KaryoNIM® Leukemia

For your future

nimgenetics®

Chronic lymphocytic leukemia (CLL)

Chronic lymphocytic leukemia (CLL) is the most frequent adult leukemia in Western countries.

It accounts for 30% of the leukemias in this population and affects mainly older individuals.[1]

- **Establishing the prognosis, treatment options, and monitoring of CLL requires the identification of Identification of genetic biomarkers.**
- **Highly effective treatment options based on monoclonal antibodies or tyrosine kinase inhibitors depend on the presence or absence of deletions 17p and 11q.[3-5]**

CNVs are the main chromosomal and genetic abnormalities seen in CLL, and are powerful prognosis markers.[2]

The mutational status determines the prognosis and treatment of CLL

Risk group	Frequency	Mutation	Survival at 5 years	Survival at 10 years
High	27%	del(17p)-TP53 and/or BIRC3	51%	29%
Intermediate	39%	NOTCH1 and/or SF3B1 and/or del(11q23)	66%	37%
Low	17%	Normal karyotype or Trisomy 12	78%	57%
Extremely low	17%	Del(13q14)	87%	69%

KaryoNIM®Leukemia

Genomic platform for the identification of biomarkers for CLL

KaryoNIM®Leukemia improves upon conventional techniques.
Designed by NIMGenetics, it combines **Oligonucleotide Array-Based CGH and SNParray technologies.**

aCGH

- More sensitive whole-genome CNV analysis
- More accurate CNV detection

SNPs

Detection of LOH* due to uniparental disomy

Proprietary design

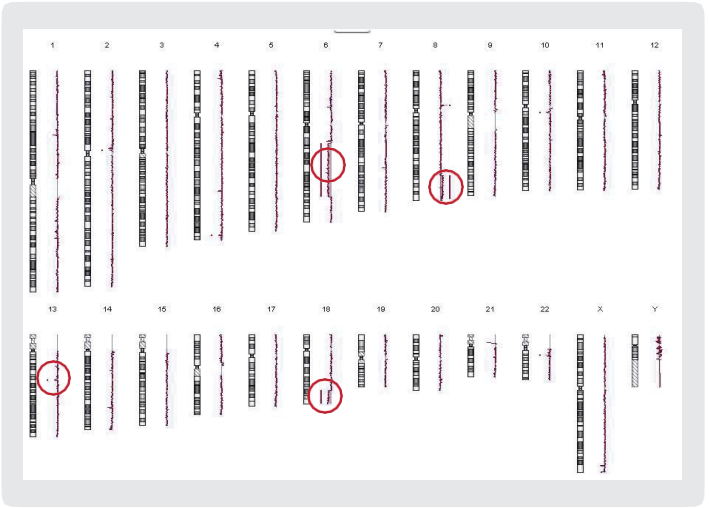
Specifically targets CLL biomarkers

LOH: Lost of heterozygosity

Array CGH: assessing prognosis in CLL

aCGH is the technique of choice for prognostic assessment in CLL:

- ✓ **It offers whole genome information**
- ✓ **It improves performance testing**
  70% of cases with CLL showed genetic alterations detected by aCGH compared with 50% of cases diagnosed by FISH.
- ✓ **It simplifies the transport and handling of samples.** The cellular status of the sample is not a limiting factor since the test uses DNA. Cell culturing is not required.



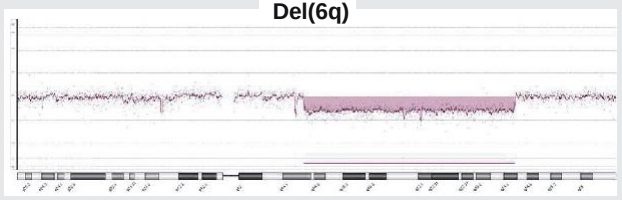
aCGH from a sample of CLL with multiple CNVs.

a

Array Comparative Genomic Hybridization (aCGH) is the most efficient genetic test to diagnose chromosomal alterations in CLL.[6-9]

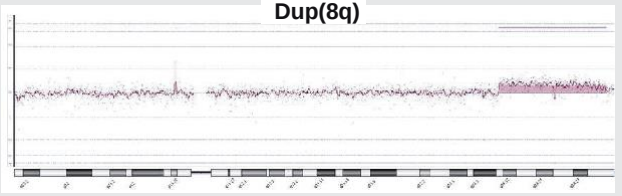
Not detected by FisH

Del(6q)



