

# **Recurrence of free trisomy 21: parental mosaicism in a couple with four trisomy 21 conceptions**

**Dra. Carmen Mediano. Hospital Vall  
d'Hebron. BARCELONA (Spain)**

# Free trisomy 21

- **95% Down syndrome cases**
- **ERR: 1-2%, increasing with maternal age**
- **Recurrent cases are rare**

# Recurrence of free trisomy 21

## THREE GROUPS:

1. Young mothers (< 28 y. First Down)  
Probably parental mosaicism.
2. Non-disjunction meiotic predisposition:  
genetic factor. That would produce  
other aneuploidies
3. Aged mothers (>33 y.) CHANCE

# **FAMILY A.F.**

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP
  3. Pregnancy (28 y.) Amnio: 46,XX. Healthy girl

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP
  3. Pregnancy (28 y.) Amnio: 46,XX. Healthy girl
  4. Pregnancy (31 y.) Spt. Miscarriage. Down (XY+21)

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP
  3. Pregnancy (28 y.) Amnio: 46,XX. Healthy girl
  4. Pregnancy (31 y.) Spt. Miscarriage. Down (XY+21)
  5. Pregnancy (33 y.) CVS: Down (XY+21) TOP

# FAMILY A.F.

- **Non-consanguineous healthy couple.  
Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP
  3. Pregnancy (28 y.) Amnio: 46,XX. Healthy girl
  4. Pregnancy (31 y.) Spt. Miscarriage. Down (XY+21)
  5. Pregnancy (33 y.) CVS: Down (XY+21) TOP
  6. **PARENTAL STUDIES: NORMAL (2006)**

# FAMILY A.F.

- **Non-consanguineous healthy couple. Unremarkable family history**
- **TEPAL: 16051**
  1. Pregnancy (26 y.) Spontaneous miscarriage
  2. Pregnancy (27 y.) Alt.Screening. Down(XY+21) TOP
  3. Pregnancy (28 y.) Amnio: 46,XX. Healthy girl
  4. Pregnancy (31 y.) Spt. Miscarriage. Down (XY+21)
  5. Pregnancy (33 y.) CVS: Down (XY+21) TOP
  - 6. PARENTAL STUDIES: NORMAL (2006)**
  7. Pregnancy (35 y.) CVS: Down (XX+21) TOP

# Cytogenetic parental studies (2006)

- **MOTHER:**

Blood karyotype: 46,XX (336)/47,XX+21(2).

FISH: 2 signals (162)/3 signals(2).

FISH buccal smear: 2 signals (483)/3 signals(3)/  
1signal (16).

