# BeSHG course 19-01-2024
# PROGRAM

**09:30-11:00** *Damien Lederer and Stéphanie Moortgat*

- **Disorders of the autosomes** (cytogenetics/molecular abnormalities and clinical aspects) (Chap. 6, part 1)

*11:00-11h15 coffee break*

**11:15-12:45** *Isabelle Maystadt*

- **Disorders of gonadal and sexual development** (gonadal embryogenesis, cytogenetics/molecular abnormalities, and clinical aspects) (Chap. 6, part 2)

*At the end of the course, we kindly ask you to complete an evaluation form.*
*You can access this form through the QR code or link below.*
*Thank you and enjoy the meeting!*

**13:30-15**

- **Devel**

**15:30-16**

- **Treat**

https://docs.google.com/forms/d/1nLyuFvBs-L0Z0T9ec6l9R4_jsWo6sOr5r9RmRf6v58g/prefill

# Chapter 6

1. Autosomal Disorders
   (*Dr S. Moortgat and Dr D. Lederer*)
   - Numerical disorders
   - Structural disorders

2. The sex chromosomes and their abnormalities (*Pr I. Maystadt*)

# Numerical Autosomes Disorders

# Numerical autosomes abnormalities

- Most of them are spontaneously aborted (94%)
- Incidence in newborns: 1/160 births (0.5-0.7%)

| | Pregnancies (incidence) | % Spontaneous abortions | % Live births |
|---|---|---|---|
| **Total** | **10000** | **1500 (15%)** | **8500 (85%)** |
| **Abnormal chromosomes** | **800 (8%)** | **750 (94%)** | **50 (6%)** |
| **Triploid/tetraploid** | **170 (1.7%)** | **170 (100%)** | **0** |
| **Trisomy 16** | **112 (1.1%)** | **112 (100%)** | **0** |
| **Trisomy 18** | **20 (0.2%)** | **19 (95%)** | **1 (5%)** |
| **Trisomy 21** | **45 (0.4%)** | **35 (78%)** | **10 (22%)** |
| **Other trisomy** | **209 (2%)** | **208 (99.5%)** | **1 (0.5%)** |

***Incidence of aneuploidies in 10000 pregnancies (Table 5-2)***

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# Numerical autosomes abnormalities

- 3 well-defined non mosaic chromosome numerical disorders compatible with postnatal survival:
  - Trisomy 21 (previously called “Down syndrome”)
  - Trisomy 18
  - Trisomy 13

| | Number | Approximate incidence |
|---|---|---|
| **Total** | **68.159** | |
| **Trisomy 21** | **82** | **1/830** |
| **Trisomy 18** | **9** | **1/7500** |
| **Trisomy 13** | **3** | **1/22700** |
| **Other aneuploidy** | **2** | **1/34000** |
| **All aneuploidies** | **96** | **1/700** |

***Incidence of autosomal aneuploidies in newborn surveys***

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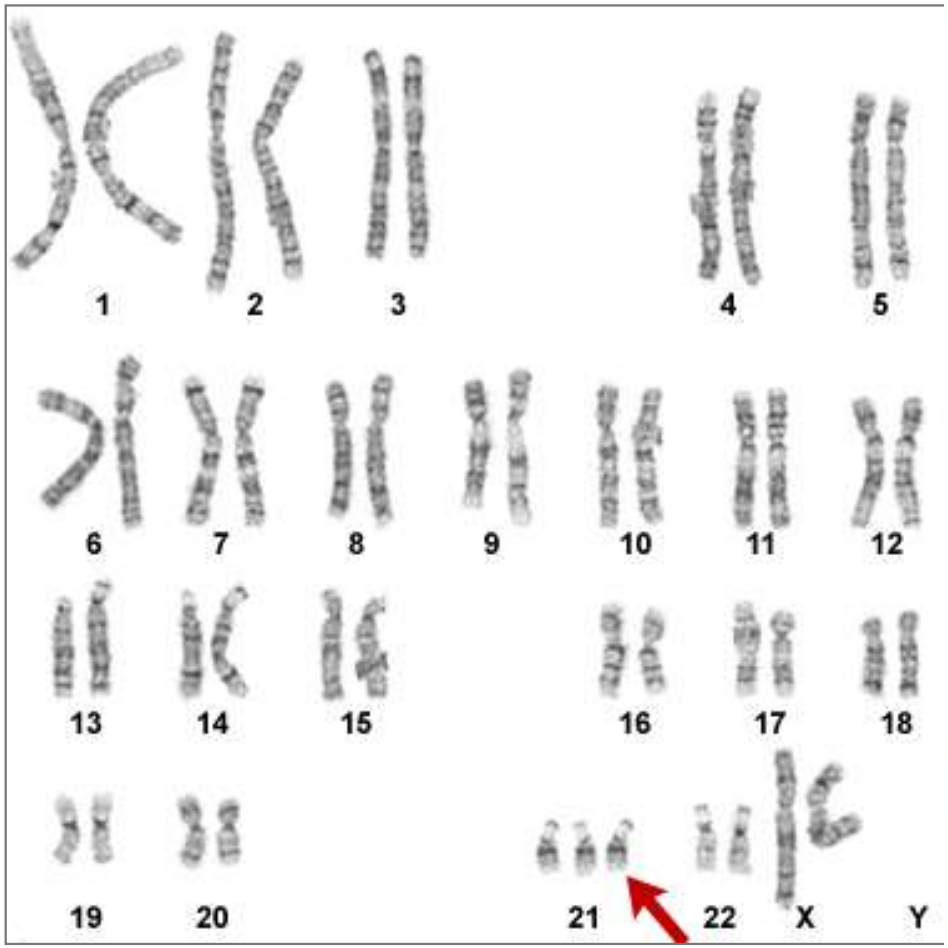
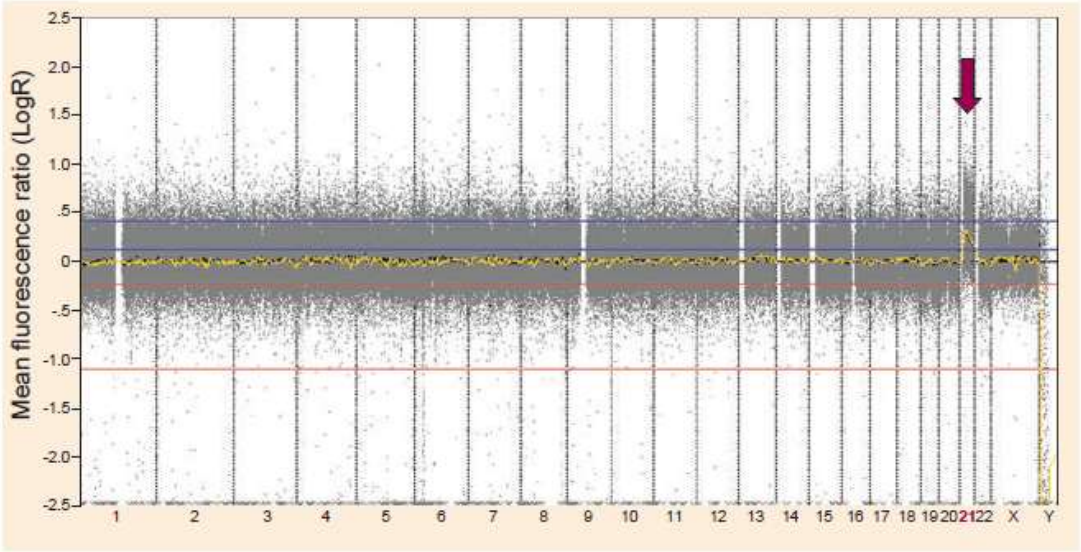
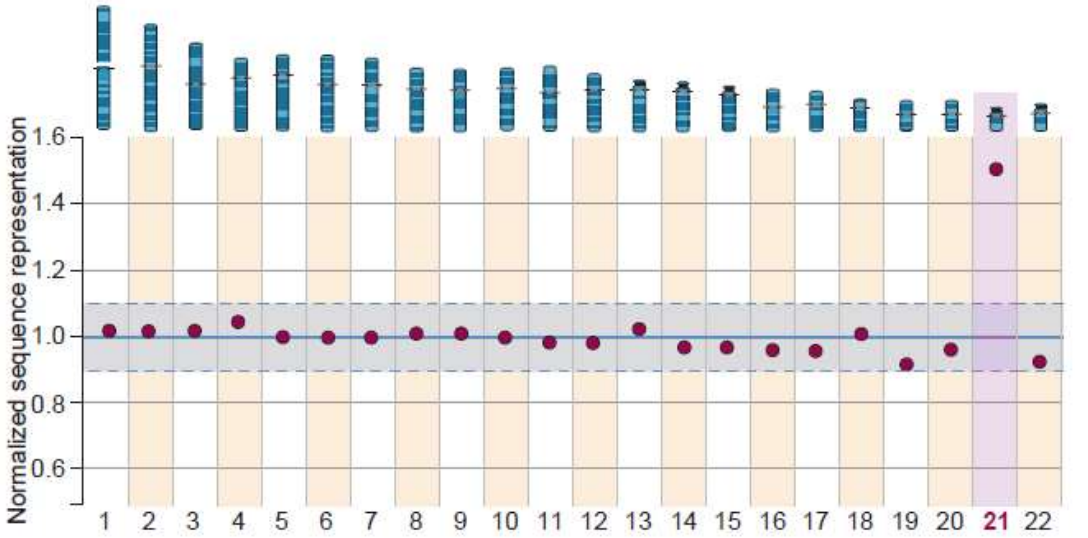
# Trisomy 21 (Down syndrome)

## Chromosomal and genomic approaches to the diagnosis of trisomy 21




47,XX,+21

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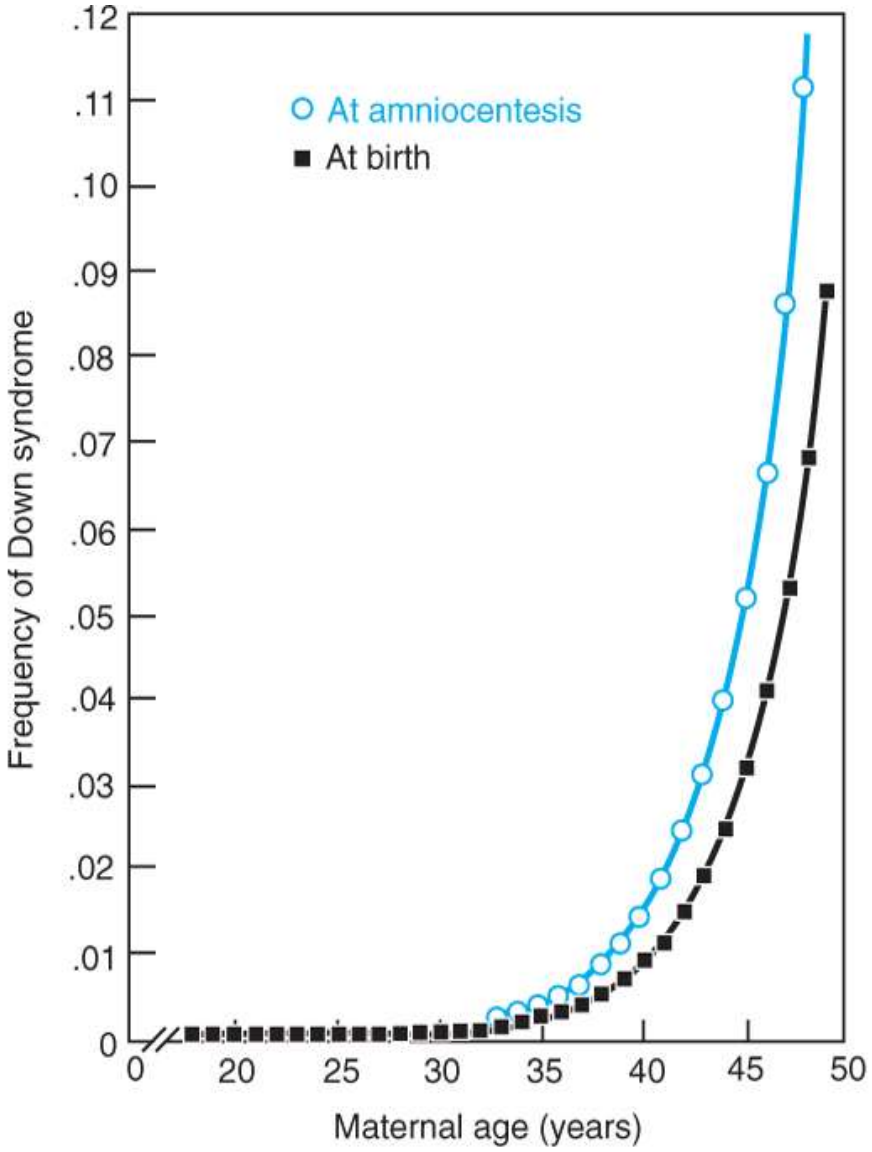
# Trisomy 21

- 1/800 live births
- increased risk with higher maternal age




| Mat age (years) | At birth | Amn Liq (16w) | CVS (9-11w) |
|---|---|---|---|
| 15-19 | 1/1250 | - | - |
| 20-24 | 1/1400 | - | - |
| 25-29 | 1/1100 | - | - |
| 33 | 1/625 | 1/420 | 1/370 |
| 35 | 1/385 | 1/250 | 1/250 |
| 38 | 1/175 | 1/115 | 1/115 |
| 40 | 1/100 | 1/70 | 1/80 |
| 42 | 1/65 | 1/40 | 1/30 |
| ≥50 | 1/25 | 1/20 | 1/15 |

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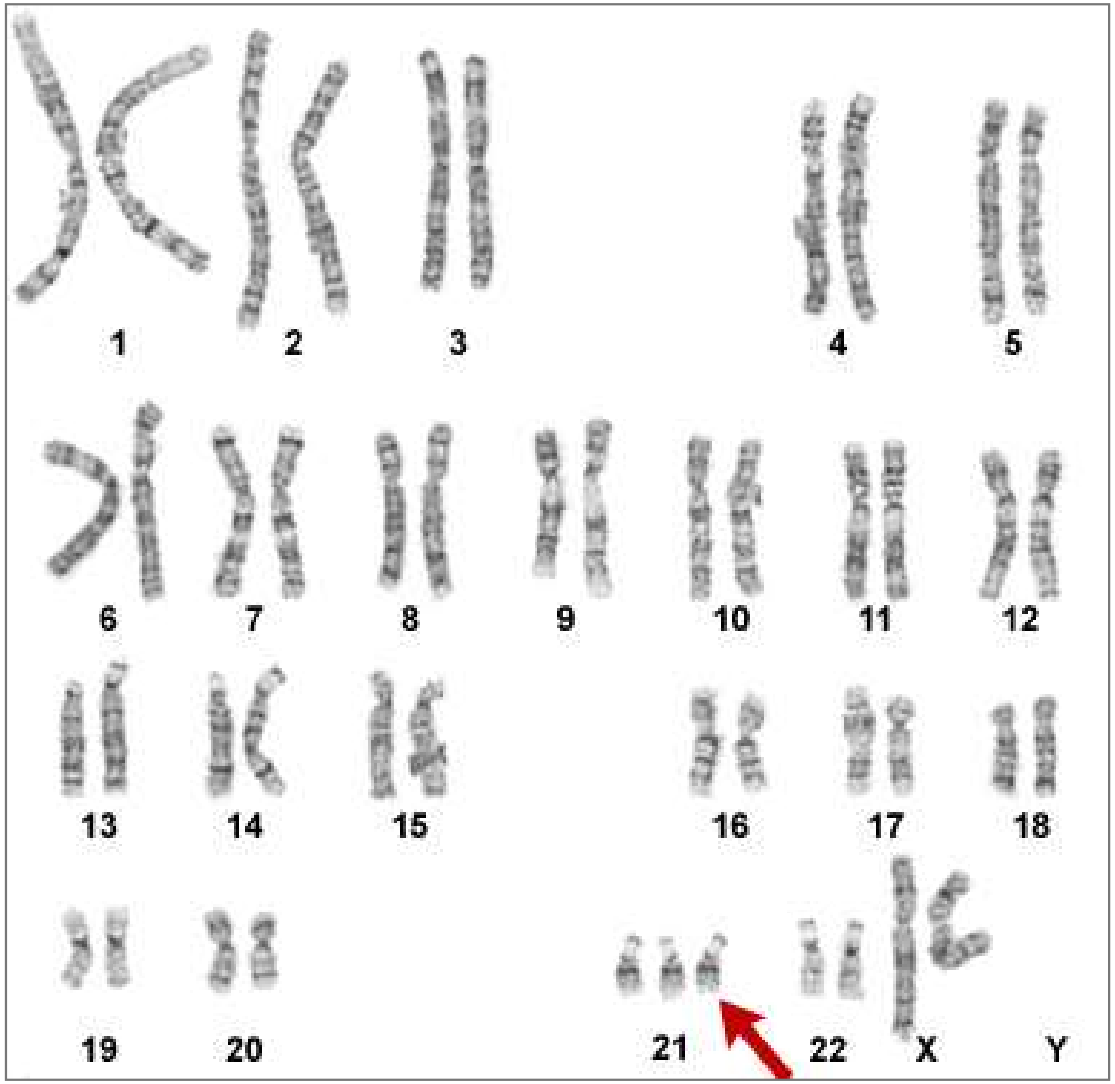
# Trisomy 21

- 95% = meiotic nondisjunction of the chromosome 21 pair
  - ↳ 90% maternal meiosis I, 10% paternal meiosis II
  - ↳ « old egg » model




***STANDARD TRISOMY 21***

Recurrence risk: 1%

→ 1.4% <30y

→ age-related risk >30y

47,XX,+21

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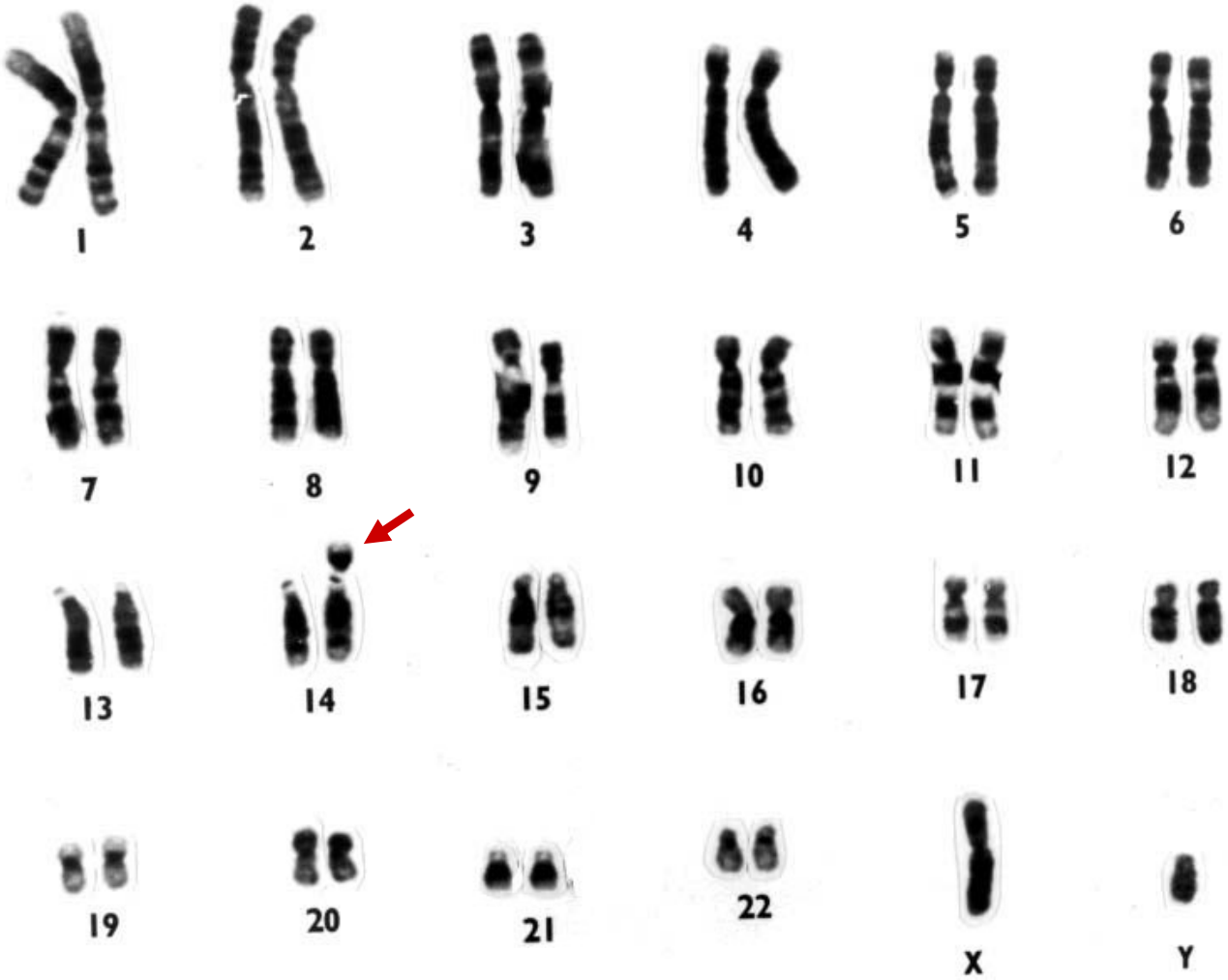
# Trisomy 21

- 4% = Robertsonian Translocation
  der(14;21), der(21;22), der(21;21)




**46,XY,rob(14;21)(q10;q10),+21**

***TRISOMY 21***

***by translocation***

Recurrence risk: ↑↑

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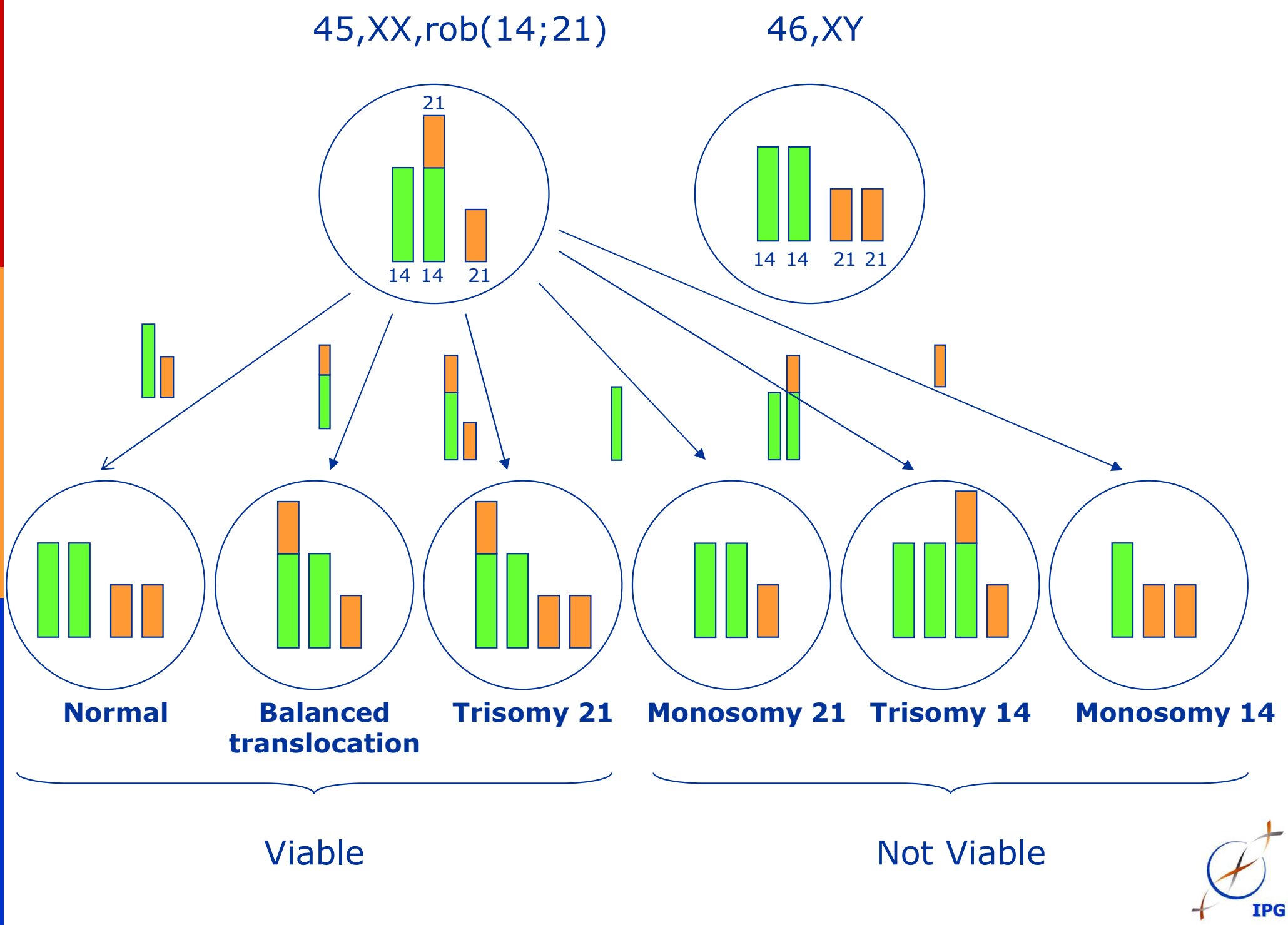
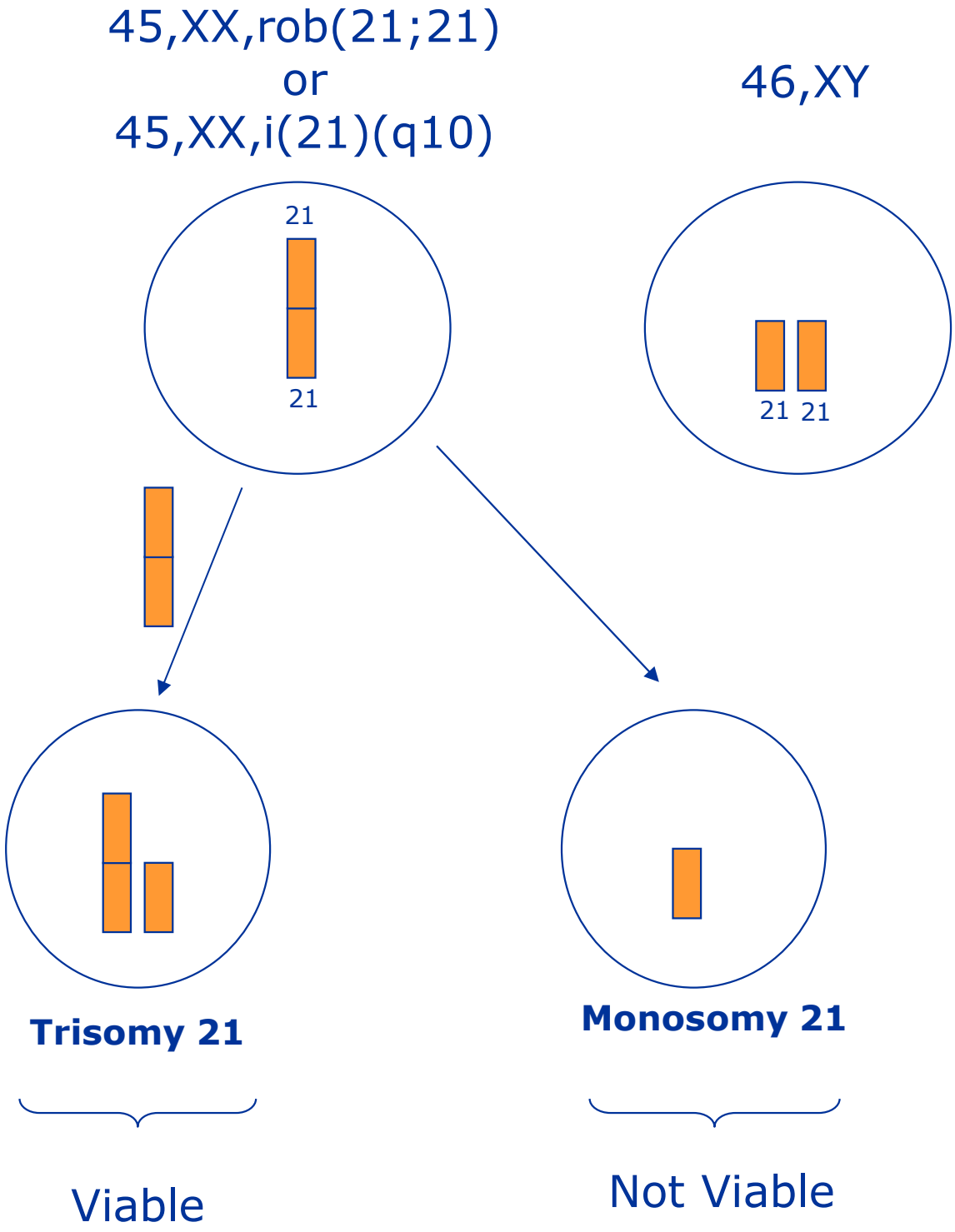

