HUMAN HEALTH

ENVIRONMENTAL HEALTH

# VALIDATED SOLUTIONS FOR MOLECULAR CYTOGENETICISTS

## PRODUCTS AND METHODOLOGIES

Not for distribution in the USA

PerkinElmer®
*For the Better*

PerkinElmer is working with its sizeable customer base (in the regions marked blue on the map) to advance health care.

# PERKINELMER - INNOVATORS IN MOLECULAR CYTOGENETICS

## Faster results – higher sensitivity

**PerkinElmer is bringing the newest molecular techniques to cytogenetics laboratories.**

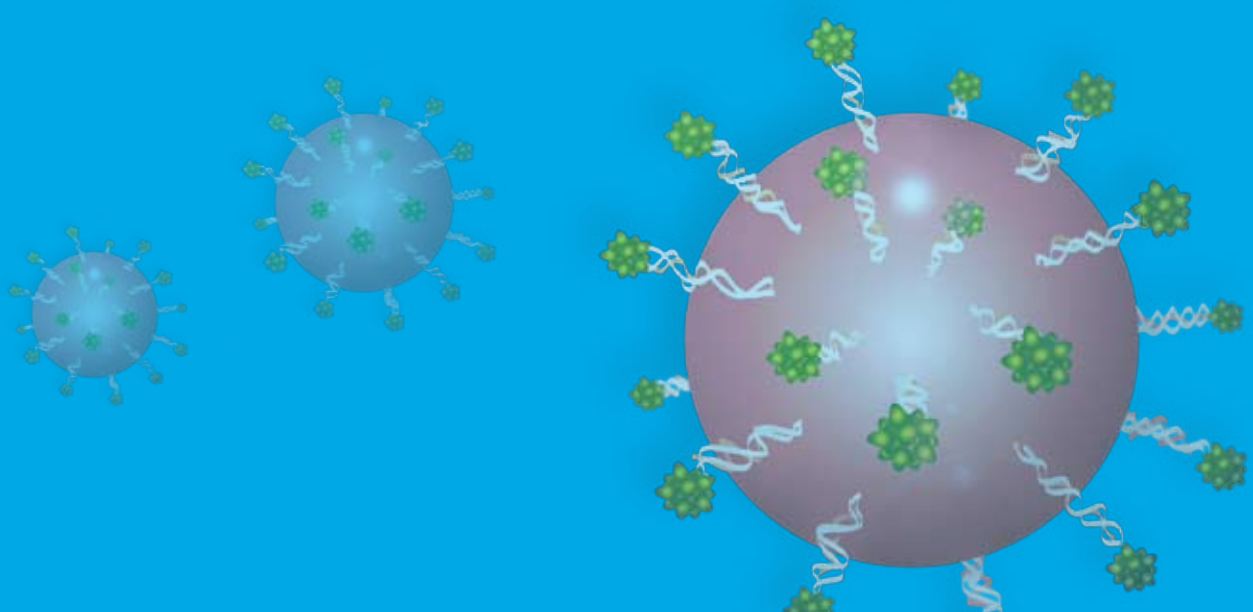
**Our innovative methodologies support:**

- **Higher detection rates**
- **More results - faster & cheaper**
- **Fewer unclear results**
- **Streamlined processes**

**Oligonucleotide-based microarrays and bead-based multiplex BACs-on-Beads (BoBs) products have been specifically designed, developed and validated by cytogeneticists for cytogeneticists performing molecular karyotyping.**

- **Rapid methods for prenatal diagnostics**
- **Tools for molecular karyotyping**
- **Software for easy interpretation of the results**
- **DNA amplification reagents***

** Products are For Research Use Only. Not for use in diagnostic procedures.*



# SIGNATURE GENOMIC LABORATORIES – CYTOGENETICS PIONEER

## A Global Leader in Human and Environmental Health

PerkinElmer is a global scientific leader that is taking action to improve the health and safety of people and their environment. We are committed to protecting the health of expectant mothers, babies and families. PerkinElmer is the world's leading supplier of newborn screening systems, a pioneer in methods for risk assessment during pregnancy and a leader in cord blood banking. Following its acquisition by PerkinElmer in 2010, Signature Genomics has enhanced PerkinElmer's molecular cytogenetics expertise.

## Validated Solutions in Molecular Cytogenetics

Signature Genomics has established cutting-edge methodologies that are now standard in molecular cytogenetics. Founded in 2003 Signature Genomic Laboratories has analyzed over 50,000 cytogenetic samples and established a powerful database of abnormalities. Based on this information a unique aCGH array design has been defined that targets relevant regions for molecular cytogenetic analysis.

