL clone may contribute additional prognostic value.

Of 91 total cases, only 2 abnormalities did not meet the 80% grading threshold for both the referee and participant groups. One of these, 2004B-6, had the following complex karyotype: 47,X,-Y,dup(1)(q21q25),+7,t(8;14)(q24.1;q32),+13[3] (Figure 2). Although this challenge did not meet the 80% grading threshold because both participants and referees failed to identify the 1q duplication, the t(8;14) and other abnormalities were correctly identified. The other case, 2014C-11, had the following complex karyotype: 46,XX,ins(11;5)(q23;q13q31)[3]/50,idem,+6,+9,+13,+19[2] (Figure 3). Four of 15 referees, and 58 of 296 participants misinterpreted the ins(11;5)(q23;q13q31) as a 5q deletion and an unbalanced 11;12 translocation [der(11)t(11;12)(q23;q13)]. Moreover, of the referees and participants who correctly identified the ins(11;5), chromosome 5 breakpoint designation and insertion orientation varied widely. These 2 ungraded challenges highlight the limitations the CyC faces when trying to assess participants with the types of complex cases routinely encountered in clinical practice. In addition, the fact that the CyC can provide only 5 metaphase spreads for each case and cannot provide the results of additional tests (eg, FISH, chromosomal microarray) commonly used to disambiguate such cases before reporting further complicates the ability of the CyC to appropriately test "routine clinical practice." These 2 cases illustrate the limitation that proficiency tests are at best only a partial rather than complete representation of clinical practice. While other challenges with complex karyotypes did reach 80% consensus (eg, 2007B-6, 2008B-8), the abnormalities submitted in these challenges are well described and are expected to be routinely observed and identifiable without ancillary testing in clinical practice.

The CyC accepted multiple karyotype designations in 12 cases either because limited band-level resolution of the metaphases precluded definitive characterization of the breakpoints involved in the abnormalities, or because different but correct ISCN nomenclature designations were reported. Seven deletions (2000B-7, 2005B-10d, 2007C-14, 2010C-11, 2012B-6, 2016B-10, 2018A-6) could not be consistently classified as terminal or interstitial on the basis of chromosome morphology, thus both responses were accepted. In addition to the technical limitations of banding resolution, differentiating distal interstitial from terminal deletions remains an ongoing challenge, because this distinction is often not relevant in clinical practice. Thus, the CyC may choose to accept both designations for these deletions. Three whole-arm rearrangements (2001A-4, 2011A-5, 2012B-10a) were also reported with acceptable alternative breakpoints near the chromosome centromeres, thus resulting in alternative karyotypic designations [eg, +1,der(1;14)(q10;q10) versus der(14)t(1;14)(q12;p11.2)]. Indeed, differentiating whole-arm rearrangements from unbalanced rearrangements with breakpoints located near the centromeres can be challenging for even the most experienced cytogeneticist. As such, multiple karyotype designations were accepted. Two karyotypes were accepted for 1 case (2017B-12), each with alternative interstitial deletion breakpoints that could not be easily distinguished from each other. Multiple karyotypic designations were accepted for 3 cases (2000A-3, 2000B-7, 2016B-10) where either the stemline was rewritten or the terms *idem* or *sl* were used to describe a subclone. Per the ISCN, abnormalities from the stemline (sl) can be rewritten in the subclone nomenclature, or alternatively listed as "idem" or "sl" for the purposes of brevity.[6]

Grading of each survey was performed by using the most current ISCN designated in the kit instructions for each challenge. Of 91 total cases, 4 failed to meet 80% consensus for nomenclature designation. Two of the 4 cases (2004B-6, 2014C-11; previously described above) failed because of incorrect recognition of abnormality. The remaining 2 cases each involved 3q26.2 rearrangements (1999A-3, 2005B-6). However, 1999A-3 failed to meet 80% consensus primarily because both referee and participants failed to include the number of cells in brackets in the karyotype. While this finding could indicate that a constitutional translocation [t(3;21)(q26.2;q22)] was suspected, none of the participants included "c" after the karyotype designation. This case provided an educational opportunity by means of the Participant Summary Report to convey the importance of correct ISCN nomenclature. Case 2005B-6 failed to meet 80% consensus because inv(3)(q21q26.2)[5] was incorrectly reported as inv(3)(q21q26)[5]. At the 400-band level of resolution required for this case, band 3q26 does not exist.

In conclusion, the continued monitoring of laboratories that perform and report conventional chromosome results for hematologic neoplasms is essential for optimal patient care. From 1999–2018, the CyC provided 87 challenges (91 cases) that included representative abnormalities from various hematologic neoplasms (primarily MDS, AML, and ALL) that are commonly encountered and/or are critical to detect in a routine cytogenetics laboratory. In addition to grading abnormality and nomenclature components, most Participant Summary Reports also included discussion points that address each individual challenge (Table). The discussions included, but were not limited to, the clinical associations and prognostic significance of abnormalities, potential ancillary testing to verify the abnormalities identified, newly described cytogenetic abnormalities, targeted therapies specific to certain chromosomal abnormalities, and nomenclature issues. Future efforts could include increased karyotypic complexity and/or cases that incorporate more ancillary data, although achieving an 80% consensus may be challenging with these goals.

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