45,XX,rob(14;21)
46,XY
21
14 14 21
14 14 21 21
Normal
Balanced translocation
Trisomy 21
Monosomy 21
Trisomy 14
Monosomy 14
Viable
Not Viable

# Trisomy 21

**46,XY,rob(21;21)(q10;q10),+21**

**Or 46,XY,i(21)(q10)**

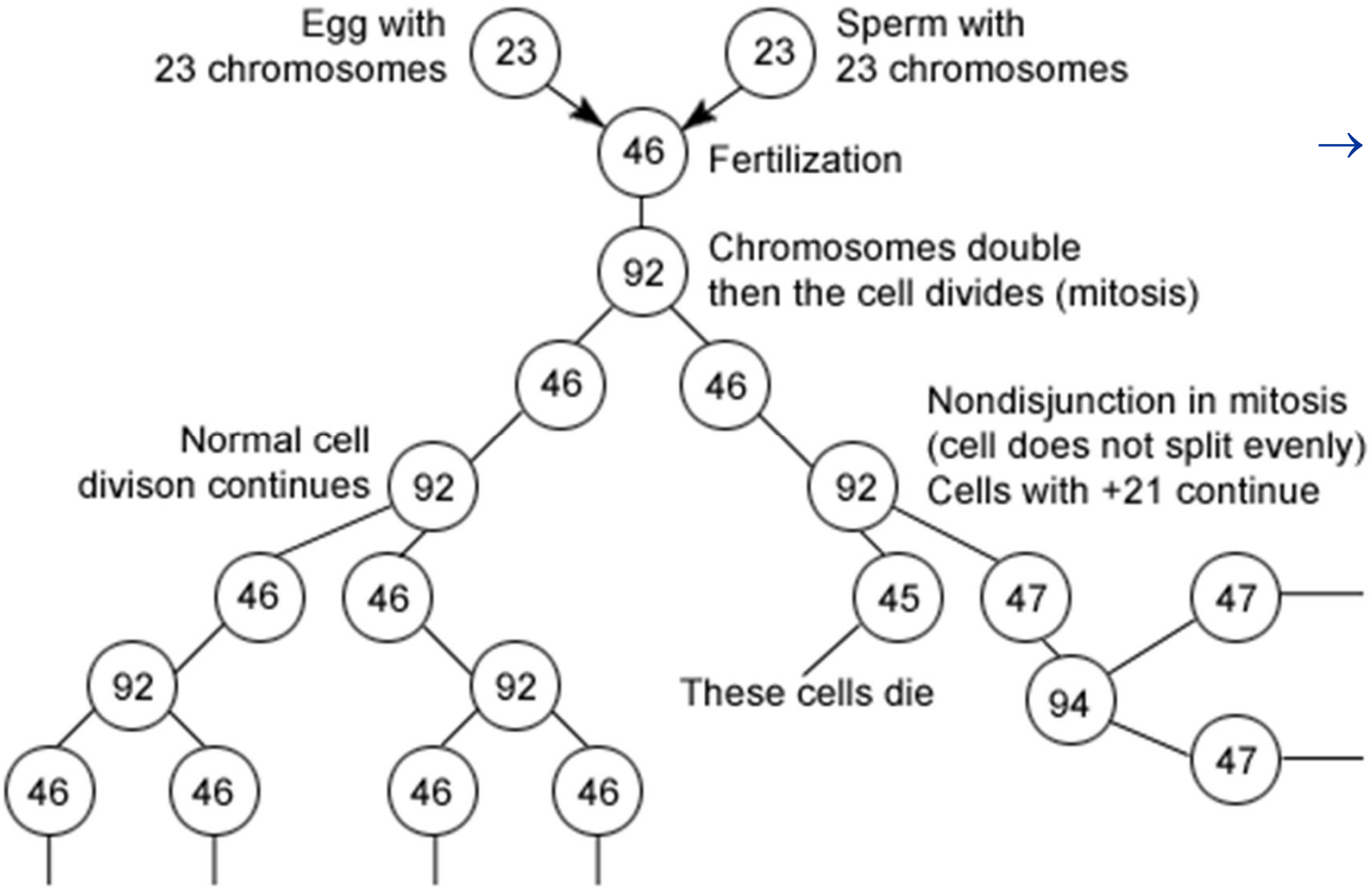

45,XX,rob(21;21)
or
45,XX,i(21)(q10)
46,XY
21
21
21 21
Trisomy 21
Monosomy 21
Viable
Not Viable

# *TRISOMY 21 by translocation : recurrence risk*

| | Maternal carrier 45,XX,rob | Paternal carrier 45,XY,rob |
|---|---|---|
| Rob (14;21) | 10-15% | 2.5% |
| Rob (21;22) | 10-15% | 2.5% |
| Rob (21;21) or i(21) | 100% | 100% |

# Trisomy 21

- 2%: mosaic Trisomy 21




→ No recurrence risk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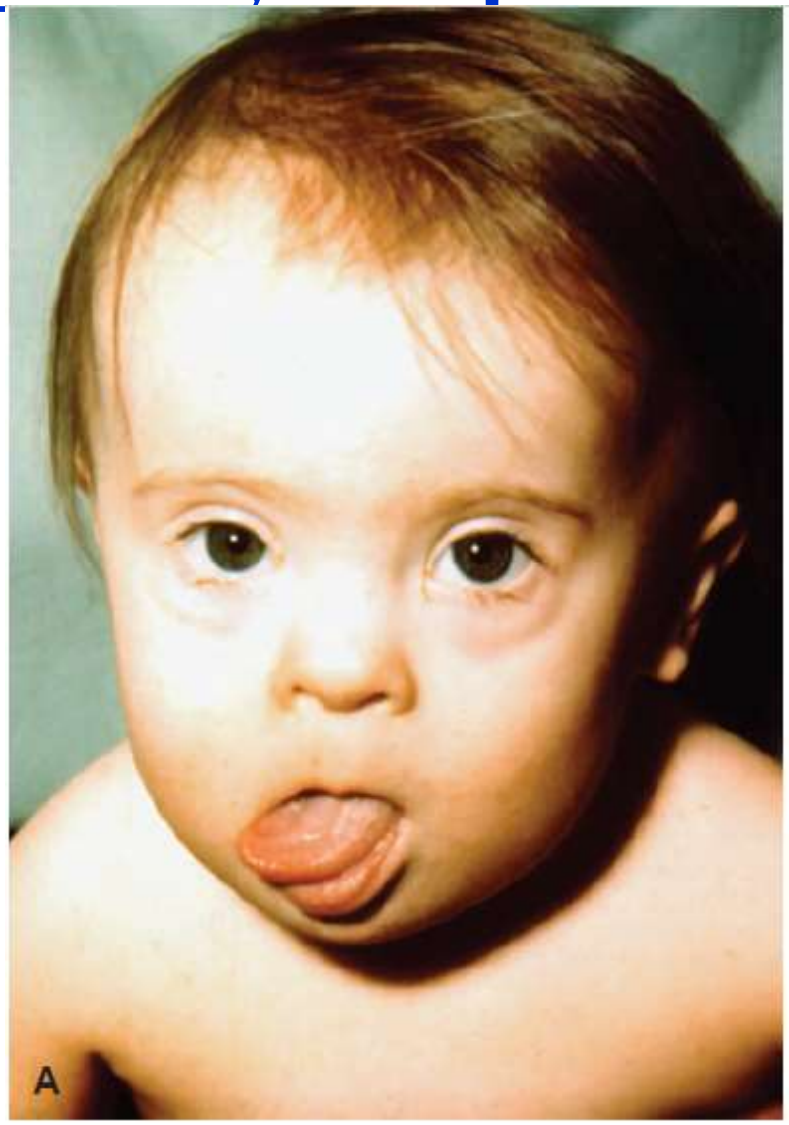
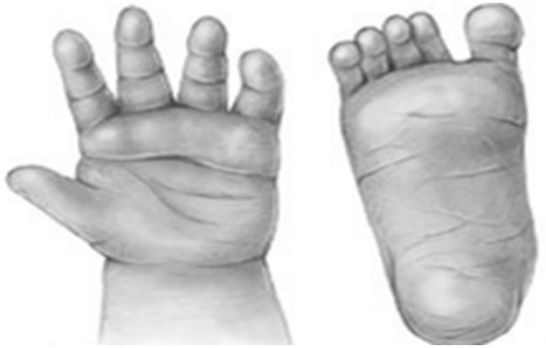
# Trisomy 21: postnatal diagnosis



- Dysmorphic features
  - **-Short stature**
  - -Flattened face
  - -Brachycephaly, flat occiput
  - -Bilateral epicanthus
  - -Upslanting palpebral fissures
  - -Brushfield spots
  - -Protruding tongue
  - -Low-set-ears
  - **-Short neck, with loose skin**
  - -Short and broad hands
  - -Single transverse palmar crease
  - -Clinodactyly
  - -« sandal » gap

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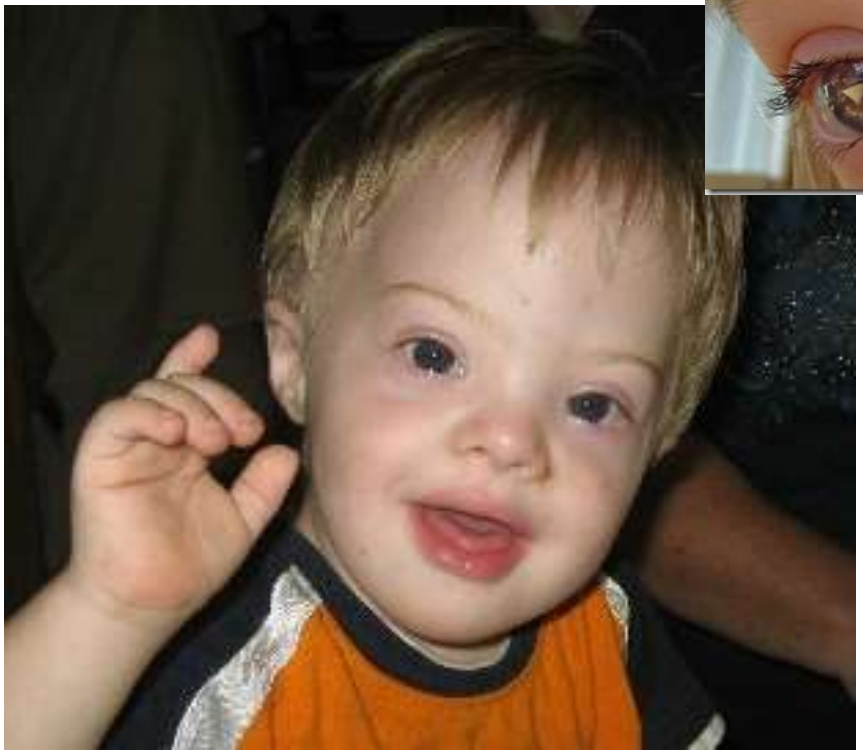


# Trisomy 21

- Hypotonia
- Intellectual disability (IQ 30-60): 100%
- Congenital heart disease: 33%

  (complete atrioventricular canal, …)
- Other congenital malformations

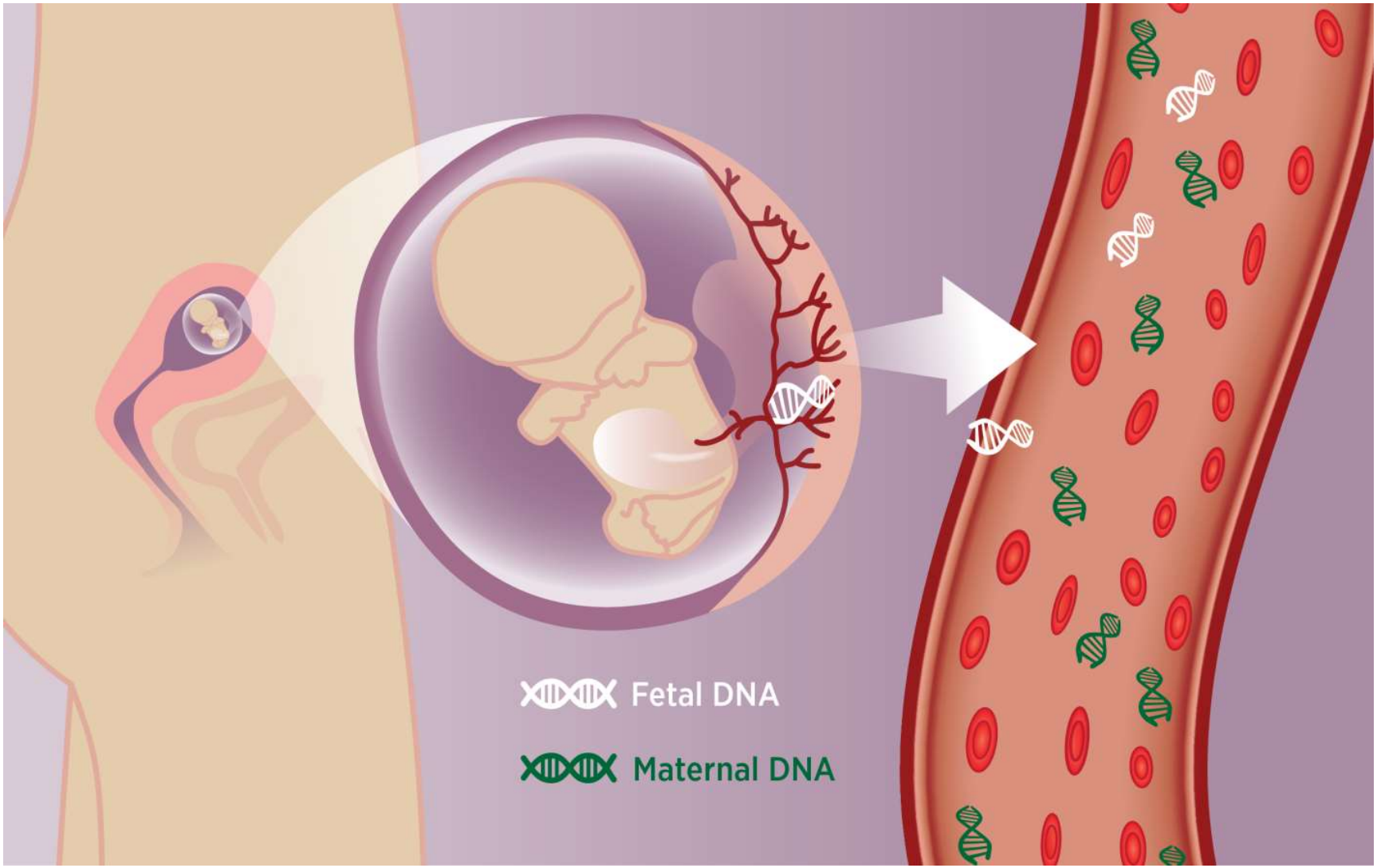
  (duodenal atresia, tracheoesophageal fistula,

  congenital cataract, Hirshprung disease, …)
- Other increased risk

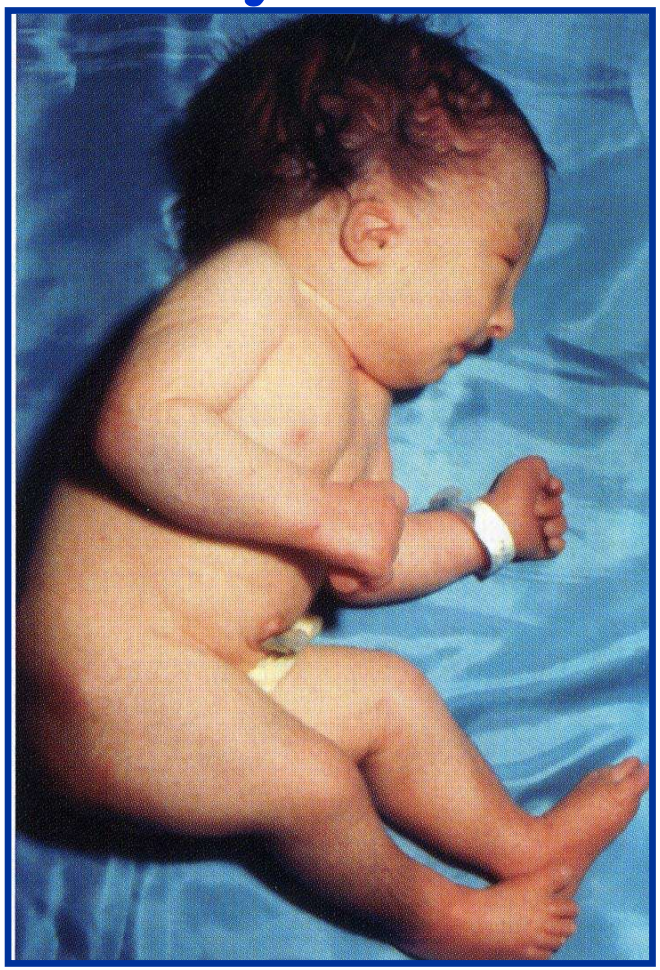
  (hypothyroidism, diabetes, leukemia, Alzheimer,…)

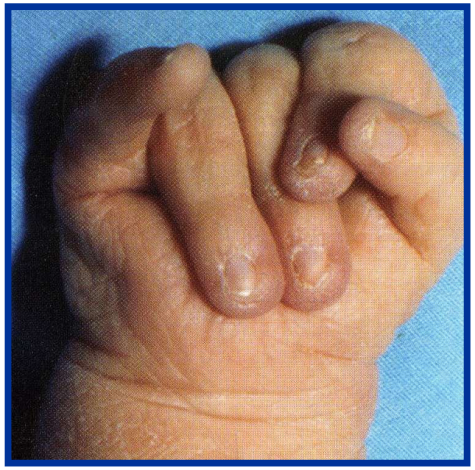
# Trisomy 21: NIPT

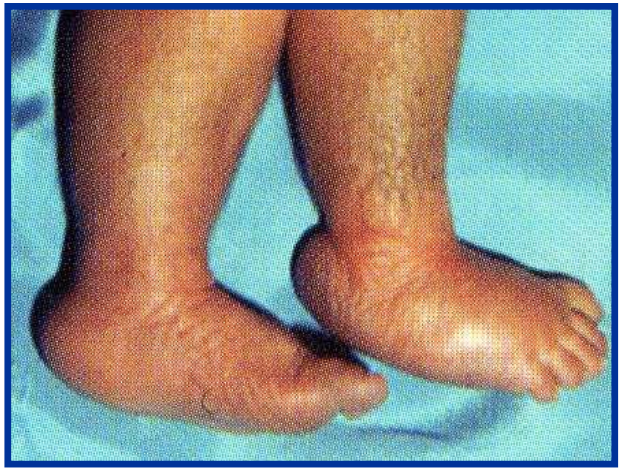
## (non invasive prenatal testing, > 10w)



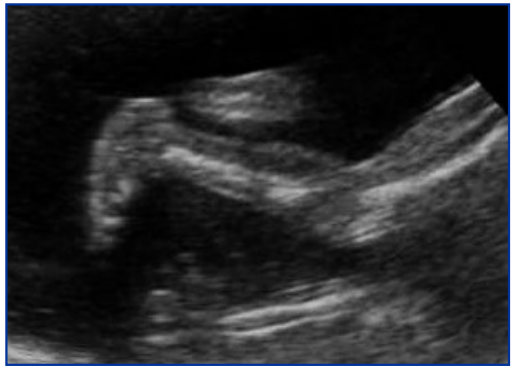
# Trisomy 18







- Intellectual disability
- **Failure to thrive**
- **Cardiac malformation**
- Hypotonia, then hypertonia
- Dysmorphic features
  - **-Prominent occiput**
  - -Retrognathia
  - -Low-set and malformed ears
  - -Short sternum
  - -Clenched hands
  - -Hypoplastic nails
  - **-Rocker-bottom feet**



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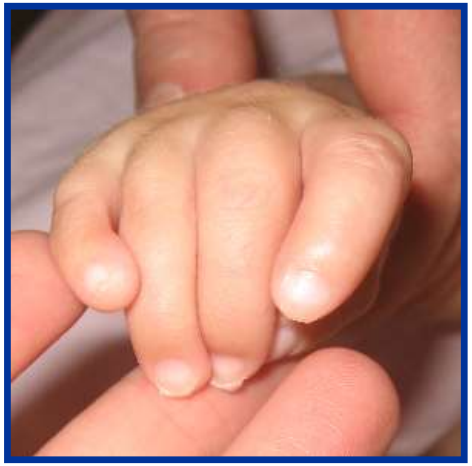
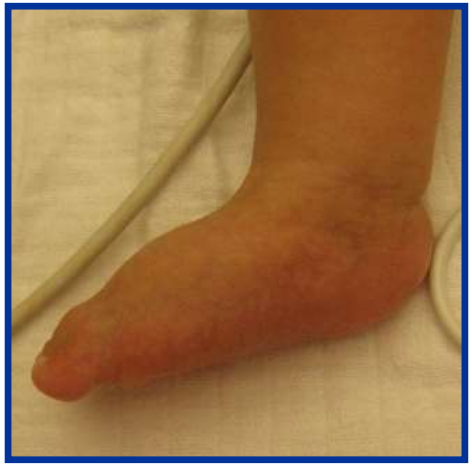
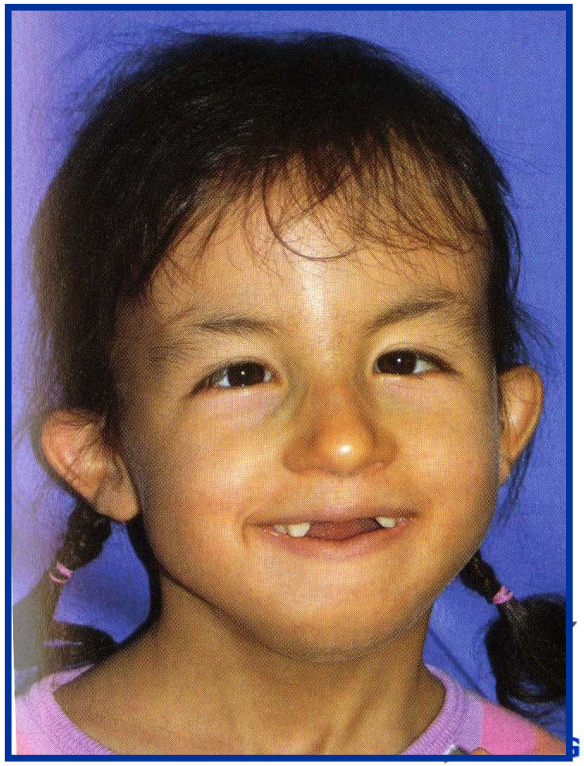
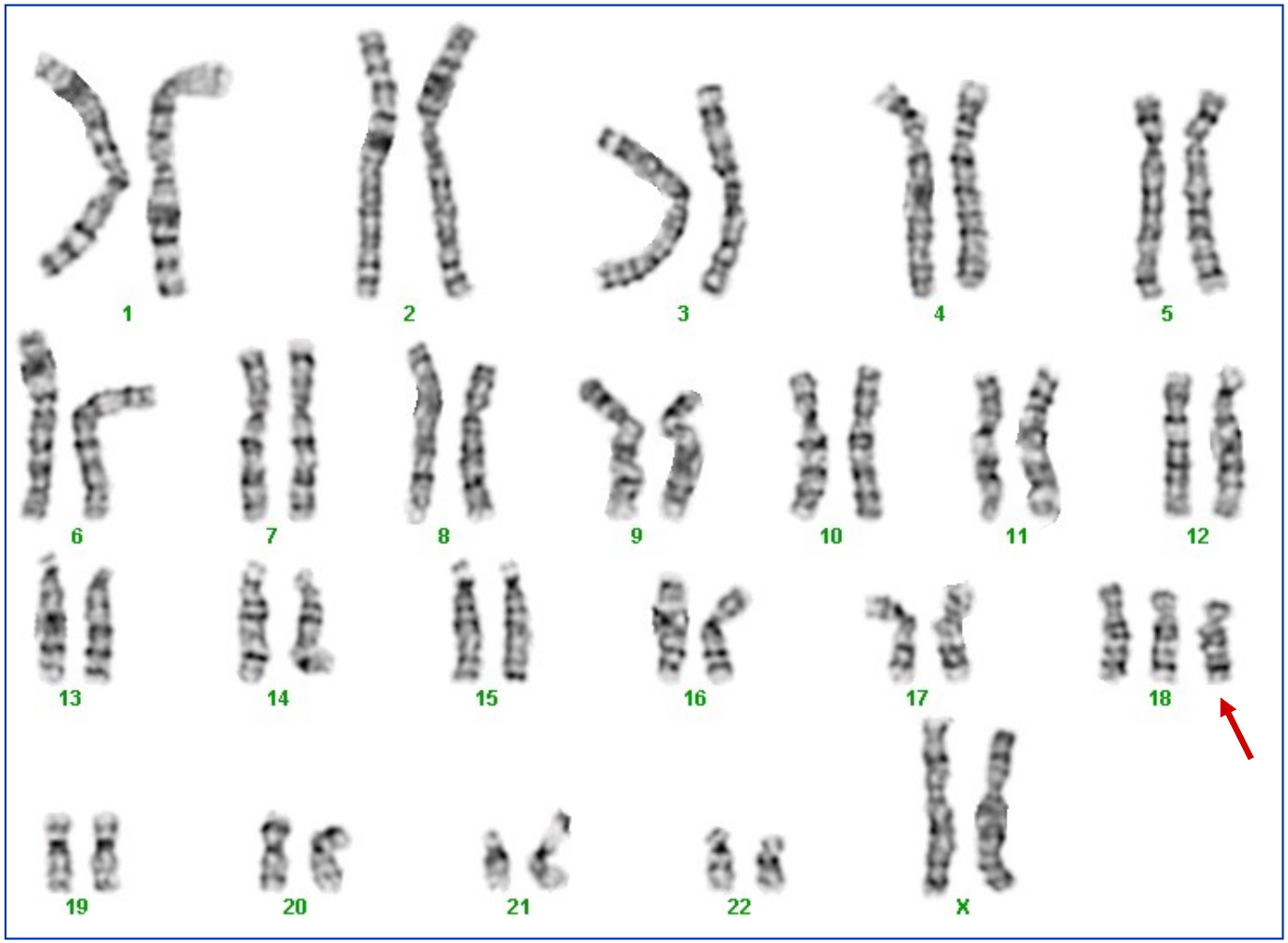