*As one of the pioneers in the field of molecular cytogenetic analysis, we continuously work toward innovation and development of cutting-edge technologies to improve human health. We aim to share our experience and expertise with the global cytogenetics community and significantly advance the field of cytogenetics.*

**Lisa Shaffer**
**Founder of Signature Genomic Laboratories**
**A PerkinElmer Company**

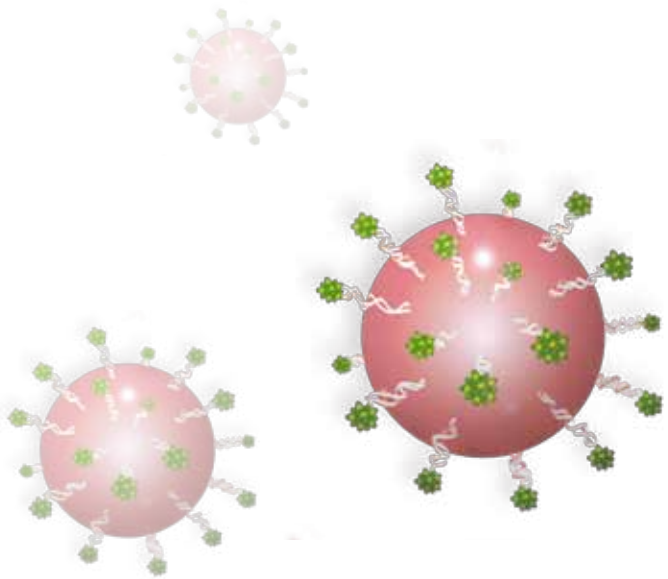
SIGNATURE GENOMICS

PerkinElmer®
*For the Better*


# THE POWER OF BACS-ON-BEADS

BoBs stands for BACs-on-Beads, an exciting new technology from PerkinElmer.

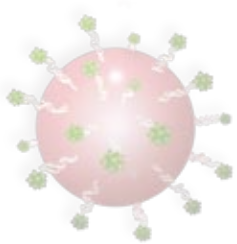
By immobilizing BAC (bacterial artificial chromosome) derived DNA probes onto Luminex® xMAP® fluorescently coded beads, BoBs enables rapid detection of copy number changes in targeted genomic regions from a minute amount of DNA. BACs-on-Beads technology supports high throughput molecular karyotyping in a microplate well which, in turn, can lead to greater laboratory efficiency and better use of resources.



## Expand on your FISH capability using BoBs technology

BACs are large cloned sequences of human DNA, typically 150,000 - 170,000 basepairs long. When coupled to Luminex® xMAP® beads, the length of the BACs is a useful property. BAC derived DNA probes have a higher signal-to-noise ratio compared to smaller DNA probes regardless of the DNA quality. This represents an important advantage when working with samples such as amniotic fluid, CVS, POC (product of conception) and DNA amplified from single or few cells. The advantage of BACs over oligos, which are less than 100 basepairs long, is that fewer probes are needed for the same coverage of a target region. Unknown clinical significance results that are common with other fast molecular karyotyping techniques are rarely encountered with the new BACs-on-Beads assays.

BAC DNA has long been used as probes for FISH (fluorescence in situ hybridization) in cytogenetic laboratories. Now, with BACs-on-Beads technology multiple FISH probes can be handled in a single well and you can perform the equivalent of tens to hundreds of FISH experiments simultaneously.



# LUMINEX XMAP TECHNOLOGY

## Assay Based on Luminex® xMAP® Technology

is an established multiplexing technology utilizing approximately 5 µm diameter polystyrene beads that have been impregnated with a specific ratio of two different fluorescent dyes.

By using ten different concentrations of each of the two dyes it is possible to generate up to 100 bead types with distinct fluorescent signatures, or spectral addresses that can be identified through excitation of the impregnated dyes when read by the Luminex 100/200™ instrument.

