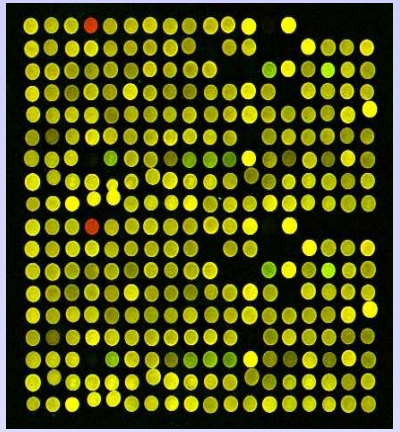
Sessió Acadèmia

15 gener 2013



Aplicabilitat clínica de les noves tecnologies genètiques

Antoni Borrell

Secció Ecografia

Societat Catalana d'Obstetrícia i Ginecologia

Aplicabilitat clínica de les noves tecnologies genètiques

1. ARRAY-CGH: Què és i com s'aplica
   Antoni Borrell (Hospital Clinic) i Miguel del Campo (Hospital Vall d'Hebron)

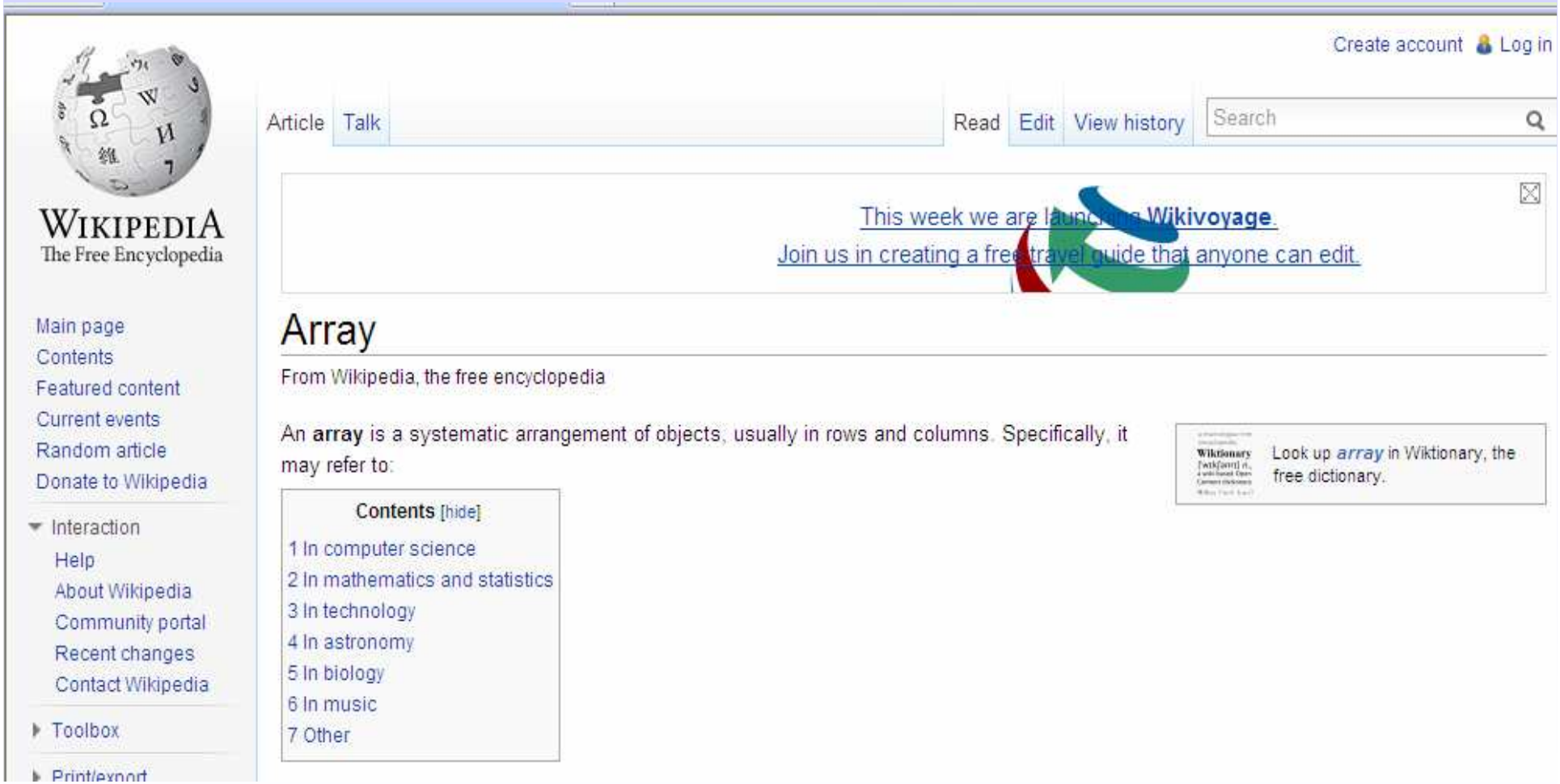
2. TEST PRENATAL NO INVASIU: en alt o baix risc?
   Vincenzo Cirigliano (LABCO-General Lab)

3. SEQÜENCIACIÓ DE L'EXOMA: el següent pas? *Lluís Armengol (Qgenomics)*

Discutidors

- Mina Comas. *Institut Universitari Dexeus, Barcelona*
- Ignacio Blanco. *Hospital Universitari Germans Trias i Pujol*
- Gerard Albaiges. *Hospital Universitari Joan XXIII, Tarragona*
- Emma Triviño. *CatLab, Terrassa*.
- Laia Alcoverro. *Metgessa resident de l'Hospital de la Santa Creu i Sant Pau*

Array



Create account Log in

WIKIPEDIA
The Free Encyclopedia

Article Talk Read Edit View history Search

This week we are launching **Wikivoyage**.
Join us in creating a free travel guide that anyone can edit.

