KaryoNIM® Prenatal

Leading genetic diagnosis

What is array-CGH?

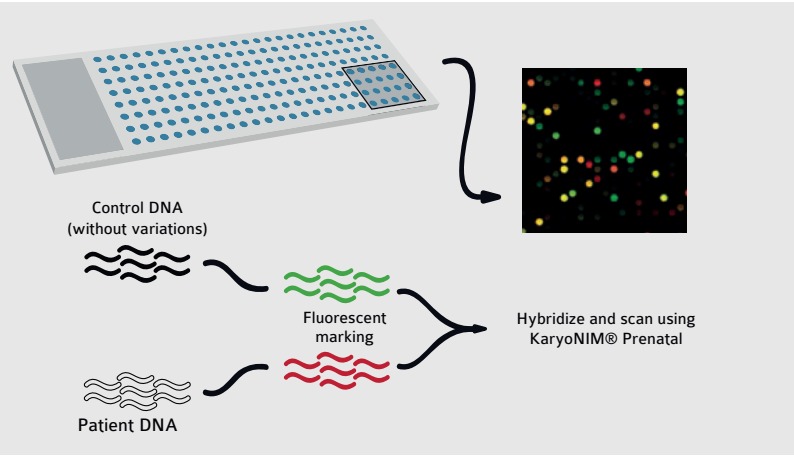
Array-CGH (Comparative Genomic Hybridization) is currently considered the newest and most powerful genomic technique in the clinical diagnosis of genetic disorders.

Array-CGH allows us to analyze the complete genome of an individual to search for possible variations due to the gain or loss of genetic material.

In addition, it is a quick and reliable test, requiring less than 2 weeks for whole genome analysis.

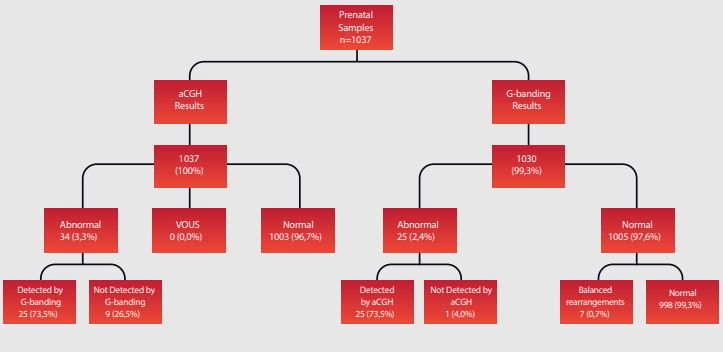
How array-CGH works

The sample DNA is compared to control DNA (without variations). Both samples are marked with different colored fluorophores and hybridized to the **KaryoNIM® Prenatal** platform. Subsequently they are scanned and the data obtained are analyzed.



More powerful than conventional tests

Array-CGH proves to be an efcient tool for the prenatal detection of chromosomal abnormalities.



Study over 1037 patients: 89% low risk patients, 11% advanced maternal age, abnormal ultrasound ndings, triple screening with abnormal results or family history of chromosomal abnormalities.

"Chromosomal abnormalities were identied in 34 cases (3.3%). In 9 of those (26.5%) aCGH detected copy number variations that would not have been identied with only a standard karyotype. aCGH was also able to detect chromosomal mosaicisms at as low as a 10% level. There was complete concordance between conventional karyotyping and aCGH results, except for 2 cases that were correctly diagnosed by aCGH."

Introducing array comparative genomic hybridization into routine prenatal diagnosis practice: a prospective study on over 1000 consecutive clinical cases. Fiorentino F, et al., Prenatal Diagnosis 2011; 31: 1270-1282.

"Current data demonstrates that the use of array-CGH in prenatal diagnosis constitutes a very useful diagnostic tool. Array-CGH designed and aimed at regions responsible for pathologies in prenatal diagnosis increases the detection of fetal genomic abnormalities It´s cost-efficient and generally well accepted by couples. It is currently the most powerful method for detecting variations in the fetus's genome in high- risk pregnancies."

J.C. Cigudosa. Coordinator of the document "Consenso para la Implementación de los Arrays [CGH y SNP-arrays] en la Genética Clínica". Instituto Roche, 2012 (may be accessed at www.institutoroche.es).

KaryoNIM® Prenatal is a platform based on array-CGH technology that simultaneously detects the presence or absence of gains or losses of genomic and chromosomal regions (such as deletions, amplications, or trisomies), responsible for up to 124 genetic syndromes, with a resolution that is 20 times higher than the conventional g-banded karyotyping.

Reasons for using KaryoNIM® in prenatal diagnosis

KaryoNIM® uses array-CGH technology and includes 60,000 probes across the complete human genome. Its designis aimed at genetic diagnosis, and it enables the detection of variations of at least 1 Mb on the complete genome, 10 times higher than conventional Karyotyping.