# Trisomy 18

- 95% sponteaneously aborded
- 1 / 7500 live births
- increased risk with higher maternal age




***80%: standard trisomy 18***

***20%: translocation (de novo or inherited)***

47,XX,+18

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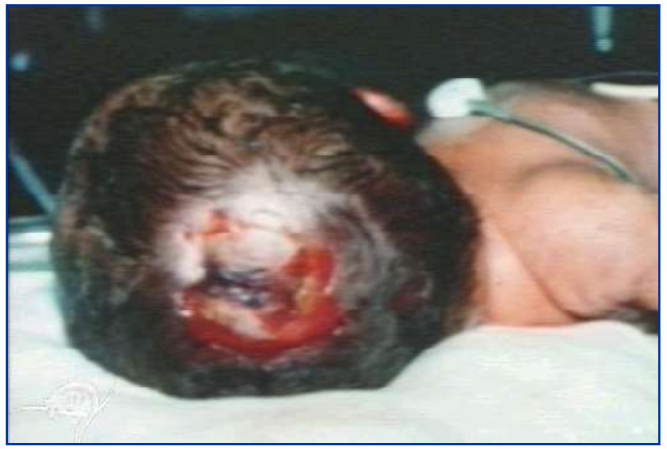
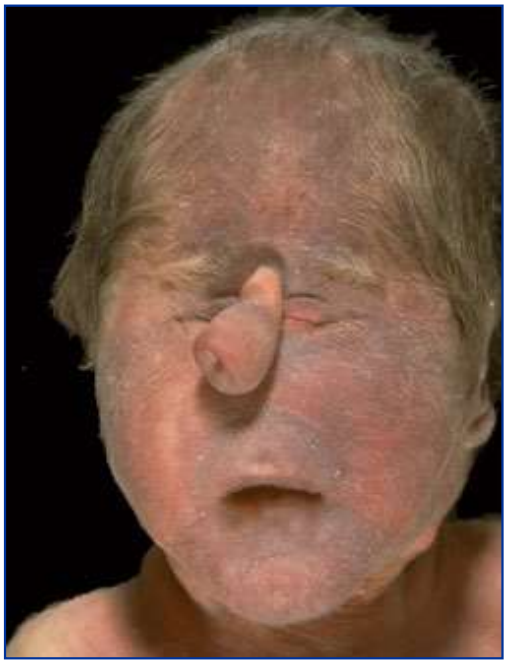
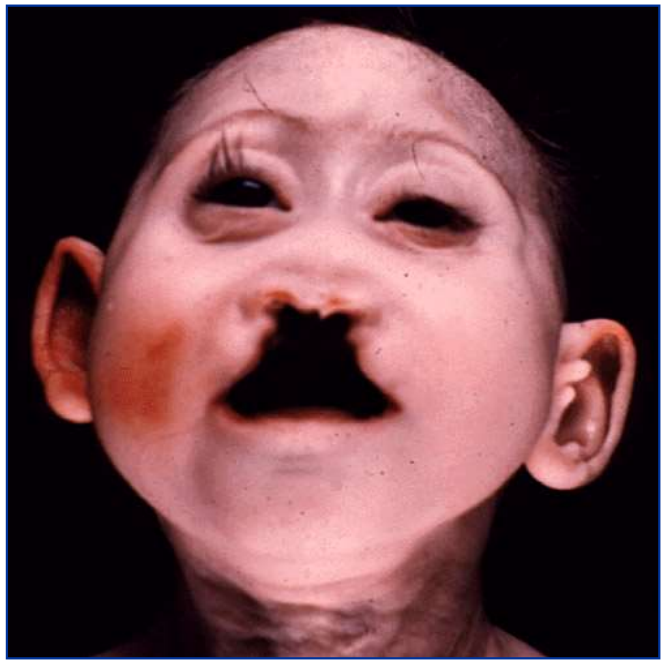
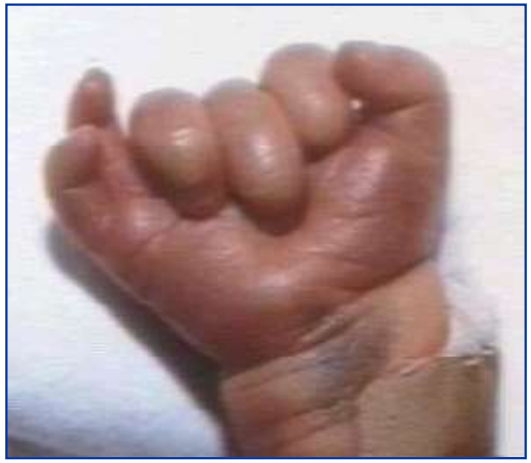
# Trisomy 13

- Mental retardation
- Growth retardation
- **CNS malformation** (holoprosencephaly,…)
- Congenital heart defect
- Urogenital anomalies
- Dysmorphic features
  - -Microcephaly
  - -Sloping forehead
  - -Scalp defect
  - -**Cleft lip/palate**
  - -**Eye anomalies**
    (microphtalmia, iris coloboma,…)
  - -Post-axial **polydactyly**
  - -Clenched hands
  - -Rocker-bottom feet









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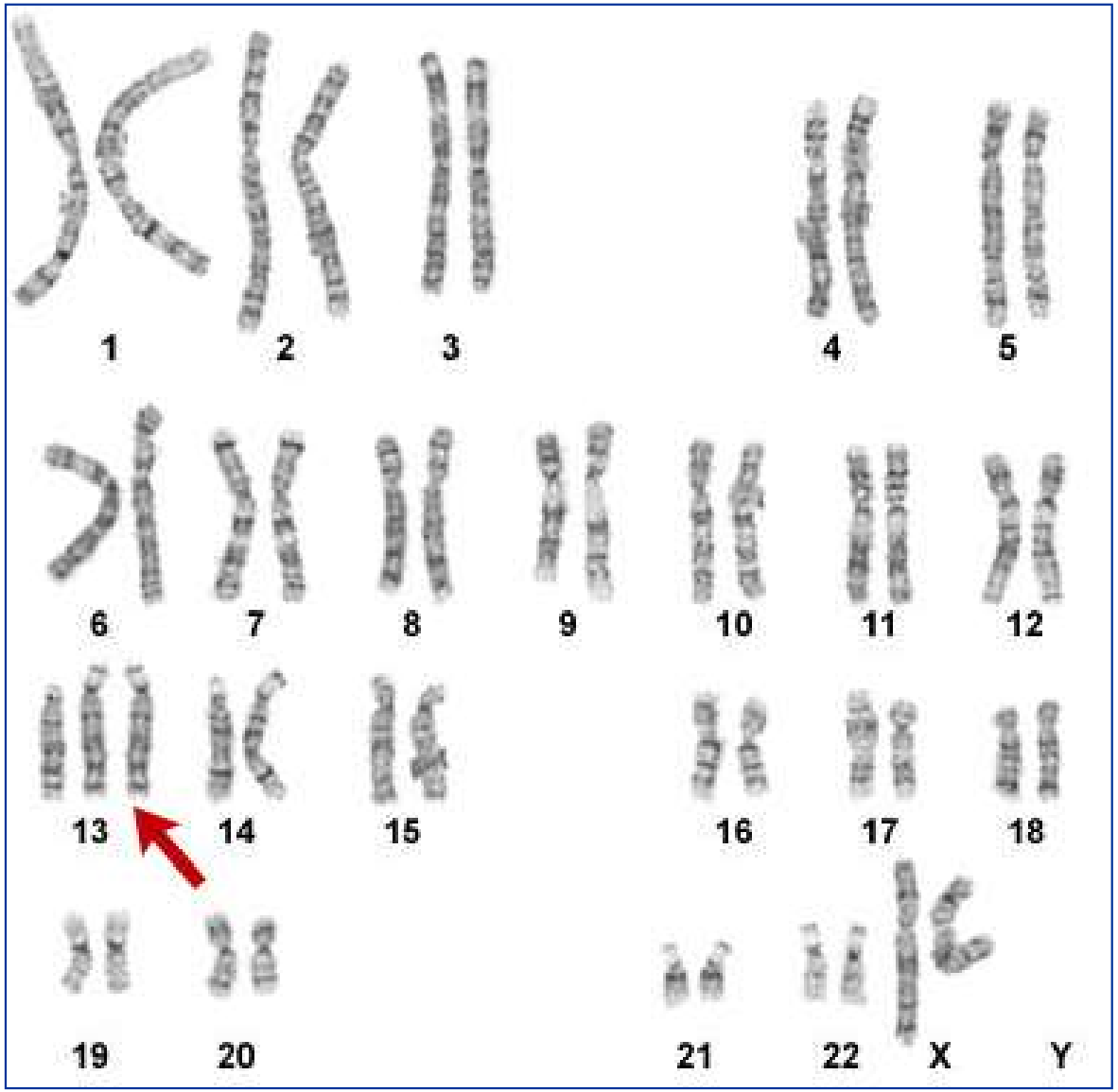
# Trisomy 13

- 95% sponteaneously aborded
- 1 / 15000 – 1 / 25000 live births
- increased risk with higher maternal age




***80%: standard trisomy 13***

***20%: unbalanced translocation***

→ Low recurrence risk (<2%)

47,XX,+13

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# Structural Autosomes Disorders

# Structural autosomes abnormalities

- Most of unbalanced rearrangements are spontaneously aborted (85%) – *see table 5-5*
- But some of them are viable

| | Number | Approximate incidence |
|---|---|---|
| **Total** | **68.159** | |
| **Balanced rearrangement** | **139** | **1/490** |
| **Unbalanced rearrangement** | **43** | **1/1585** |
| **All structural rearrangements** | **182** | **1/375** |

***Incidence of structural abnormalities in newborn surveys (Table 5-3)***

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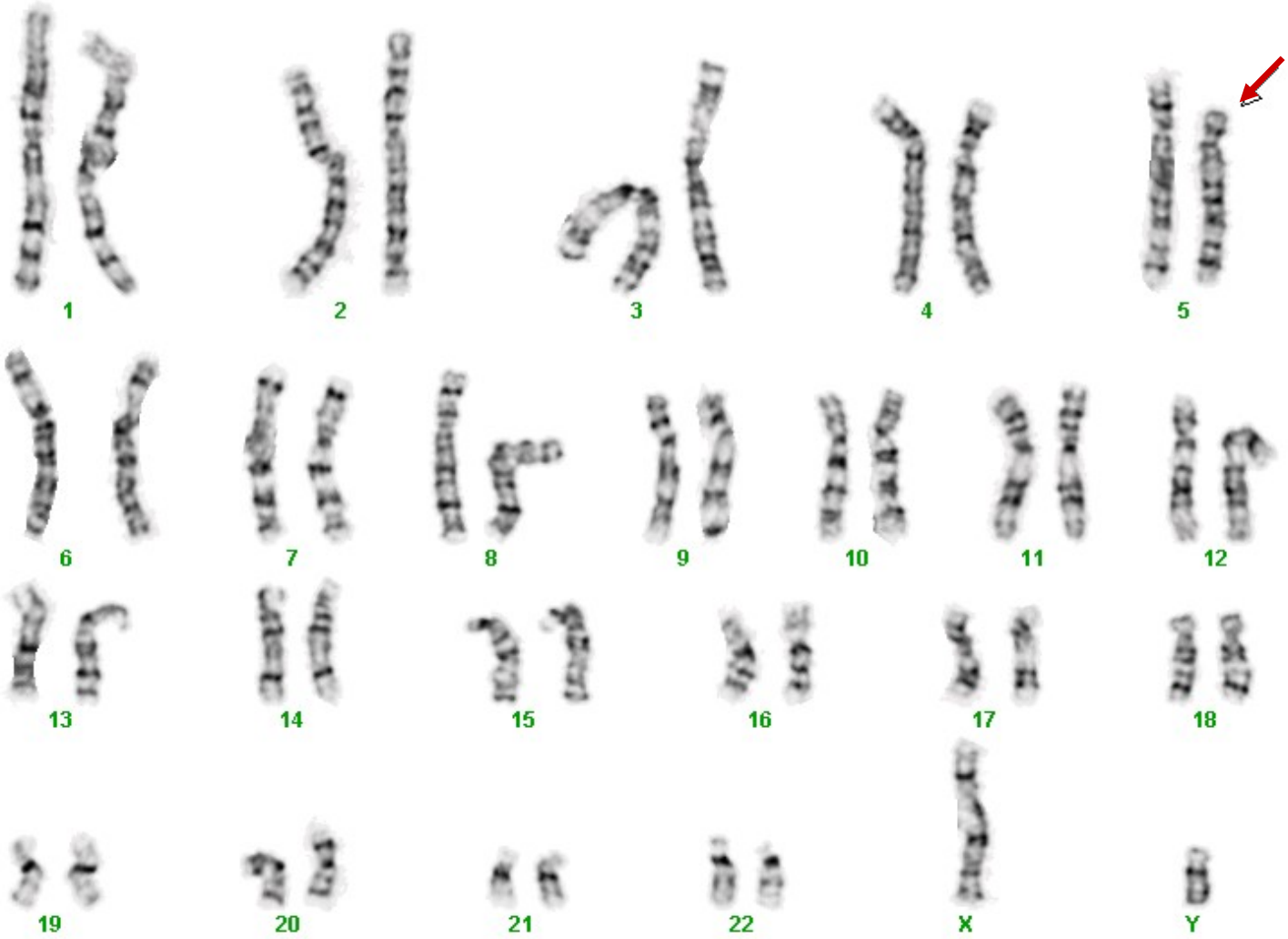
# Autosomal deletion syndromes

- cytogenetically visible autosomal deletion: 1/7000 live births
- some clearly recognizable syndromes
  (5p-, 4p-, 9p-, 9q-, 18p-, …)




**example: 46,XY, del(5)(pter→p14.2)**

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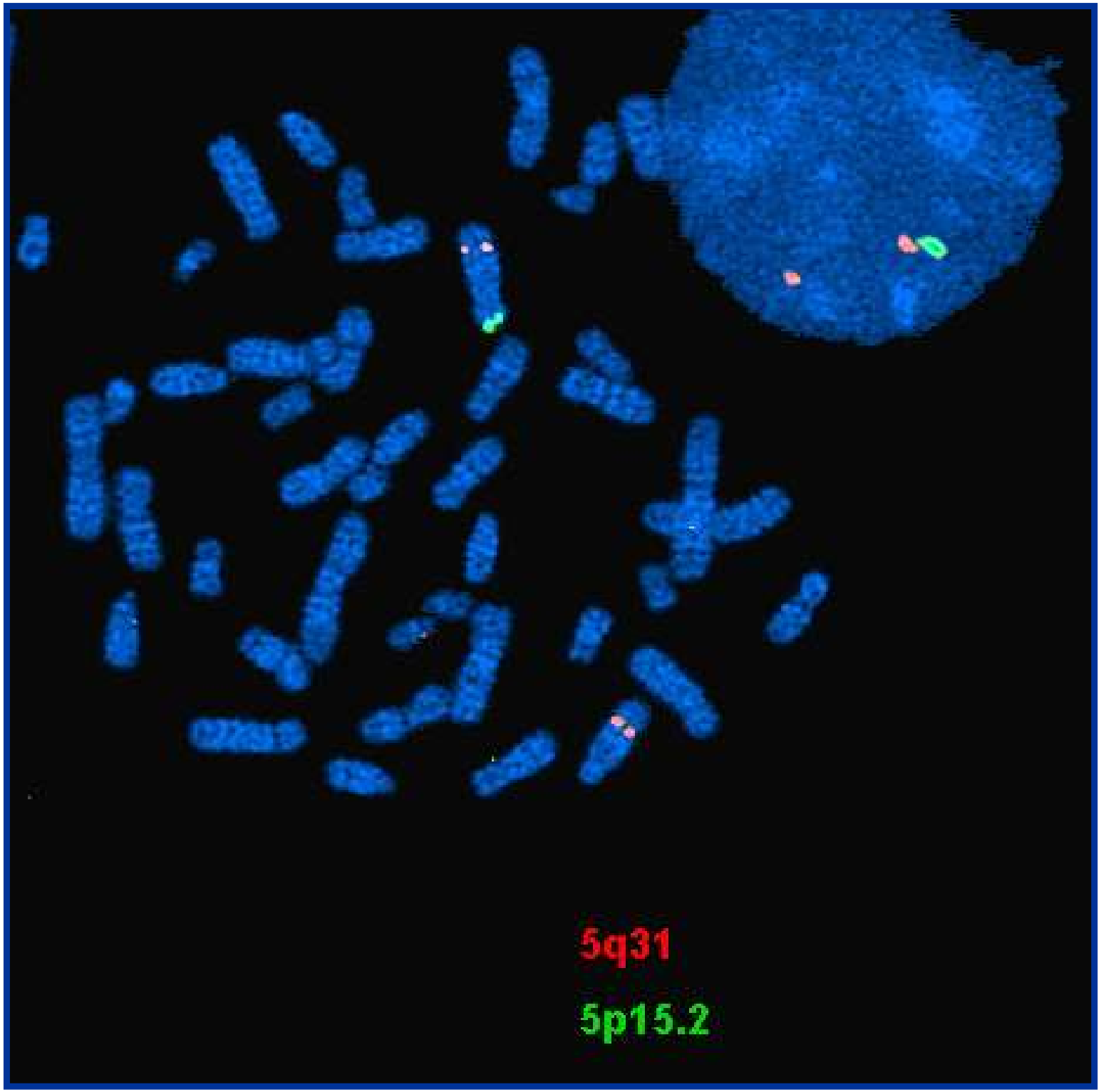
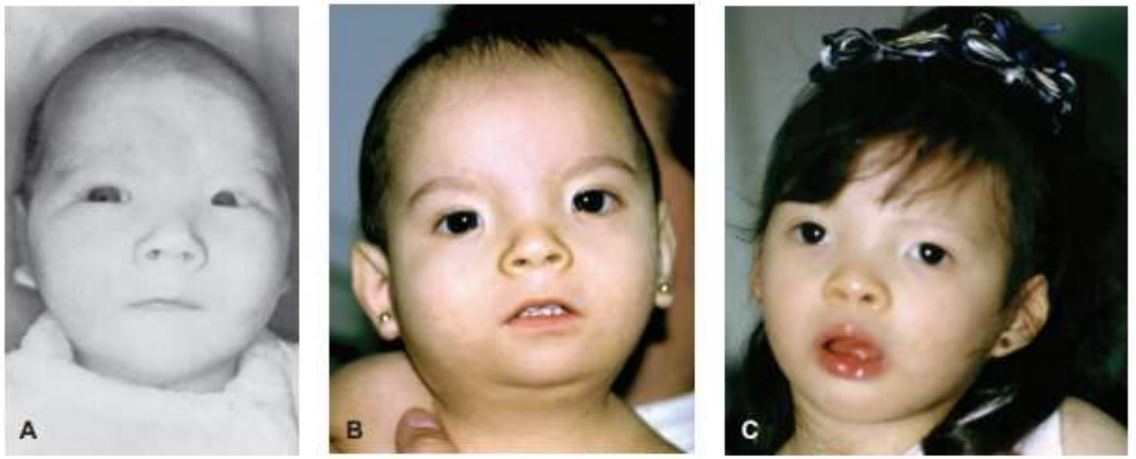

5q31
5p15.2

# Cri du Chat syndrome (5p-)

- Mental retardation
- Cry like a mewing cat
- Heart defect
- Dysmorphic features
  - -Microcephaly
  - -Hypertelorism
  - -Epicanthal folds
  - -Low-set ears
  - -Preauricular tags
  - -Micrognathia

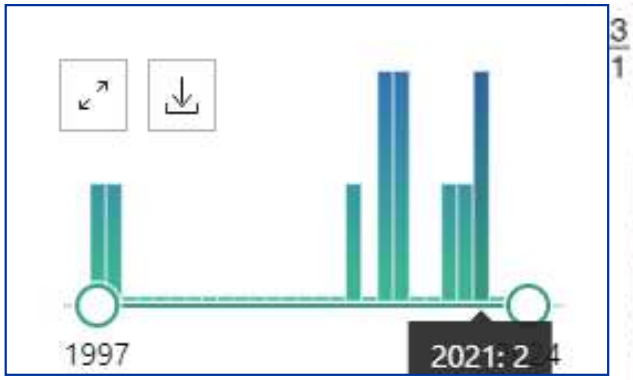



***85-90%: de novo (sporadic)***

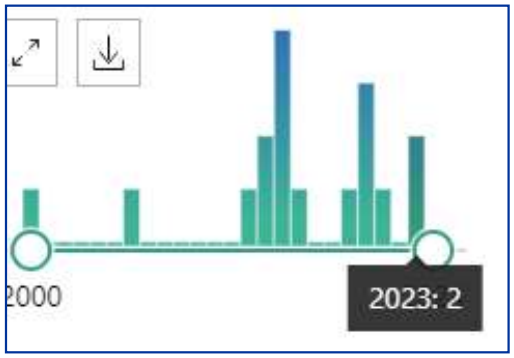
***10-15%: parental translocation***

# Cri du Chat syndrome (5p-)

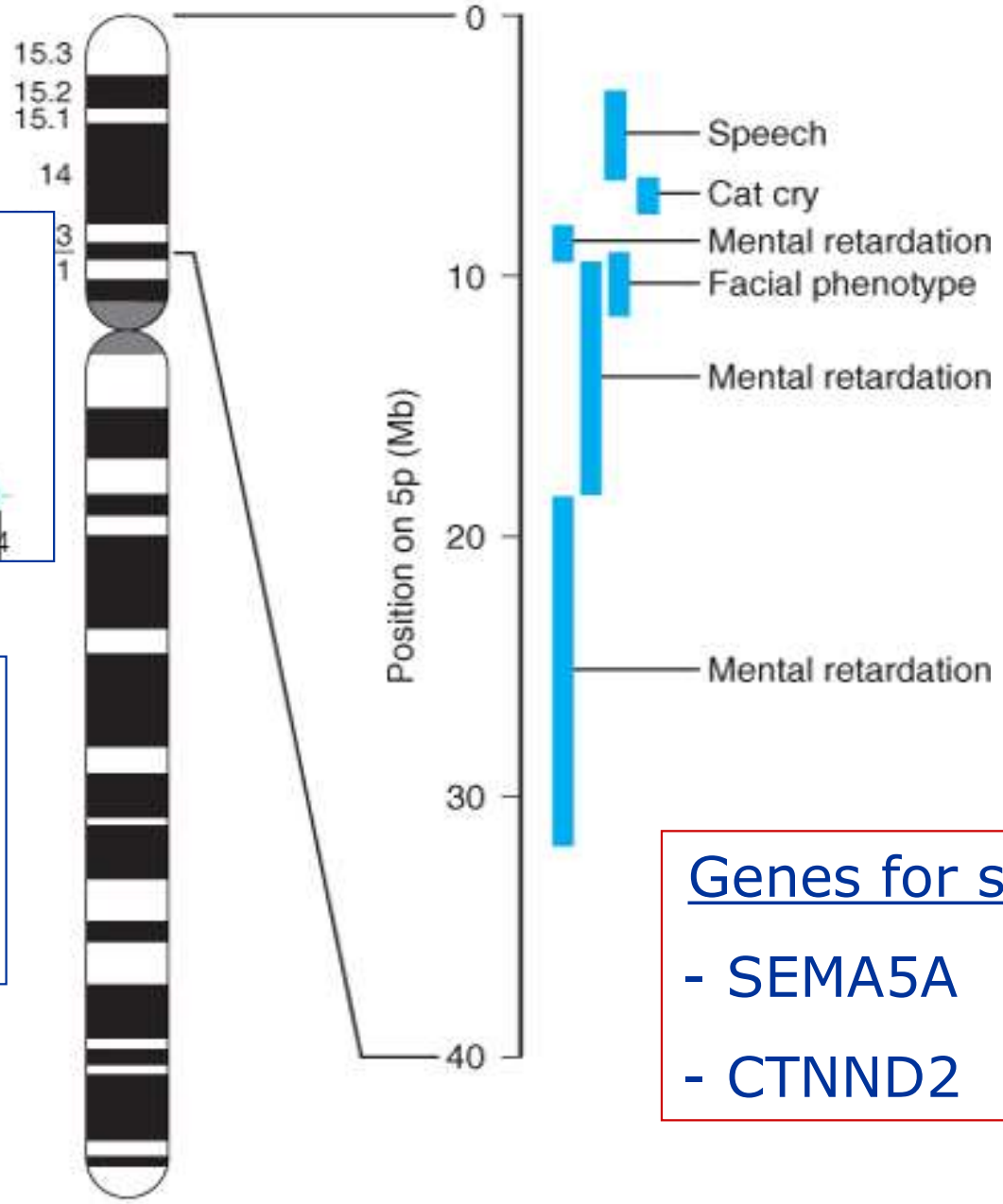
- Genotype-Phenotype correlations




SEMA5A and ID




CTNND2 and ID




Genes for severe MR

- SEMA5A
- CTNND2

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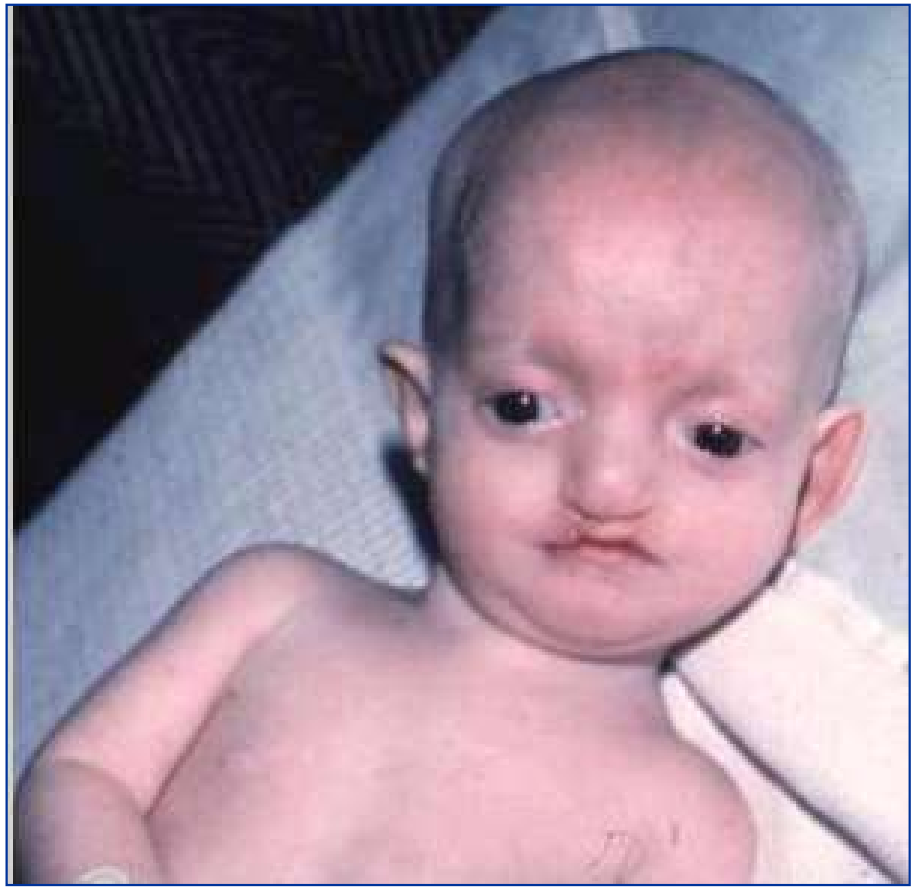
# Autosomal deletion syndromes: other examples