Main page
Contents
Featured content
Current events
Random article
Donate to Wikipedia

Interaction
Help
About Wikipedia
Community portal
Recent changes
Contact Wikipedia

Toolbox

Print/export

Array

From Wikipedia, the free encyclopedia

An **array** is a systematic arrangement of objects, usually in rows and columns. Specifically, it may refer to:

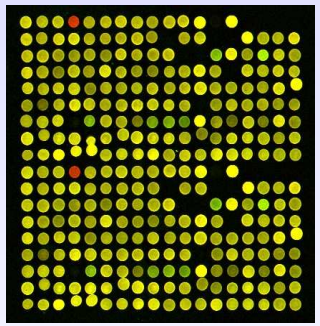
Look up *array* in Wiktionary, the free dictionary.

Contents [hide]

1 In computer science
2 In mathematics and statistics
3 In technology
4 In astronomy
5 In biology
6 In music
7 Other

Array-CGH

- QUÈ ÉS? un suport sòlid (microarray/microxip), sobre el qual es disposen, de manera ordenada, un gran nombre de fragments de DNA que s'utilitzen com a sondes per interrogar el genoma.



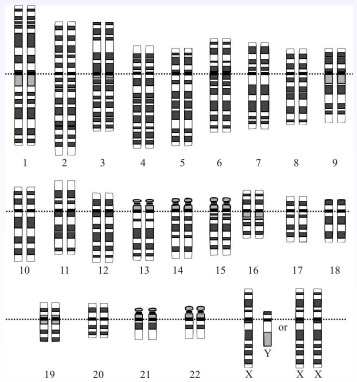
- COM FUNCIONA? Interroga l'existència de guanys i pèrdues de DNA en milers de loci al llarg del genoma complet, en un únic experiment, en poc temps i amb una alta resolució.

Resolució tècniques de citogenètica

CITOGENÈTICA CONVENCIONAL

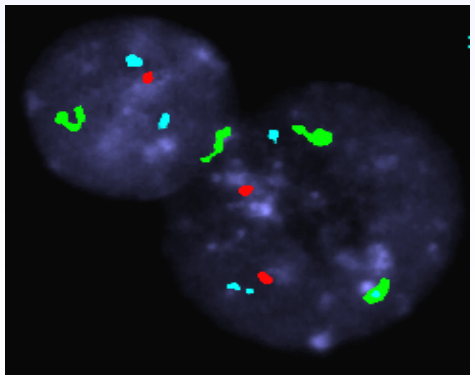
CITOGENÈTICA MOLECULAR

~5-10 Mb

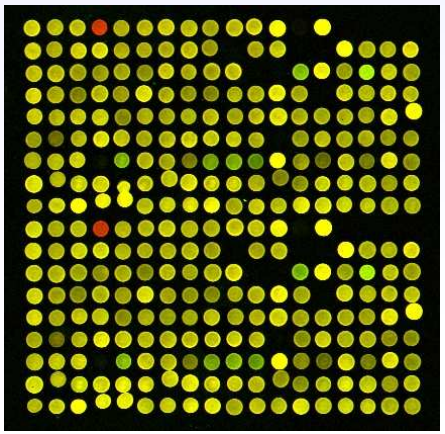


3.000 Mb

FISH
~200 Kb
(sonda-específica)