**The advantage of the Luminex® instrument platform lies in the fact that up to 100 different bead types can be mixed together and the experiment can be performed in a multiplexed fashion using microplates.**

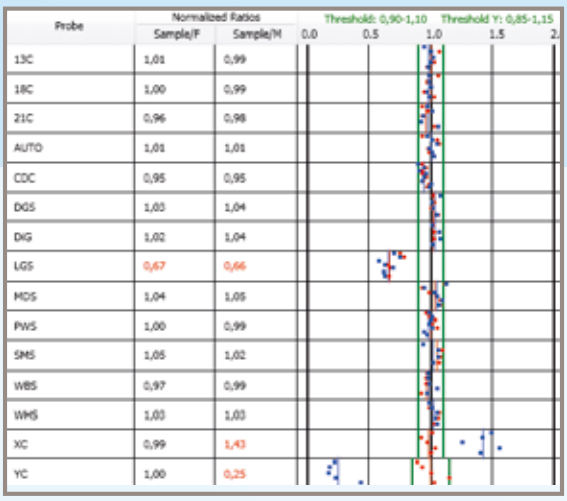
The instrument can automatically aspirate the beads from each well of a 96-well plate, and by use of a flow system that allows one bead to be interrogated by two lasers simultaneously, all beads can be classified and quantified within the assay in a short amount of time.

### Easy interpretation of the Copy Number Changes with BoBsoft™ Analysis Software

BoBsoft™ analysis software takes the output file generated by the Luminex® 100/200™ instrument, and analyzes the data. The signal intensities from the sample and reference DNA are compared to provide a clear display of any copy number changes in the targeted regions.

### BOBS PRODUCTS BRING THESE BENEFITS TO YOUR WORK

- **Robust assay with low quality DNA from various sample types**
- **Enables high throughput analysis as tens of samples can be run simultaneously reducing the hands-on time**
- **Resources are optimized as sample volume can be increased without increasing staffing**
- **Complete procedure from extracted DNA to result availability takes less than 24 hours**
- **Results are clear and easy to interpret**
- **More information due to the multiplexing power of xMAP®**



# PRENATAL BOBS

## A more informative option than FISH and QF-PCR for IVD Labs

Prenatal BoBs™ is a CE-marked IVD product based on BACs-on-Beads technology. In addition to detecting copy number changes of chromosomes 13, 18, 21, X and Y, the product enables detection of 9 additional chromosomal regions in which a clear correlation between a loss and an adverse outcome has been demonstrated.[1] Gains and losses in these targeted regions could easily be missed with other commonly used methods.

### Low Input Material – Fast Results

Analysis using Prenatal BoBs typically requires only 150 ng genomic DNA, an amount which can be obtained from 3 - 5 mL of amniotic fluid or from 1 villus. Results are ready in 24-48 hours from the time of sampling.

### Clear Result Interpretation

In Prenatal BoBs a gain or loss of a region is called if three or more probes within a given target region exceed the cut-off for gain or loss.

Frequencies of aneuploidies and single microdeletion syndromes vary from quite common to rare. Combining the frequency rates (using the most conservative frequency rate) it is expected that there is a finding of an aneuploidy or microdeletion syndrome region with the Prenatal BoBs kit in every 1/288 births.

| Aneuploidies | Cytoband |
|---|---|
| Trisomy 13: Patau Syndrome | Chr 13 |
| Trisomy 18: Edwards Syndrome | Chr 18 |
| Trisomy 21: Down Syndrome | Chr 21 |
| Sex Chromosome Abnormalities | Chr X, Chr Y |

| Microdeletion Syndrome | Cytoband |
|---|---|
| DiGeorge Syndrome | 22q11.2 |
| DiGeorge 2 Syndrome | 10p14 |
| Williams-Beuren Syndrome | 7q11.2 |
| Prader-Willi Syndrome | 15q11-q12 |
| Angelman Syndrome | 15q11-q12 |
| Smith-Magenis Syndrome | 17p11.2 |
| Wolf-Hirschhorn Syndrome | 4p16.3 |
| Cri du Chat Syndrome | 5p15.3-p15.2 |
| Langer-Giedion Syndrome | 8q23-q24 |
| Miller-Dieker Syndrome | 17p13.3 |