**4p deletion (Wolf-Hirshhorn)**

**9p deletion**

# Genomic disorders:

## Microdeletion and microduplication syndromes

- small deletions or duplications, most often cryptic

  ⇒ - high-resolution karyotype

  - FISH analysis

  - MLPA (multiple ligation-dependant probe assay)

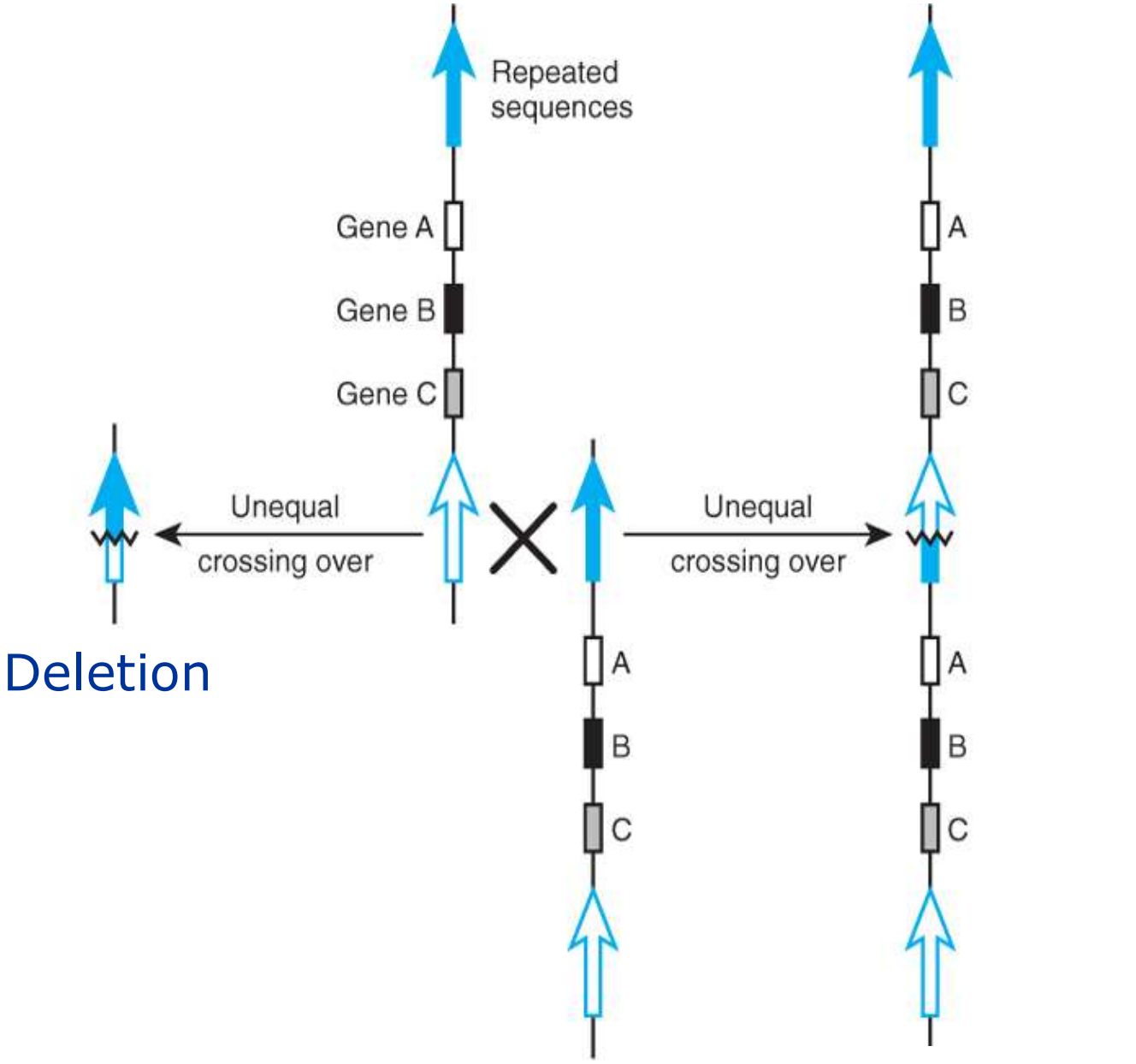
  - array-CGH - SWGS

- several clinically recognizable syndromes

  including « contigous gene syndromes »

# Genomic disorders:

## Microdeletion and microduplication syndromes



# Genomic disorders:

## Microdeletion syndromes

| Disorder | Location | Rearrangement Type | Rearrangement Size (kb) |
|---|---|---|---|
| Smith-Magenis | 17p11.2 | Deletion | 4000 |
| HNLPP | 17p12 | Deletion | 1400 |
| Velo-cardio-facial | 22q11.2 | Deletion | 3000,1500 |
| Prader Willi/ Angelman | 15q11-q13 | Deletion | 3500 |
| Williams | 7q11.23 | Deletion | 1600 |
| Neurofibromatosis | 17q11.2 | Deletion | 1400 |
| Sotos | 5q35 | Deletion | 2000 |
| Azoospermia (AZFc) | Yq11.2 | Deletion | 3500 |

***Examples of genomic disorders due to recombination between low-copy repeat sequences (Table 6-1)***

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# Genomic disorders:

## microduplication syndromes

| Disorder | Location | Rearrangement Type | Rearrangement Size (kb) |
|---|---|---|---|
| Charcot-Marie-Tooth1A | 17p12 | Duplication | 1400 |
| Cat-eye syndrome | 22q11.2 | Triplication | 3000,1500 |

***Examples of genomic disorders due to recombination between low-copy repeat sequences (Table 6-1)***

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# Genomic disorders:

## microduplication syndromes

| Disorder | Location | Rearrangement Type | Rearrangement Size (kb) |
|---|---|---|---|
| Charcot-Marie-Tooth1A | 17p12 | Duplication | 1400 |
| Cat-eye syndrome | 22q11.2 | Triplication | 3000,1500 |
| (Smith-Magenis) | 17p11.2 | Dup 17p11.2 | 4000 |
| (Velo-cardio-facial) | 22q11.2 | Dup 22q11.2 | 3000,1500 |
| (Prader Willi/ Angelman) | 15q11-q13 | Dup 15q11-q13 | 3500 |
| (Williams) | 7q11.23 | Dup 7p11.23 | 1600 |
| (Neurofibromatosis) | 17q11.2 | Dup 17q11.2 | 1400 |

***Examples of genomic disorders due to recombination between low-copy repeat sequences (Table 6-1)***

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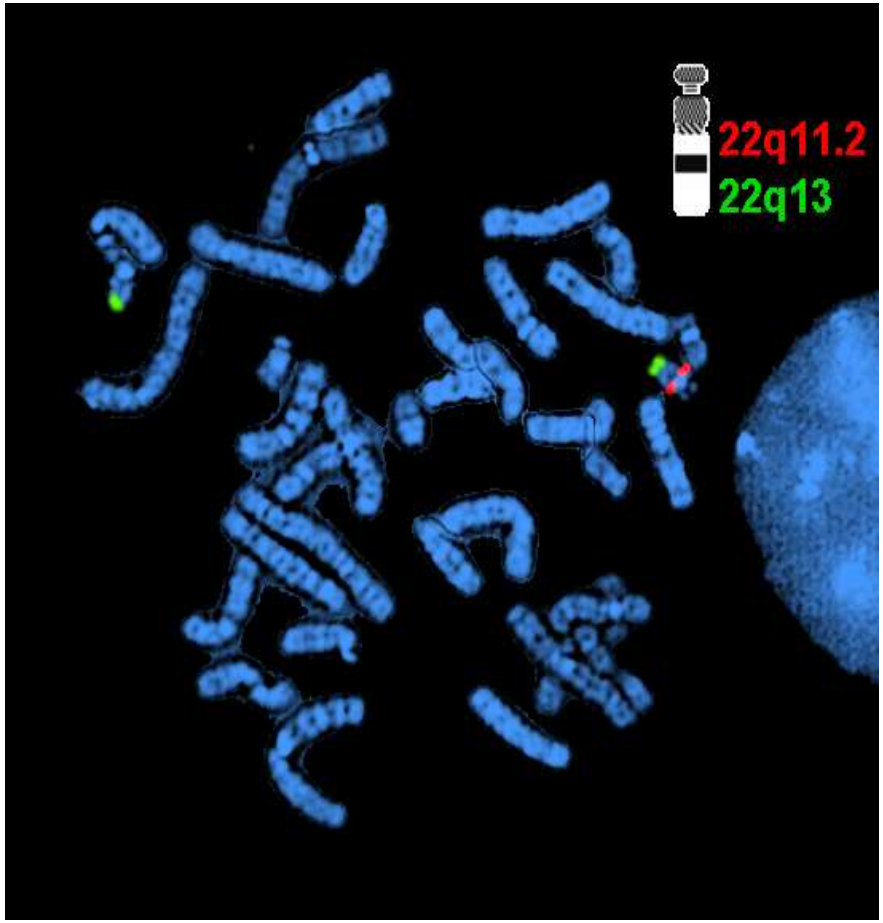
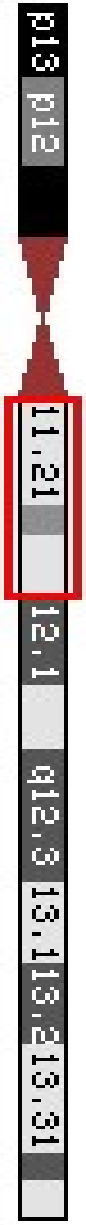
# Region 22q11

## *Deletion*

**Velo-cardio-facial syndrome**



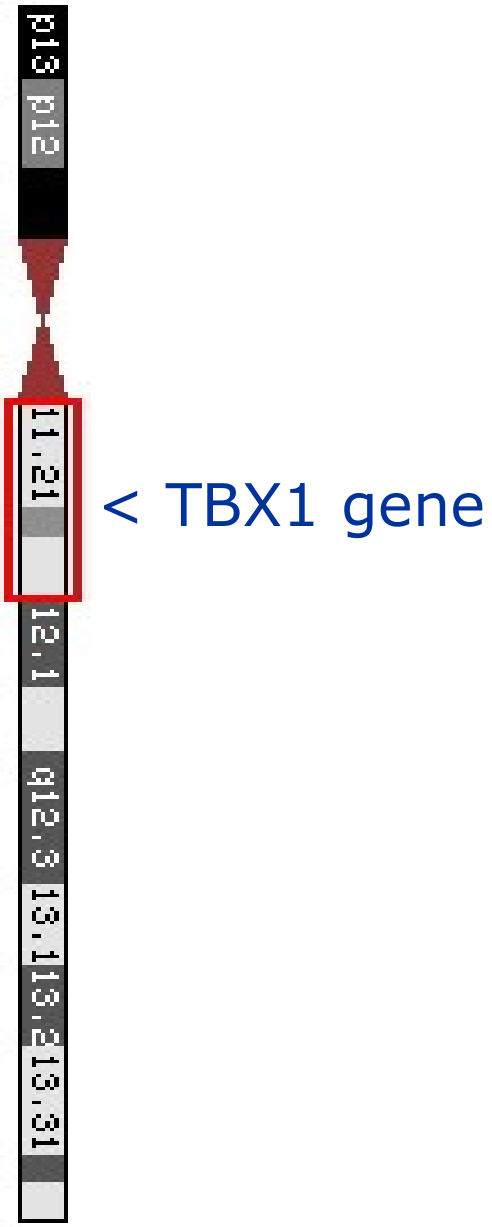

IPG

# Region 22q11

## *Deletion*

**Velo-cardio-facial syndrome**

- 1/2000-1/4000 live births
- Learning difficulties (60%)
- Psychiatric disorders (10%)
- Heart defects (65%)
- Velar incompetence (95%)
- Facial dysmorphy




IPG

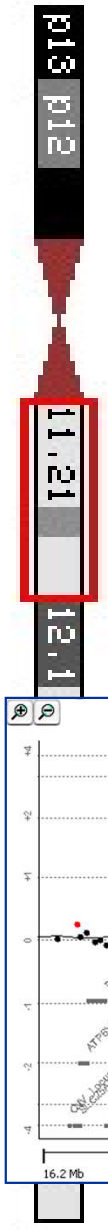
# Region 22q11

## *Deletion*

### Velo-cardio-facial syndrome

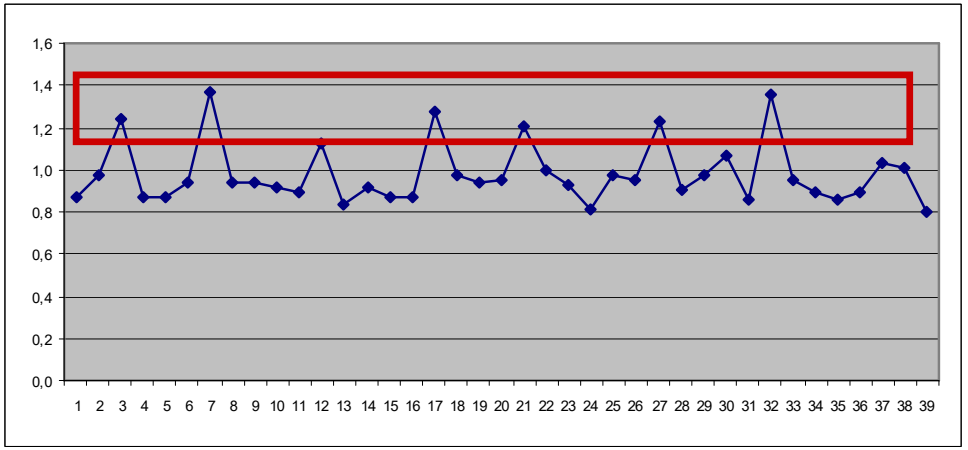
- 1/2000-1/4000 live births
- Learning difficulties (60%)
- Psychiatric disorders (10%)
- Heart defects (65%)
- Velar incompetence (95%)
- Facial dysmorphy

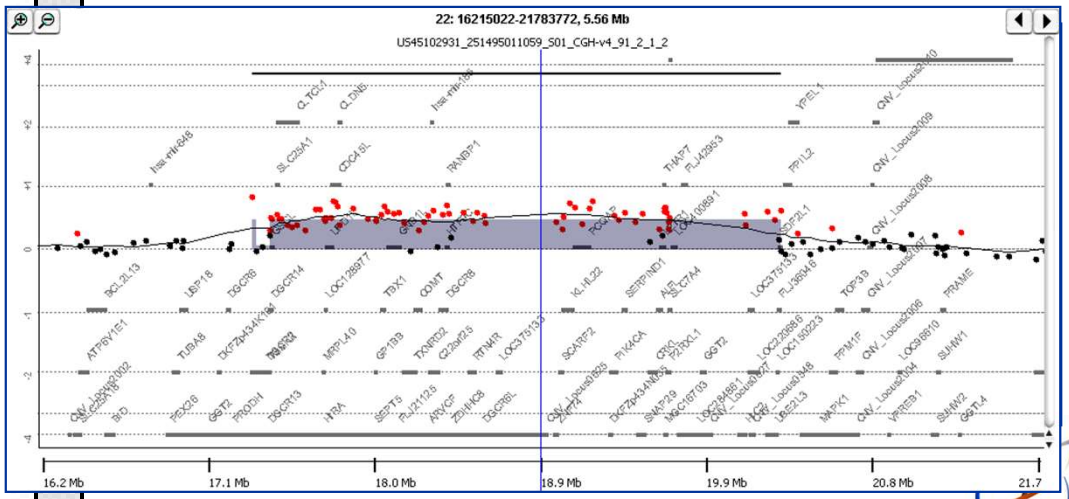
Ch 22




## *Duplication*

### Dup (22)(q11.2)




IPG

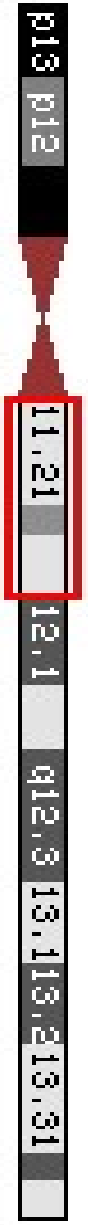
# Region 22q11

## *Deletion*

**Velo-cardio-facial syndrome**

- 1/2000-1/4000 live births
- Learning difficulties (60%)
- Psychiatric disorders (10%)
- Heart defects (65%)
- Velar incompetence (95%)
- Facial dysmorphy

Ch 22




## *Duplication*

**Dup (22)(q11.2)**

- Learning difficulties (100%)
- Behavioral problems (50%)
- Heart defects(15-20%)
- Velar incompetence (70%)

IPG

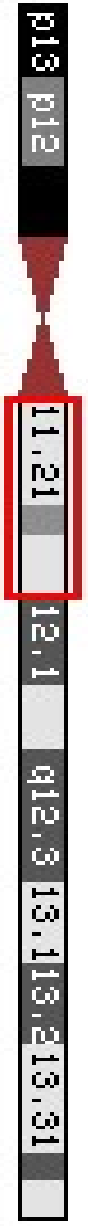
# Region 22q11

## *Deletion*

### Velo-cardio-facial syndrome

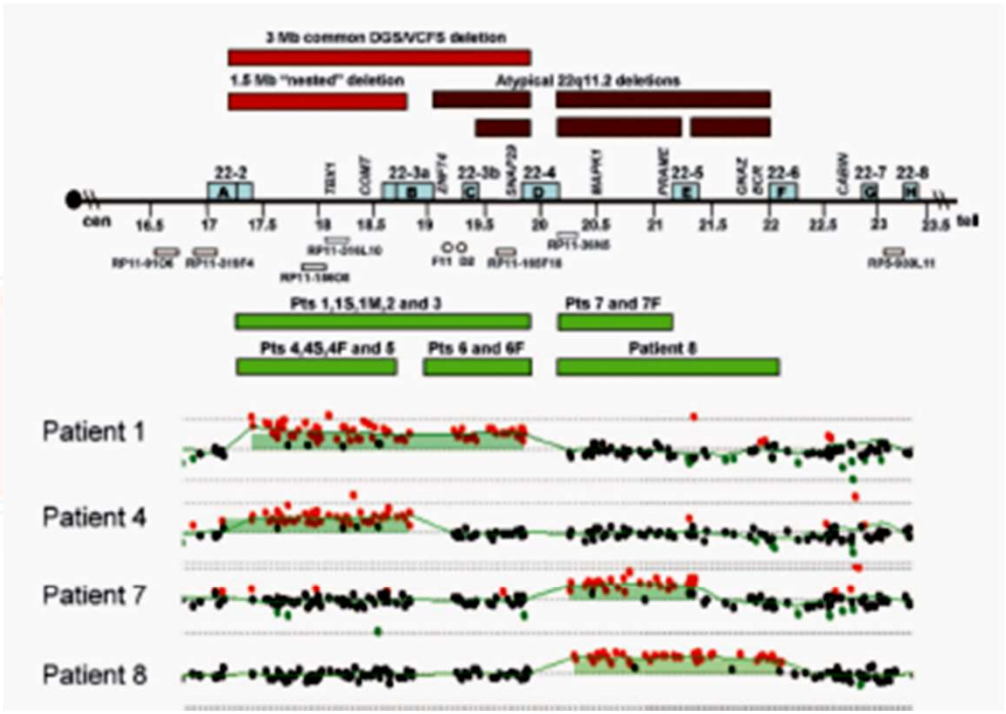
- 1/2000-1/4000 live births
- Learning difficulties (60%)
- Psychiatric disorders (10%)
- Heart defects (65%)
- Velar incompetence (95%)
- Facial dysmorphy

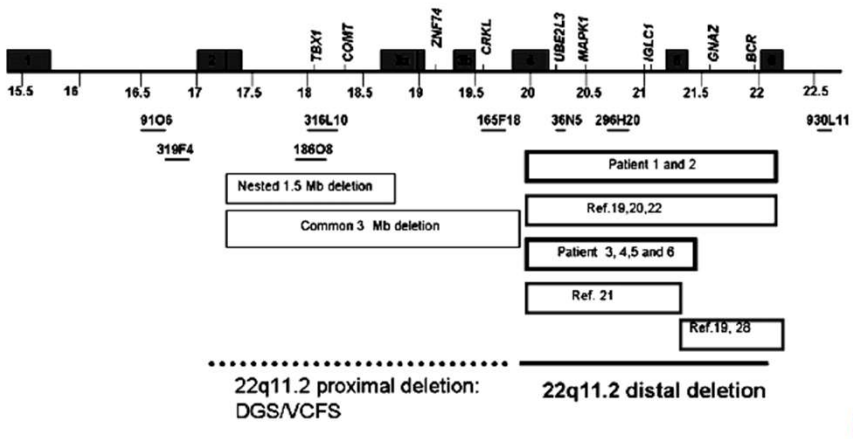
Ch 22




## *Duplication*

### Dup (22)(q11.2)

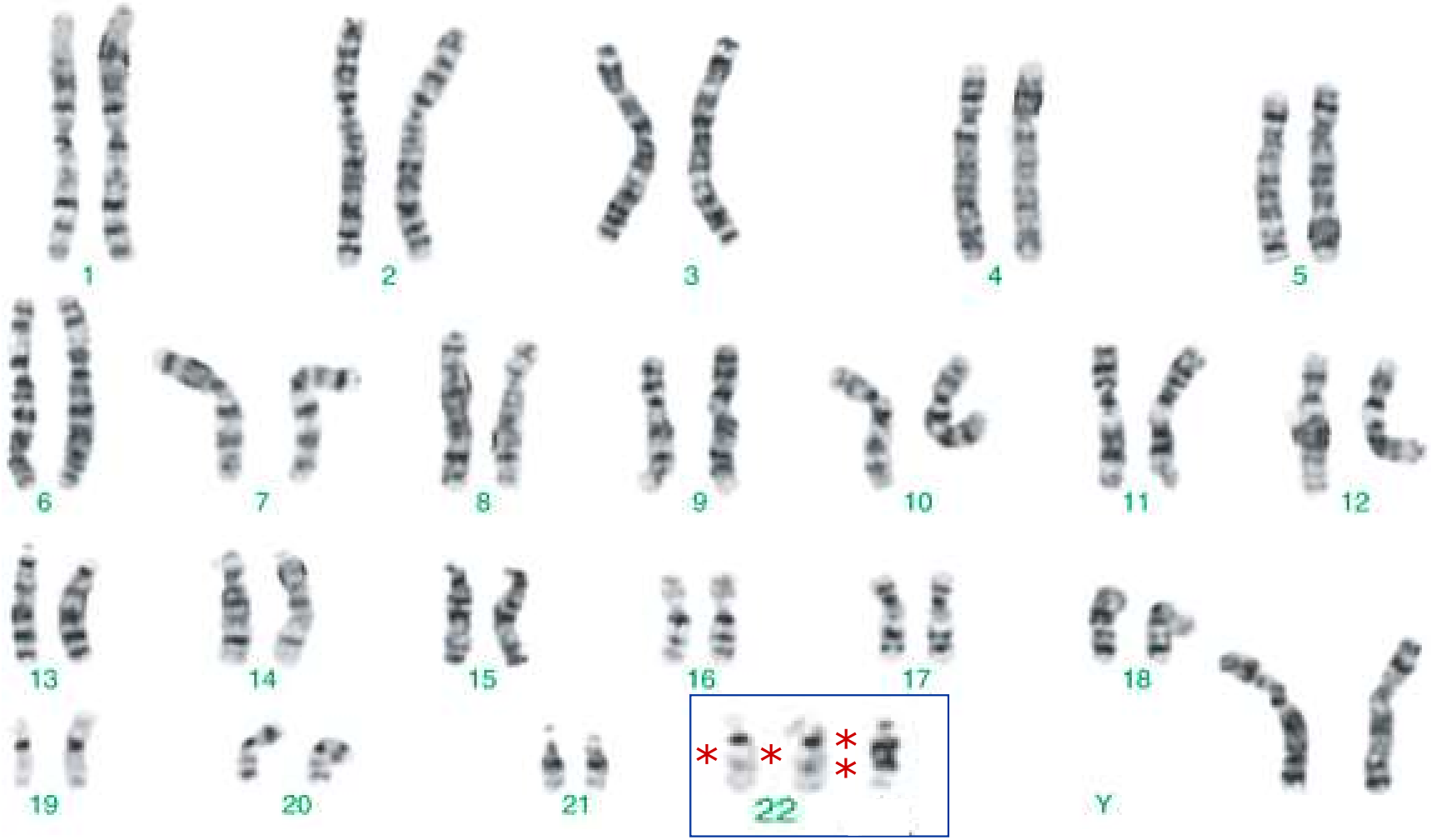



IPG

# Region 22q11

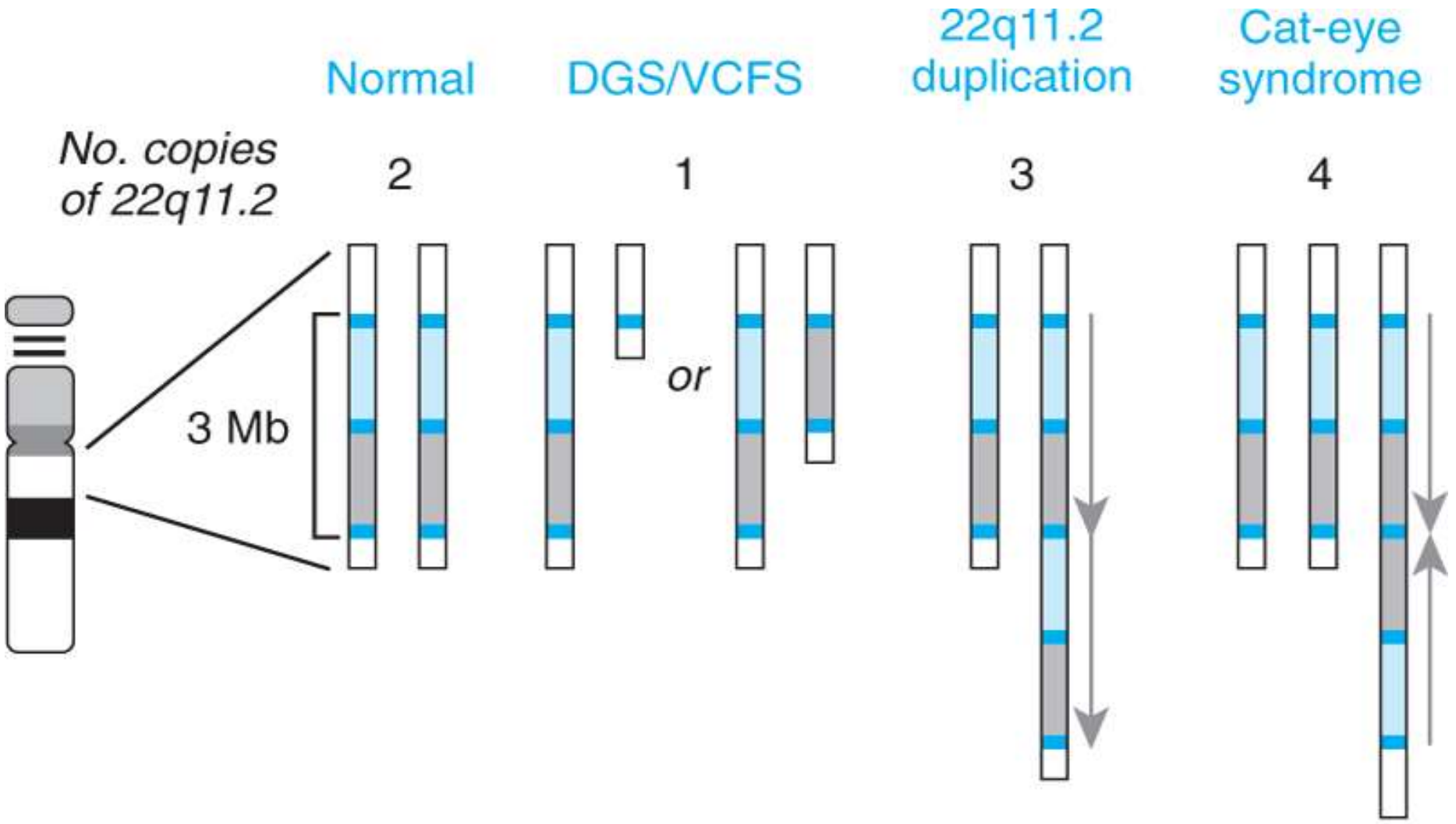
## Tetrasomy 22q11→ Cat-eye syndrome




47,XX,+inv dup(22)(pter→q11.2)