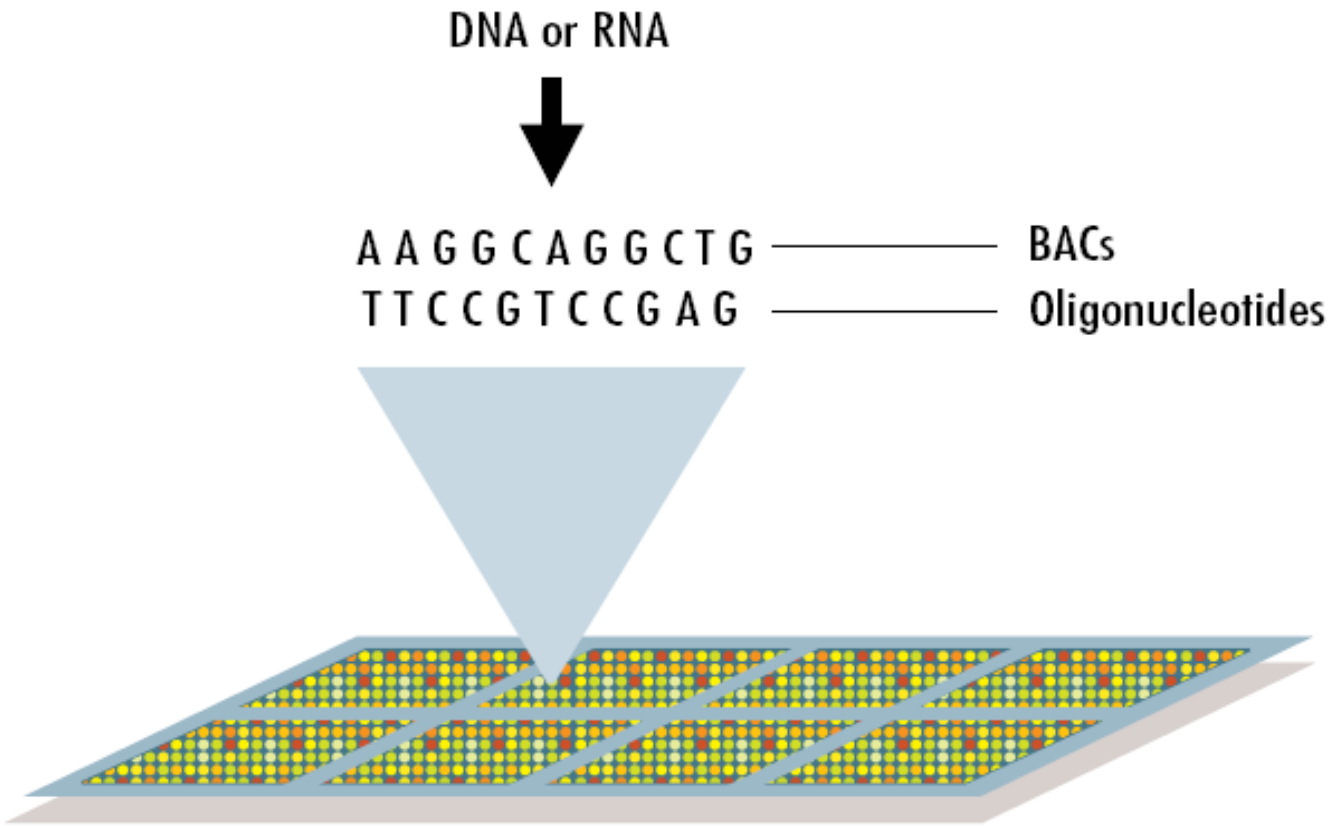


arrayCGH
10Kb-1Mb



CGH-array

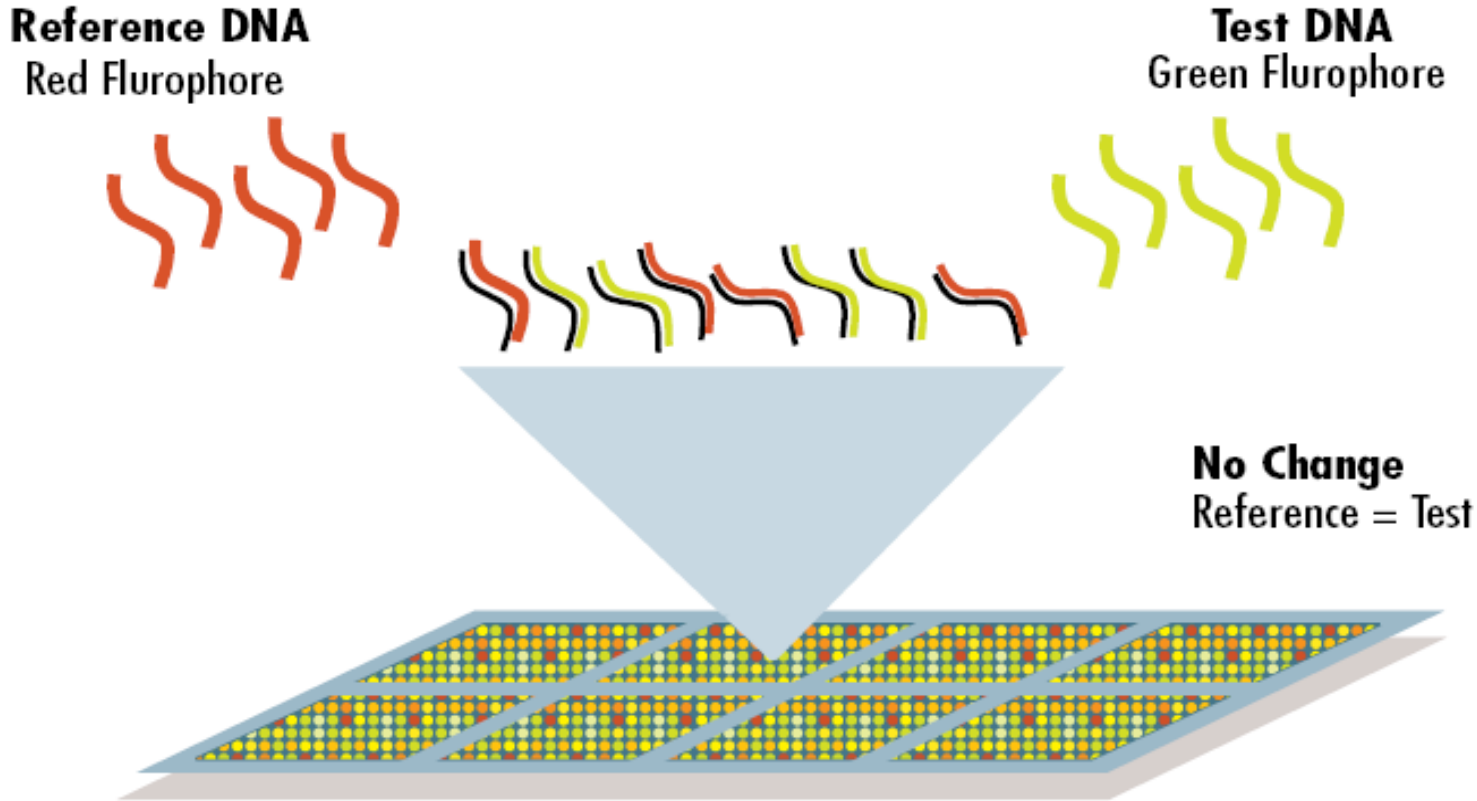
Genomic Microarrays-1



Revised from Vysis/Abott

CGH-array

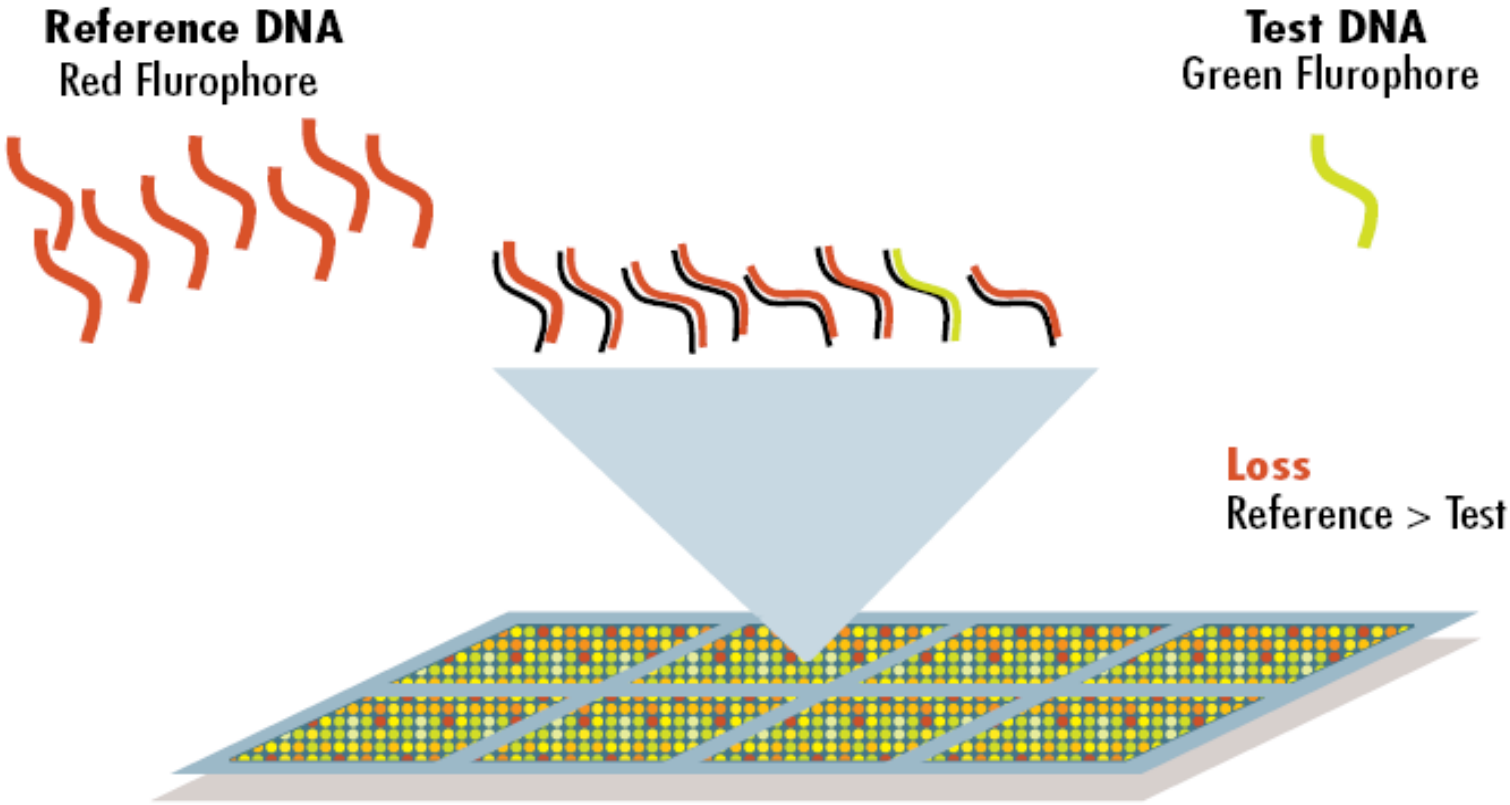
Genomic Microarrays-2



Revised from Vysis/Abott

CGH-array

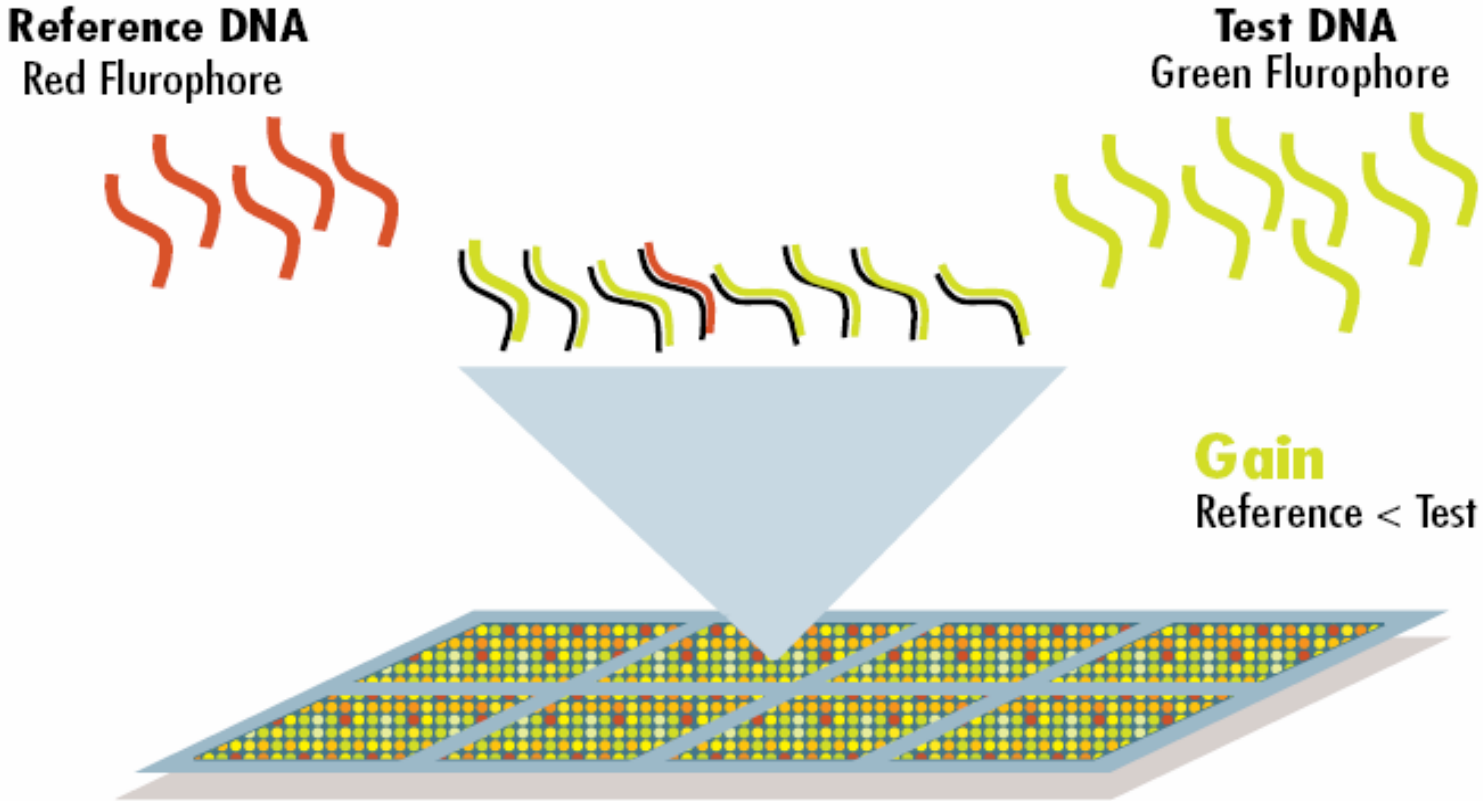
Genomic Microarrays-3