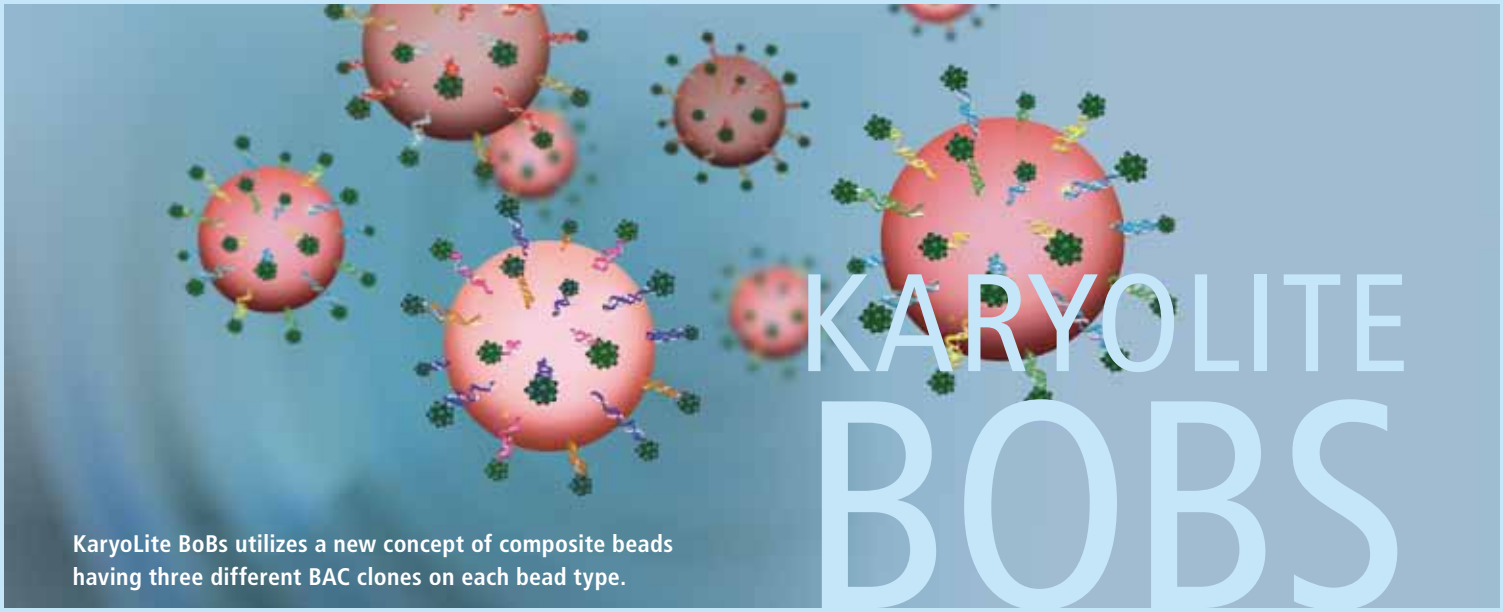
*Prenatal BoBs reagents are not available in the USA and Canada.*
*In other countries please check availability with your PerkinElmer sales representative.*

**LITERATURE:**

1. OMIM: http://www.ncbi.nlm.nih.gov/omim/ #105830, #123450, #150230, #176270, #182290, #188400, #194050, #194190, and #247200

**See also**

Gross SJ et al. Rapid and novel prenatal molecular assay for detecting aneuploidies and microdeletion syndromes, Prenat Diagn. 2011 Mar;31(3):259-66.
Vialard F et al. Prenatal BACs-on-Beads: a new technology for rapid detection of aneuploidies and microdeletions in prenatal diagnosis, Prenat Diagn. 2011 May;31(5):500-8.
Shaffer LG et al. The development of a rapid assay for prenatal testing of common aneuploidies and microdeletion syndromes, Prenat Diagn. 2011 Aug;31(8):778-87.
Popowski T et al. Williams-Beuren Syndrome: the prenatal phenotype, Am. J. Obs & Gyn. 2011.



KaryoLite BoBs utilizes a new concept of composite beads having three different BAC clones on each bead type.