IPG

# Region 22q11



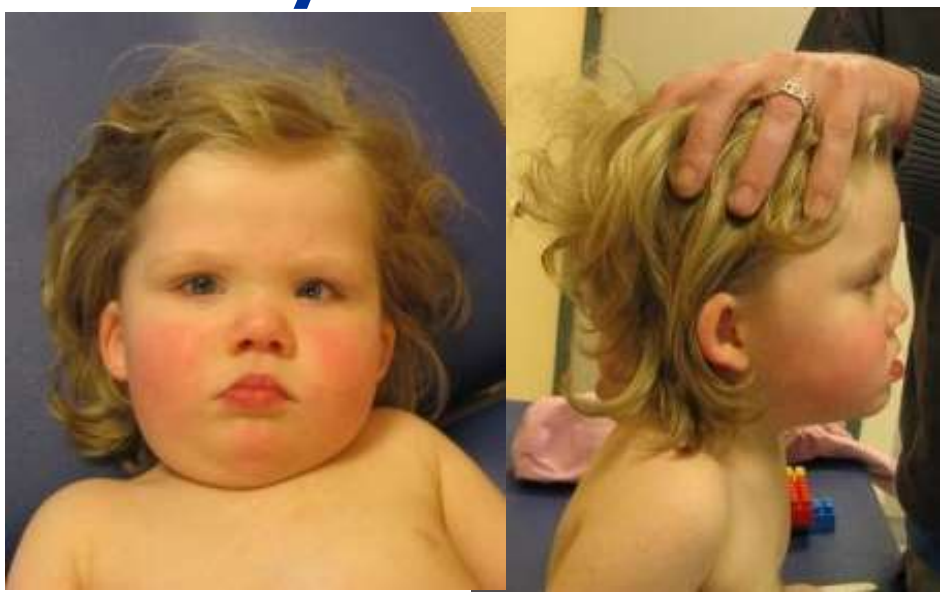



IPG

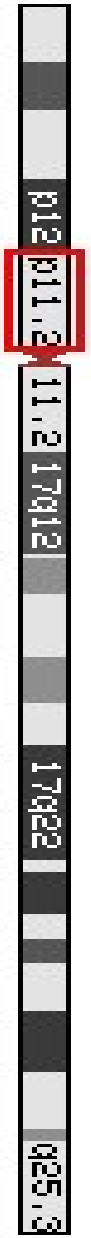
# Region 17p11.2

## *Deletion*

**Smith-Magenis syndrome**

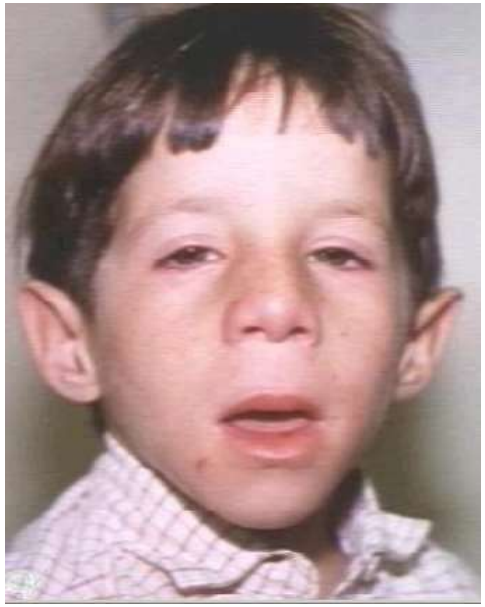


- Mental retardation, speech delay
- Self-destructive behavior
- Sleep disorders
- Flat midface, brachycephaly
- Brachydactyly
- Congenital anomalies




## *Duplication*

**Dup (17)(p11.2)**



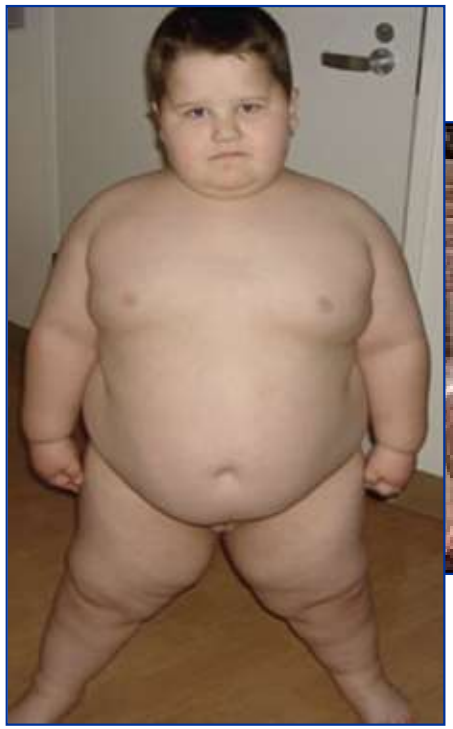
- Dvpt delay, speech delay
- Poor feeding, growth retardation
- Autistic features
- Cardiac defect

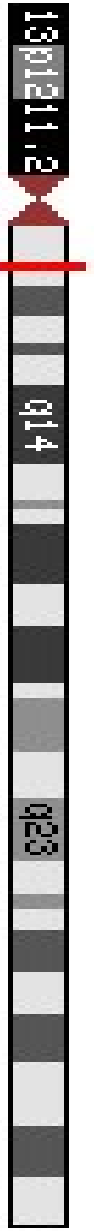
IPG

# Region 15q11-q13

## *Paternal Deletion* Ch 15

**Prader-Willi syndrome**

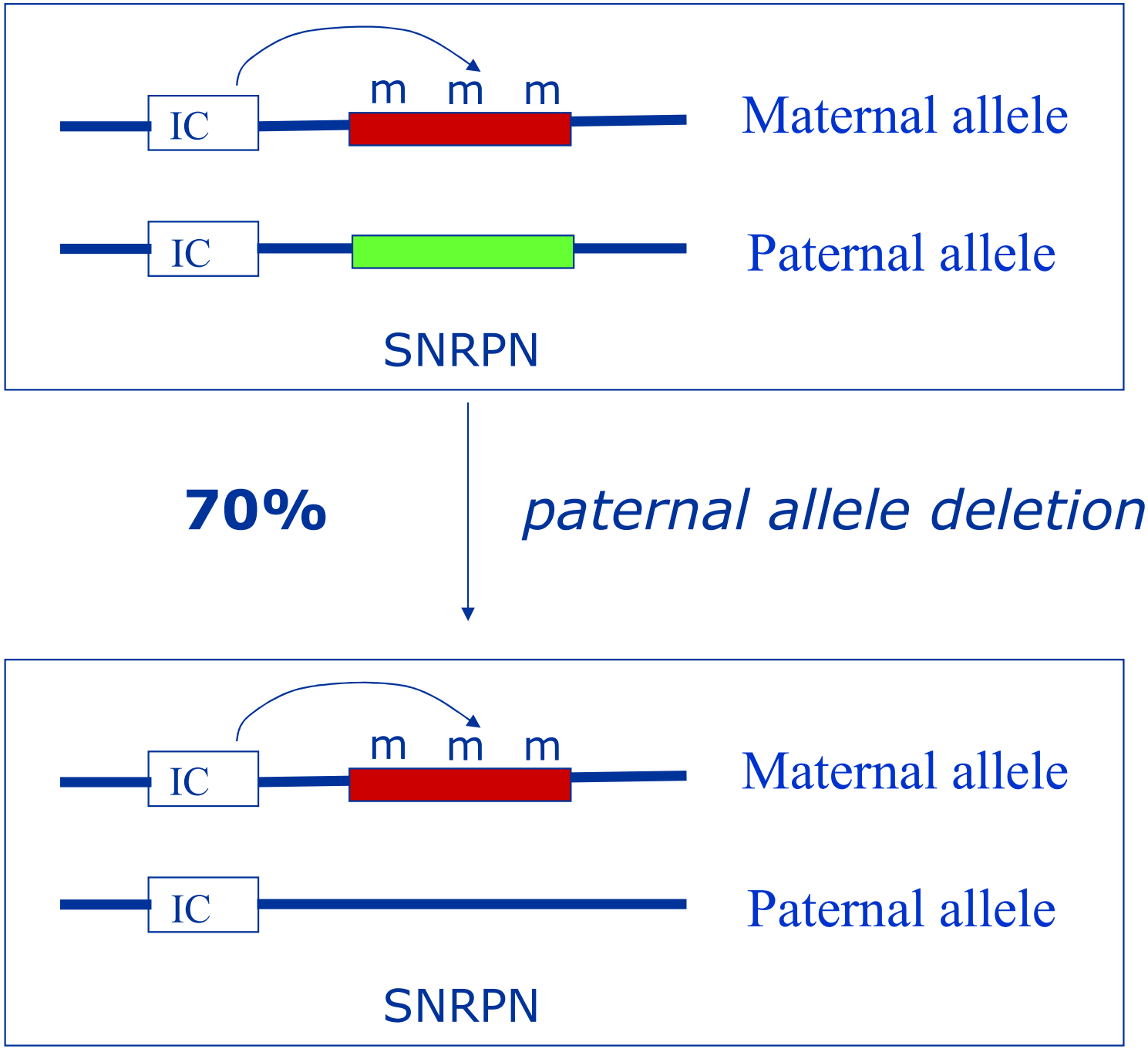




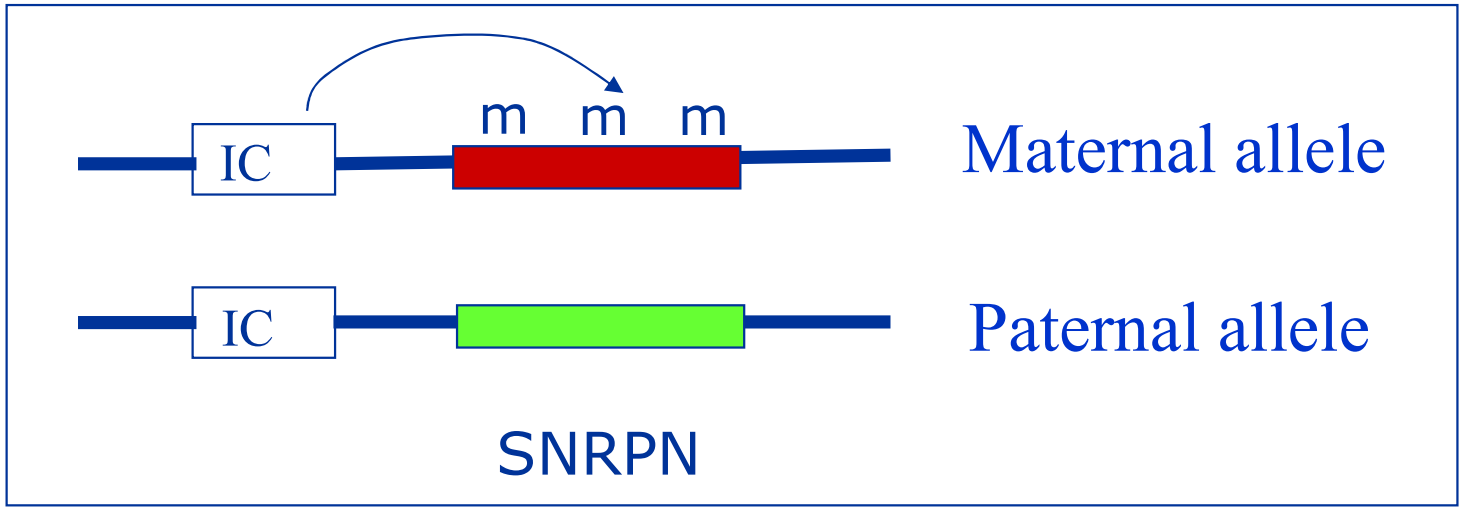

- Mental retardation
- Behavior problems
- Neonatal hypotonia
- Hyperphagia, morbid obesity
- Hypogonadism