Revised from Vysis/Abott

CGH-array

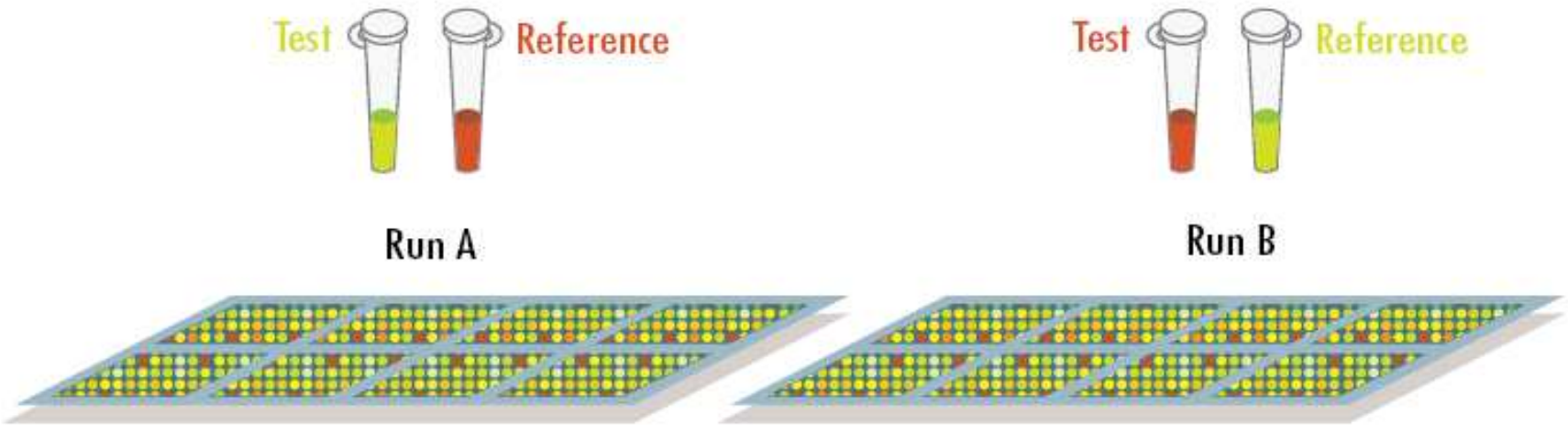
Genomic Microarrays-4



Revised from Vysis/Abott

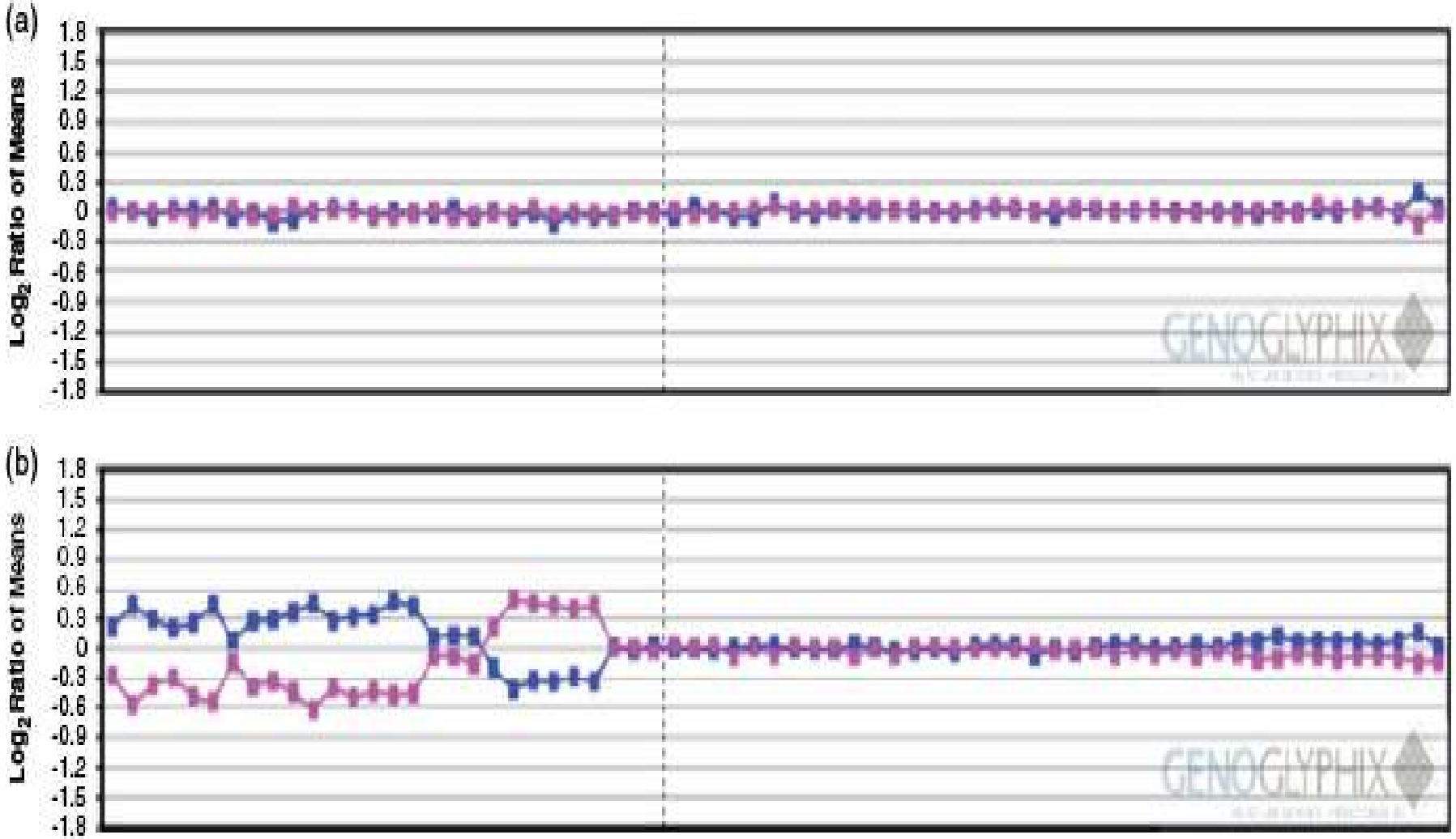
CGH-array

Genomic Microarrays-5: Dye Swap and Analysis



Revised from Spectral Genomics

Resultat Array-CGH



Tipus d'arrays-CGH

1. **Repercussió clínica de les sondes**
   - Whole Genome Array
   - Targeted Array: sondes malaltia-específiques

2. **Tipus de les sondes de DNA**
   - BAC (bacterial artificial chromosomes) 100-200 Kb
   - Oligonucleòtids 25-75 Kb
   - SNP (single nucleotide polymorphism) 1bp

3. **Resolució**

1.- Repercussió clínica de les sondes

1) **Whole-genome array**
   - estudi general genoma = cariotip d'alta resolució (fins a 1 milió sondes amb resolució 10Kb)
   - CNV (Copy Number Variation): 12% del genoma
     - » benignes
     - » patogèniques
     - » incertes (VOUS: Variants Of Unknown Significance)

2) **Targeted array**
   - sondes malaltia-específiques= múltiples FISH
   - sense problemes d'interpretació
   - més adequat per a Prenatal