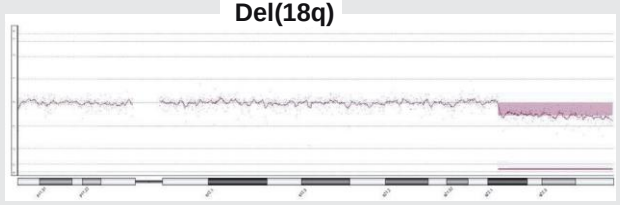
Not detected by FisH

Dup(8q)



Not detected by FisH

Del(18q)

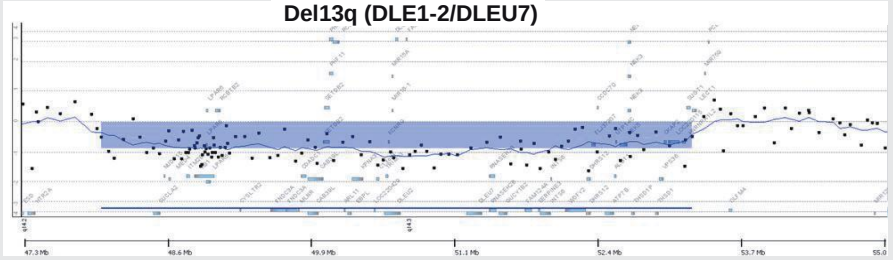


✓ **It can change prognosis**

FISH technology does not analyze the whole genome, only a defined group of alterations.

Not detected by FisH

Del13q (DLE1-2/DLEU7)



✓ **It increases resolution:**

- Completely defines CNV
- Identifies the genes involved.

Complete coverage of the classical regions for CLL prognosis	Locus	
	DETECTION CAPACITY	RESOLUTION
Trisomy of chromosome 12	130 kb	1 probe/25.5 kb
Deletion **11q23**, including the gene ***ATM***		
Deletion **13q14**, including the ***DLEU*** region		
Deletion **17p13**, including the gene ***TP53***		

OTHER REGIONS/GENES OF INTEREST	DETECTION CAPACITY
Genes of interest in CLL *ATM, BIRC2, BIRC3, IKZF1, KLHL6, MYB, MYD88, NOTCH1, POT1, SF3B1, TP53, XPO1*	<17 kb
LOH regions	10 Mb
Genes included in Cancer Consensus	Complete coverage

KaryoNIM® Leukemia

The best aCGH for the evaluation of CLL

- ✓ **Improves the detection of CNVs in regions of prognostic interest.**
- ✓ **Provides relevant information on:**
  - genes related to CLL
  - clonality and loss of heterozygosity
- ✓ **Increases the diagnostic effectiveness by 20% with respect to those cases detected by FISH.**
- ✓ **Easier handling of the sample as no cell culturing is required.**
- ✓ **More complete prognosis: examines all regions of the genome compared with those by routine FISH.**
- ✓ **Maximum precision in defining the alteration and its boundaries, revealing the genes involved thanks to its superior resolution.**[6-9]
- ✓ **Provides the medical team with the most current genetic diagnosis of CLL, in accordance with international guidelines and the most advanced laboratories worldwide.**[10]

Sample handling and shipping:

- **Type of sample:** 3-5 mL of blood or bone marrow in EDTA. Ship at room temperature within 48 hours of sample collection.
- **DNA sample:** 500 ng of DNA at a concentration greater than 10 ng/µL dissolved in TE *low* buffer or H_2O. Ship at room temperature.
- **Documents to be included with the sample:** Informed consent form
  Request form
- **Delivery of results:** 15 working days

Bibliography

1: dighiero G, Hamblin T. Chronic lymphocytic leukaemia. Lancet, 2008; 371: 1017–29

2: Eichhorst B, dreyling M, et al. Chronic lymphocytic leukemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol, 2011; 22 Suppl 6: 50–54

3: rossi d, rasi s, et al. Integrated mutational and cytogenetic analysis identifies new prognostic subgroups in chronic lymphocytic leukemia. Blood, 2013; 121 (8): 1403-1412

4: Wierda WG, Kipps TJ, et al. Chemoimmunotherapy with O-FC in previously untreated patients with chronic lymphocytic leukemia. Blood 2011; 117:6450

5: Hillmen p,skotnicki AB, et al. Alemtuzumab compared with chlorambucil as first-line therapy for chronic lymphocytic leukemia. J Clin Oncol 2007; 25:5616