IPG

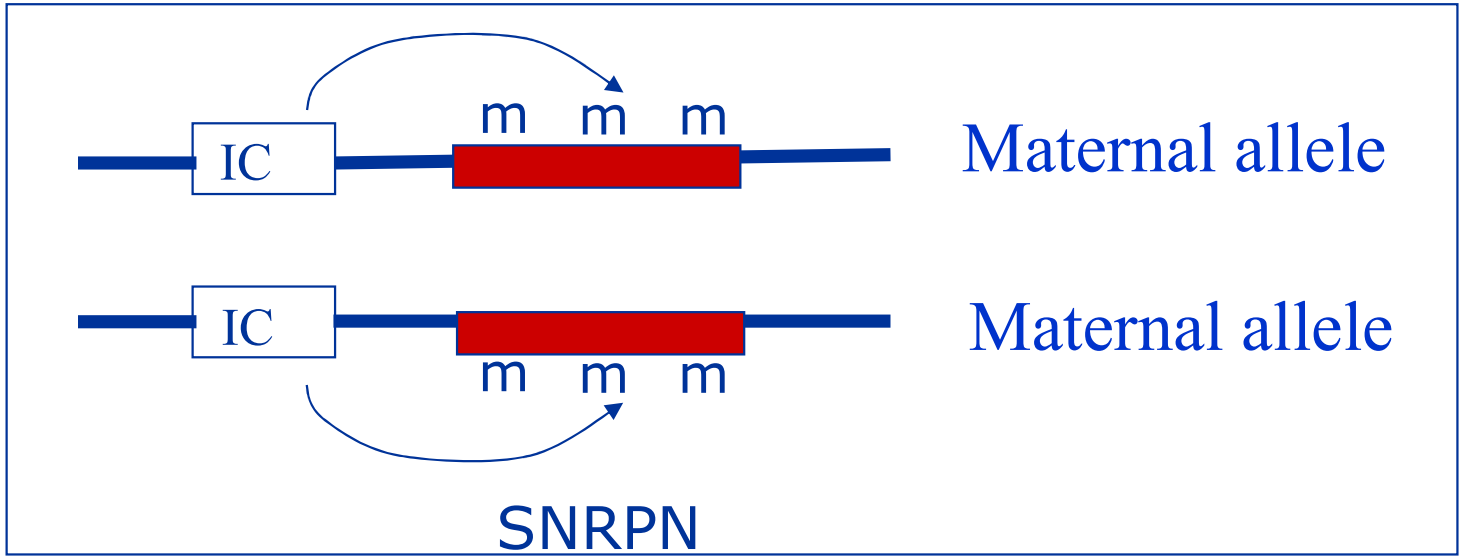
# Region 15q11-q13



# Region 15q11-q13

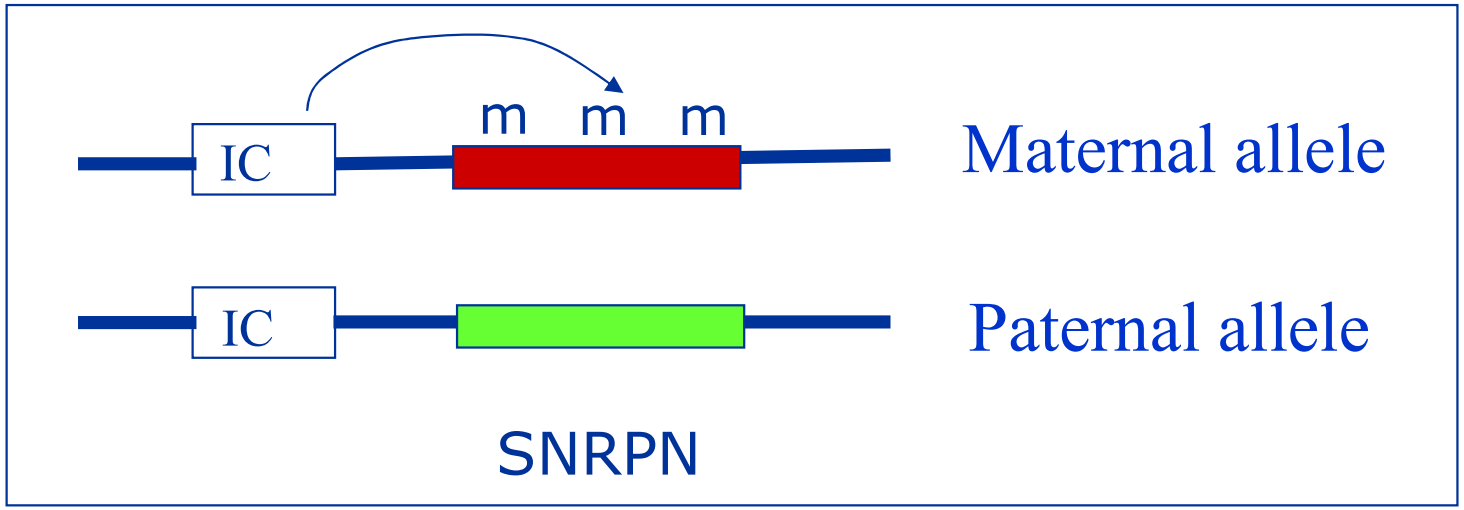



**25-30%** *maternal uniparental disomy*

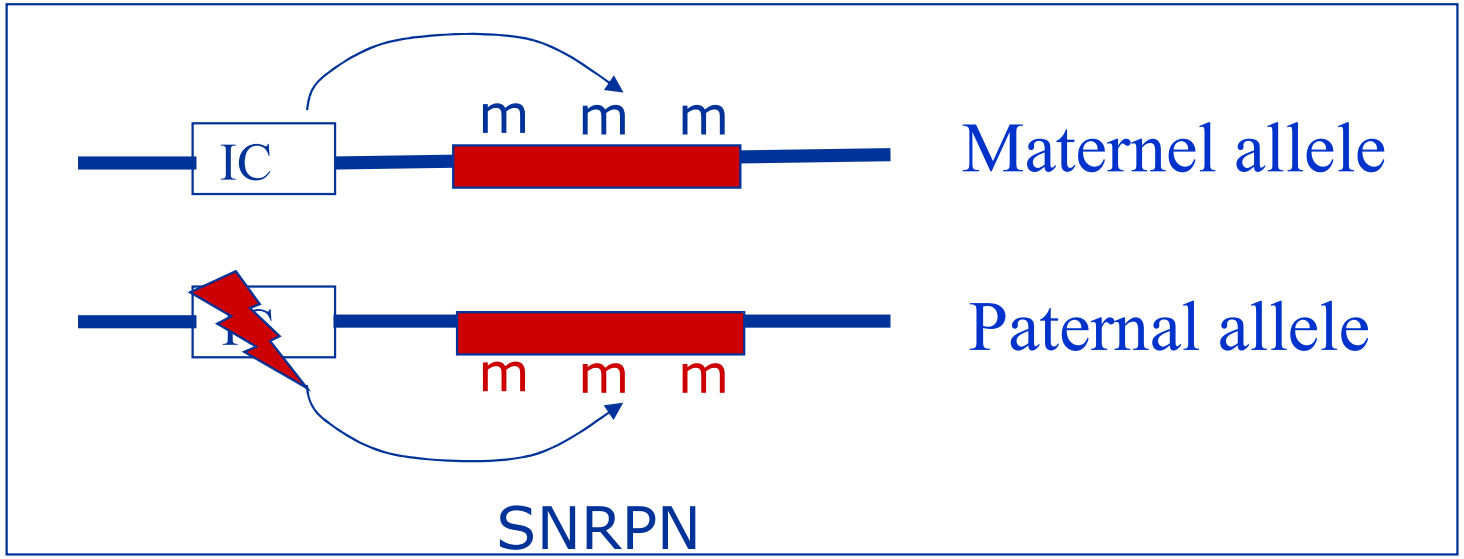



IPG

# Region 15q11-q13




**<5%** *defect in the imprinting center*

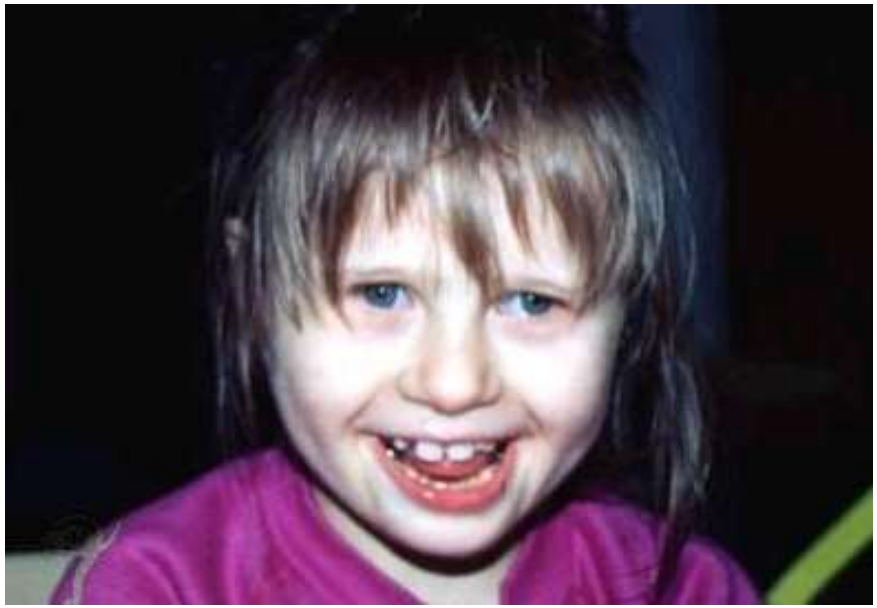


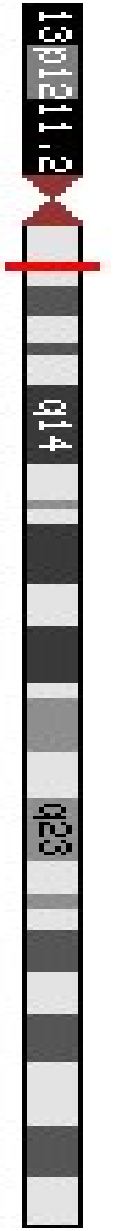

IPG

# Region 15q11-q13

## *Maternal Deletion* Ch 15

**Angelman syndrome**

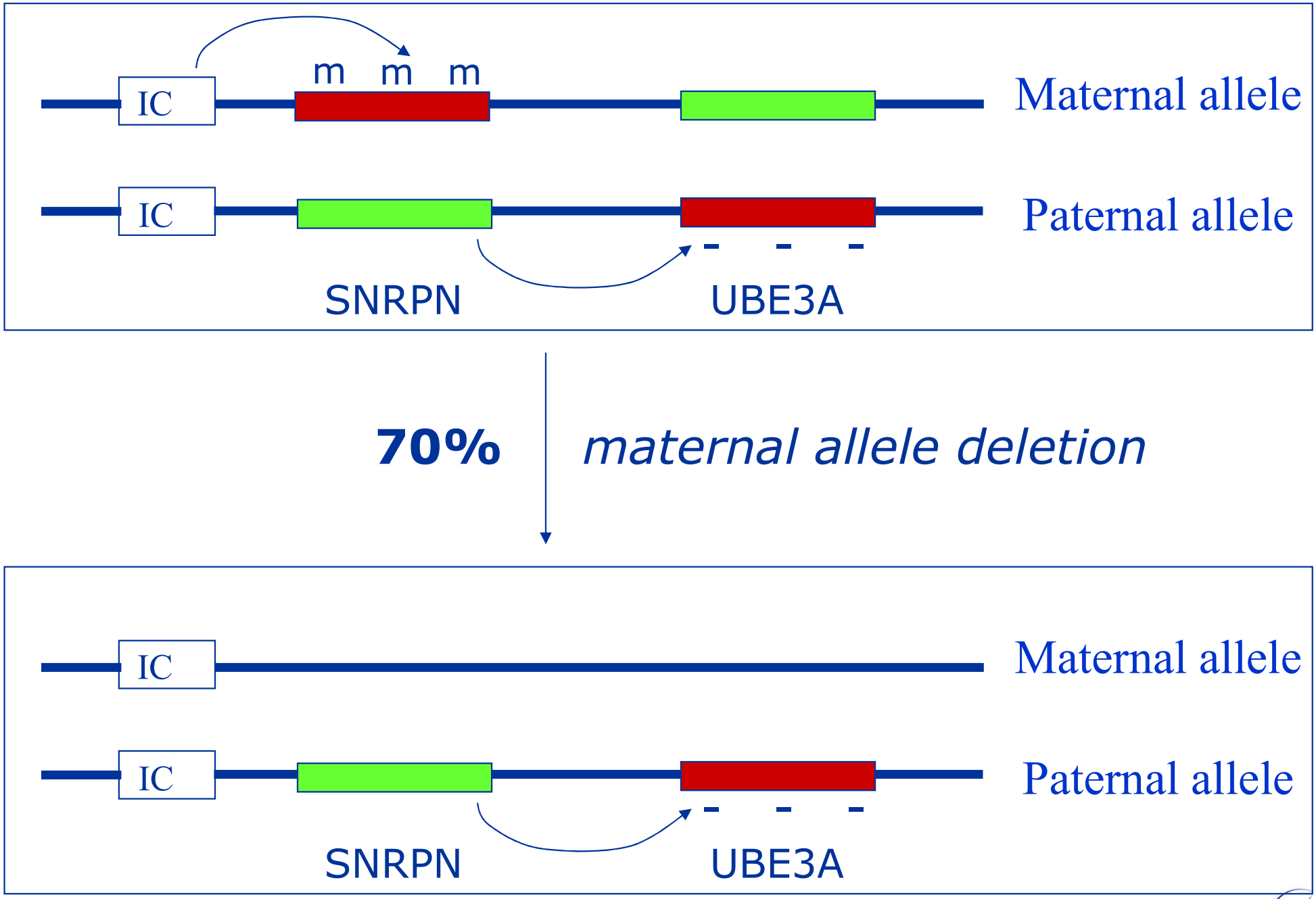




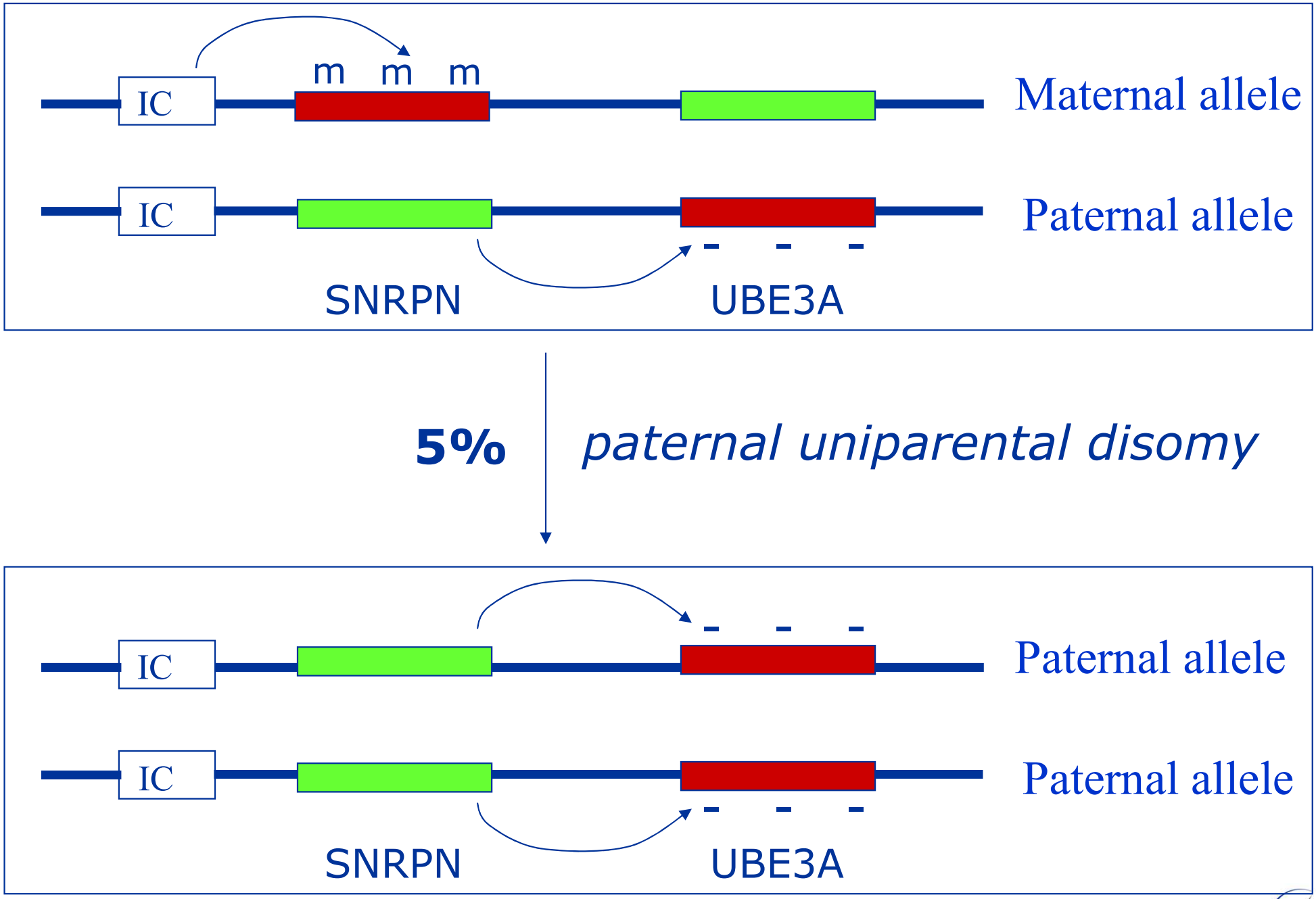

- Severe mental retardation
- Ataxia
- Epilepsy
- Happy behavior

IPG

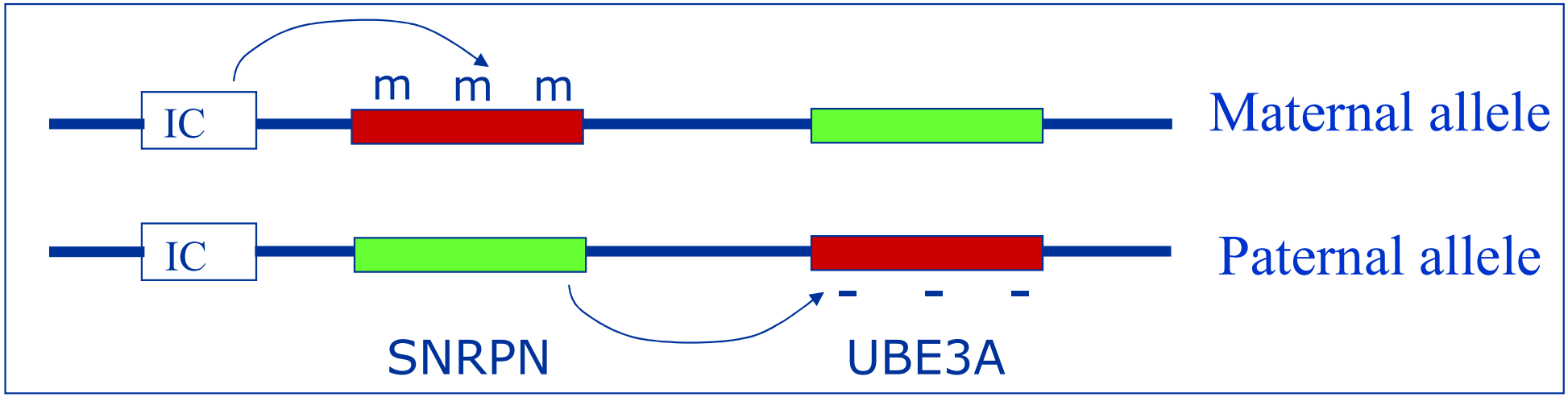
# Region 15q11-q13



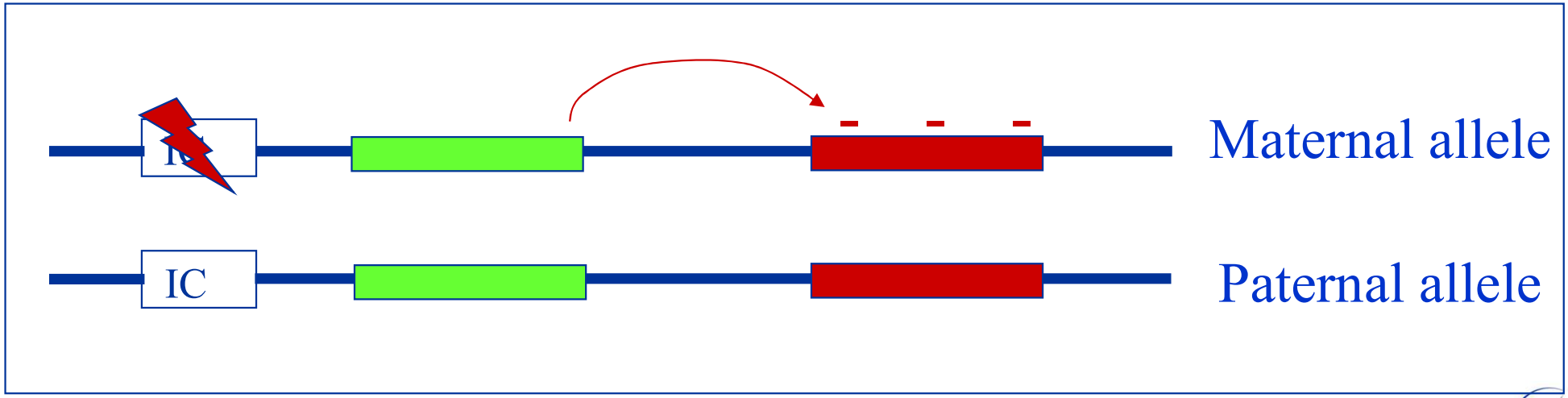
# Region 15q11-q13



# Region 15q11-q13

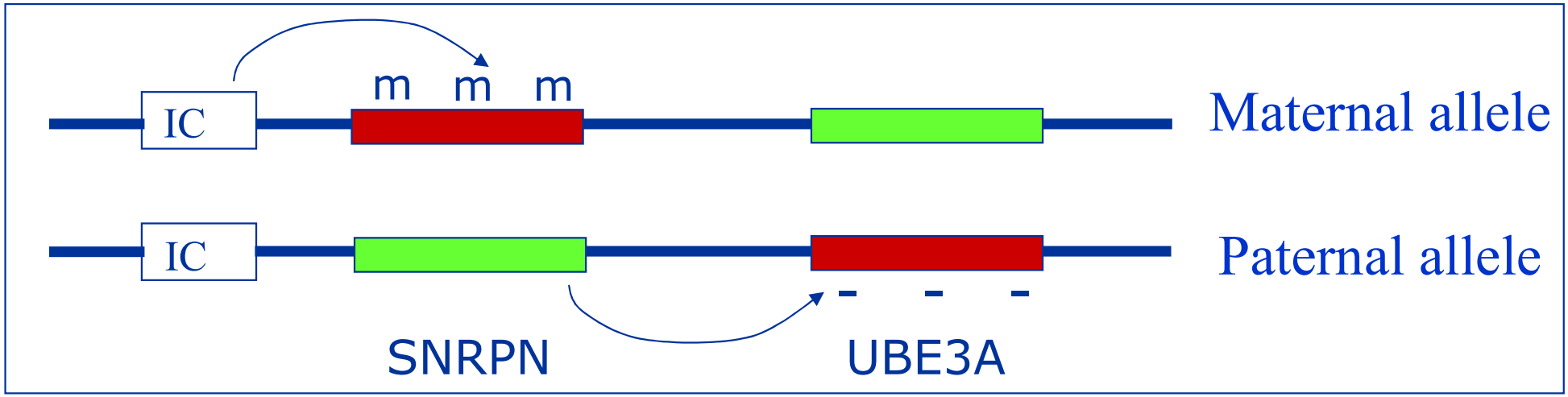



**5%** *defect in the imprinting center*

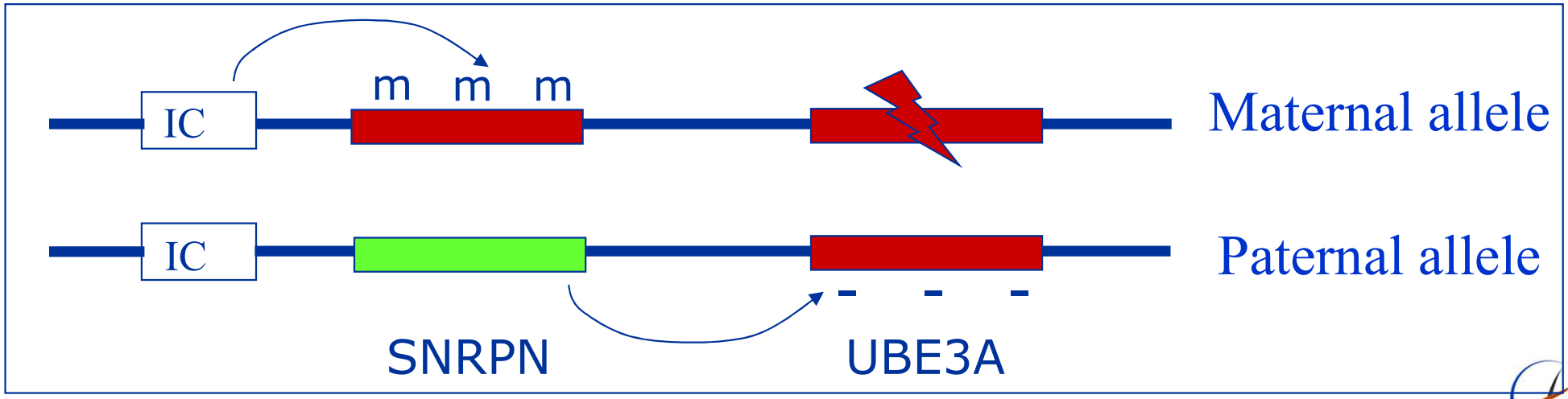



IPG

# Region 15q11-q13

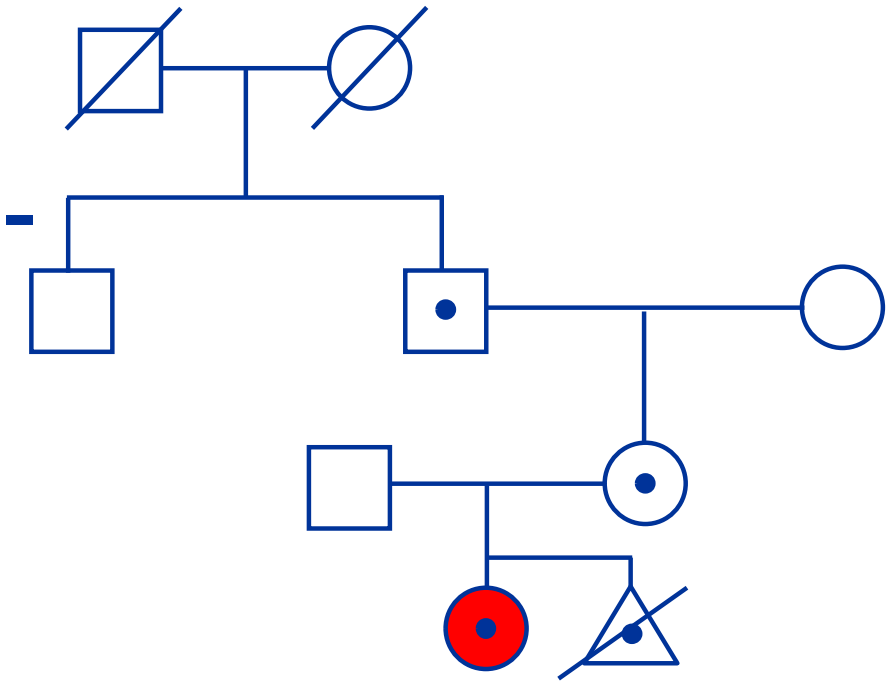


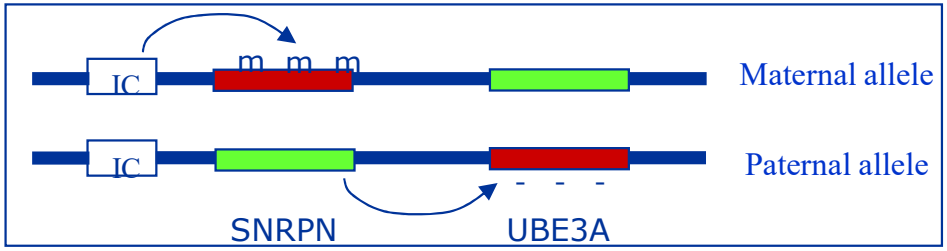

**10%** *mutation in UBE3A gene*



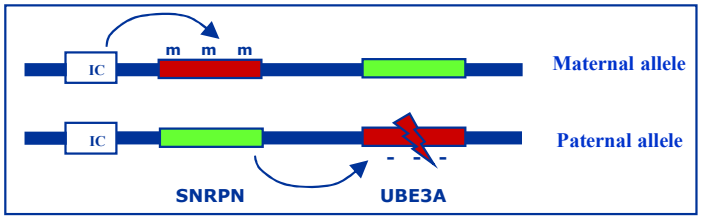

IPG

# UBE3A point mutation

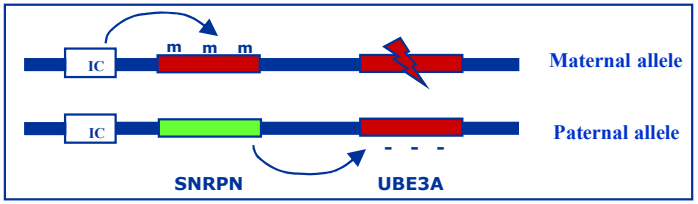





## Normal




Asymptomatic carrier




Angelman

Carrier Angelman syndrom

Tested negative

Angelman syndrome

| | PW | Angelman |
|---|---|---|
| **Deletion** | **70% (pat)** | **70% (mat)** |
| **Uniparental Disomy (UPD)** | **20-30% (mat)** | **7% (pat)** |
| **Single gene mutation** | **Rare** | **10%<br>Familial cases** |
| **Imprinting Center Mutation** | **2,5%** | **3%** |
| **Unidentified** | **<1%** | **10%** |

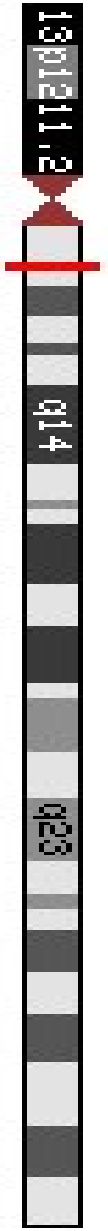
*Table 6-4: Molecular mechanisms causing Prader-Willi and Angelman syndromes*

# Region 15q11-q13

## *Paternal Deletion*

**Prader-Willi syndrome**

Ch 15




## *Duplication*

**Dup (15)(q11-q13)**

## *Maternal Deletion*

**Angelman syndrome**

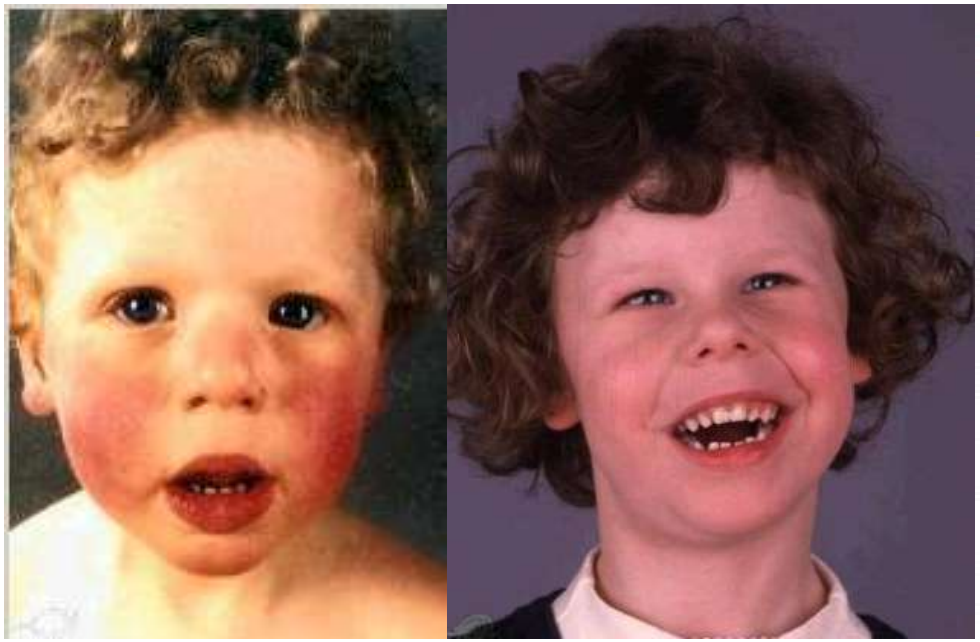
- Mental retardation
- Autism

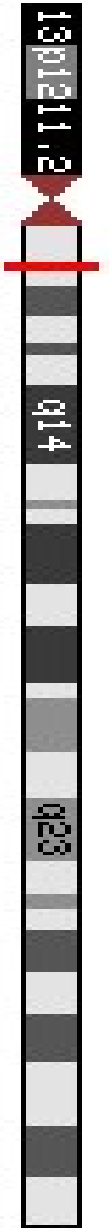
IPG

# Region 7q11

## *Deletion*

**Williams syndrome**





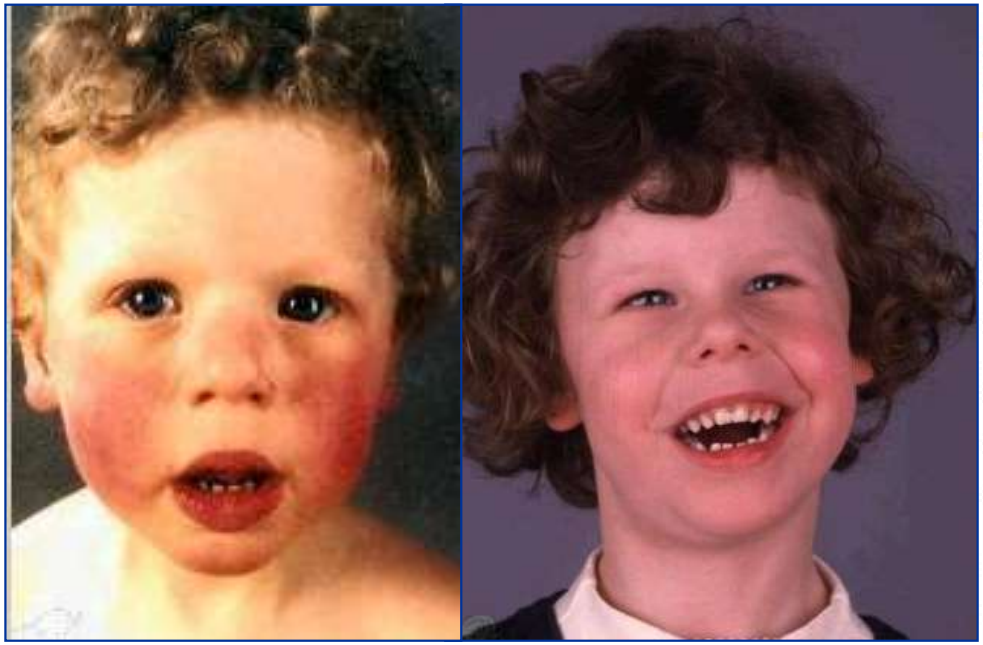

- Cardiovascular anomalies
- Distinctive facies
- Mental retardation
- Friendly personality

IPG

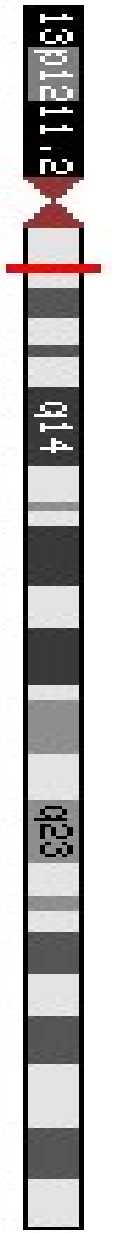
# Region 7q11

## *Deletion*

**Williams syndrome**



- Cardiovascular anomalies
- Mental retardation
- Friendly personality




## *Duplication*

**Dup (7)(q11)**

- Mental retardation
- Speech delay
- Behavioral problems

IPG

# Microdeletions/microduplications syndromes:

BeSHG

COLLEGE GENETICS

**Table of susceptibility loci in context of invasive prenatal testing**

prepared by the BeSHG Prenatal Committee on 17.09.2022

| chr | start in Mb (hg19) | stop in Mb (hg 19) | size in kb | CNV | gene | phenotype | morph. anomaly | return? | OMIM | update May 2017 | update December 2021 | update June / September 2022 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 146.57 | 147.39 | 820 | distal 1q21.1 dup | *GJA5 (CX40)* | ID, DD, ASD, schizophrenia | macrocephaly, CHD | YES | 612475 | YES | | YES |
| 1 | 146.57 | 147.39 | 820 | distal 1q21.1 del | *GJA5 (CX40)* | ID, DD, ASD, SZ, facial dysmorphism | microcephaly, CHD, renal and urinary tract anomalies | YES | 612474 | YES | | YES |
| 1 | 171.81 | 172,38(?) | 57 | 1q24.3 del | *DNM3* | ID | IUGR, microcephaly, brachydactyly | YES | | | | YES |
| 2 | 50 | 51.11 | 1110 | 2p16.3 del (exon 6-24 del) | *NRXN1* | ID, ASD, SZ, DD, dysmorphic features | none | YES | 614332 | | added to YES (pubmed ID 31932357 and discussion in consortium 18/06/2020) | YES |
| 15 | 31.13 | 32.48 | 1350 | 15q13.3 del | *CHRNA7* | DD, ID, ASD, epilepsy, SZ | microcephaly, CHD | YES | 612001 | YES | | YES |
| 15 | 99.36 | 102.52 | 3160 | 15q26 del | *IGF1R* | MR | IUGR | YES | | YES | | |
| 16 | 28.74 | 28.96 | 220 | 16p11.2 distal del | *SH2B1* | obesity, DD, ID, SZ | none | YES | 613444 | YES | | YES |
| 16 | 29.59 | 30.19 | 600 | 16p11.2 proximal dup | *TBX6* | ASD, ID, DD, SZ, anorexia | microcephaly | YES | 614671 | moved to YES since actionable; penetrance del and dup comparable | | YES |
| 16 | 29.59 | 30.19 | 600 | 16p11.2 proximal del | *TBX6* | ID, DD, ASD, obesity, SZ, speech delay | macrocephaly, vertebra | YES | 611913 | YES | | YES |
| 17 | 34.82 | 36.21 | 1390 | 17q12 deletion syndrome RCAD (renal cysts & diabetes) | *TCF2* | facial dysmorphy, genital abnormalities, ID, DD, ASD, MODY | renal anomalies | YES | 614527 | YES | | YES |
| 22 | 19.02 | 20.29 | 1270 | 22q11.2 dup | *TBX1* | ASD, ID, DD, dysmorphic features | microcephaly, CHD | YES | 608363 | YES | | YES |
| 1 | 144.97 | 146.61 | 1640 | 1q21.1 dup | *HFE2* | DD, ASD | CHD | NO | | NO | | NO |
| 2 | 50 | 51.11 | 1110 | 2p16.3 del (whole gene, intronic, exon 1-5) | *NRXN1* | ID, ASD, SZ, DD, dysmorphic features | none | NO | 614332 | NO | NO in case of whole gene del, intronic del or exon 1-5 del (pubmed ID 31932357 and discussion in consortium 18/06/2020) | NO |
| 2 | 110.87 | 110.98 | 110 | 2q13 dup | *NPHP1* | ASD, ID | none | NO | | NO | | NO |
| 2 | 111.4 | 113 | 1600 | 2q13del | | ID, DD, dysmorphic features | CHD | | | NO (Govaerts 2017) | | NO |
| 3 | 1.7 | 2.8 | 1100 | 3p26.3 del | *CNTN4* | ASD | | | | NO (Govaerts 2017) | | NO |
| 3 | 195.7 | 197.30 | 1600 | 3q29 dup | | MR, DD | none | NO | | NO | | NO (note: coordinates corrected) |
| 10 | 49 | 52.4 | 3400 | 10q11.22q11.23 del | | ID, DD | | | | NO (Govaerts 2017) | | NO |
| 10 | 49 | 52.4 | 3400 | 10q11.22q11.23 del | | ID, DD | | | | NO (Govaerts 2017) | | NO |
| 13 | 20.81 | 21.01 | 1200 | 13q12 dup | *CRYL1* | | | NO | | NO | | NO |
| 15 | 22.8 | 23.09 | 290 | 15q11.2 dup | *NIPA1* | DD, motor delay, speech delay, ASD | none | NO | | NO (likely benign) | | NO |
| 15 | 22.8 | 23.09 | 290 | 15q11.2 del | *NIPA1* | ID, DD, epilepsy | CHD | NO | 615656 | NO (likely benign) | | NO |

