Chromosomal Abnormalities

1- Numerical Abnormalities
2- Structural Abnormalities

Numerical Abnormalities Gains and losses of whole chromosomes in the karyotype string are usually denoted by the use of either a plus (+) or minus (−) sign before the aberrant chromosome; for example, 47,XY,+21. The exception is the sex chromosomes in constitutional studies, where sex chromosome gains and losses are indicated by listing the chromosome(s) present (e.g., 45,X or 47,XXY) without use of plus or minus signs. Acquired sex chromosome aberrations are written with plus and minus signs.

Ploidy refers to the number of sets of chromosomes present. Thus, diploid refers to the normal situation of two sets of each chromosome (e.g., 46,XX or 46,XY). A haploid, triploid, or tetraploid karyotype is evident from the chromosome number; for example, 23,X, 69,XXY, or 92,XXYY, respectively.

If additional chromosome changes are evident, these are expressed in relation to the appropriate ploidy level. The ploidy levels most commonly used in human karyotyping, most often in acquired diseases, are:

• Near-haploid (1n), which describes chromosome counts up to 34 chromosomes; numerical abnormalities are expressed in relation to 23 chromosomes.

• Near-diploid (2n), which describes counts with 35–57 chromosomes; numerical abnormalities being expressed in relation to 46 chromosomes.

• Near-triploid (3n), which describes karyotypes with 58–80 chromosomes; numerical aberrations are expressed in relation to 69 chromosomes.

• Near-tetraploid (4n), which describes karyotypes with 81–103 chromosomes; numerical changes are expressed in relation to 92 chromosomes.

25, X, +4, +10

This represents a near-haploid karyotype with two copies of chromosomes 4 and 10 and single copies of all other chromosomes.

70, XXY, +13

This describes a near-triploid karyotype with four copies of chromosome 13 and three copies of all other chromosomes.

At times, the biology of the study or the chromosome number will vary between two ploidy levels. Because precise communication of the karyotypic data is key, these cases may be written with the ploidy level in angle brackets "< >" immediately after the chromosome number and before the sex chromosome complement. For example, high hyperdiploidy, a favorable finding in pediatric acute lymphoblastic leukemia (ALL), may be written relative to 2n ploidy even

though it represents a near-triploid clone; for example, 59<2n>,XX,+X,+4,+5,+6,+10,+10,+14,+14,+17,+17,+18,+18,+21.

Endoreduplication (end) is a special form of duplication of the genome without mitosis, giving rise to four-stranded chromosomes at prophase and metaphase. Endoreduplication

should be written as end 46, XY. Note the space after the triplet and before the chromosome number.

Structural Chromosome Abnormalities

Abbreviations are used to specify structural abnormalities and precede the chromosome(s) involved in the aberration in the nomenclature string.

Deletions (del)

Deletions result in loss of a chromosome segment.

Terminal deletions are caused by a single break with loss of the segment distal to the break.

Interstitial deletions result from two breaks in a chromosome, loss of the intervening segment, and reunion of the breakpoints.

del (5)(p15.3)
This describes a terminal deletion of the short arm of chromosome 5. All chromosomal material distal to band p15.3 is missing.

del (20) (q11.2q13.3)
an interstitial deletion of the long arm of chromosome 20. The material between bands q11.2 and q13.3.

Ring Chromosomes (r)

Ring chromosomes, or rings, are donut-shaped structures that may involve one or more chromosomes.

46,XX,r(7)(p22q36)

This describes a ring derived from chromosome 7. Breaks have occurred at bands p22 and q36, and the ends of the segment between the breakpoints have re-joined. The acentric (without a centromere) segments distal to the breakpoints have been lost.

Inversions (inv)

In an inversion, a chromosomal segment breaks, reorients 180°, and reinserts itself. If an inversion involves the centromere, with one break in each chromosome arm, it is said to be pericentric. A paracentric inversion is isolated to one chromosome arm and does not involve the centromere.

46, XX,inv(16)(p13.1q22)

This is a pericentric inversion of chromosome 16. A break has occurred in the short arm at band 16p13.1 and the long arm at band 16q22. The chromosome segment between these bands is present but inverted. This aberration is commonly observed in acute myelomonocytic leukemia with eosinophilia

46,XY,inv(3)(q21q26.2)

This is a paracentric inversion involving bands q21 and q26.2 in the long arm of chromosome 3. This rearrangement is also seen in acute myeloid leukemia.

Duplications (dup)

The orientation of duplications is either direct or inverted and is indicated by the order of the bands with respect to the centromere in the karyotype designation.

The band closest to the centromere is written first in the short system; only the detailed system can pinpoint the exact location of the duplicated segment.

46,XY,dup(1)(q21q42)

This is a direct duplication of the segment between bands q21 and q42 in the long arm of chromosome 1.

46,XX,dup(13)(q34q21)

This is an inverted duplication of the segment between bands q21 and q21 in the long arm of chromosome 13.

Insertions (ins)

An insertion involves the movement of a segment of intrachromosomal material from one chromosomal location into another. The recipient can be another chromosome or a different part of the chromosome of origin.

The orientation of the inserted segment may be direct, retained in its original orientation, or inverted. In inverted insertions, the “normal” orientation of the bands will be reversed with respect to the centromere.

Translocations (t)

A translocation is an abnormality resulting from an exchange of genetic material between two chromosomes.

46,XY,t(12;14)(q13;q32)

This is a translocation involving two chromosomes. Breaks have occurred at bands q13 and q32.

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Robertsonian Translocations (rob)

Robertsonian translocations are a special type of translocation in humans involving the acrocentric chromosomes (chromosomes 13, 14, 15, 21, and 22).

Typically, the participating chromosomes break in their short arms and give the appearance that the long arms fuse to form a single chromosomea with a single centromere. If the location of the breakpoints is unproven, “rob” may be used.

Because the short arms of acrocentric chromosomes contain repetitive ribosomal gene clusters, loss of these arms due to this type of translocation has no phenotypic consequences.

A karyotype with a single Robertsonian translocation by definition will have a 45-chromosome count.

Isochromosomes (i)

An isochromosome is an abnormal chromosome with two identical arms due to duplication of one arm and loss of the other arm (mirror image of a chromosome from its centromere).

46,XY,i(6)(p10)

An isochromosome for the short arm of chromosome 6 has replaced one copy of chromosome 6.

46,X,i(X)(q10)

This is a female with one normal X chromosome and one isochromosome for the long arm of the X chromosome. This karyotype is a frequent finding in patients with Turner syndrome

Dicentric (dic), Isodicentric (idic) Chromosomes

These are structurally altered chromosomes with two centromeres.

In the karyotype description, both dicentric and isodicentric chromosomes are counted as one chromosome without the need to indicate the missing normal chromosome(s).

45,XY,dic(14;14)(q11.2;q32)

This represents a dicentric chromosome formed by breakage and reunion at bands 14q11.2 and 14q32 on the two homologous chromosomes 14. However, if a dicentric chromosome is proven to originate through breakage and reunion of sister chromatids, it may be designated as dic (14) (q11.2q32).