

Public Meeting on the Guidance Document for IVDMIAs

February 8, 2007

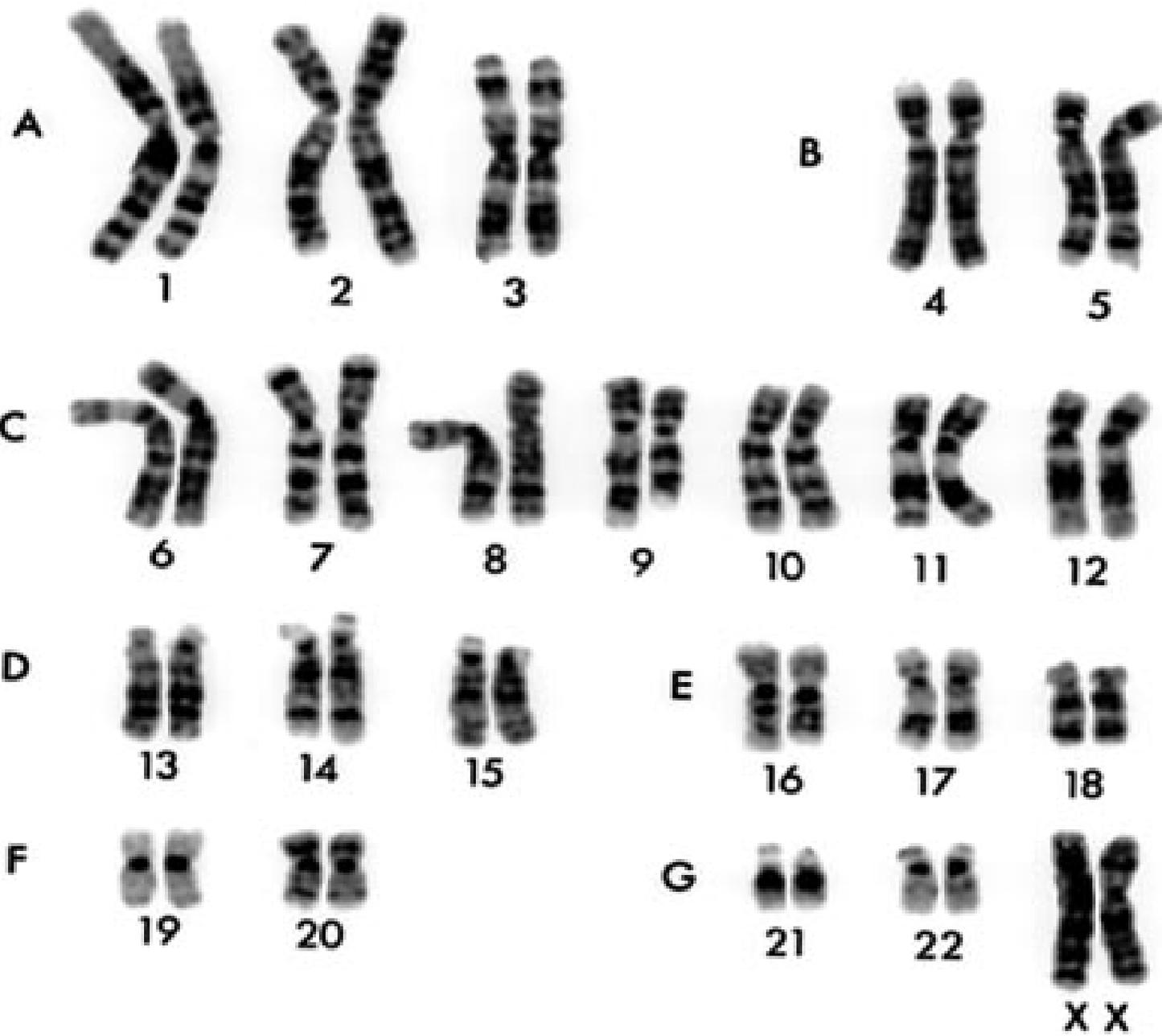
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