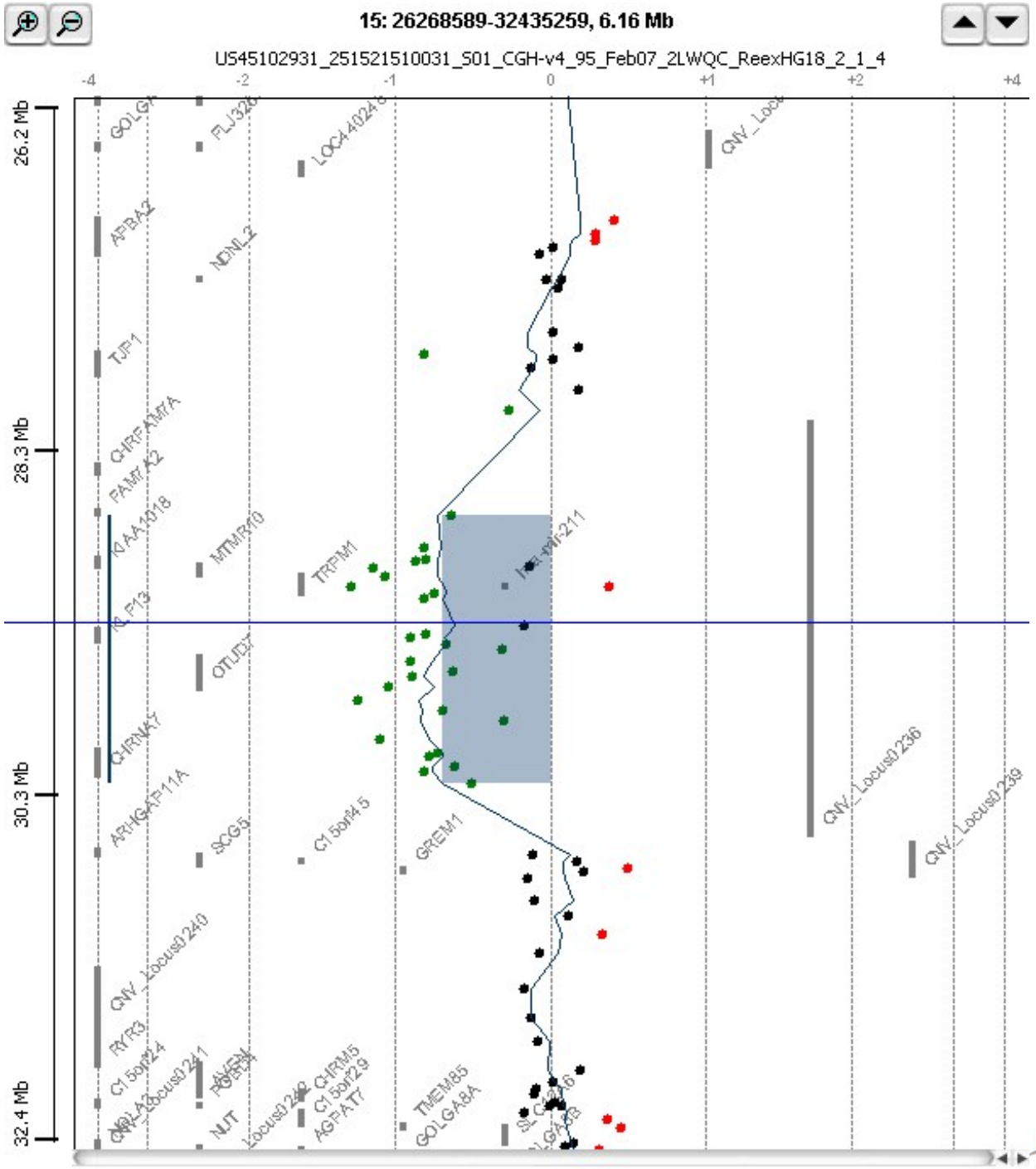
**> Highly variable expressivity**

IPG

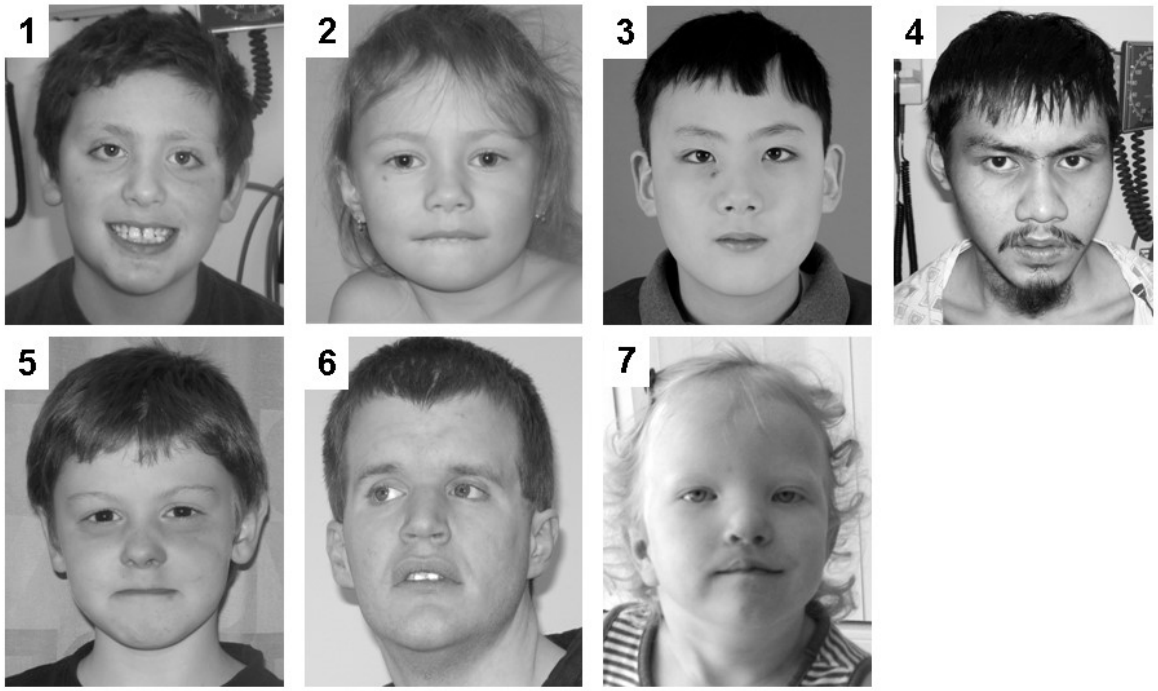
# Exemple: 2 brothers

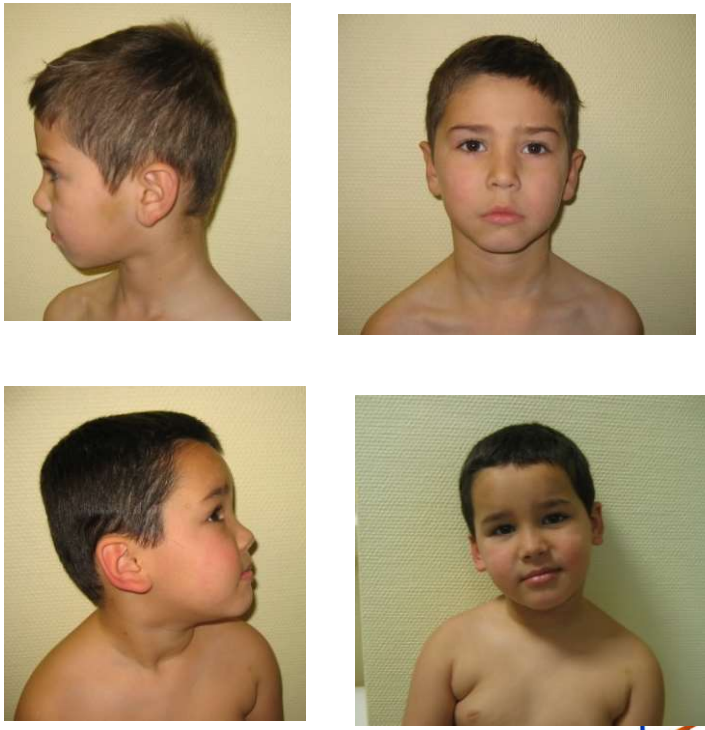
- Developmental delay
  - Walk > 18 months
  - Speech delay
- Learning difficulties
- Epilepsy
- Behavioral problems

# 15q13.3 deletion (1,5 Mb)



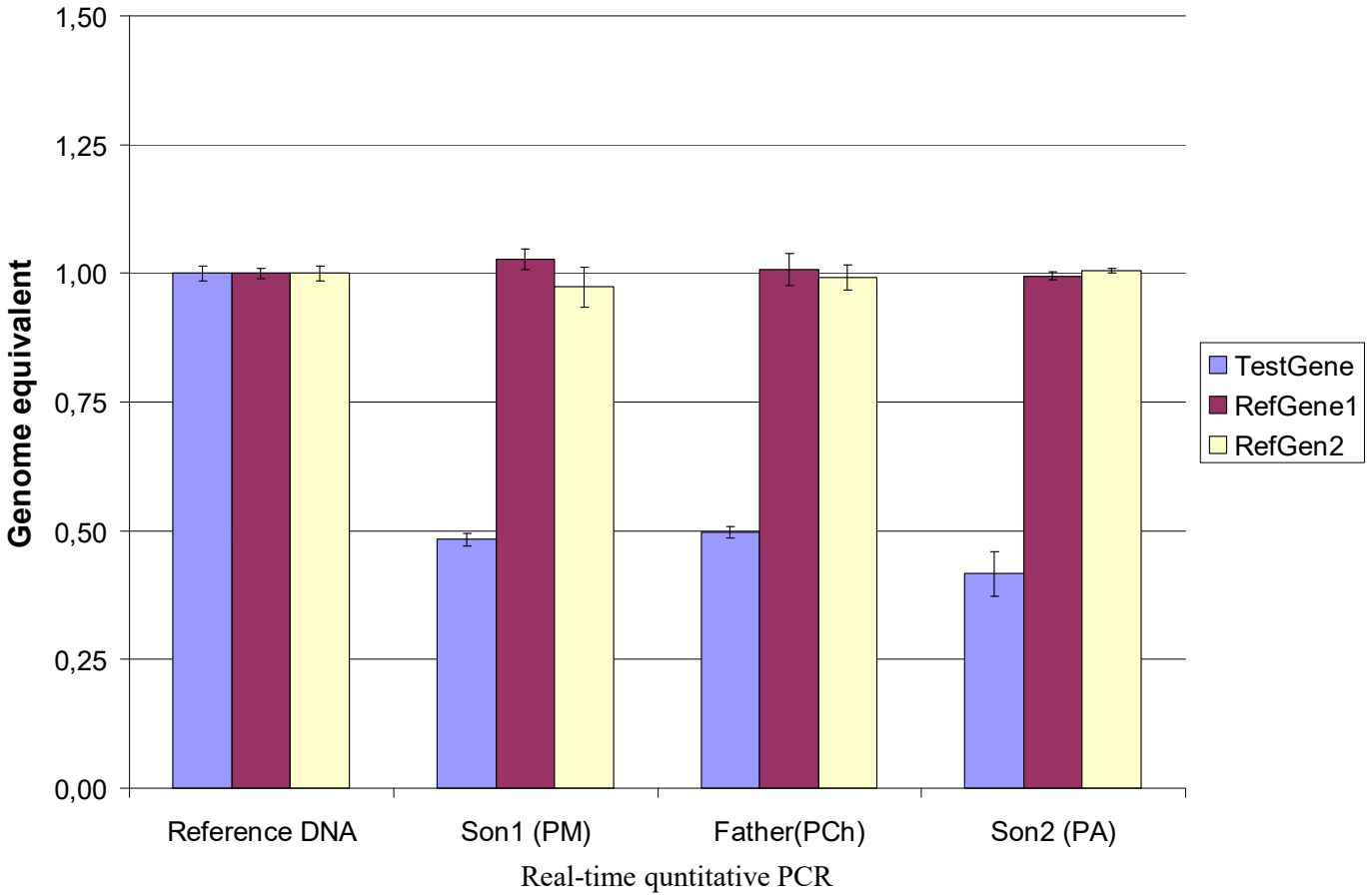
## Sharp et Al (Nat Genet 2008)

## Miller et Al (J Med Genet 2008)

# Familial screening (Q-PCR)




**2 brothers** : 15q13.3 délétion
**Father** : 15q13.3 délétion

**→ inherited rearrangement from an asymptomatic father**

# A recurrent 15q13.3 microdeletion syndrome associated with mental retardation and seizures

Andrew J Sharp[1,15], Heather C Mefford[1], Kelly Li[2], Carl Baker[1], Cindy Skinner[3], Roger E Stevenson[3], Richard J Schroer[3], Francesca Novara[4], Manuela De Gregori[4], Roberto Ciccone[4], Adam Broomer[2], Iris Casuga[2], Yu Wang[2], Chunlin Xiao[2], Catalin Barbacioru[2], Giorgio Gimelli[5], Bernardo Dalla Bernardina[6], Claudia Torniero[6], Roberto Giorda[7], Regina Regan[8], Victoria Murday[9], Sahar Mansour[10], Marco Fichera[11], Lucia Castiglia[11], Pinella Failla[11], Mario Ventura[12], Zhaoshi Jiang[1], Gregory M Cooper[1], Samantha J L Knight[8], Corrado Romano[11], Orsetta Zuffardi[4,13], Caifu Chen[2], Charles E Schwartz[3] & Evan E Eichler[1,14]

**Nat Genet, 2008 : 40(3), 322-328**

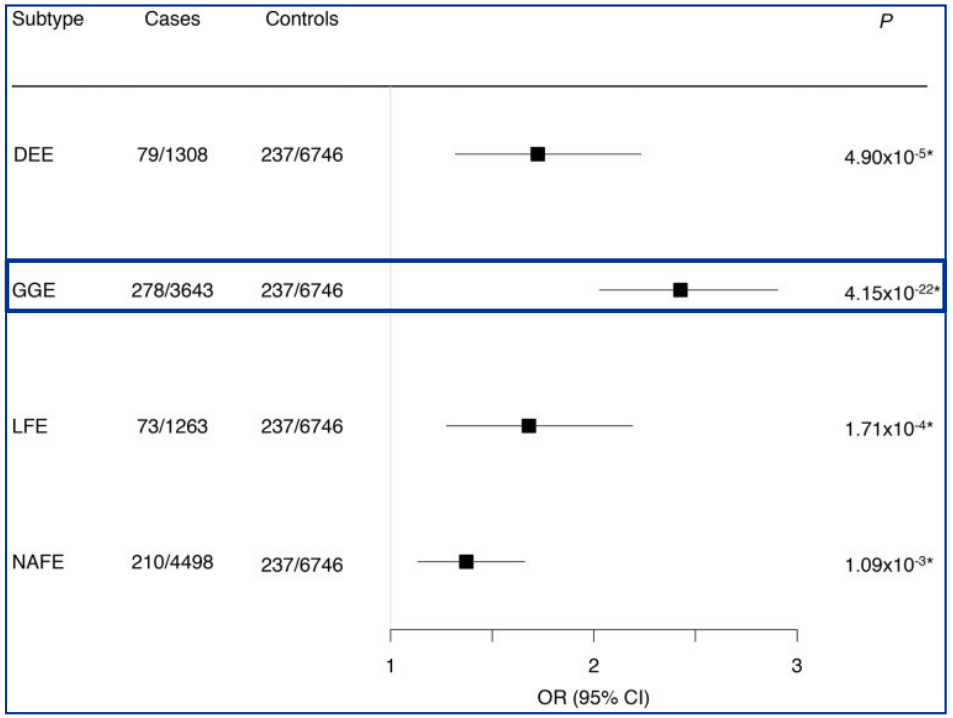
Incomplete penetrance

Variable Expressivity

IPG

# Epilepsy and deletion/duplication

- 1q21.1
- 15q11.2
- 15q13.3
- 16p11.2
- 16p12.1
- 16p13.11
- 22q11.2 (Di George)



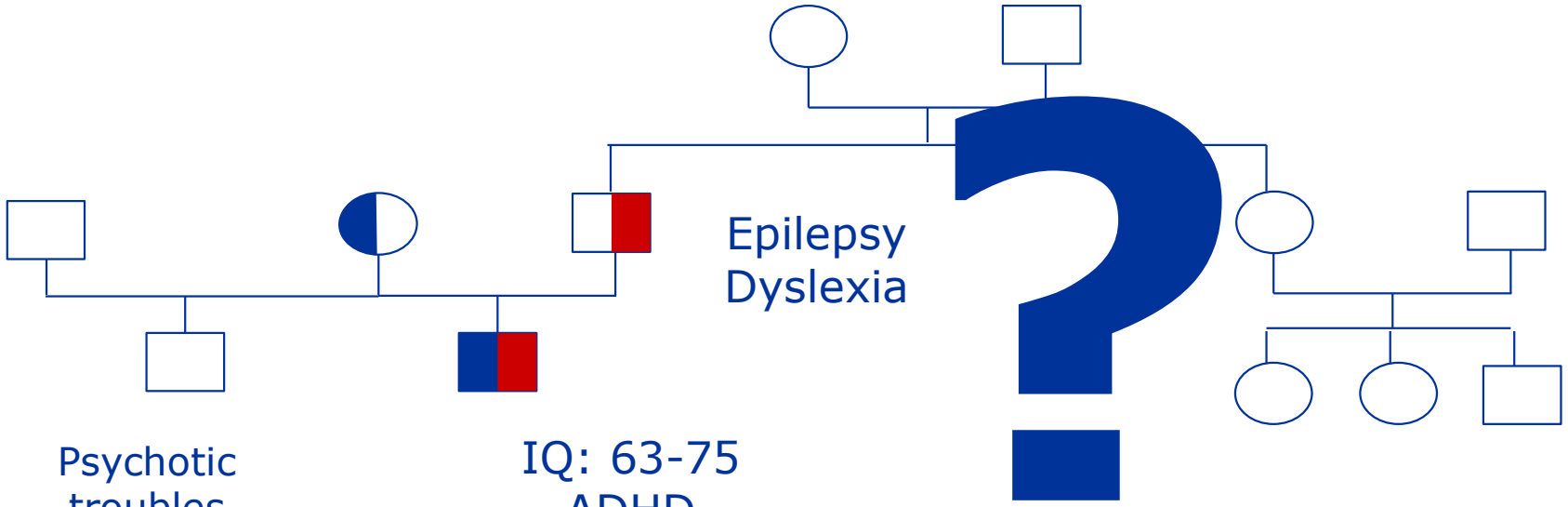

Mainly generalised epilepsy

Niestroj Brain 2020

IPG

# CGH: clinical case

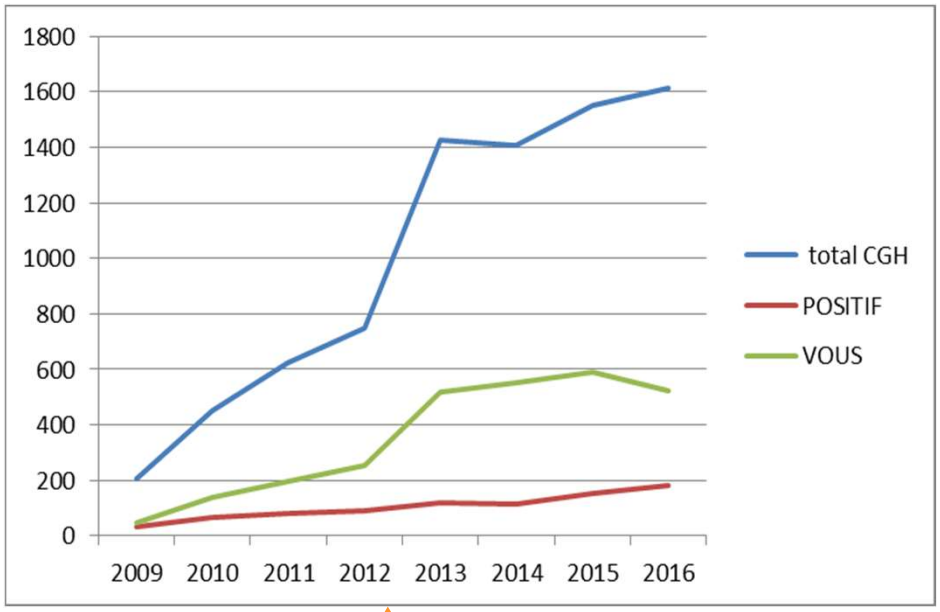
## Borderline IQ and ADHD




Del 22q11 distal
Del 1p31.1

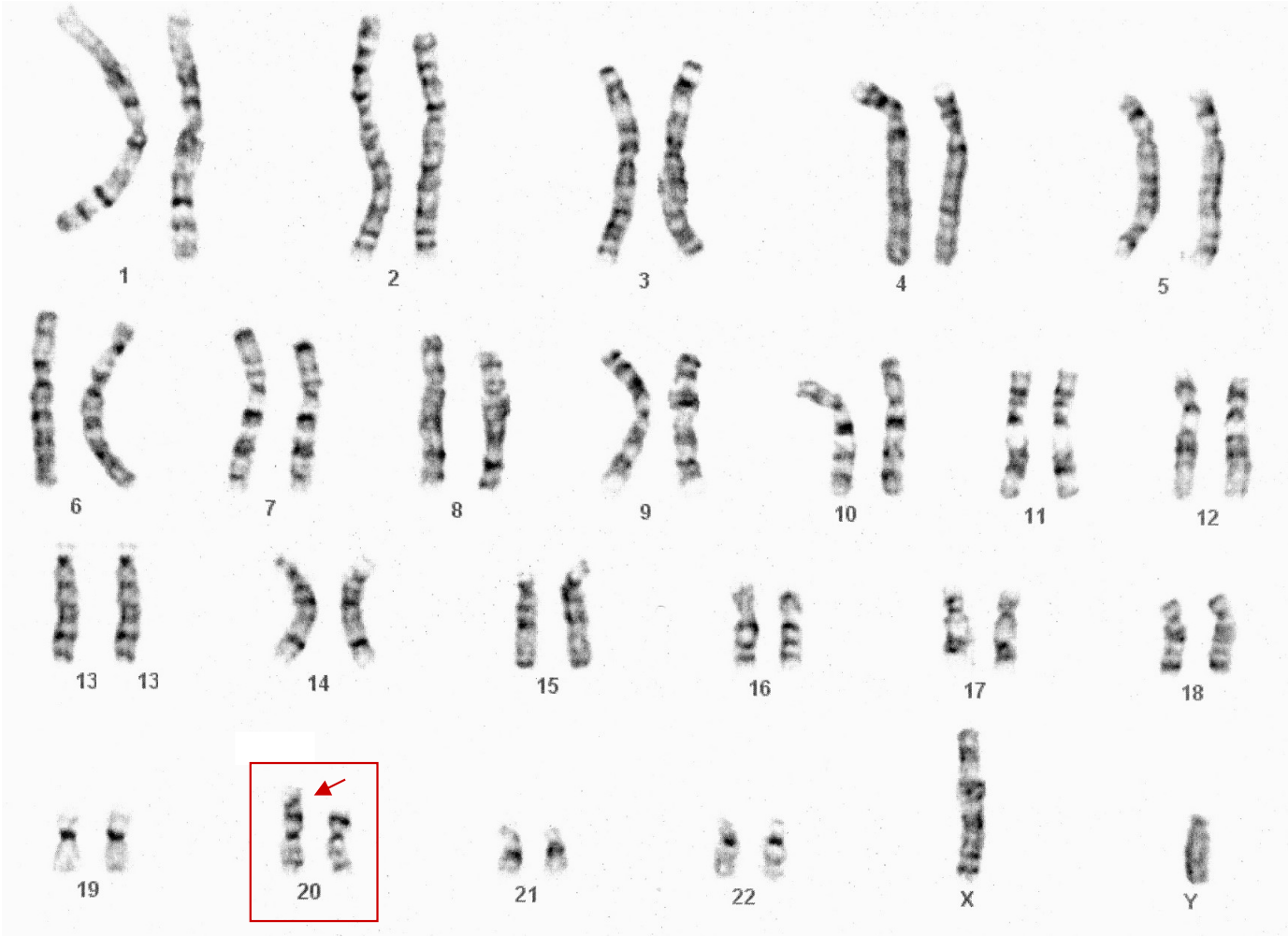
# CGH: IPG 2009-2016

- 8035 analyses
  - 834 positifs (10,4%)
  - 2824 variants ofunknown signification (VUS) (35%)




