

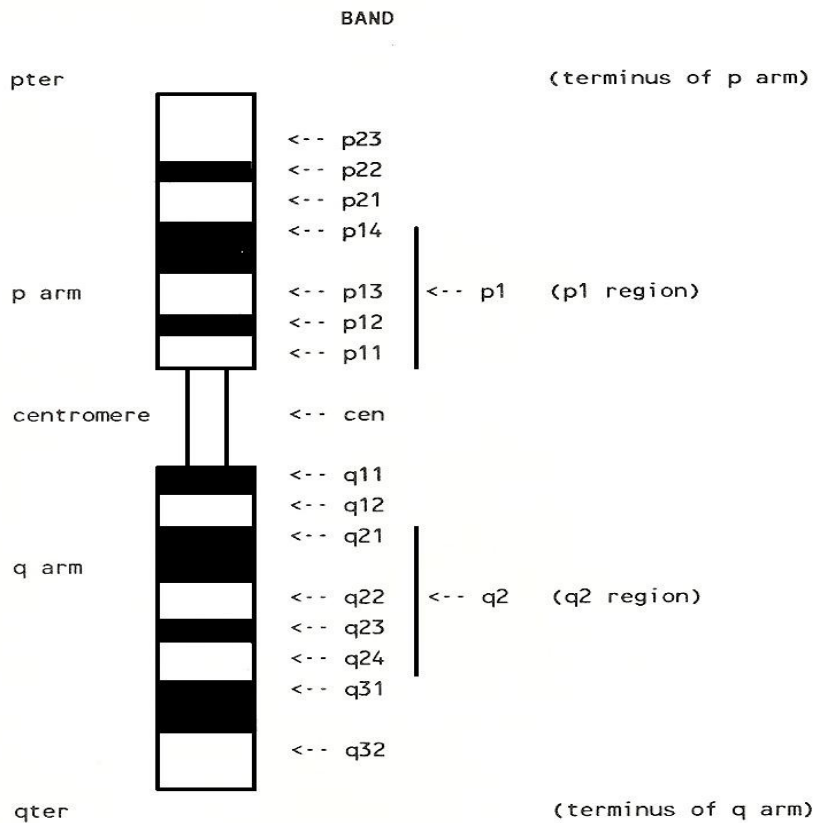
## Interpreting Chromosomal Abnormalities

This project, co-authored with J.M. Friedman, MD, PhD, FAAP, FABMG, FCCMG, FRCPC of UBC Medical Genetics, developed an Expert System to interpret standard notation used to represent human chromosomal abnormalities.

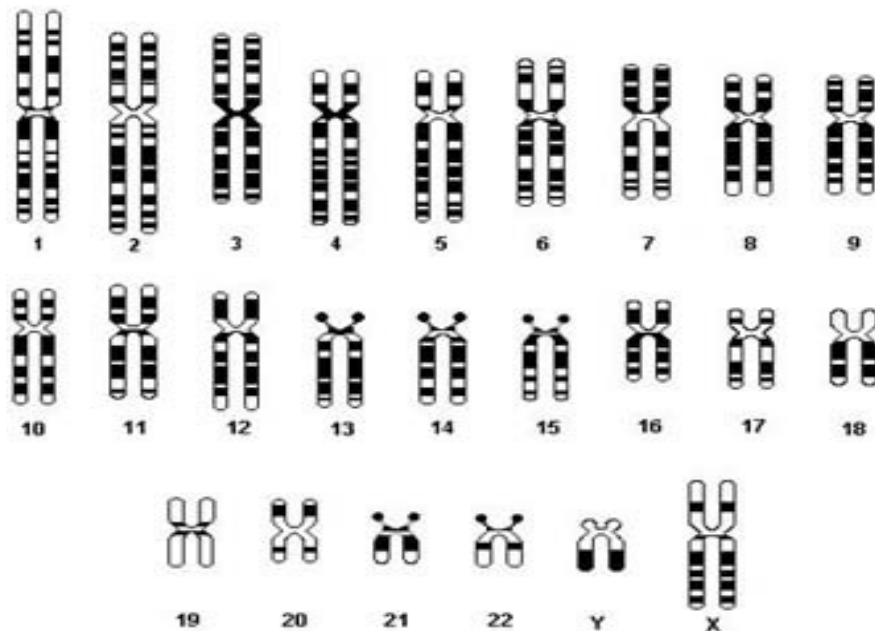
The genetic material of cells is contained in DNA molecules. Normal human cells contain 46 chromosomes arranged in 23 pairs. One of the pairs, called the sex chromosomes, determines whether the individual is a male or female. Females have two identical sex or "X" chromosomes. Males have one X chromosome like that in the female, but their other sex chromosome is a smaller one called "Y". Males are designated XY and females, XX. The other 22 pairs of chromosomes appear the same in males and females and are called autosomes. Each pair of autosomes is designated by a number from 1 to 22.