# KARYOLITE BOBS

## 24 Chromosomes in 24 Hours

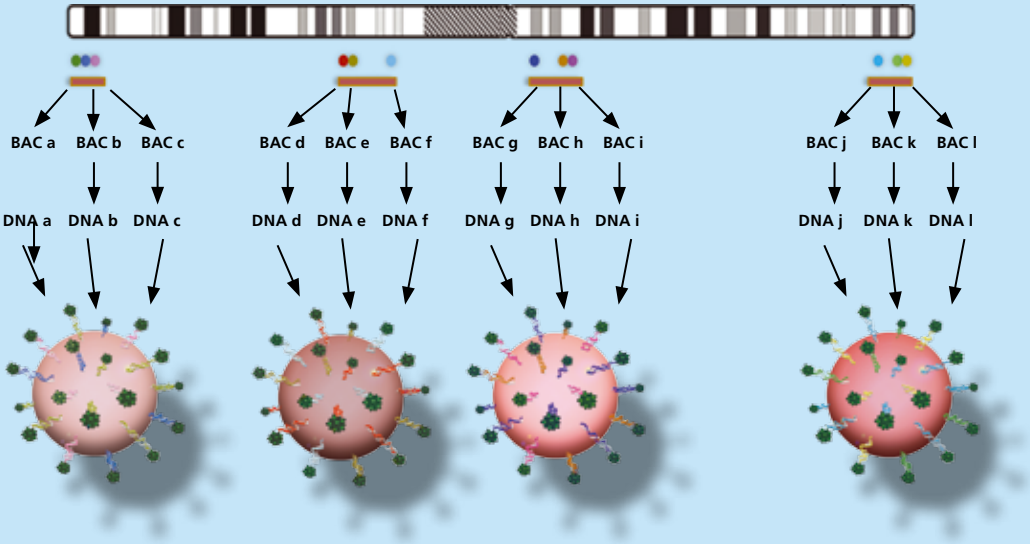
KaryoLite BoBs™ has been developed to detect arm specific aneuploidies in all 24 chromosomes in a single assay for research use only. The product covers p and q arms of all chromosomes 1-22, X and Y. Based on the BACs-on-Beads technology, it consists of BAC DNA immobilized onto polystyrene microspheres distinguishable by the Luminex® instrument system.

KaryoLite BoBs utilizes a new concept of composite beads having DNA from three different BAC clones on each bead type. The composite clone format expands the region of chromosomal DNA interrogated by each bead.

Research may be performed with KaryoLite BoBs using only 50 ng of genomic DNA extracted directly from amniotic fluid, chorionic villae or fetal tissue. As no cell culturing is required with any BoBs assay, KaryoLite BoBs offers a clear advantage over conventional cytogenetic techniques in cases in which cell culture is problematic, for example in POC (product of conception) analysis.

### Results in Under 24 hours with Hands-On Time ~ 3.5 h

The probes used have been carefully selected to give information about the whole chromosome including the distal and proximal region of the chromosome arms. For acrocentric chromosomes (13, 14, 15, 21 and 22) three beads have been selected to cover exclusively the q-arms.




*KaryoLite BoBs reagents are for Research Use Only. Not for use in diagnostic procedures.*



# ARRAY CGH

## Oligonucleotide Array CGH Solution from Signature Genomics

Traditional karyotyping methods, such as FISH or G-banding, are well established for detecting chromosomal aberrations, however, these methods are limited by speed, throughput and resolution.

While these traditional methods are able to detect visible chromosomal alterations, such as an extra chromosome band, smaller gains or losses in the genome cannot be found reliably. Array CGH enables higher resolution genome analysis and allows the detection of submicroscopic chromosomal imbalances across the genome in one single experiment.

As one of the pioneers in the field of molecular cytogenetics analyses, Signature Genomics, a PerkinElmer company, has early on established cutting-edge technologies that are now the standard for detection of chromosomal abnormalities.

**Signature Genomics' newest innovation stems from the 'genotype-first' approach and provides the basis for unprecedented sensitivity. This new array design has led to a partnership between Signature Genomics Laboratories, PerkinElmer and Roche NimbleGen.**

SIGNATURE GENOMICS

NimbleGen

**This partnership allows clinical researchers access to relevant cytogenetic content through the use of robust array technology - the CGX Cytogenetics Solution.**

PerkinElmer®
*For the Better*

ARRAY COMPARATIVE GENOMIC HYBRIDIZATION TECHNOLOGY

# CGX OLIGO ARRAYS

## CGX Oligo Arrays™ are oligonucleotide-based microarrays

specifically designed, developed and validated by Signature Genomics for detection in research applications of small genetic aberrations associated with learning disability and dysmorphic features.

The 135,000 features on CGX Oligo Arrays cover regions known to be involved in cytogenetic abnormalities, including over 200 common, known syndrome regions, genes involved in development, pericentromeric regions, and subtelomeres, with a probe spacing of one probe every 35 kb throughout the genome and one probe every 10 kb in the targeted regions.

### Almost every abnormality detected by CGX Oligo Arrays can be visualized by FIS.

FISH confirmation might be required to identify structural changes and the possible source of any change. With the possibility for ordering FISH probes for confirmation purposes, PerkinElmer offers a total solution package consisting of discovery and confirmation options.