Phenotype	Genes	Cytogenetics
Perisylvian polymicrogyria (Polymicrogyria, bilateral perisylvian; BPP)	SRPX2	Xq22.1
10q22q23 deletion	NRG3, GRID1	10q22q23 deletion
11q11–q13.3 duplication/multiple craniosynostoses, congenital heart defect	FGF3, FGF4	11q13.3 duplication
12q14.1q15 microdeletion	GRIP1	12q14.3 deletion
12q24.21-q24.23 microduplication	THRAP2, NOS1, RFC5	12q24.21-q24.23 duplication
13q33q34 deletion/ genital malformation in males/Microcephaly/MR	ERNB2, ARHGEF7	13q33.3q34 deletion
14q11.2 deletion syndrome	SUPT16H, CHD8	14q11.2 deletion
14q12 deletion syndrome	FOXG1B	14q12 deletion
15q21 microdeletion syndrome		15q21.2 deletion
15q24 deletion	HCN4	15q24.1
15q24 microdeletion	PML	15q24.1 deletion
15q26.3 deletion, Severe IUGR, developmental delay, postnatal growth retardation	IGF1R (insulin-like growth factor -1 receptor	15q26.3 deletion
16p11.2p12 deletion		16p12.1 deletion
17q21.31 microdeletion/microduplication syndrome	MAPT, CRHR1	17q21.31 deletion
1q21.2 deletion/duplication		1q21.2 deletion/ duplication
1q41q42 deletion	DISP1	1q41 deletion
20q13.33 deletion/Autosomal-dominant nocturnal frontal lobe epilepsy,Benign familial neonatal convulsions (type 1), hypotrichosis–lymphedema–telangiectasia	ARFGAP1, CHRNA4, KCNQ2, SOX18	20q13.33 deletion
22q11.2 duplication syndrome reciprocal to DGS deletion	TBX1 T-box 1 ?	22q11.2 duplication
22q13.3 deletion/Autism	SHANK3	22q13.33 deletion
2p15-p16.1 microdeletion		2p15-p16.1 deletion
2q22.3 deletion		2q22.3 deletion

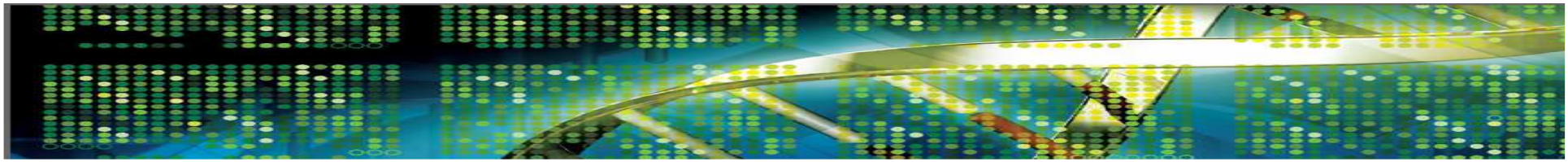
Phenotype	Genes	Cytogenetics
2q22.3q23.3	MBD5, KIF5C	2q23.1
2q35	IHH	2q35
2q37 deletion/brachydactyly-MR/obesity/Albright hereditary osteodystrophy	CENTG2, GPC1, GPR35, ATSV/ KIF1A, STK25	2q37.3 deletion
3p25 deletion	CNTN4	3p25.3 deletion
3q29 deletion syndrome/Autism	FAK2, DLG1	3q29 deletion
5q14.3 deletion	MEF2C	5q14.3
5q21q31 deletion syndrome		5q21q31 deletion
6q24.3q25.1(Diabetes mellitus, insulin-dependent, 5; IDDM5)	SUMO4	6q25.1
7q11.23 duplication (WBS region)		7q11.23 duplication
7q21.13q22.1 deletion/Ectrodactyly/Deafness	CUTL1 (CUX1), FZD1	7q22.13q22.1 deletion
8p23.1 inverted duplication/deletion		8p22p23 inversion
9q34.3 deletion syndrome	NOTCH1, EHMT1	9q34.3 deletion
Acheiropody/ and preaxial polydactyly	LMBR1	7q36.3 deletion
Action myoclonus-renal failure syndrome (AMRF)	SCARB2	4q21.1 deletion
Adrenal hyperplasia, congenital (CAH) due to 21-alpha hydroxylase deficiency	CYP21A2	6p21.32 deletion
Adrenal hypoplasia congenital (AHC)	NROB1 nuclear receptor family 0 B1 (DAX1)	Xp21.2 deletion
Adrenoleukodystrophy; (ALD)	ABCD1	Xq28 deletion
Alagille syndrome (AGS)	JAG1 jagged 1	20p12.2 deletion
P henotype	Genes	Cytogenetics
Albinism, ocular type 1	GPR143/OA1	Xp22.2 deletion
All 41 unique subtelomeric regions	Multiple	41 sites
All 43 unique pericentromeric regions	Multiple	43 sites
Allan-Herndon-Dudley syndrome, X-linked mental retardation (XLMR)	SLC16A2	Xq13.2 deletion
Alpha thalassemia-MR syndrome	HBA2 & HBA1	16p13.3 deletion

Phenotype	Genes	Cytogenetics
Alport syndrome, X-linked (ATS)	COL4A5	Xq22.3 deletion
Andersen syndrome	KCNJ2	17q24.3 deletion
Androgen insensitivity syndrome (AIS)	AR	Xq12 deletion
Aneuploidy for 24 chromosomes	Multiple	24 chromosomes
Angelman syndrome (AS)	UBE3A ubiquitin ligase 3A, AS-SRO,	15q11.2-q12 deletion
Angelman syndrome (AS)	AS imprinting center	15q11.2 deletion
Aniridia II (AN2)	PAX6 paired box gene 6	11p13 deletion
Anterior segment mesenchymal dysgenesis (ASMD)/ Cataract	PITX3	10q24.32 deletion
Arthropathy, progressive pseudorheumatoid, of childhood; (PPAC)	WISP3	6q21 deletion
Ataxia	ITPR1	3p26.2 deletion
Ataxia teleangiectasia	ATR	3q23 deletion
Atrial septal defect	GATA4	8p23.1 deletion
ATRX, XLMR-Hypotonic facies syndrome, ATR-X, and others	ATRX	Xq21.1 deletion/ duplication
Autism		4q32.1 deletion
Autism	DLX5	7q21.3 deletion
Autism	JMJD1C, TRIP8, REEP3	10q21.3 deletion
Autism	NURP1	13q14.12 deletion
Autism	NRXN3	14q31.1 deletion
Autism	A2BP1	16p13.2 deletion
Autism	DLG4	17p13.1 deletion
Autism	NURP2	17q11.2 deletion
[illegible]	[illegible]	[illegible] tion
Autism	ASMT (ASMTL)	Xp22.33 deletion
Autism	DPP10	2q14.1 deletion
Autism	DPP6	7q36.2 deletion

Array-CGH: què detecta?