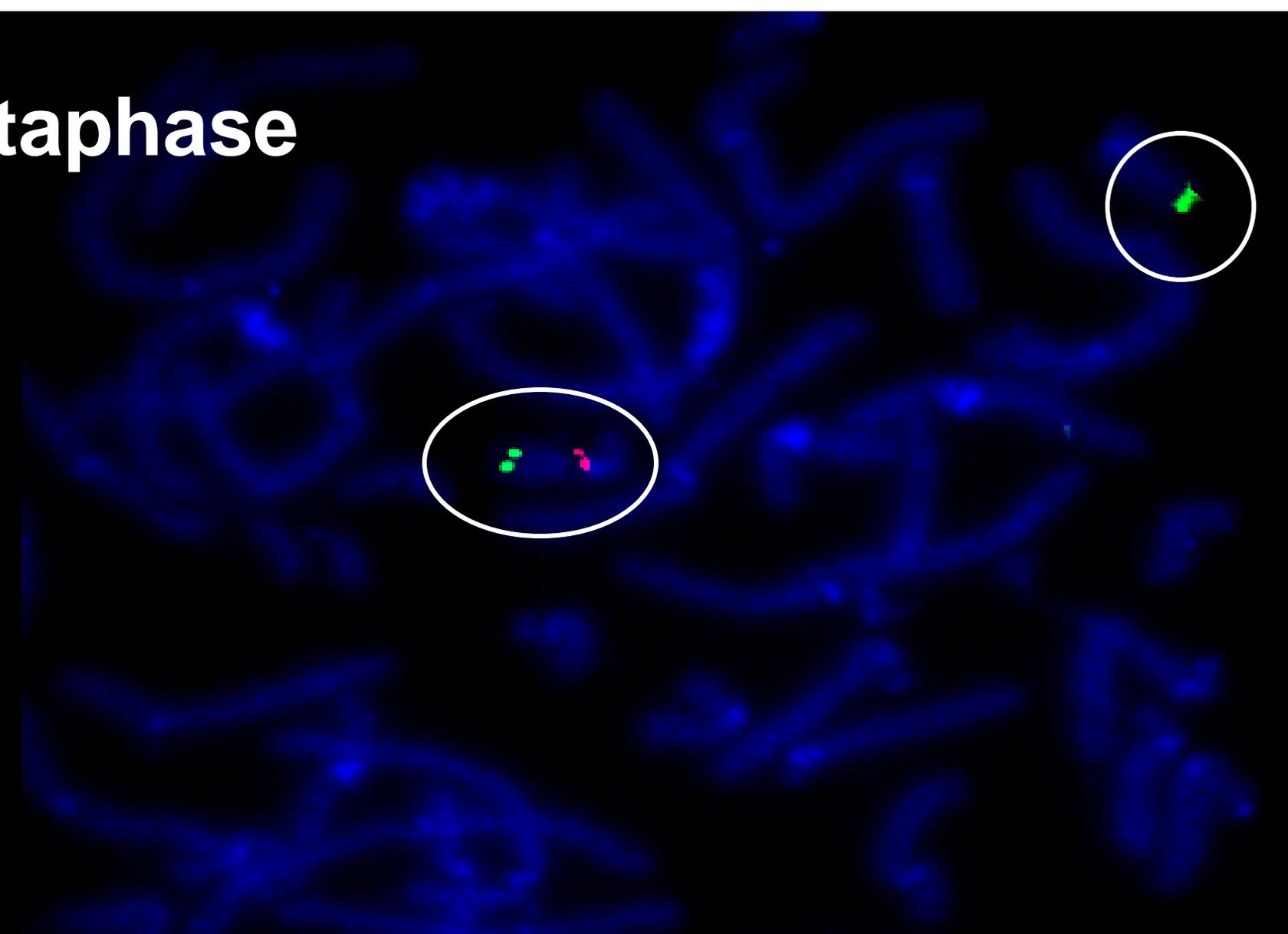
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**Points to Consider
on
Proposed Guidance
for
IVDMIAs**