### CGX OLIGO ARRAYS CHARACTERISTICS THAT WILL BENEFIT YOUR WORK

- **135,000 features evaluated in each experiment, representing over 200 known syndromic regions, plus all 41 unique subtelomeric regions, and all 43 unique pericentromeric regions**
- **Probe spacing of one probe every 35 kb throughout the genome, and one probe every 10 kb within targeted regions**
- **Pseudoautosomal probes detect sex chromosome numerical abnormalities**
- **Pericentromeric probes detect marker chromosomes**
- **12-plex, 6-plex and 3-plex formats allowing laboratories to adjust throughput**

*CGX Oligo Arrays are Research Use Only products.*
*Not for use in diagnostic procedures.*
*CGX Oligo Arrays are designed by Signature Genomics and manufactured by Roche Nimblegen.*

# CGX HYBRIDIZATION SYSTEM

## CGX Hybridization System

added to your DNA microarray processing workflow will improve throughput and produce consistent and reproducible results. The 4-bay system is a compact benchtop instrument representing an optimal microarray processing solution.

- **Active Mixing**
  Improves hybridization kinetics; ensures uniform hybridization.
- **Consistent Data**
  Reproducible results; increased sensitivity and specificity.
- **Easy-to-use Components**
  All four bays can be accessed independently to allow continuous use of the system.


### 4-BAY HYBRIDIZATION SYSTEM - MAIN SPECIFICATIONS

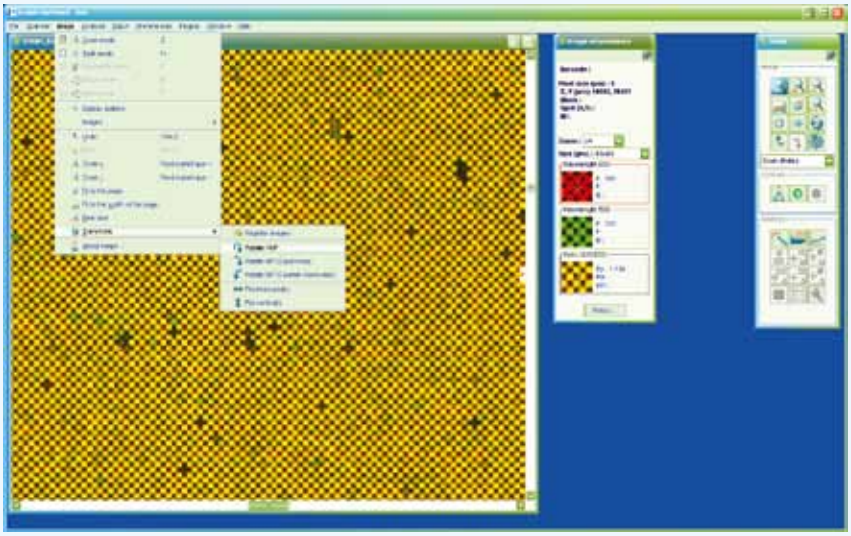
- **Physical dimensions: 200 x 370 x 170 mm³**
- **Weight: 7.9 kg**
- **Capacity: 4 slides**
- **Slide formats: 24.9 - 25.5 mm x 75.4 - 76.4 mm**
- **Incubation temperature range: 42 - 65°C**
- **Temperature control precision: ±1.0°C**

# SCANNING AND VISUALIZATION

## Fast and Sensitive Scanning with ScanRI

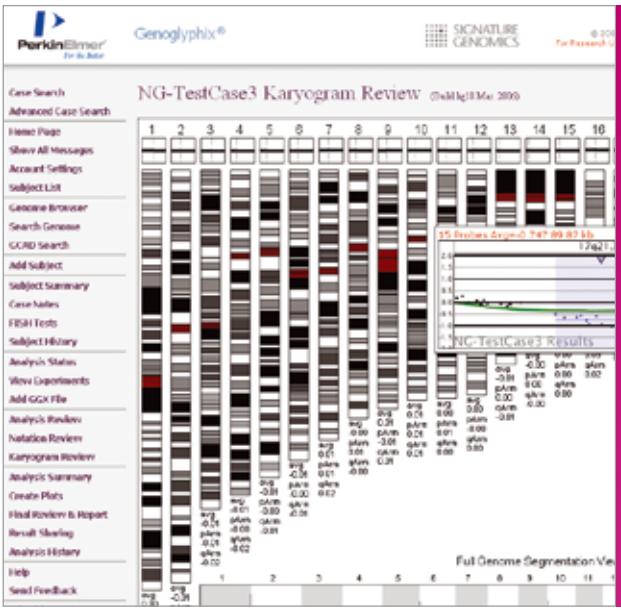
ScanRI™ is one of the fastest microarray scanners on the market enabling the capture of images in approximately 20 min when scanned at 3 µm resolution.