The DNA of each chromosome forms a specific linear sequence of genes. One member of each pair of chromosomes (and, consequently, one member of each pair of genes) is inherited from the father and the other member is inherited from the mother. During reproduction, one member chosen at random from each pair of chromosomes enters the egg or sperm. When the mother's egg and the father's sperm unite at conception, the embryo again has 46 chromosomes. It is this way that children inherit half of their genes from each parent.

Every chromosome has a characteristically placed central constriction, the centromere, which divides the chromosome into a short "p" and a long "q" arm. Although one cannot see individual genes under the microscope, one can tell the chromosomes from each other because each pair exhibits a different specific pattern of light and dark bands when stained appropriately. Schematically, one may view a chromosome as a series of alternating bands lined up in a row:



Each band contains many genes. The bands are customarily grouped into regions and are numbered from the centromere outward to the chromosome tips, which are labeled pter and qter. In the chromosome represented above, for example, region p1 is divided into bands p11, p12, p13, and p14. The next region up is p2, and it is divided similarly. Depending on the degree of resolution achieved by the specific method of chromosome preparation used, some of the bands may be seen to be further divided into subbands. Subbands are labeled as decimal fractions of the parent band, for example, p12.1, p12.2, and p12.3 or p12.21, p12.22, and p12.23.



Normal cells contain 2 copies of each autosome (1-22) plus two sex chromosomes (XX or XY)

Normal embryonic development is critically dependent on having the right number and combination of genes present. Thus, whenever a chromosome, chromosome arm, region, or even band is present in too many or too few copies, serious abnormalities of physical and mental development can occur. For example, Down syndrome results from the presence of three, rather than the normal two, copies of the smallest chromosome (number 21). In other circumstances, all of the normal amount of chromosomal material is present, but it is rearranged. This may or may not be associated with physical abnormalities or mental retardation, but almost always causes problems with transmission of the genetic material to the eggs and sperm. Individuals who carry such balanced (but abnormal) chromosomal rearrangements therefore have an increased risk of having children with physical abnormalities and mental retardation.

Cytogeneticists describe patients with chromosomal abnormalities using standard notation known as the **International System for Human Cytogenetic Nomenclature (ISCN)**. ISCN is an elegant way to express chromosomal abnormalities, but it is very densely packed with information. In a single formula of about 50 characters, one can describe a patient with:

- Abnormal amounts of specific blocks of genetic material
- Rearrangements of various chromosomes
- A change in the total number of chromosomes
- An alteration of sex determination
- The specific mechanism that brought about the abnormalities
- The parent from whom they were inherited

Storing these formulas is easy, but searching for them on the basis of cytogenetically useful criteria is beyond the capacity of conventional software that relies on string matching to distinguish records. That's because a specific alteration of cytogenetic interest (eg. loss of a certain chromosome segment) may occur in a variety of ways, each of which would be written differently in ISCN. The ISCN standard also allows the same abnormality to be written in several different formats and treats similar alterations of sex chromosomes and autosomes differently.

This project created a software program called ISCN Expert that transforms any ISCN formula to a more descriptive formula that describes in greater detail the linear sequence of bands present. Such formulas act like an "exploding parts" catalog, on which searches for specific rearrangements may be performed. The program was written in Prolog (PROgramming in LOGic), where each ISCN formula is regarded as a mathematical structure (much like an algebraic expression). Such expressions are naturally parsed by Prolog, where its "logical variable" is used to represent unknown material. These exploded parts are searched by the same program for abnormalities, using a large rule base.

Prolog's logical variables behave identically to their mathematical counterparts in equation solving. Consequently, Prolog programmers enjoy the same advantage as those using algebra to solve problems involving unknown quantities. For example, a data structure can be partially instantiated when passed to and from a predicate (ie. subroutine), allowing each rule to fill in the result of a query incrementally. With this feature, Prolog code is powerful and compact. ISCN Expert uses the logical variable everywhere, such as when building or searching linear structures representing abnormal chromosomes. It also makes rules bases very easy to build or read.

A simple example of a normal "karyotype" is an ordinary male, represented by

**46, xy**

The program's output for this ISCN string would be:

```
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 x y
| | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |
Sex model is male
```

Here, | represents one chromosome. So there are two of them for each chromosome 1 to 22, one for x, and one for y.