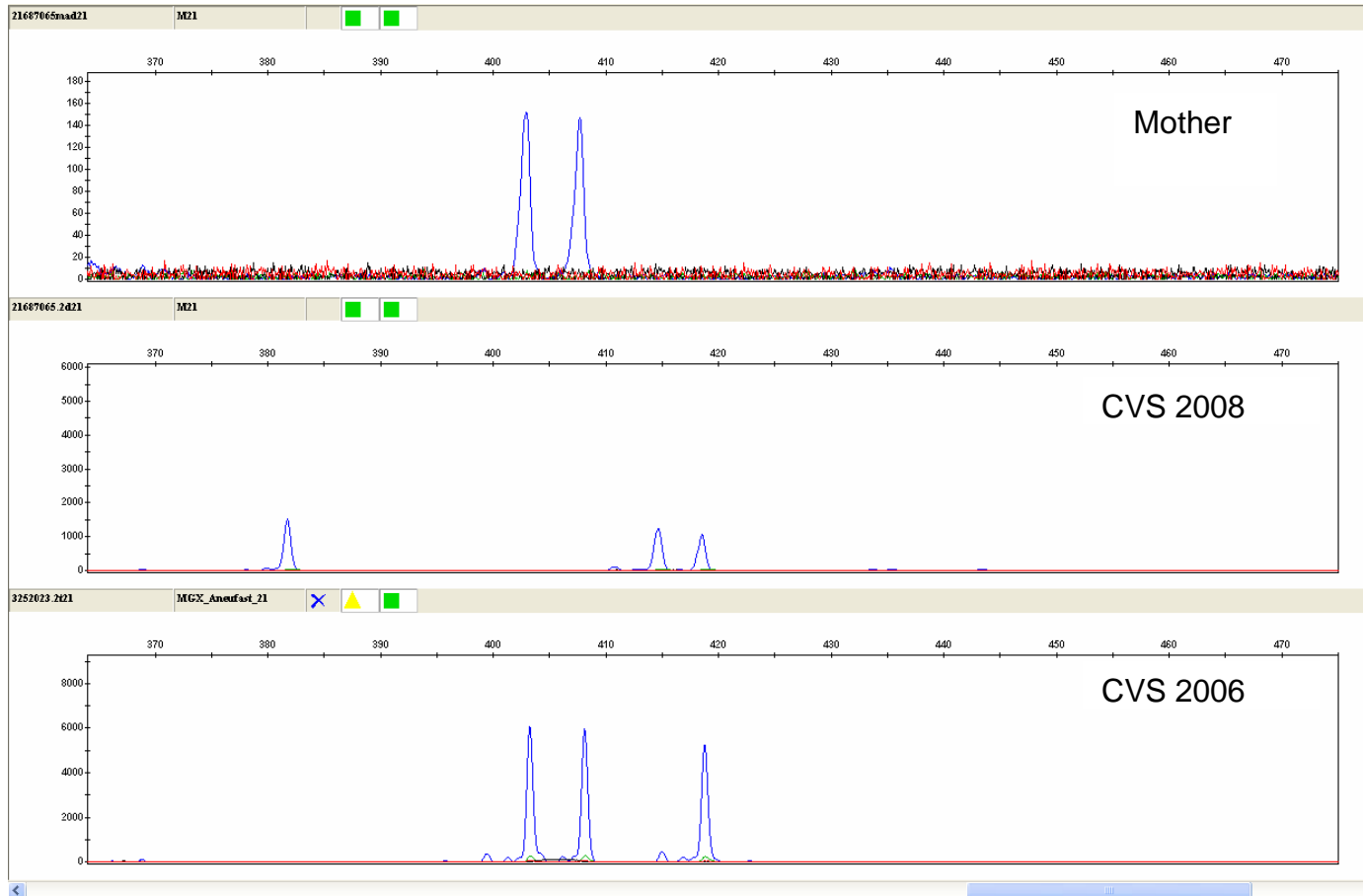
- **FATHER:**

Blood karyotype: 46,XY(50)

FISH: 2 signals (57)/3 signals (1)

FISH buccal smear: 2 signals (226/ 1 signal (3)

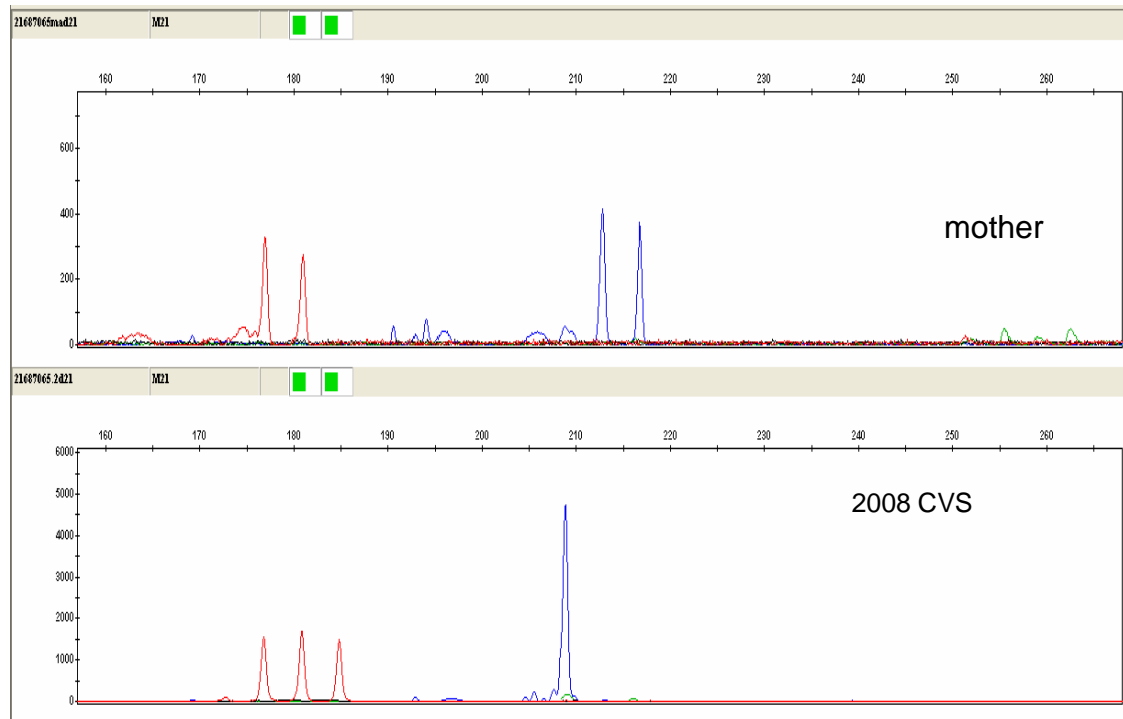
# QF-PCR detection of recurrent T21 in CVS



D21S1442

Both Maternal alleles are absent in the trisomic (2008) fetus. CVS 2006 T21 apparently of maternal origin

# QF-PCR detection of recurrent T21 in CVS



D21S1437 (red) compatible with maternal origin.

D21S12008 (blue): The trisomic fetus is homozygous so as for D21S1412, also at this locus there are three fetal alleles which are absent in the mother.

# Recurrence of free trisomy 21: Parental Mosaicism

- Search for mosaicism in blood and other tissues: cytogenetics, FISH
- Low level mosaicism (1-2%) is enough.
- DNA markers:
  1. maternal/paternal alleles +1
  2. Three alleles: 1 paternal+1 maternal +  
1 NOVEL: would indicate that parent  
being originally trisomic embryo with  
rescued and then mosaic.

# FREE TRISOMY 21: VALL D' HEBRON DATA

- N= 194
- GROUPS:
  - I) Advanced maternal age(>37y.)= 107(55%)
  - II) Maternal age:30-36 years = 68 (35%)
  - III) Young mothers (<30y.)= 19(10%)
- **Couples with spontaneous miscarriages and or recurrence free trisomy 21 =4**



**C. Mediano**

**T. Vendrell**

**A. Plaja**

**M. Jallas**

**L. Espi**

**B. F. Diaz**

**E. Arantegui**

**A. Fernandez**

**L. Fernandez**

**L. Perez-Jurado**

**M. A. Sanchez-Duran**

**J. Sagalà**

**V. Cirigliano**

**E. Ordoñez**