It provides simultaneous 2-color image acquisition with scanning resolution from 3 µm to 40 µm. Combined with its small size, low background noise and high sensitivity, ScanRI provides an attractive solution for array users.



### SCANRI SCANNER - MAIN SPECIFICATIONS

- **Weight 15.5 kg**
- **Dimensions 278 x 457 x 369 mm³**
- **Laser excitation wavelengths of 532 nm and 635 nm**
- **Simultaneous 2-color scanning**
- **Scanning resolution from 3 µm to 40 µm**
- **Low background noise and high sensitivity**
- **Uniform scanning across the microarray slide**




# PERKINELMER ARRAY SOFTWARE SOLUTIONS

## Genoglyphix: turning 50,000 samples into meaning

A powerful data visualization software and database, based on the analysis of over 50,000 cytogenetic samples already (and still growing), Genoglyphix® turns complexity into meaning. Designed and used by cytogeneticists Genoglyphix offers a proven analysis solution with an intuitive and complete workflow including sample tracking, aberration characterization, data interpretation, report creation utility, and data sharing options with other Genoglyphix users.

### Designed by cytogeneticists for cytogeneticists

Genoglyphix sets a new standard for array based cytogenetics analysis. Developed by Signature Genomics Laboratories and available exclusively with CGX arrays, Genoglyphix genome browser software provides intuitive data visualization and annotation features for streamlined and rapid analysis of CGX data.

*Genoglyphix software is for Research Use Only. Not for use in diagnostic procedures.*

### GENOGLYPHIX – BRINGING MULTIPLE GENETIC DATABASES INTO ONE TOOL

- **A database of over 15,000 genetic alterations identified in over 50,000 samples**
- **Direct link to the database of Database of Genomic Variants (DGV)**
- **Known genes compiled with information from databases such as PubMed, DGV, OMIM,UCSC and Ensembl**
- **Secure web based (128-bit encryption) access to Genoglyphix database and software**

### GENOGLYPHIX EASILY GUIDES CYTOGENETICISTS THROUGH ANALYSIS WITH CONVENIENT TOOLS

- **Generate user defined databases with MyGCAD and add custom tracks such as abnormal results, copy number variants and analysis notes**
- **User definable reporting features**
- **Easy-to-use- workflow: sample tracking, aberration characterization, data interpretation, report creation utility, and data sharing options**

**Figure 1: Data visualization in Genoglyphix**.


< Graphical representation of aberration

< Identify BAC clones

< Genes aligned by genomic coordinates with links to OMIM, PubMed, and the UCSC databases

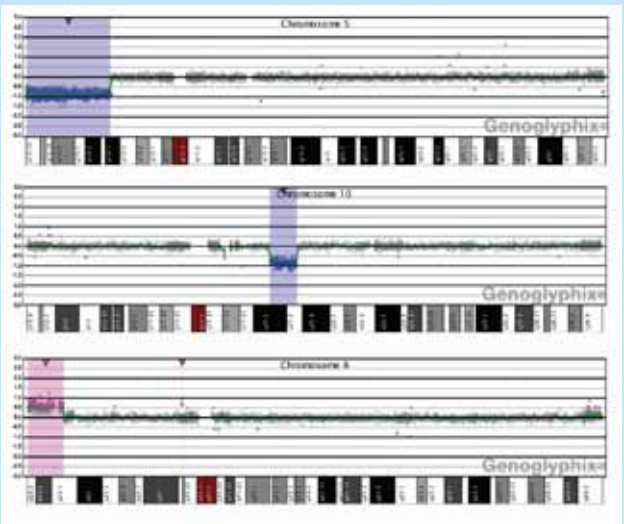
< Database of Genomic Variants

< Signature Genomics database of over 10,000 aberrations

< Track your own samples in MyGCAD

< Genes listed in the RefSeq Database

**Figure 2: Example data for various chromosomes shown in Genoglyphix.**




Top track: A 26.2 Mb deletion on chromosome 5p.

Middle track: A 6.3 Mb deletion on chromosome 10q.

Bottom track: A 9.1 Mb duplication on chromosome 8p.

# EASYAMP

## Single Cell Whole Genome Amplification with EasyAmp™

EasyAmp™ is a single cell whole genome amplification (WGA) kit that can be used when the amount of DNA is not sufficient to perform the direct analysis, e.g. research in vitro fertilization (IVF) applications on single cells. EasyAmp WGA is based on technology from Rubicon Genomics.