A simple example of an abnormal karyotype is Down syndrome, interpreted by the program as follows:

**47, xy, +21**

```
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 x y
| | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |
Sex model is male
Exactly 3 whole copies of chromosome 21
```

A more complicated example is a rearrangement, in which a segment of one chromosome has moved to another chromosome. This rearrangement may or may not be reciprocal (ie. the two chromosomes may or may not exchange segments):

**46, xx, -18, +der(13q18q), t(13;18)(13q18q;13p18p)pat**

```
Paternal origin
46, xx, -18, +der(13q18q), t(13;18)(13q18q;13p18p)pat

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 x y
| | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |
Cell observation is whole arm translocation
Chromosome with centromeres 13 18 is 13qter->cen->18qter
Sex model is female
Exactly 1 whole copies of chromosome 18
WAU(13,18) = unbalanced segregant of translocation (whole arm)
```

Here a chromosome 18 has been replaced by a more complicated chromosome involving material from a chromosome 13. So there is one normal 18, and one abnormal 18 whose linear sequence of genetic material is exactly described in the output:

13qter->cen->18qter

This automatic transformation of the original (short) formula to the so-called "long" formula is the essence of the program. It allows geneticists to easily decipher the composition of the abnormal chromosome, showing that it is composed of the long arms of 13 and 18 joined in the middle by their centromeres. More importantly, it allows database software to locate this abnormality in any database of short formulas, by using the long formulas generated by the program.

**46,XX,-2,+der(2),ins(Y;2)(p1;q21q22)**

```
1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 X  Y
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Cell observation is direct insertion between two chromosomes
Chromosome 2 is 2pter->2q21::2q22->2qter
Sex model is female
Exactly 1 whole copies of chromosome 2
DXD(Y,2) = Deleted der chrom from DIRINS - 2 chrom (IDR)
IDR(2) = Interstitially deleted chromosome replaced normal
```

In this example, a Y chromosome appears in the formula but not in the cell line, so the sex model is female. This shows that searching for male cell lines by merely string searching for the character "Y" in short (or long) formulas would be inadequate. ISCN Expert, on the other hand, computes the sex model by "knowledge searching" each abnormality for the correct sex model.

**46,XX,del(2)(q21q22)**

```
1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 X  Y
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Cell observation is interstitial deletion
Chromosome 2 is 2pter->2q21::2q22->2qter
Sex model is female
Exactly 1 whole copies of chromosome 2
IDR(2) = Interstitially deleted chromosome replaced normal
```

This example is structurally equivalent to the previous abnormality, but results from a different aberration. ISCN Expert recognizes this by providing the same structural interpretation. In other words, the two short formulas are completely different but their long forms are identical. ISCN Expert understands this.

**47,XX,dup(Y)(q11.21 to q11.22)**

```
1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 X  Y
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Cell observation is direct duplication
Chromosome Y is Ypter->Yq11.22::Yq11.21->Yqter
Sex model is male
Exactly 0 whole copies of chromosome Y
Exactly 2 whole copies of chromosome X
DDR(Y) = Direct duplication replaces normal
XNX(X) = Extra whole normal chrom (trisomy, XXY, or XYY)
```

In this example ISCN Expert regards one of the X chromosomes as "extra", since there are two of them in a male model. But another interpretation could have been that the Y chromosome is extra, since there are two normal X's. However, the program adopts the convention that the sex model determines how many sex chromosomes of each type are expected. Ordinary string searching would be unable to determine whether X or Y is "extra" in any formula where X appears twice and Y appears once.

Other examples are (input is boldfaced, output is shaded):

**46,x,-x,-5,+der(x),+der(5),dirins(x;5)(q26.1;p12p13)**

```
1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 x  y
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Cell observation is direct insertion between two chromosomes
Chromosome x is xpter->xq26.1::5p12->5p13::xq26.1->xqter
Chromosome 5 is 5pter->5p13::5p12->5qter
Sex model is female
Exactly 1 whole copies of chromosome x
Exactly 1 whole copies of chromosome 5
```



