Nomenclature Evolution: Changes in the ISCN from the 2005 to the 2009 Edition

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Abstract

The Committee for the International System for Human Cytogenetic Nomenclature (ISCN) has recently met and published a revised version, ISCN 2009. Multiple changes in nomenclature guidelines are presented in that updated version. This review will highlight changes to the idiograms and specific changes in respective chapters of the 2009 version compared with the previous version of the ISCN published in 2005. These highlights are meant as a guide for the cytogeneticist to assist in the transition in the use of this updated nomenclature for describing cytogenetic and molecular cytogenetic findings in both clinical and research reports.

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The International System for Human Cytogenetic Nomenclature (ISCN) has served as the central reference for describing the human chromosome complement since 1960 [Denver Conference, 1960]. Multiple iterations of this system have evolved, and a historical record of that

evolution is presented in the most recent version of the ISCN, published in 2009 [ISCN, 2009]. The world-wide cytogenetic community strives for consistency in the descriptive and interpretive reporting of both normal and abnormal karyotypes, regardless of which technical evaluation method was used. As the field of cytogenetics continues to expand to include several molecular-based technologies, concurrent revisions of cytogenetic nomenclature are critical for accurate descriptions of the new technologies. In addition, as the use of cytogenetics in oncology continues to increase, the use of cytogenetic nomenclature for neoplasms continues to become more well-defined.

The ISCN committee, comprised of an elected panel of expert cytogeneticists representing each continent, convenes periodically to address changes in the field which are summarized in updated versions of the ISCN. The use of the most current ISCN nomenclature is required for cytogenetic publications, proficiency-testing mechanisms such as those administered through the College of American Pathologists/American College of Medical Genetics, and for laboratory accreditation. When ISCN versions are updated, the cytogenetics community enters a learning curve during a transition period while

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Table 1. Idiogram changes between ISCN 2005 and 2009

Chromosome	Region	Resolution (bhs)	Comment
1	q23–q25.2	550 and higher	distinct sub-bands defined
1	q32.12	850	distinct sub-bands defined
2	p21.1	850	distinct sub-bands defined
4	q35.2	700	eliminated q35.3
5	q13.2	850	distinct sub-bands defined
6	p23–21.1	700 and higher	distinct sub-bands defined and re-drawn
8	q24.2	550	distinct sub-bands defined
9	q34.1–q34.2	850	sub-bands eliminated
10	p12.3–p11.21	850	sub-bands re-drawn
11	q24	550	distinct sub-bands defined
14	q22–q31	400	re-drawn
15	q12	400	band eliminated
15	q26.2	400	band added
16	q12–q23	300	re-drawn
16	q12–q13	400	sub-bands eliminated and re-drawn
18	q21.1–q22	400	distinct sub-bands defined
X	p22.33–p22.1	550	distinct sub-bands defined
Y	q11.2	400	distinct sub-bands defined

bhs = Bands per haploid set.

the changes are adapted for use in both research and clinical reporting.

This report highlights the major changes in the most current version of the ISCN compared to ISCN [2005]. Karyotype examples are critical for illustrating nomenclature concepts, and new examples given will be noted by ISCN [2009] chapter. Descriptions of changes, with references to corresponding ISCN [2009] sections, can serve as a starting point in understanding and converting to ISCN [2009] nomenclature.

Chapter 2: Normal Chromosomes

One of the most obvious changes in the ISCN [2009] is the re-drawing of many of the idiograms representing chromosomes at various levels of banding resolution. It is important that all cytogeneticists become familiar with these new idiograms, as they contain multiple changes over those originally described by Francke [Francke, 1981]. These new idiograms and their derivation are described by Chia [2009] and summarized in table 1. It should be noted that many of the drawings have slightly different size designations for sub-bands, and it is suggested that the cytogeneticists perform a visual comparison between idiograms from ISCN [2005]

and ISCN [2009]. The revisions of the idiograms were accomplished by a subgroup of the ISCN committee and based on a comparison of multiple chromosomes from synchronized peripheral blood cultures, unsynchronized peripheral blood, oncology, prenatal and fibroblast cultures representing respective band resolutions. Major changes to the idiograms depicted in ISCN [2009] (fig. 5, Chapter 2) are shown in table 1. Additional changes are highlighted below in the respective chapters of the ISCN [2009].

Chapter 3: Symbols and Abbreviated Terms

Several symbols and abbreviations used in the description of chromosomes and chromosome abnormalities listed in Chapter 3 were redefined or clarified as shown in table 2.

Chapter 4: Karyotype Designation

Clarification for designating the band composition of a chromosome is provided in section 4.3.2.2. A new example karyotype is provided in section 4.3.1.2 (Three-Break Rearrangement).

Table 2. Symbol and abbreviated term changes (specific section specified), all new except expanded definitions noted in bold

amp	Denotes an amplified signal (13.2)
approximate sign (~)	Denotes intervals and boundaries of a chromosome segment or number of chromosomes, fragments, or markers (5.2); also used to denote a range of number of copies of a chromosomal region when the exact number cannot be determined (14.2)
arr	Microarray (14.3)
hmz	Homozygous, homozygosity; used when one or two copies of a genome are detected, but previous, known heterozygosity has been reduced to homozygosity through a variety of mechanisms, e.g. loss of heterozygosity (LOH) (14.2)
htz	Heterozygous, heterozygosity (14.2)
mlpa	Multiple ligation-dependent probe amplification (MLPA) (14.1, 14.4)
multiplication sign (×)	Multiple copies of rearranged chromosomes (9.3) or number of copies of a chromosomal region (14.2)
period (.)	Separates various techniques (13.2)
++	2 hybridization signals or hybridization regions on a specific chromosome (13.2)

Chapter 5: Uncertainty in Chromosome or Band Designation

A new example karyotype is provided in section 5.4 (Incomplete Karyotype).