Stop routine caryotype

# Autosomes structural anomalies: particular examples (non recurrent)



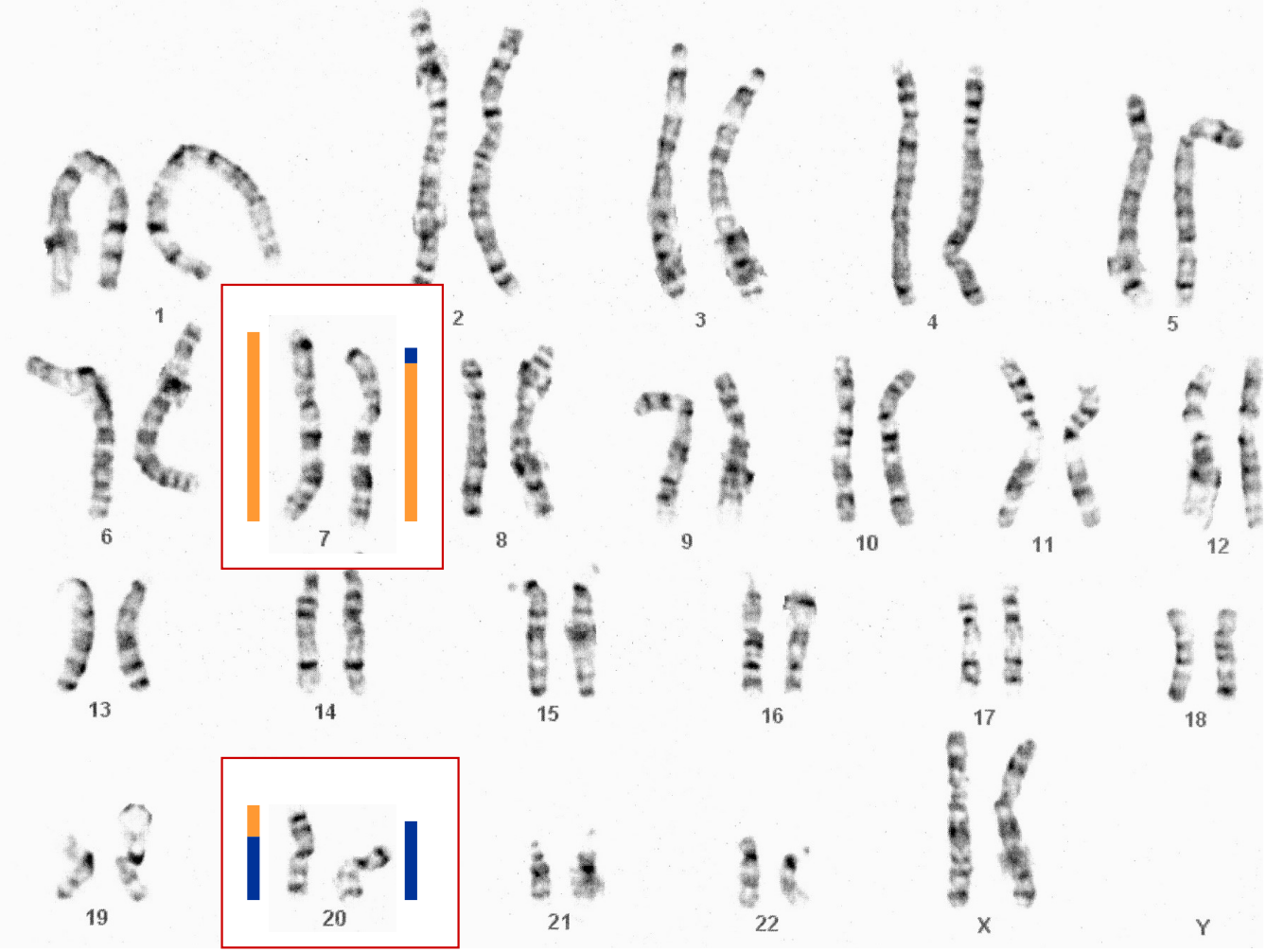

- Mental retardation
- Autistic features
- Facial dysmorphy

46,XY,der(20)

IPG

# Autosomes structural anomalies: particular examples

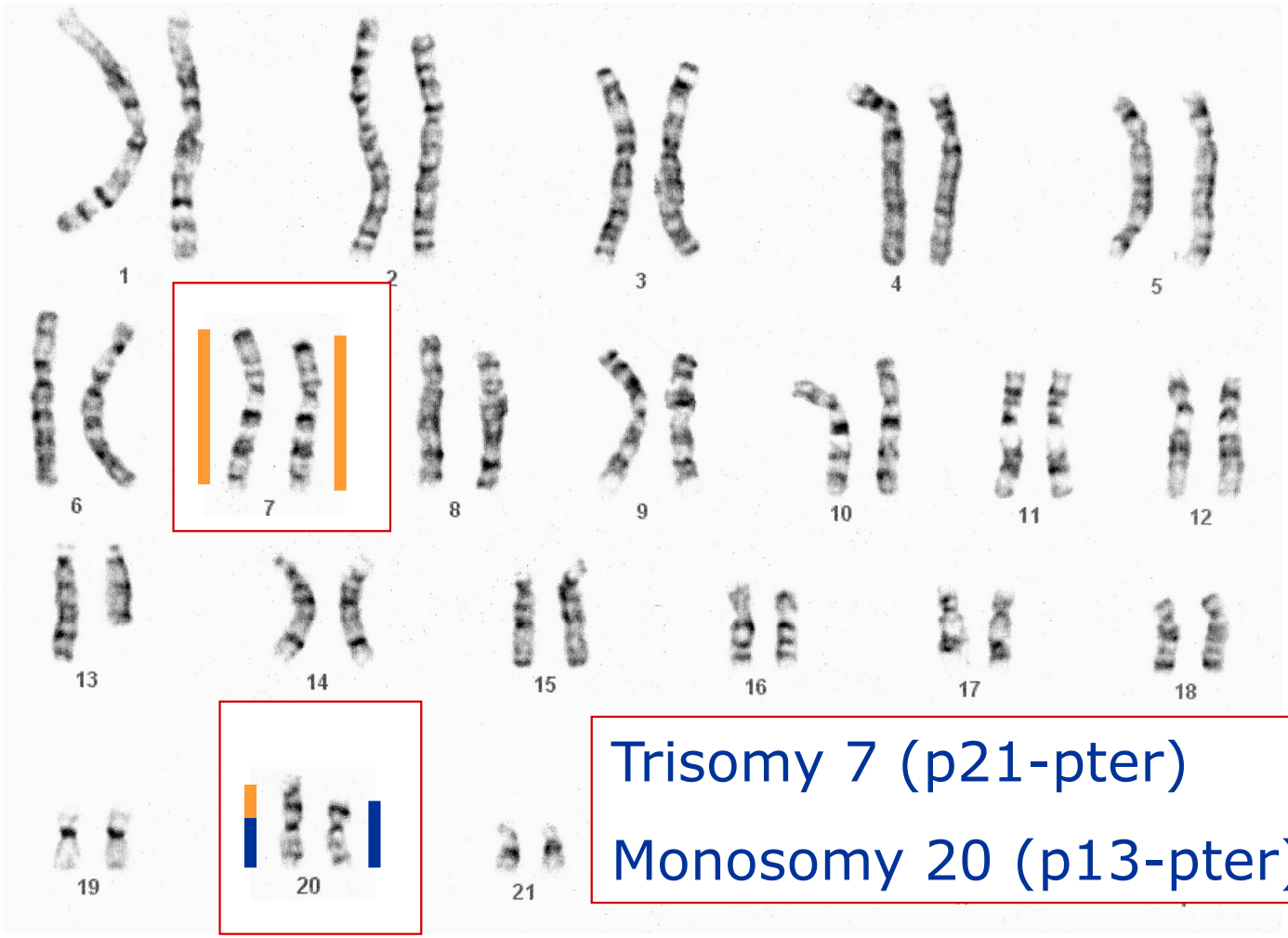
Mother's karyotype:




46,XX,t(7;20)(p21;p13)

# Autosomes structural anomalies: particular examples

⇒ patient's karyotype:



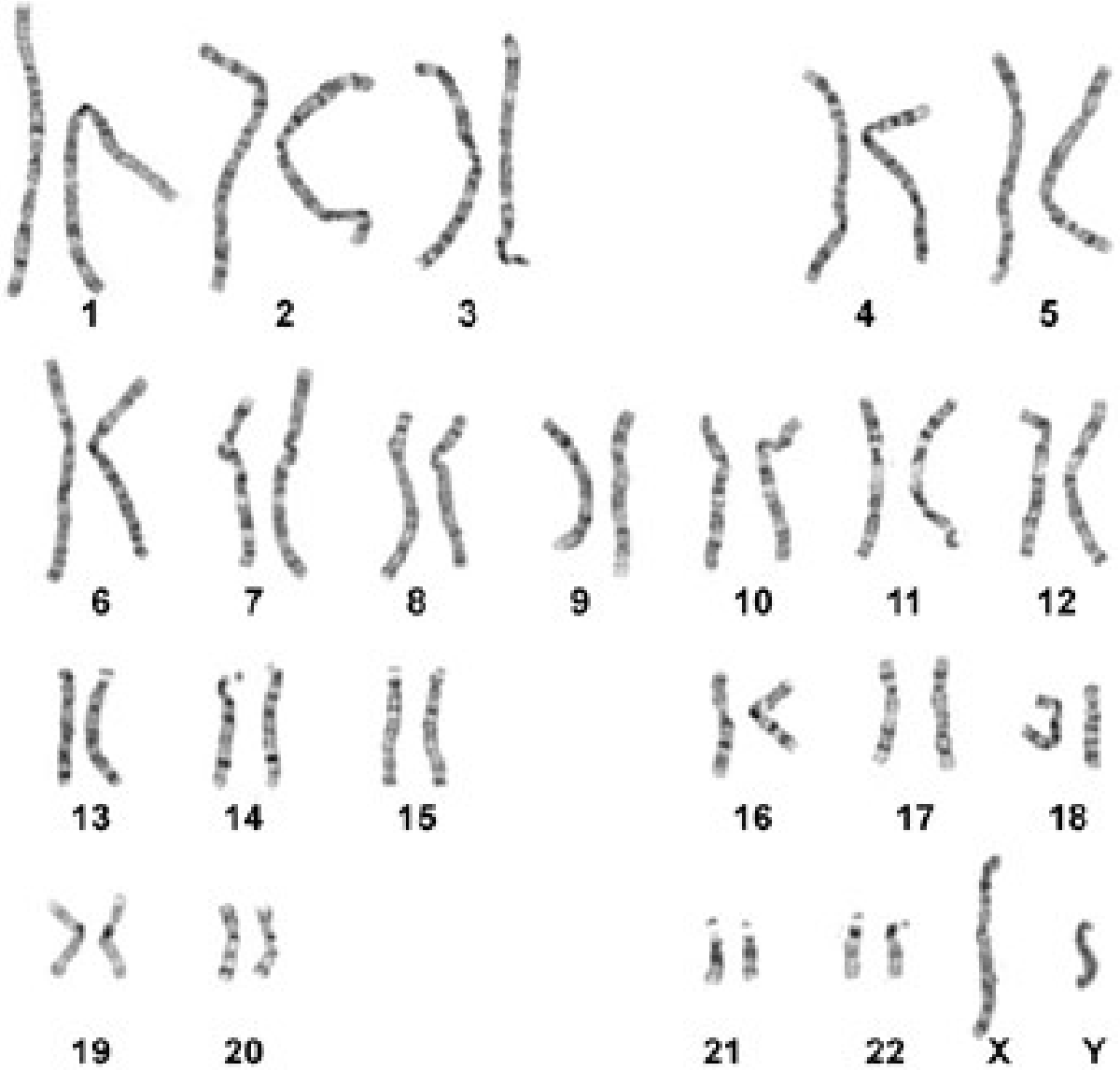

Trisomy 7 (p21-pter)

Monosomy 20 (p13-pter)

46,XY,der(20)t(7;20)(p21;p13)mat

IPG

# Autosomes structural anomalies: particular examples

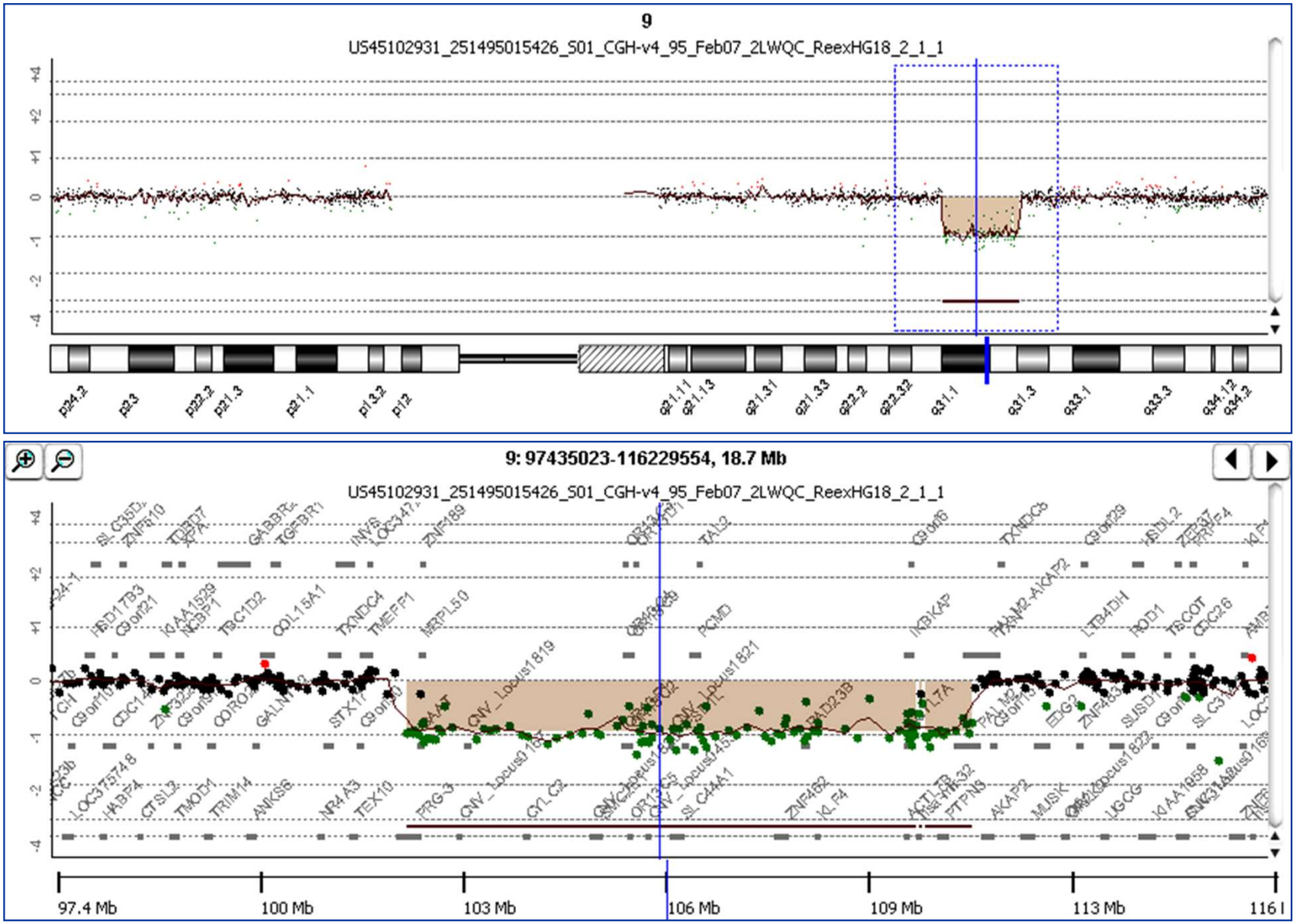



- Mental retardation
- Autistic features
- Facial dysmorphy

46,XY

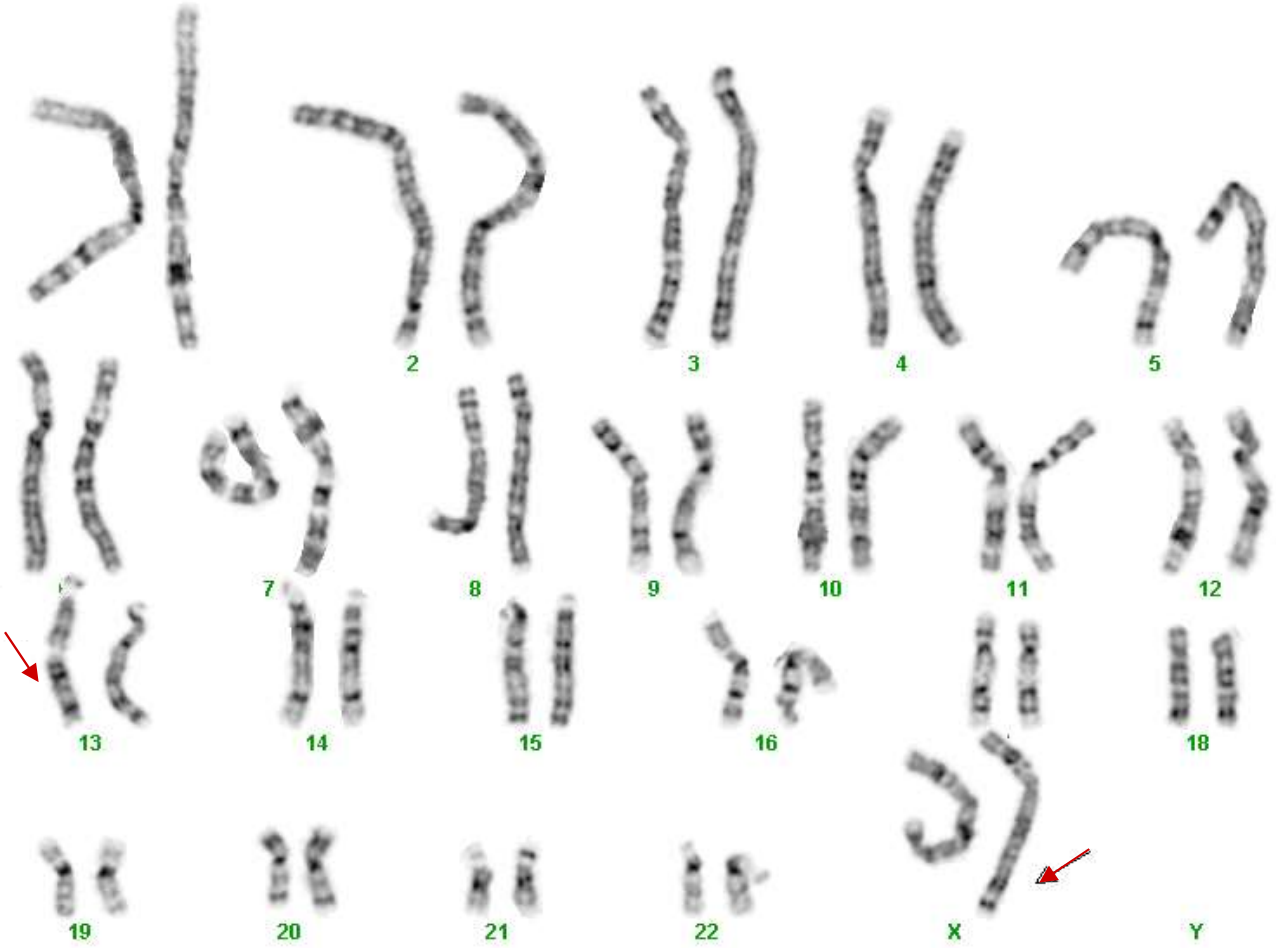
IPG

# Autosomes structural anomalies: particular examples




De novo 8.7 Mb deletion on 9q31.1-q31.3

# Autosomes structural anomalies: particular examples




- **Mental retardation**
- **Facial dysmorphy**
- **Supernumerary nipple**

46,X,t(X;13)(q24;q22),inv(9)(p12q13)

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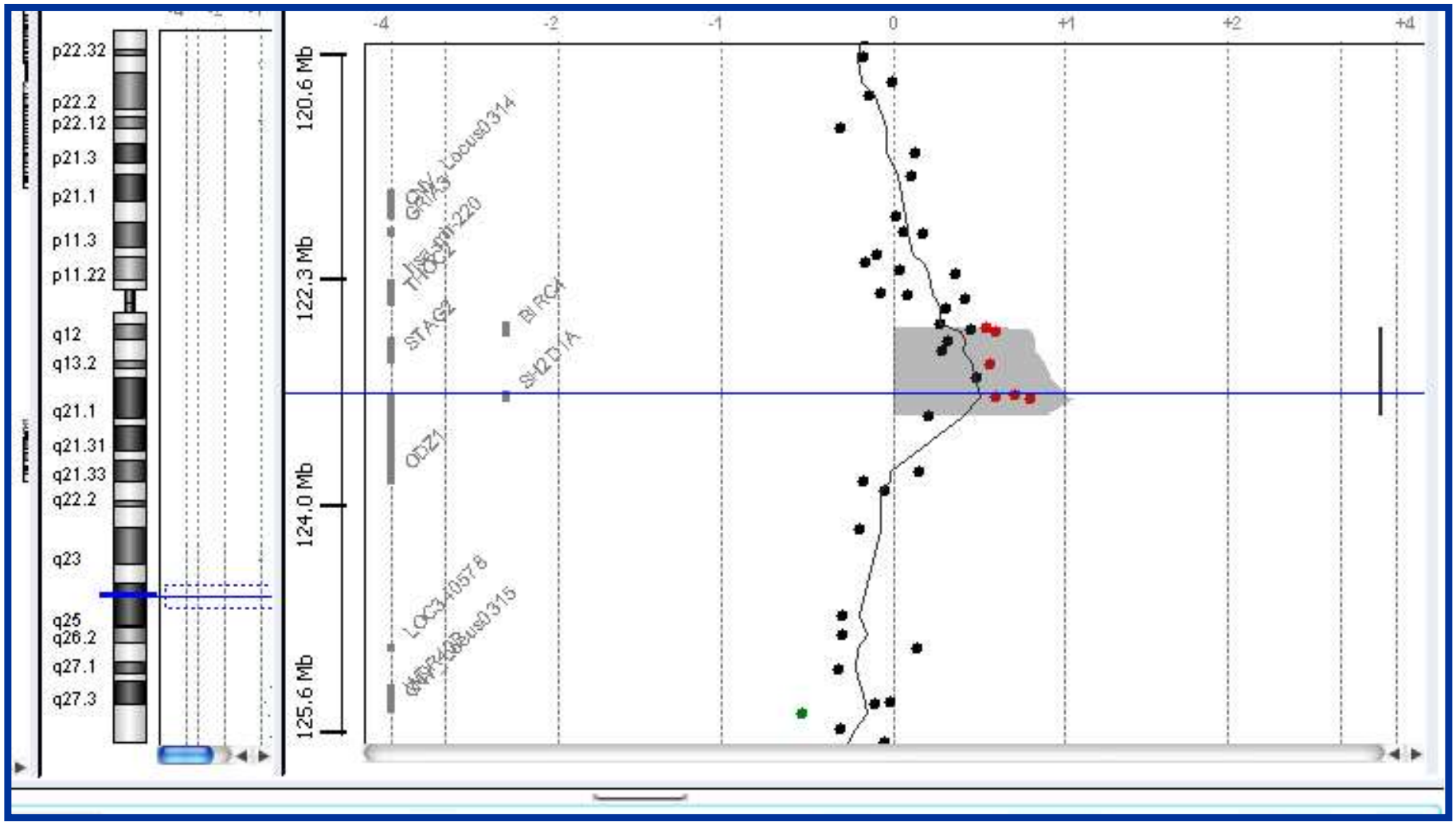
# Microarrays: Microduplication Xq25




Microrearrangement at the breakpoint on chromosome X

IPG

# CONCLUSIONS

- ***Numerical autosomes abnormalities:***
  - frequent spontaneous abortions
  - Trisomy 13, trisomy 18, trisomy 21
    - ↳ *low recurrence risk if no parental rearrangement*
  - pigmentary changes, corporal asymmetry
    - ↳ *skin biopsy (mosaicism)*
    - ↳ *low recurrence risk*
  - supernumerary marker chromosomes
    - ↳ *low recurrence risk*

IPG

# CONCLUSIONS

- ***Structural autosomes abnormalities:***

  - cytogenetically detectable (karyotype)

    ↳ *autosomal deletion syndromes*

  or genomic disorders (FISH, MLPA, arrays,…)

    ↳ *microdeletion and microduplication syndromes*

  - well-defined syndromes

    ↳ *sporadic or inherited (! variable expressivity)*

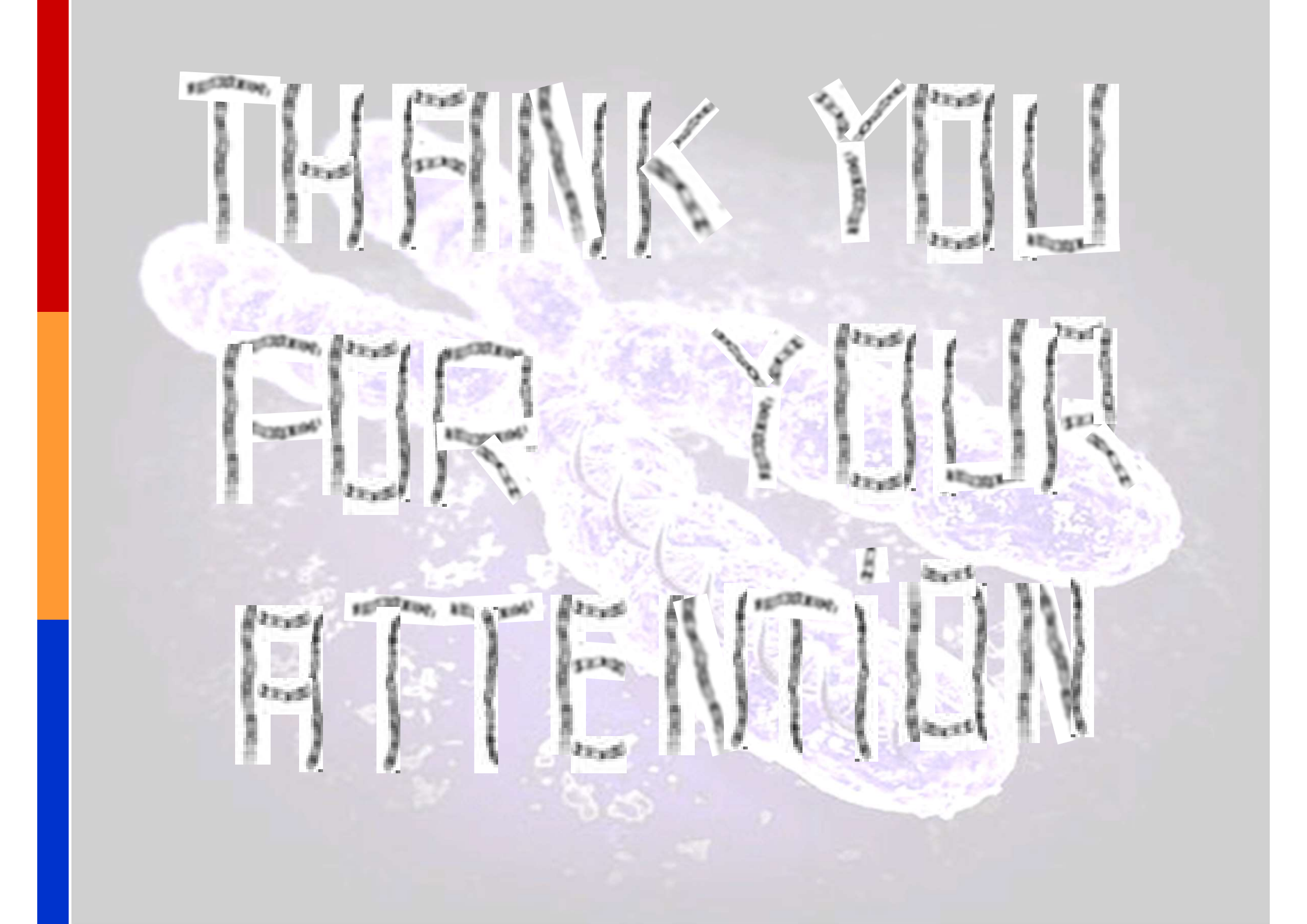
  or particular cases

    ↳ *low recurrence risk if no parental rearrangement*

  - apparently balanced translocations

    ↳ *microarrays if abnormal phenotype*

IPG


THANK YOU
FOR YOUR
ATTENTION