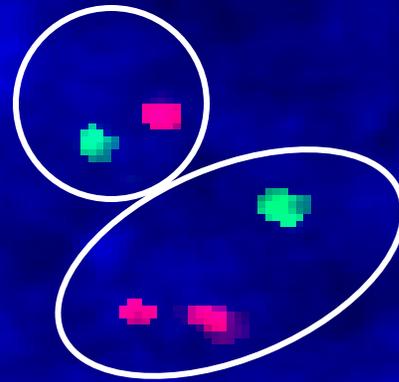


Metaphase



Fluorescence in situ hybridization (FISH)

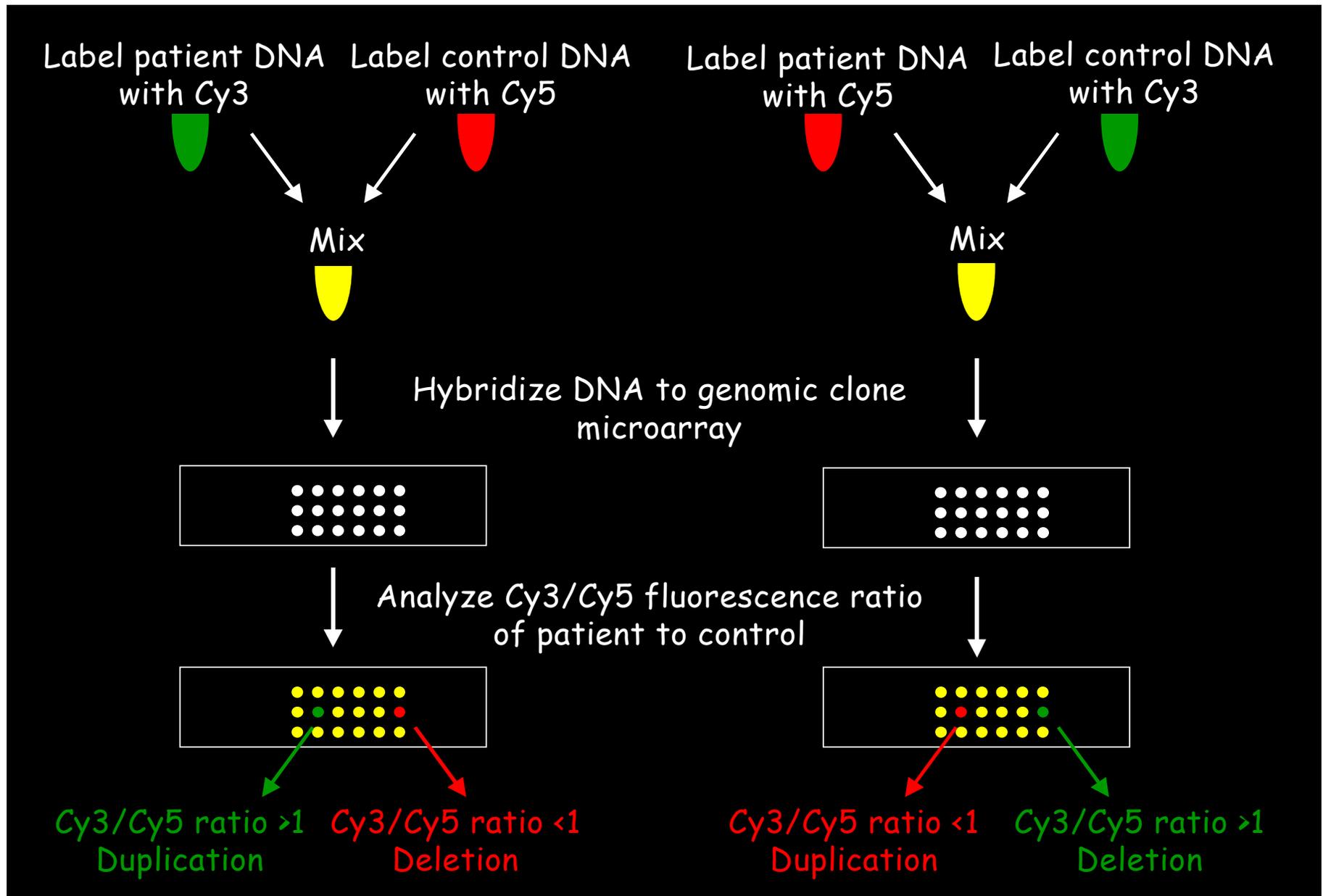