2 extra isochromosomes which are the same	Inverted chrom replaced normal (from peri INV)
2 extra isochromosomes which are different	Unbalanced recombinant resulting from peri INV
Isochromosome replaces 1 normal chromosome	Extra inverted chrom (from pericentric INV)
1 isochromosome replaces 2 normal chromosomes	Ring chromosome replaced normal
Extra isochromosome	Extra ring chromosome
Interstitially deleted chromosome replaced normal	Unbalanced 3:1 segregant with 1 derivative
Extra interstitially deleted chromosome	Unbalanced 3:1 segregant with 2 derivatives
Balanced carrier of inverted INS - 1 chrom	Unbalanced 3:1 segregant with 3 derivatives
Normal karyotype (from INVINS - 1 chrom)	Unbalanced adjacent-1 segregant
Unbalanced recomb result from INVINS - 1 chrom	Balanced carrier of reciprocal translocation
Inverted insertion in extra chromosome	Unbalanced 1:3 segregant with derivative
Balanced carrier of INVINS - 2 chrom	Unbalanced adjacent-2 segregant
Deleted der chrom from INVINS - 2 chrom (IDR)	Unbalanced 1:3 segregant - monosomy
Derivative chrom with INVINS - 2 chrom	Normal karyotype (from recip trans)
Normal karyotype (from INVINS - 2 chrom)	Terminal rearrangement replaces 1 chromosome
Chromosome with unknown segment deleted	2 same ter rea's replace 1 normal chromosome
Extra chromosome with unknown segment deleted	Terminal rearrangement replaces 2 chromosomes
Balanced carrier of unspecified INS - 1 chrom	Terminal rearrangement chromosome is extra
Normal karyotype (from unspec INS - 1 chrom)	Terminally deleted chromosome replaced normal
Unbalanced resulting from unspec INS - 1 chrom	Extra terminally deleted chromosome
Balanced carrier of unspec INS - 2 chrom	Tetraploid (4n = 92)
Deleted der chrom from unspec INS - 2 chrom (IDR)	Triploid (3n = 69)
Derivative chrom with unspec INS - 2 chrom	Unbalanced segregant with 2 extra chrom (tandem)
Normal karyotype (from unspec INS - 2 chrom)	Balanced carrier from tandem translocation
Marker chromosome	Unbalanced segregant miss a chrom (tandem trans)
Miscellaneous (double) deletion	Normal karyotype (from tandem translocation)
Missing whole chromosome (monosomy)	Unbalanced segregant with extra chrom (tandem)
Normal karyotype (from paracentric INV)	Balanced carrier of translocation (whole arm)
Inverted chrom replaced normal (from para INV)	Normal karyotype (from whole arm translocation)
Unbalanced resulting from paracentric INV	Unbalanced segregant of translocation (whole arm)
Extra inverted chrom (from paracentric INV)	Chromosome with extra unknown piece attached
Pseudodicentric replaces 1 chromosome	Extra chromosome with extra unknown piece attached
2 same psu dic's replace 1 normal chromosome	Dbl trisomy/auto trisomy plus XXX/XXY/YYY
Pseudodicentric replaces 2 chromosomes	2 ex whole normal chroms (tetra, XXXY, XXYY, YYYY)
Pseudodicentric chromosome is extra	Extra whole normal chrom (trisomy/XXY/YYY)
Normal karyotype (from pericentric INV)	

Suppose we wanted to search the following database of ISCN expressions for all abnormalities contained in the program's rule base:

**Case ISCN expression**

- 1 44,X,terrea(1;1)(q44;q44)
- 2 45,-X,-5,+der(X),+der(5),dirins(X;5)(q21.3;p12p13)
- 3 45,-X,-X,dic(X)(q12)
- 4 45,-X,-X,dic(X)(q25)
- 5 45,X,-1,+der(1),ins(1;1)(q1;q1q2)
- 6 45,X,-21,+dic(X;21)(q26;p12)
- 7 45,X,-21,+psudic(21)t(21;Y)(q2;q12)
- 8 45,X,-21,+psudic(21;X)(p12;q26)
- 9 45,X,-21,+psudic(X)t(X;21)(q26;p12)
- 10 45,X,-21,+psudic(X;21)(q26;p12)
- 11 45,X,-21,+terrea(21;X)(q22;q28)
- 12 45,X,-21,+terrea(X;21)(q28;q22)
- 13 45,X,-X,-21,+psudic(21;X)(p12;q26)
- 14 45,X,-X,-21,+psudic(X)t(X;21)(q26;p12)
- 15 45,X,-X,-21,+psudic(X;21)(q26;p12)
- 16 45,X,-X,-21,+terrea(21;X)(q22;q28)
- 17 45,X,-X,-21,+terrea(X;21)(q28;q22)
- 18 45,X,-X,dic(X;21)(q26;p12)
- 19 45,X,-X,psudic(X)t(X;21)(q26;p12)
- 20 45,X,-X,terrea(X;21)(q28;q22)