Chapter 6: Order of Chromosome Abnormalities in the Karyotype

A new example karyotype is provided on page 52.

Chapter 7: Normal Variable Chromosome Features

In section 7.1, the term ‘variation’ is defined.

Chapter 8: Numerical Chromosome Abnormalities

Two new example karyotypes have been added to section 8.2 (Sex Chromosome Abnormalities). The second example indicates that for constitutional markers, there is a space between ‘mar’ and ‘c’ in the karyotype. A new karyotype example is also presented in section 8.4 (Uniparental Disomy).

Chapter 9: Structural Chromosome Rearrangements

Several revisions were made to chapter 9 including the addition of numerous karyotype examples describing various derivative chromosomes. New karyotypes have been added to the following sections: 9.1 (General Principles), 1 additional example; 9.2.2 (Deletions), 1 additional example; 9.2.3 (Derivative Chromosomes), 3 additional examples; 9.2.4 (Dicentric Chromosomes), 1 additional example; 9.2.9 (Insertions), 2 additional examples; 9.2.11 (Isochromosomes), 1 additional example; and in 9.2.13 (Neocentromeres), 1 additional example. Several karyotypes listed in the ISCN [2005] had erroneous chromosome counts when describing derivatives involving dicentric chromosomes; those examples have been corrected in ISCN [2009] to indicate the correct 45 chromosome count (section 9.2.3). Clarification of the definition of a marker chromosome is provided in section 9.2.12. Revisions have been made to the detailed system of designating structural abnormalities in several karyotypes in section 9.2.3. It is recommended that cytogeneticists carefully review the numerous revisions in that chapter, as descriptions of derivative chromosomes have traditionally been challenging.

Chapter 11: Neoplasia

The chapter on neoplasia has been extensively revised to include several alternative karyotypes that use either 'sdl' (sideline) or 'idem' to describe subclones. Section 11.1.4 clarifies the proper use of both 'sdl' and 'idem' for describing sidelines and has expanded explanations for some karyotypes illustrating the proper use of these terms. A new example karyotype is also present in section 11.1.3 (Mainline). It is known that cancer karyotypes can be extremely complex, and having a good understanding of the nomenclature of the examples provided can tremendously simplify report writing and interpretation.

Chapter 13: In situ Hybridization

Single additional karyotype examples have been added to sections 13.3.1 (Use of dim and enh), 13.4.2.3 (Dual Fusion Probes), and 13.4.2.4 (Break-Apart Probes). Two additional examples are included in sections 13.3 (Prophase/Metaphase in situ hybridization) and 13.9 (Partial Chromosome Paints). Section 13.4.1, describing number of signals, has been significantly expanded to include 9 new karyotype examples. Similarly, section 13.7 has 7 new examples illustrating nomenclature for chromosome comparative genomic hybridization. Alternative ways of writing the nomenclature to describe a relative position of signals are illustrated in section 13.4.2. Several karyotypes have also been revised throughout the chapter.

Chapter 14: Copy Number Detection

The final significant change to the ISCN [2009] is the addition of a new chapter with 55 new nomenclature examples describing copy number detection. As the field of microarray technology has advanced at a rapid pace, this section is critical for understanding how to communicate results from assays which detect gain or loss of genomic segments. The microarray nomenclature has been simplified from that which was initially described in 2005 to the symbol 'arr' which now can encompass array technology using multiple different platforms (CGH and others). Examples of normal and abnormal genomes are shown in section 14.3. The normal results are shortened over the previous designation and abnormal results again only describe specific abnormalities, leaving the assumption that all other regions gave a normal result. There is now the option to write a 'short' version, showing only the abnor-

mal nucleotides, or a detailed version, showing normal flanking nucleotides. Because SNP arrays can reveal genotypes, nomenclature for homozygosity (hmz) and heterozygosity (htz) have been introduced. Lastly, there is now a description of how to designate nomenclature for MLPA (multiple ligation-dependent probe amplification) (section 14.4.). It is expected that as molecular technologies evolve, the nomenclature will continue to be modified to meet the needs of the cytogeneticist.

Conclusion

In conclusion, as the field of cytogenetics and molecular genetics evolves, a standardized nomenclature is critical for describing karyotypes and genomic changes accurately and concisely. This report summarizes the major changes noted in the ISCN [2009]. Cytogeneticists are encouraged to carefully review the new version and become familiar with all differences introduced. While band designations described on the idiograms appear to more precisely indicate actual bands seen at different levels of resolution, one should also be cautioned that there may be discrepancies in genomic map locations at sites described previous to the publication of the ISCN 2009 and that the idiograms and genomic browsers have not been compared and reconciled. Careful identification of these potential discrepancies is recommended and is beyond the scope of this review.

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