Interphase FISH duplication



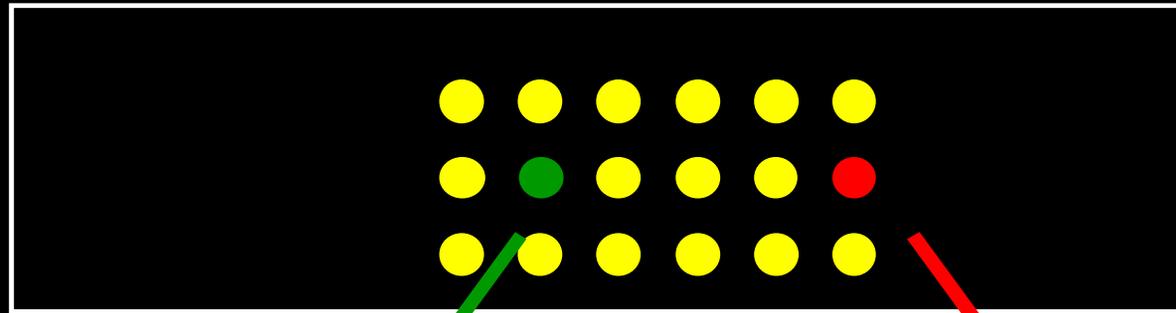
**Array Comparative Genomic
Hybridization (Array CGH)**