21 45, X, -Y, -21, +dic(Y;21) (q12;q2)  
22 45, X, -Y, -21, +psudic(21)t(21;Y) (q2;q12)  
23 45, X, -Y, psudic(21)t(21;Y) (q22;q12)  
24 45, X, -Y, psudic(Y;21) (q12;q22)  
25 45, X, -Y, terrea(21;Y) (q22;p11)  
26 45, X, dic(X;21) (q26;p12)  
27 45, X, dic(Y;21) (p11;q11)  
28 45, X, dic(Y;21) (q12;q22)  
29 45, X, ins(1) (p1q1q2)  
30 45, X, psudic(X)t(X;21) (q26;p12)  
31 45, X, psudic(X;21) (q26;p12)  
32 45, X, psudic(21)t(21;Y) (q21;q12)  
33 45, X, terrea(21;Y) (q22;p11)  
34 45, X, terrea(Y;21) (p11;q22)  
35 45, XX, -12, -14, +terrea(12;14) (p13;q32)  
36 45, XX, -14, -21, +dic(14;21) (p11;p12)  
37 45, XX, -14, -21, +psudic(14)t(14;21) (p11;p12)  
38 45, XX, -14, -21, +psudic(14)t(14;21) (p13;p13)  
39 45, XX, -14, -21, +psudic(14;21) (p11;p12)  
40 45, XX, -14, -21, +psudic(14;21) (p13;p13)  
41 45, XX, -21, -21, +dic(21) (p12)  
42 45, XX, -21, dic(21) (p12)  
43 45, XX, -21, idic(21) (p12)  
44 45, XX, -21, psudic(21) (p12)  
45 45, XX, dic(14;21) (p11;p12)  
46 45, XX, dic(15;21) (q1;q22)  
47 45, XX, dic(15;21) (q26;q22)  
48 45, XX, dic(1;1) (p1;p1)  
49 45, XX, dic(1;2) (p1;p1)  
50 45, XX, psudic(14;21) (p11;p12)  
51 45, XX, psudic(1;1) (q1;q1)  
52 45, XY, -21, -21, +psudic(21) (p12)  
53 45, XY, -21, dic(21) (p12)  
54 45, XY, -21, psudic(21) (p12)  
55 45, XY, dic(14;21) (p11;p12)  
56 45, XY, psudic(14)t(14;15) (p13;p13)  
57 45, XY, psudic(14)t(14;21) (p11;p12)  
58 45, XY, psudic(14;21) (p11;p11)  
59 45, XY, terrea(14;12) (q32;p13)  
60 45, XY, terrea(1;1) (q44;q44)  
61 45, Y, -21, +psudic(X), t(X;21) (q26;p12)  
62 45, Y, -X, -21, +psudic(X)t(X;21) (q26;p12)  
63 45, Y, dic(X;21) (q27;p12)  
64 45, Y, dic(Y;21) (q12;p12)  
65 45, Y, ins(1) (p1q1q2)  
66 45, del(y) (p)  
67 45, dic(X) (q21)  
68 45, dic(X;X) (q21;q22)  
69 45, dic(X;Y) (q21;q12)  
70 45, dic(Y;Y) (q12;q12)  
71 45, psudic(X) (q21)  
72 45, psudic(X) (q21)  
73 45, xy, -1, del(1) (p)  
74 46, X, +ins(1) (p1q1q2)  
75 46, X, +terrea(X;Y) (q28;p11)  
76 46, X, -9, +del(9) (pter->cen:), +del(9) (qter->cen:)  
77 46, X, -X, +der(X), ins(X;1) (p1;q1q2)  
78 46, X, -X, -5, +der(X), +der(5), dirins(X;5) (q26.1;p12p13)  
79 46, X, -X, dic(X) (q11)  
80 46, X, -Y, -5, +der(Y), +der(5), invins(Y;5) (q11.2;p14p12)  
81 46, X, -Y, psudic(21)t(21;Y) (p11;q11), +21  
82 46, X, -Y, psudic(X;Y) (q1;q1)  
83 46, X, -Y, psudic(Y)t(Y;21) (q11;p11), +21