RUBICON GENOMICS
breaking the sample barrier

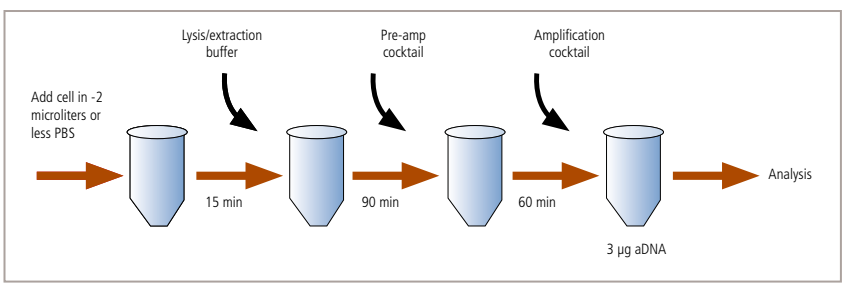
### Reliable and Reproducible Amplification Technology

EasyAmp enables the researcher to obtain the amount of DNA from only one cell that previously required over 10,000 cells for subsequent analyses. EasyAmp, in contrast with other single cell amplification methods, delivers amplified genomic DNA that reproducibly represents all sequences with low allele drop out. EasyAmp can be used on polar bodies, blastomere or blastocyst cells for preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) research applications.

### RAPID AND ROBUST ONE-TUBE PROTOCOL

- **Simple 1-tube, 3-step and 3 hour protocol**
- **Eight components sufficient to perform 50 (or 12) reactions**
- **About 1 million fold amplification of a single cell to produce 3-5 micrograms of DNA**
- **Low background**
- **Reproducible locus amplification**
- **No allele bias**

*EasyAmp reagents are for Research Use Only. Not for use in diagnostic procedures.*




The EasyAmp™ whole genome amplification process amplifies a single cell's DNA approximately one million-fold to give 3-5 micrograms of amplified DNA.

# ORDERING INFORMATION

| Product Number | Product Name | Comments |
|---|---|---|
| **BACS-on-Beads** | | |
| 3100-0020 | Prenatal BoBs™ | |
| 4500-0020 | Constitutional BoBs | Research Use Only |
| 4501-0010 | KaryoLite™ BoBs™ | Research Use Only |
| 4502-0010 | EasyAmp 50 reaction WGA kit | Research Use Only |
| 4503-0010 | EasyAmp 12 reaction WGA kit | Research Use Only |
| 1014-0020 | Luminex® 200 w/ xPONENT® | |
| 5012-0010 | BoBSoft research Analysis Software | Research Use Only |
| 5012-0020 | BoBsoft™ Analysis Software | |
| **CGX** | | |
| 4092-0010 | CGX-3 array 2/pack | Research Use Only |
| 4093-0010 | CGX-3 array 4/pack | Research Use Only |
| 4094-0010 | CGX-3 10 mixers/pack | Research Use Only |
| 4095-0010 | CGX-6 array 1/pack | Research Use Only |
| 4096-0010 | CGX-6 array 4/pack | Research Use Only |
| 4097-0010 | CGX-6 10 mixers/pack | Research Use Only |
| 4098-0010 | CGX-12array 1/pack | Research Use Only |
| 4099-0010 | CGX-12array 2/pack | Research Use Only |
| 4100-0010 | CGX-12 10 mixers/pack | Research Use Only |
| 4101-0010 | CGX Hybridization Kit (small) | Research Use Only |
| 4102-0010 | CGX Hybridization Kit (large) | Research Use Only |
| 4103-0010 | CGX labeling and hybridization control kit for 96 samples | Research Use Only |
| 4104-0010 | CGX Sample Tracking Control Kit | Research Use Only |
| 4105-0010 | CGX Wash Buffer Kit | Research Use Only |
| 4106-0010 | CGX Dual-Color DNA Labeling kit for 24 samples | Research Use Only |
| 4107-0010 | CGX Dual-Color DNA Labeling kit for 96 samples | Research Use Only |
| 1015-0010 | Hybridization System 4 | |
| 1013-0010 | ScanRI | |
| 1013-0020 | ScanRI PC | |
| 5016-0010 | Genoglyphix SW | Research Use Only |

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ISO 14001
OHSAS 18001

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1244-9963-02, January 2012 Printed in Finland