**Chromosomal Microarray
Analysis (CMA)**

CMA Methodology



CMA Methodology



Cy3/Cy5 ratio >1
Duplication

Cy3/Cy5 ratio <1
Deletion

Normal female vs normal male

Raw

Normalized

Combined

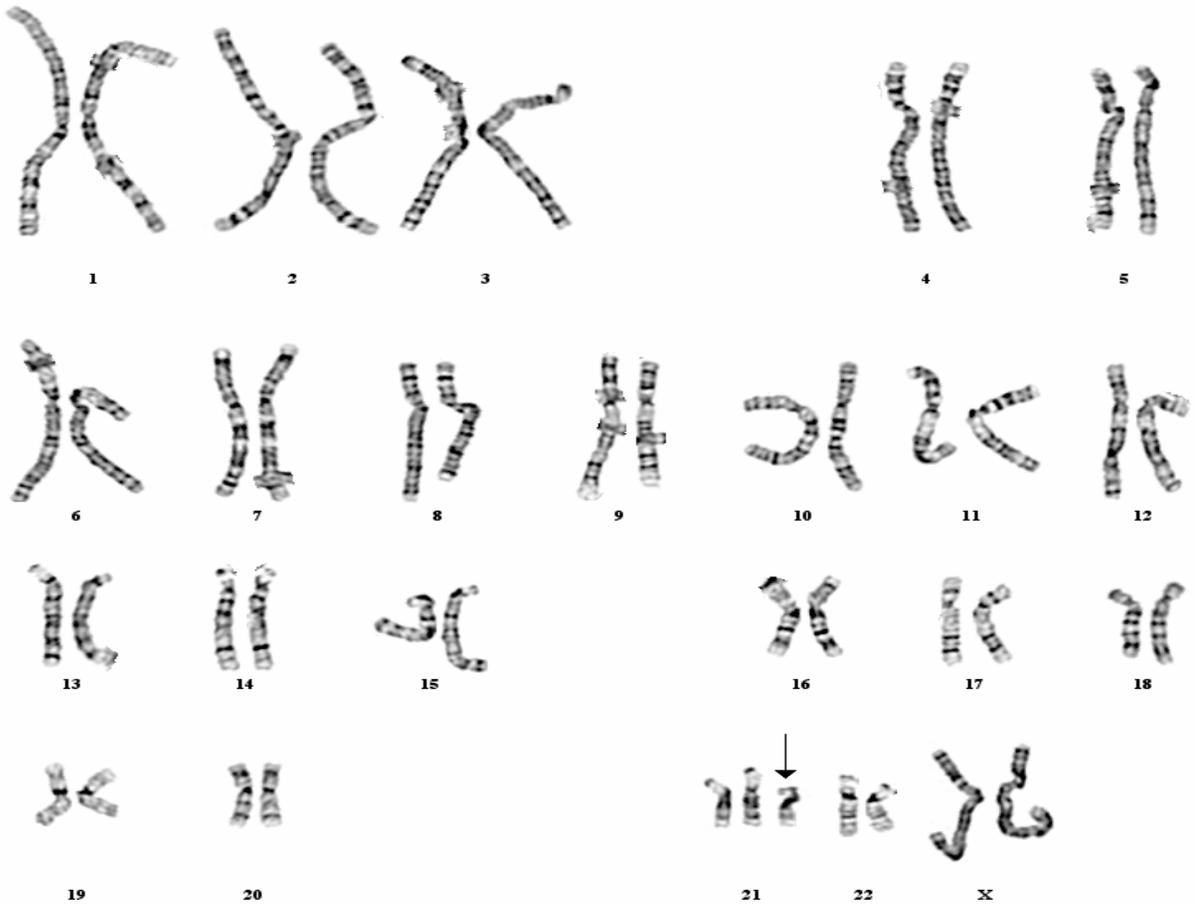
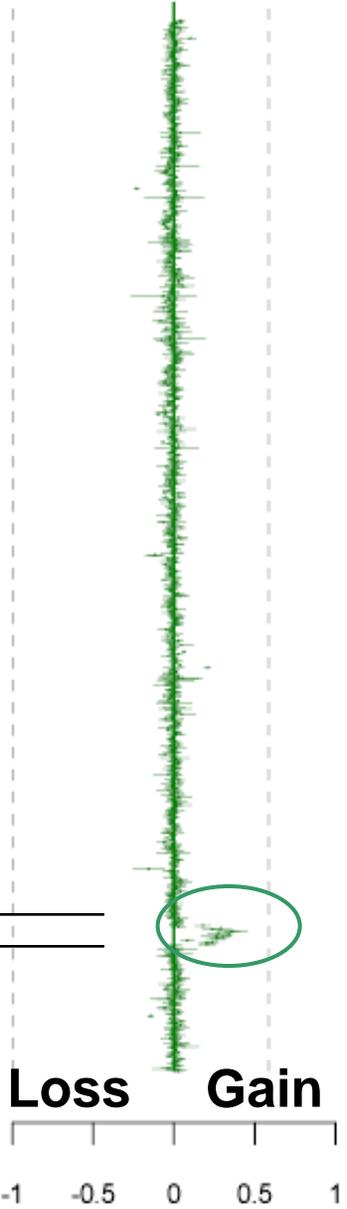
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- X
- Y



Loss Gain

Trisomy 21 (Down syndrome)