84 46, X, -Y, psudic (Y;21) (q12;p12), +21  
85 46, X, der (X), dirins (X;5) (q11;p11p14)  
86 46, X, der (X), ins (X;1) (q11;p1p2)  
87 46, X, dic (X) (q11)  
88 46, X, dic (X) (q27)  
89 46, X, dic (X;21) (q27;p12), +21  
90 46, X, dic (X;X) (q21;q22)  
91 46, X, dic (X;Y) (q21;q12)  
92 46, X, dic (Y) (p11)  
93 46, X, dic (Y;Y) (q12;q12)  
94 46, X, dirins (5;X) (p12;q21q24)  
95 46, X, dirins (5;X) (p13;q13q23)  
96 46, X, dirins (5;Y) (p11;q11.2q12)  
97 46, X, dirins (X) (q13q24q27)  
98 46, X, dirins (X;5) (q21;p13p14)  
99 46, X, dirins (Y;5) (q11.2;p12p13)  
100 46, X, fra (X) (q27)  
101 46, X, idic (X) (q2)  
102 46, X, idic (Y) (p11)  
103 46, X, ins (X) (p1q1q2)  
104 46, X, invins (5;X) (p14;q24q23)  
105 46, X, invins (5;Y) (p12;q12q11.2)  
106 46, X, invins (X) (q13q27q24)  
107 46, X, invins (X;5) (q11;p13p12)  
108 46, X, invins (Y;5) (q11.2;p14p12)  
109 46, X, psudic (21)t (21;Y) (p11;q11), +21  
110 46, X, psudic (21;Y) (p11;q11), +21  
111 46, X, psudic (X) (q11)  
112 46, X, psudic (X;X) (q1;p1)  
113 46, X, psudic (Y) (p11)  
114 46, X, psudic (Y)t (Y;21) (q11;p11), +21  
115 46, X, psudic (Y;21) (q12;p12), +21  
116 46, X, terrea (X;Y) (p22.33;p11)  
117 46, X, terrea (X;Y) (p22;q12)  
118 46, X, terrea (Y;Y) (p11;p11)  
119 46, XX, -1, +der (1), -1, +der (1), ins (1;1) (q1;p2p1)  
120 46, XX, -1, +der (1), -2, +der (2), ins (1;2) (q1;p2p1)  
121 46, XX, -1, +der (1), ins (1;2) (p1;q1q2)  
122 46, XX, -1, -2, +der (1), +der (2), ins (1;2) (q1;p1p2)  
123 46, XX, -12, +terrea (12;14) (p13;q32)  
124 46, XX, -14, +terrea (12;14) (p13;q32)  
125 46, XX, -15, +dic (15;21) (p11;p12)  
126 46, XX, -15, +dic (15;21) (q26;q22)  
127 46, XX, -15, +psudic (21), t (21;15) (p12;p11)  
128 46, XX, -15, +psudic (21), t (21;15) (q22;q26.3)  
129 46, XX, -15, +psudic (21)t (21;15) (p12;p11)  
130 46, XX, -2, +der (2), ins (1;2) (p1;q2q1)  
131 46, XX, -2, +der (2), ins (Y;2) (p1;q32q22)  
132 46, XX, -2, +der (2), invins (5;2) (p11;q32q22)  
133 46, XX, -21, +dic (21) (p12)  
134 46, XX, -21, +dic (X;21) (q26;p12)  
135 46, XX, -21, +psudic (21;15) (p12;p11)  
136 46, XX, -21, +psudic (X;21) (q26;p12)  
137 46, XX, -21, +psudic (21)t (21;15) (p12;p11)  
138 46, XX, -21, +psudic (21)t (21;15) (p13;p13)  
139 46, XX, -5, +der (5), dirins (5;X) (p14;q23q24)  
140 46, XX, -5, +der (5), invins (X;5) (q1;p14p12)  
141 46, XX, der (1), ins (1;2) (p1;p1p2)  
142 46, XX, der (2), ins (1;2) (p1;p2p1)  
143 46, XX, dic (12) (q12)  
144 46, XX, dic (13) (q12)  
145 46, XX, dic (15;21) (p11;p12), +15  
146 46, XX, dic (21) (p12)

147 46,XX,dic(X;21) (q26;p12)  
148 46,XX,dic(Y;21) (q12;p12)  
149 46,XX,dirins(1;3) (p22;q21q25)  
150 46,XX,ins(1;2) (q1;q1q2)  
151 46,XX,ins(1;2) (q1;q2q1)  
152 46,XX,psudic(21) (p12)  
153 46,XX,psudic(21)t(21;15) (p12;p11),+21  
154 46,XX,psudic(21)t(21;15) (p13;p13),+21  
155 46,XX,psudic(21;15) (p12;p11),+15  
156 46,XX,psudic(21;15) (q22;q26),+15  
157 46,XX,psudic(X)t(X;21) (q26;p12)  
158 46,XX,psudic(21)t(21;15) (p12;p11),+15  
159 46,XX,tdic(15;21) (p11;p12),+21  
160 46,XX,terrea(12;14) (p13;q32),+12  
161 46,XX,terrea(12;14) (p13;q32),+14  
162 46,XX,terrea(X;21) (q28;q22)  
163 46,XXq+  
164 46,XY,-15,+psudic(21;15) (p12;p11)  
165 46,XY,-2,-5,+der(2),+der(5),invins(5;2) (p13;q32q22)  
166 46,XY,-21,+dic(15;21) (p11;p12)  
167 46,XY,-21,+dic(21) (p12)  
168 46,XY,-21,+psudic(21) (p12)  
169 46,XY,-21,+psudic(21;Y) (p12;q12)  
170 46,XY,-21,+psudic(21) (p12)  
171 46,XY,-21,+psudic(21)t(21;Y) (p12;q11)  
172 46,XY,-21,+psudic(Y)t(Y;21) (q11;p11)  
173 46,XY,-21,+terrea(21;X) (q22;q28)  
174 46,XY,-21,+terrea(X;21) (q28;q22)  
175 46,XY,-5,+der(5),invins(Y;5) (q11.2;p14p13)  
176 46,XY,13ss,14ph-  
177 46,XY,1p+  
178 46,XY,1p-  
179 46,XY,1ps,13ps-qs  
180 46,XY,1qh+,1qh-  
181 46,XY,del(13) (p1)  
182 46,XY,der(2),dirins(5;2) (p12;q22q32)  
183 46,XY,der(2),invins(5;2) (p14;q32q22)  
184 46,XY,der(2)dirins(5;2) (p11;q22q32)  
185 46,XY,der(5),invins(5;Y) (p12;q12q11.2)  
186 46,XY,dic(X;21) (q26;p12)  
187 46,XY,dic(Y;21) (q12;p12)  
188 46,XY,dirins(1) (q42q2q3)  
189 46,XY,dirins(5;2) (p15.31;q22q32)  
190 46,XY,dirins(1) (p1q1q2)  
191 46,XY,dirins(1;3) (p22;q24q25)  
192 46,XY,frac(11) (q13q23)  
193 46,XY,frac(2) (q11)  
194 46,XY,ins(1) (p1q1q2)  
195 46,XY,ins(1) (p1q1q2)  
196 46,XY,ins(2) (p13q2q3)  
197 46,XY,ins(2) (p13q31q21)  
198 46,XY,invins(1) (q42q31q11)  
199 46,XY,invins(2) (p13q3q2)  
200 46,XY,invins(5;2) (p15.3;q32q22)  
201 46,XY,inv(1) (p1q1),inv(1qh)  
202 46,XY,psudic(21;15) (p12;p11),+21  
203 46,XY,psudic(Y;21) (q12;p12)  
204 46,XpsXpsqs  
205 46,Xq-Yp-  
206 46,Y,+terrea(X;Y) (q28;p11)  
207 46,Y,-X,+der(X),dirins(5;X) (p14.3;q21q22)  
208 46,Y,-X,+der(X),ins(5;X) (p1;q21q23)  
209 46,Y,-X,+der(X),ins(X;1) (p1;q1q2)