KaryoNIM® is aimed at detecting genetic variations related to genetic syndromes. In the critical regions that cause these syndromes, resolution is 20 times higher than in a conventional karyotype, being able to detect, in some cases, altered regions smaller than 200 Kb. With this design we avoid unnecessary information relating to sensitive samples, such as prenatal ones, focusing the analysis on regions associated to known diseases.

1 Because the protocol is based on DNA and not on cell cultures.

KaryoNIM® does not require cell cultures to obtain metaphase cells. It would only need a small amount of DNA from the sample (200 to 500 nanograms), which can be obtained from approximately 4-5 ml of amniotic fluid. The quality of the genetic material is a key factor, and therefore precautions must be taken when handling the sample, in particular at the DNA extraction stage.

2 Because results are fast and reliable

The time span from the reception of the sample until the issuance of the report ranges from 5 to 10 days. The analysis is carried out by our team of geneticists and bioinformatics who are experts in the use of the appropriate advanced software for obtaining results.

The detection of variations is very objective and based on statistical parameters that comply with qualitative and quantitative standard criteria.

Preparation of reports for clinical purposes

The report is intended for clinical use and provides a clear answer on the presence or absence of the genomic variation analyzed, for each of the syndromes specically included in the array. In addition, any gain or loss larger than 1 Mb (such as complete trisomies) will be stated in the report. The clinical relevance of the findings will always be explained in a direct and clear way, easing the ow of information from the doctor to the patient.

To reinforce reliable clinical interpretation, this report does not include syndromes of reduced penetrance or those unclear with regards to their inheritance pattern. The report always takes into account the limitations of this technique, and it will therefore not be possible to detect through array-CGH any variations due to uniparental disomies or gene mutations, balanced chromosomal relocations, complete polyploidies, or the presence of mosaics of variations that affect less than 30% of the cell population.

In prenatal diagnosis, **KaryoNIM®** is a technology that complements conventional karyotyping and substitutes prenatal FISH or MLPA, by being able to simultaneously detect up to 124 severe genetic syndromes.

NIMGenetics, offers a comprehensive diagnosis, including conventional karyotyping, for those centers that request it. For additional information, procedures and prices, please contact **NIMGenetics**.

Syndromes included in KaryoNIM Prenatal 60k

OMIM	SYNDROME
607872	Chromosome 1p36 deletion syndrome
613735	Chromosome 1p32-p31 deletion syndrome
612530	Chromosome 1q41-q42 deletion syndrome
612337	Chromosome 1q43-q44 deletion syndrome
164280	Feingold syndrome
606407	Hypotonia-cystinuria syndrome
157170	Holoprosencephaly 2
612513	Chromosome 2p16.1-p15 deletion syndrome
613564	Chromosome 2p11-p11.2 deletion syndrome
605274	Mesomelic Dysplasia Savariayan type
609583	Joubert syndrome 4
256100	Nephronophthisis 1
606708	Split/hand foot malformation 5
612345	Chromosome 2q31 deletion syndrome
612313	Chromosome 2q32-q33 deletion syndrome
605934	Holoprosencephaly 6
600430	Brachydactyly-mental retardation syndrome
110100	Blepharophimosis, ptosis and epicanthus inversus
220200	Dandy-Walker syndrome
206900	Syndromic Microphthalmia 3
605289	Split/hand foot malformation 4
609425	Chromosome 3q29 deletion syndrome
611936	Chromosome 3q29 duplication syndrome
194190	Wolf-Hirschhorn syndrome
613509	Chromosome 4q31 deletion syndrome
180500	Axenfeld Rieger syndrome
123450	Cri-du-chat syndrome (includes distal region)
122470	Cornelia de Lange syndrome
613174	Chromosome 5p13 duplication syndrome
612881	Periventricular Heterotopia associated with chromosome 5q deletion
613443	Chromosome 5q14.3 deletion syndrome
117550	Sotos syndrome
612582	Chromosome 6pter-p24 deletion syndrome
119600	Cleidocraneal dysplasia
613544	Chromosome 6q11-q14 deletion syndrome
176270	Syndrome similar to the Prader-Willi syndrorme in chromosome 6
612863	Chromosome 6q24-q25 deletion syndrome
101400	Saethre-Chotzen syndrome
175700	Creig Cephalopolysyndactyly syndrome
194050	Williams-Beuren syndrome
609757	Williams-Beuren region duplication syndrome
606382	Williams-Beuren syndrome associated to infantile spasms
183600	Split-hand/foot malfomation 1
142945	Holoprosencephaly 3
222400	Diaphragmatic Hernia 2
214800	CHARGE syndrome
150230	Langer Giedion syndrome
190350	Trichorhinophalangeal syndrome type I
179613	Recombinant chromosome 8 syndrome
154230	Chromosome 9p24.3 deletion associated to XY sex reversal 46, partial or complete
158170	Chromosome 9p deletion syndrome
610828	Holoprosencephaly 7
161200	Nail-patella syndrome