Combined

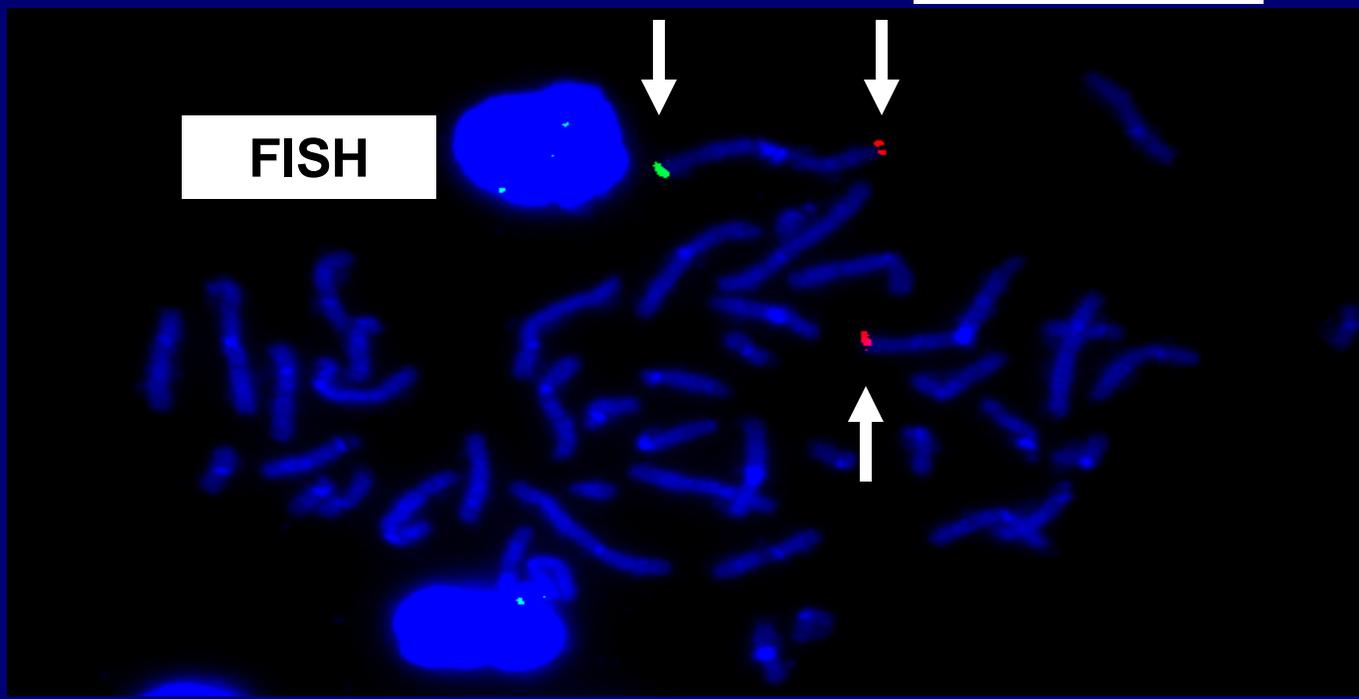
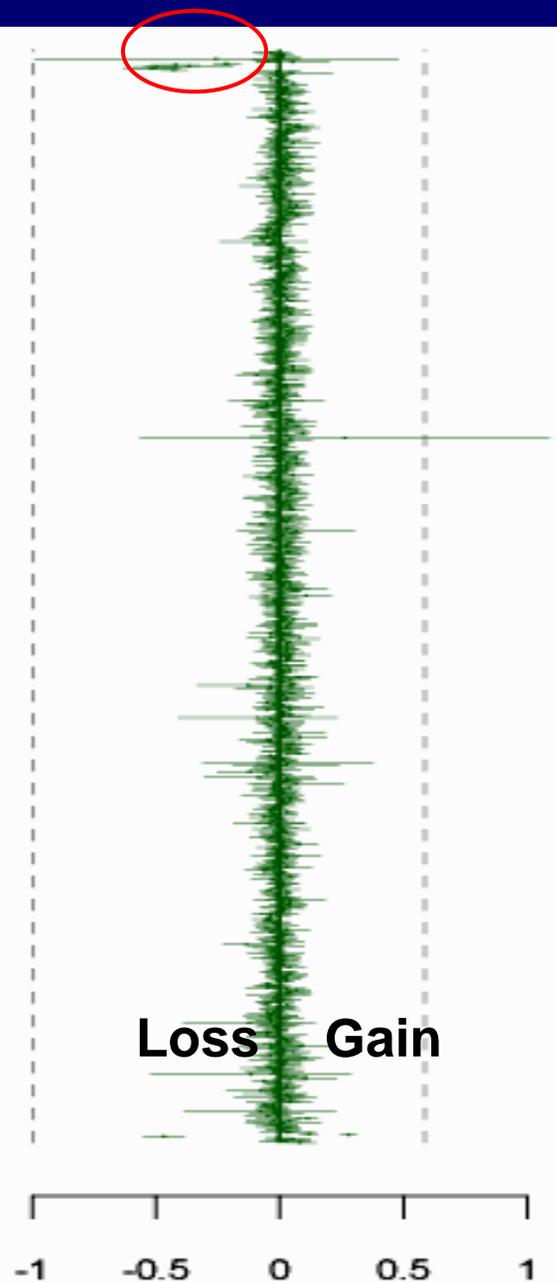


Karyotype

Case 2: Previous result : 46,XX (at birth)