210 46, Y, -X, psudic(21;X) (p12;q27), +21\*  
211 46, Y, -X, psudic(X;Y) (p1;q1)  
212 46, Y, -X, terrea(21;X) (q22;q28), +21  
213 46, Y, -X, terrea(X;21) (q28;q22), +21  
214 46, Y, dic(X;X) (q21;q22)  
215 46, Y, dic(X;Y) (q1;q12)  
216 46, Y, dic(Y;Y) (q11;q12)  
217 46, Y, dirins(5;X) (p1;q1q2)  
218 46, Y, dirins(X;5) (q11;p12p13.1)  
219 46, Y, ins(X;5) (q21;p14p15)  
220 46, Y, invins(5;X) (p15;q24q21)  
221 46, Y, invins(X;5) (q21;p14p11)  
222 46, Y, psudic(X;Y) (p1;q1)  
223 46, Y, terrea(21;X) (q22;q28), +21  
224 46, Y, terrea(X;21) (q28;q22), +21  
225 46, Y, terrea(X;X) (q28;q28)  
226 46, Y, terrea(Y;Y) (p11;p11)  
227 46, Yq+Yq-  
228 46, dic(X) (q27), Y  
229 46, idic(X) (q27), Y  
230 46, psudic(X) (q27), Y  
231 46, x, del(x) (p)  
232 46, xy, -1, +del(1) (p)  
233 46, xy, del(1) (p)  
234 47, X, +Xp, +Xq  
235 47, X, +Yp, +Yq  
236 47, XX, +dic(15;21) (q11;q21)  
237 47, XX, +dic(15;21) (q26;q22)  
238 47, XX, +dic(X;21) (p22;p11)  
239 47, XX, +idic(15) (q11)  
240 47, XX, +psudic(15) (q11)  
241 47, XX, +psudic(X;21) (q26;p11)  
242 47, XX, +psudic(X;Y) (q1;p1)  
243 47, XX, +psudic(21)t(21;15) (q11;p11)  
244 47, XX, +psudic(21)t(21;Y) (p1;q1)  
245 47, XX, dic(X) (q1)  
246 47, XX, dic(X;X) (q1;q2)  
247 47, XX, dic(X;Y) (q21;q1)  
248 47, XX, dic(Y;Y) (q12;q12)  
249 47, XX, fra(X) (q27)  
250 47, XX, idic(15) (q11), +15  
251 47, XX, idic(15) (q12), +15  
252 47, XX, idic(X) (q1)  
253 47, XX, ins(X) (p1q1q2)  
254 47, XX, psudic(X;Y) (q1;p1)  
255 47, XXpsXpsqs  
256 47, XY, +1, del(13) (p1)  
257 47, XY, +dic(15;21) (q11;q11)  
258 47, XY, +dic(15;21) (q11;q22)  
259 47, XY, +dirins(1) (q2q31q42)  
260 47, XY, +ins(1) (p1p2p3)  
261 47, XY, +ins(1) (p1p3p2)  
262 47, XY, +ins(1) (p1q1q2)  
263 47, XY, +ins(1) (p1q3q2)  
264 47, XY, +ins(1) (p3p1p2)  
265 47, XY, +ins(1) (p3p2p1)  
266 47, XY, +ins(1) (q1p2p3)  
267 47, XY, +ins(1) (q1p3p2)  
268 47, XY, +ins(1) (q1q2q3)  
269 47, XY, +ins(1) (q1q3q2)  
270 47, XY, +ins(1) (q3q1q2)  
271 47, XY, +ins(1) (q3q2q1)  
272 47, XY, +invins(1) (q21q42q31)