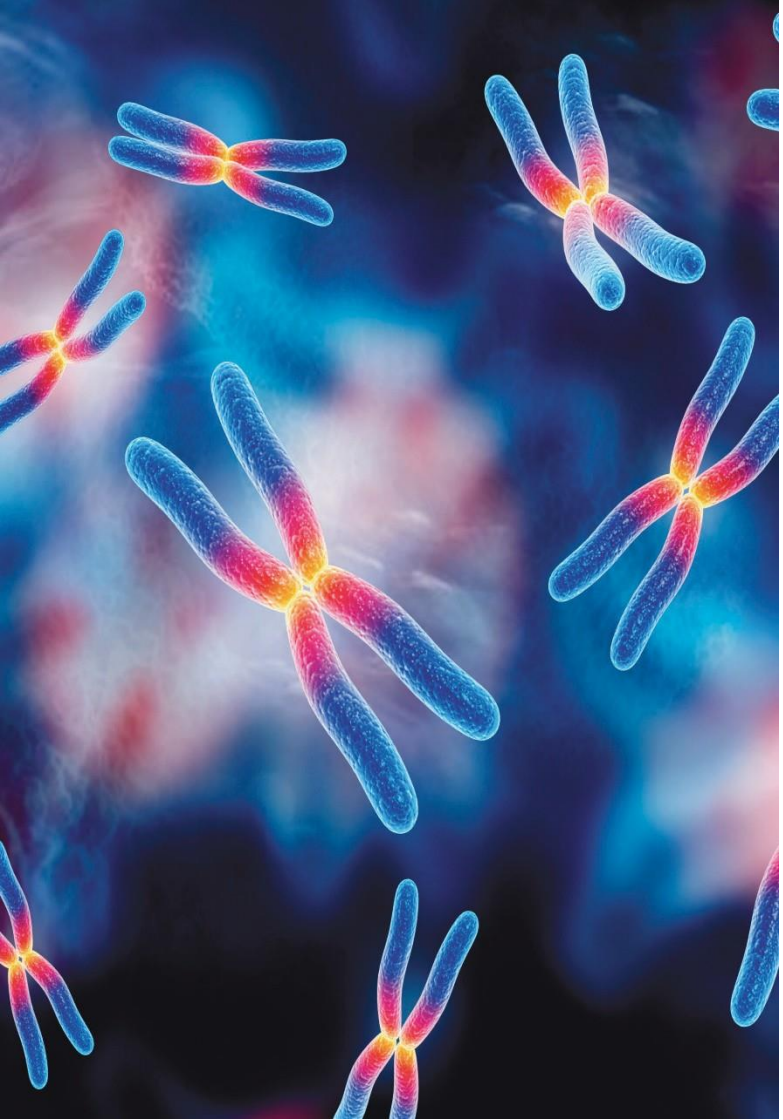
6: Ferreira Bi, Garcia JF, et al. Comparative genome profiling across subtypes of low-grade B-cell lymphoma identifies type-specific and common aberrations that target genes with a role in B-cell neoplasia. Haematologica, 2008; 93(5):670-9

7: Kolquist KA, schultz rA, et al. Evaluation of chronic lymphocytic leukemia by oligonucleotide-based microarray analysis uncovers novel aberrations not detected by FISH or cytogenetic analysis (2011). Mol Cytogenet, 2011; 16;4:25

8: Edelmann J, Holzmann K, et al. High-resolution genomic profiling of chronic lymphocytic leukemia reveals new recurrent genomic alterations. Blood. 2012;120(24):4783-94

9: peterson JF, Aggarwal N, et al. Integration of microarray analysis into the clinical diagnosis of hematological malignancies: How much can we improve cytogenetic testing?. Oncotarget 2015; 6(22):18845-62

10: schoumans J, suela J et al. Guidelines for genomic array analysis in acquired haematological neoplastic disorders. Genes Chromosomes Cancer, 2016; 55(5):480-91



Comprehensive approach to the diagnosis of CLL

- **Integrated solutions. NIMGenetics** has an extensive portfolio of molecular genetic tests to meet the needs of the patient. Including:

  NIMFISH probes, to monitor CLL. Unique catalog of probes characterized by their high specificiy, precision and luminiscence, which are regularly updated.

  TP53 sequencing
  Our NGS platform for TP53 is certified by ERIC (European Research Initiative on CLL).

- **Opinion leaders in Oncology.** Our team has published more than 200 scientific articles on genetics and oncohematology in international journals.

- Our laboratories follow the quality control standards of **EMQN** (*European Molecular Genetics Quality Network*).

- We are accredited by the Spanish Association of Human Genetics: *Asociación Española de Genética Humana* (**AEGH**).

- The reports by **NIMGenetics** are rated as excellent by opinion leaders in oncology, clinical genetics, and other disciplines.