- **At two months of age**
- **Facial dysmorphism**
- **Bilateral cleft lip and palate**
- **Growth parameters <5th percentile**
- **Congenital heart disease**
 - **AV canal type VSD and a small ASD**

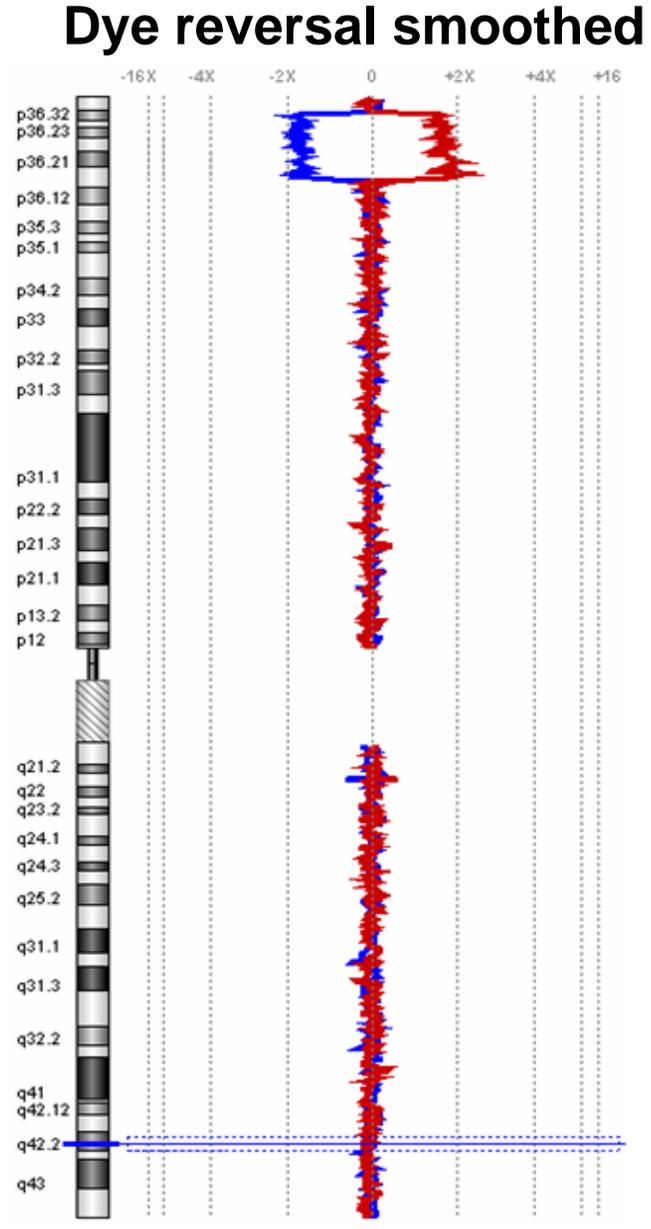
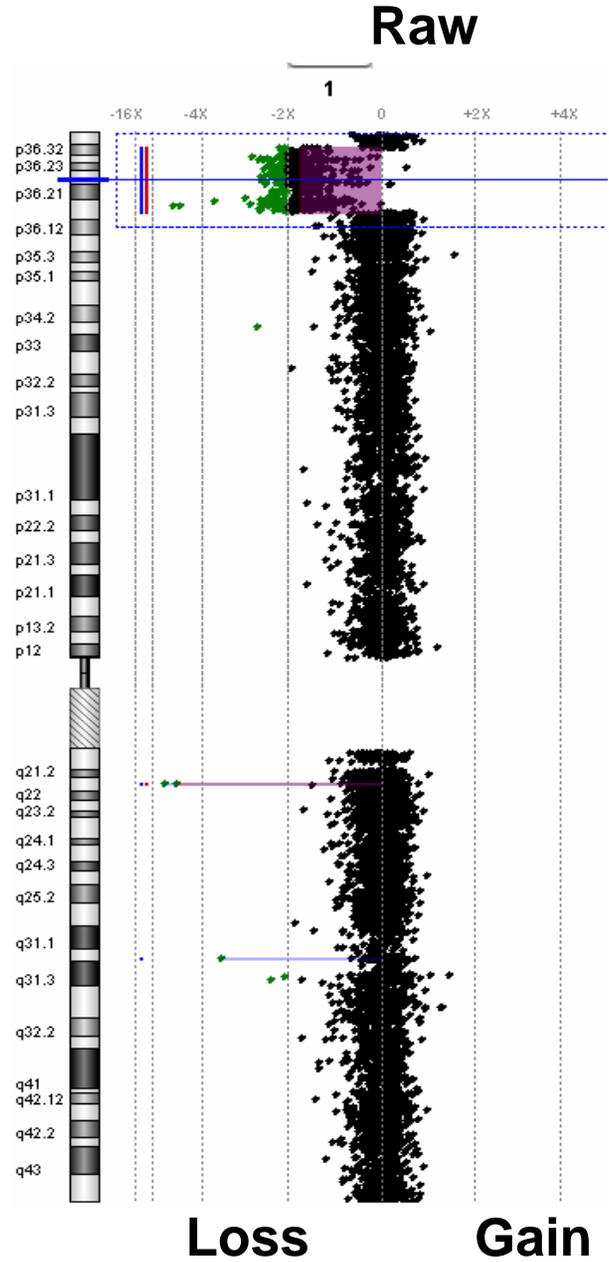
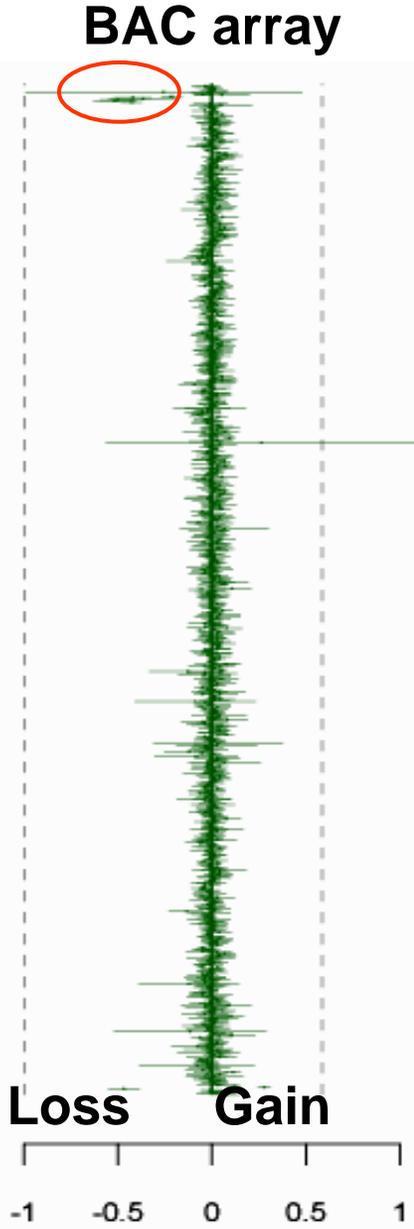
Deletion chromosome 1p (short arm)



PLATFORM EQUIVALENCY

- Many different platforms can provide equivalent data regarding gain or loss of copy number (BAC, oligonucleotide, or bead arrays).
- Results can be specified for genomic segments tested using nucleotide designations for human genome.

Oligonucleotide array



Array CGH Advantages

- **Detects many abnormalities missed by karyotype.**
 - Many absolutely undetectable
 - High variability in karyotype quality.
- **Equivalent to hundreds or thousands of FISH tests at low cost.**
- **Particularly good for duplications.**

Suggested array CGH Guidance

- Analogy to imaging devices (e.g., MRI of brain or mammography); all platforms equivalent.
- Four components
 - Raw image data.
 - Algorithm to process data.
 - Interpretation by board certified laboratorian for result; regions with gain or loss and associated possible phenotypes (like radiologist).
 - Clinician integrates result in clinical context.

Array CGH as a general test of genome copy number

- We believe that array CGH is the biggest advance in genetic diagnosis in decades.**
- We believe that array CGH should replace karyotype as the primary cytogenetic test.**
- Delay is depriving families of valuable diagnostic and counseling information.**
- Array CGH can be less costly than karyotype.**
- Array CGH is applicable to prenatal diagnosis.**

END

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