273 47,XY,+psudic(15)(p12)  
 274 47,XY,+psudic(21;15)(q11;q11)  
 275 47,XY,+psudic(21;15)(q11;q26)  
 276 47,XY,+psudic(Y)t(Y;21)(q11;p11)  
 277 47,XY,+psudic(Y)t(Y;21)(q12;p12)  
 278 47,XY,+psudic(Y;Y)(q1;q1)  
 279 47,XY,+psudic(X;X)(q1;p1)  
 280 47,XY,+psudic(Y;21)(q11;p11)  
 281 47,XY,+terrea(14;12)(q32;p13)  
 282 47,XY,+terrea(21;X)(q22;q28)  
 283 47,XY,+terrea(X;21)(q28;q22)  
 284 47,XY,+terrea(X;X)(q28;q28)  
 285 47,XY,-1,+1p,+1q  
 286 47,XY,dic(15)(q11),+15  
 287 47,XY,dic(X)(q11)  
 288 47,XY,dic(X;X)(q2;q2)  
 289 47,XY,dic(X;Y)(q1;q1)  
 290 47,XY,dic(Y)(p11)  
 291 47,XY,dic(Y;Y)(q12;q12)  
 292 47,XY,dirins(X)(q27q13q24)  
 293 47,XY,fra(X)(q27)  
 294 47,XY,ins(X)(p1q1q2)  
 295 47,XY,invins(X)(q27q24q13)  
 296 47,XY,psudic(15)(q11),+15  
 297 47,XY,psudic(X)(q21)  
 298 47,XY,psudic(X;Y)(q1;p1)  
 299 47,XY,psudic(Y)(q12)  
 300 47,XY,psudic(Y;Y)(q1;q1)  
 301 47,XY,psudic(X;X)(q1;p1)  
 302 47,XYq+Yq-  
 303 47,Y,+Xp,+Xq  
 304 47,xy,+del(1)(p)  
 305 47,xy,del(x)(p)  
 306 47,xy,del(y)(p)  
 307 48,XY,-1,+1p,+1q,+1  
 308 68,X,dic(X;X)(q21;q22)  
 309 68,X,psudic(X;X)(q1;q1)  
 310 68,XXX,psudic(1;1)(p1;p1)  
 311 91,XX,terrea(X;X)(p22;p22)  
 312 91,XXXX,terrea(1;1)(p36;p36)

ISCN Expert would convert each formula to its longer equivalent, and then use its rule base on the "exploded" versions to infer which cases have specific abnormalities:

**7 cases of dicentric replaces 2 chromosome involving 21:**

41 42 43 44 52 53 54

In other words, there are seven cases (41,42,43,44,52,53,54) in the database involving a dicentric replacing two normal chromosomes.

**5 cases of fragile site involving all:**

100 192 193 249 293

**3 cases of isochromosome replaces 1 normal chromosome involving 21:**

133 146 167

**14 cases of missing whole chromosome (monosomy) involving all:**

1 2 5 29 64 65 66 70 73 74 76 216 226 227

**57 cases of pseudodicentric replaces 1 chromosome involving all:**

75 81 82 83 84 109 110 111 112 113 114 115 116 117 118 123 124 127 128 129 135 136 137  
 138 152 153 154 155 156 157 158 160 161 162 164 168 169 170 171 172 173 174 202 203 206  
 210 211 212 213 222 223 224 225 230 242 244 254

**46 cases of pseudodicentric replaces 2 chromosomes involving all:**

1 7 8 9 10 11 12 13 14 15 16 17 19 20 22 23 24 25 30 31 32 33 34 35 37 38 39 40 44 50 51  
52 54 56 57 58 59 60 61 62 71 72 309 310 311 312

**6 cases of sex = female and missing whole chromosome (monosomy) involving X:**

1 2 5 29 74 76

**25 cases of terminal rearrangement replaces 1 chromosome involving all:**

70 75 93 116 117 118 123 124 126 128 138 154 156 160 161 162 173 174 206 212 213 223 224  
225 248

**21 cases of terminal rearrangement replaces 2 chromosomes involving all:**

1 11 12 16 17 20 23 24 25 28 33 34 35 38 40 47 56 59 60 311 312

**1 case of two extra chrom from Robertsonian segregant involving all:**

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**References**

[1] Glen Cooper, JM Friedman, "[Interpreting Chromosomal Abnormalities Using Prolog](#)", Computers and Biomedical Research 23, 153-164 (1990).

This work has been extended by others:

[2] Craig Larman, "[Learning From Knowledge Systems](#)", M.Sc. Thesis, Simon Fraser University, (1995).