- DETECTA:
  - pèrdues o guanys de < 5 Mb a les zones cobertes per les sondes
  - síndromes microdelecionals
  - markers eucromatina
  - pèrdues en els punts de ruptura de translocacions aparentment equilibrades
  - disomies uniparentals (SNP-arrays)

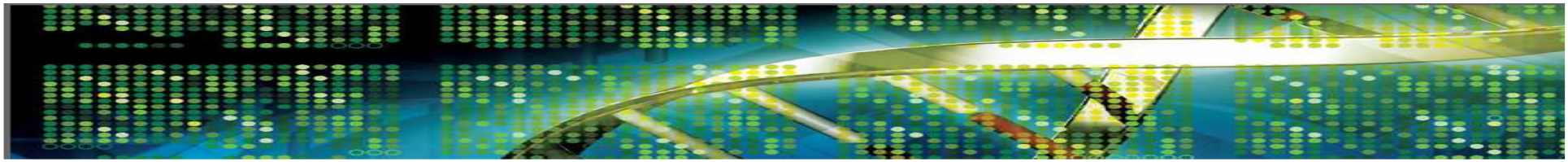
- NO DETECTA:
  - reorganitzacions equilibrades (disrupcions gèniques)
  - mosaics < 20%
  - algunes triploidies



Array-CGH: avantatges i inconvenients

- Avantatges
  - Alta resolució: típicament
    - 10 Kb targeted regions
    - 200 Kb genome backbone
  - Temps resposta curt
    - no cultiu
    - automatisme

- Inconvenients:
  - Preu: a partir de 400 €
  - "Copy Number Variations" incertes (VOUS)



Ultrasound Obstet Gynecol 2011; 37: 6–14
Published online 30 November 2010 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.7754

Additional information from array comparative genomic hybridization technology over conventional karyotyping in prenatal diagnosis: a systematic review and meta-analysis

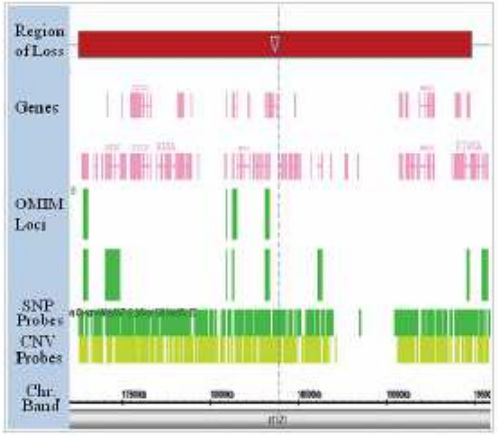
S. C. HILLMAN*†, S. PRETLOVE†, A. COOMARASAMY*, D. J. McMULLAN‡, E. V. DAVISON‡, E. R. MAHER*§ and M. D. KILBY*†

Array-CGH: metanàlisi

(Hillman et al., UOG 2011;37,6)

- aCGH dóna informació addicional al cariotip?
- Metanàlisi 10 estudis (2005-09) amb 798 casos
- 3.6% disbalanços genòmics en cariotips normals:
  - 2.5% patogènics,
  - 1.1% incerts
- 5.6% quan hi ha anomalia fetal a l'ecografia

The NEW ENGLAND JOURNAL of MEDICINE



ORIGINAL ARTICLES

Microarray vs. Karyotype for Prenatal Diagnosis

December 6, 2012 | R.J. Wapner and Others

This large, systematic study of prenatal diagnosis shows that chromosomal microarray analysis provided additional, clinically significant cytogenetic information as compared with karyotyping but did not identify triploidies and balanced translocations.

CME | Comments

Karyotype vs. Microarray Testing after Stillbirth

December 6, 2012 | U.M. Reddy and Others

Related Editorial ›

IMAGE CHALLENGE

What is the diagnosis?

Submit Answer

More Image Challenges ›

Array-CGH: darreres sèries prenatals

	n	Resolució	Anomalies addicionals	En malformac.
VanDenVeyver,09	300	44 kb	5.0%	4.6%
Maya,10	269	BAC	1.1%	2.0%
Fiorentino,11	1030	1 Mb	0.9%	7.6%
Armengol,11	900	BAC	1.6%	3.5%
Wapner,12	4401	44 kb	2.5%	5.8%
Lee,12	3171	1 Mb/60 kb	No 0.5%	8.2%
Srebniak,12	207	200 kb	-	7.7%
Breman,12	1115	44-180 kb	2.4%	-
Faas,12	220	SNP	5%	-
Schaffer,12	5003	-	5.3%	6.5%
Wapner,12	4406	75 kb	2.5%	6.0%
			2.7%	*5.8%*