OMIM	SYNDROME
610253	Kleefstra syndrome
146255	Hypoparathyroidism, sensorineural deafness and renal disease
601362	Digeorge 2 syndrome (includes Nebulette gene region)
612242	Chromosome 10q23 deletion syndrome
600095	Split-hand/foot malformation 3
609625	Chromosome 10q26 deletion syndrome
130650	Beckwith-Wiedemann syndrome
606528	Homozygous 11p15-p14 deletion syndrome
612469	Chromosome 11p13-12 deletion syndrome
194072	WAGR syndrome
601224	Potocki-Shaffer syndrome
147791	Jacobsen syndrome
601803	Pallister-Killian syndrome
163950	Noonan syndrome
-	Patau syndrome
609637	Holoprosencephaly 5
607932	Syndromic microphthalmia 6
176270	6 Prader-Willi syndrome
105830	Angelman syndrome
608636	Chromosome 15q11-q13 duplication syndrome
613406	Chromosome 15q24 deletion syndrome
142340	Congenitl piaphragmatic hernia
612626	Chromosome 15q26-qter deletion syndrome
610543	Chromosome 16p13.3 deletion syndrome
141750	Chromosome 16-related alpha-thalassemia mental retardation syndrome
600273	Infantile severe polycystic kidney disease with tuberous sclerosis
180849	Rubinstein-Taybi syndrome
613604	Chromosome 16p12.2-p11.2 deletion syndrome
247200	Miller-Dieker lissencephaly syndrome
613215	Chromosome 17p13.3 duplication syndrome
118220	Carchot-Marie-Tooth disease, demyelinating, type 1A
162500	Hereditary neuropathy with liability to pressure palsies
182290	Smith-Magenis syndrome
610883	Potocki-Lupski syndrome
613675	Chromosome 17q11.2 deletion syndrome
610443	Chromosome 17q21.31 deletion syndrome
613533	Chromosome 17q21.31 duplication syndrome
613355	Chromosome 17q23.1-q23.2 deletion syndrome
114290	Campomelic Dysplasia
146390	Chromosome 18p deletion syndrome
-	Edwards syndrome
142946	Holoprosencephaly 4
610954	Pitt-Hopkins syndrome
601808	Chromosome 18q deletion syndrome
607842	Congenital aural atresia
609334	Chromosome 18 pericentric inversion
613026	Chromosome 19q13.1 deletion syndrome
118450	Alagille 1 syndrome
190685	Down syndrome
236100	Holoprosencephaly 1
115470	Cat-Eye syndrome
188400	Digeorge syndrome
192430	Velocardiofacial syndrome
145410	Opitz-GBBB
611867	Chromosome 22q11.2 deletion syndrome, distal
606232	Chromosome 22q13.3 deletion syndrome
–	Turner syndrome
–	Triple X syndrome
–	Klinefelter syndrome
308100	Complicated X-Linked Ichthyosis syndrome
300679	Chromosome Xp21 deletion syndrome
310200	Muscular dystrophy, Duchenne-type (deletion of the DMD gene)
300578	Chromosome Xp11.3 deletion syndrome
300801	Chromosome Xp11.23-p11.22 duplication syndrome
300706	Syndromic X-linked mental retardation, Turner type
300123	X-linked mental retardation with panhypopituitarism
300475	Chromosome Xq28 deletion syndrome
300260	Chromosome MECP2 duplication syndrome
300815	Chromosome Xq28 duplication syndrome
400044	46,XY sex reversal 1
-	XYY syndrome

Sample Delivery

Samples will be collected by NIMGenetics, subject to prior notice, at the centers in which they are obtained. Samples must be kept at 4ºC until they are collected.

Sample requirements

- **Blood from the umbilical cord:**
  1ml in Heparin Tube or EDTA (green, brown or purple top).
- **Amniotic fluid:**
  5 ml sample in tube or syringe.
- **Chorionic villous biopsy:**
  2 cubic millimeter fragment of chorionic material suspended in a sterile solution (such as PBS). We recommend, in this case, a Falcon type tube with between 5 and 15 ml of solution.

Technical description

- **Total number of probes in selected syndromic regions:**
  7,500 probes
- **Average detection capacity in syndromic regions:**
  165 kb.
- **Total number of probes in critical genes:**
  655 probes
- **Coverage of critical genes in syndromic regions:**
  5 probes/gene
- **Total number of probes in the rest of the genome:**
  48,000 probes
- **Average detection capacity in the rest of the genome:**
  275 kb.

1
More powerful than conventional tests
2
Not dependent on cell cultures
3
Results in 10 days
4
Aimed at diagnosing 124 syndromes related to mental retardation and congenital anomalies
5
Written report for clinical use which provides a clear answer on the presence or absence of genomic variations analyzed for each one of the diseases included in the array

The NIMGenetics Team is committed to offering all necessary scientific and technical support in order to provide an accurate, reliable and well-defined genetic diagnosis.