

## Product survey: Microarrays

# Jam-packed Features

Though some people predict that DNA microarrays will be displaced in the near future by next generation sequencing techniques, they are still the premier choice for most researchers performing gene expression studies. Not forgetting protein microarrays, which are on the fast lane to becoming essential tools in proteomics.

When Patrick Brown tinkered with the first printed DNA microarray slide in his lab at Stanford University in the early nineties, he was probably unaware that he had just kick-started a new era in molecular detection techniques. Starting with less than 300 microarray-related papers in 2000, the number of microarray manuscripts has skyrocketed since to around 6,000 at the end of the decade. Though the majority of these papers still deals with DNA microarrays used to compare the expression of a given set of genes, non-DNA microarrays, such as peptide arrays, antibody arrays, carbohydrate arrays or even whole cell arrays, are rapidly gaining ground.

DNA microarrays are printed by spotting oligonucleotides onto glass microscope slides with a non-contact microarray spotter, which works similarly to ink jet or bubble jet printers. Instead of ink, however, the printer expels tiny spots of DNA-probes onto the glass surface. Alternatively, DNA microarrays may also be prepared with contact printers that deposit the probe solution directly on to the surface via special print pins. The printed spots or features usually reach sizes of about 100 to 150  $\mu\text{m}$ , leaving enough space to place about 10,000 to 30,000 features on a single microscope slide. DNA microarrays are typically spotted with 200 to 800 bp (base pairs) long double-stranded DNA fragments, e.g. PCR amplicons and cDNAs, or short oligos having 25 to 85 bp. Printed microarrays are favoured by many labs working with “home-brewed” microarrays since the printing procedure is relatively easy and cheap and one may adopt the probes quickly to new findings, e.g. newly-sequenced genes.

### Photolithography instead of printer

About the same time as Patrick Brown presented the printed microarray format, Affymetrix co-founder Steve Fodor, independently came up with a completely different solution to manufacture DNA microarrays. His idea was to apply semiconductor-based photochemistry to synthesise ol-

igos directly on the surface of small quartz wafers (*in-situ* synthesised oligonucleotide microarrays), instead of spotting presynthesised oligos on glass slides. In the first step of this technique, which allows very high densities of more than one million features per microarray, linkers with light sensitive protection groups are attached to the wafer's surface. The linkers are deprotected as soon as the surface is exposed to UV light and covalently bind to added nucleotides (also carrying a light-sensitive protection group at one end). The trick is to direct the UV light through a lithographic array mask, acting as a filter that either blocks or transmits light and thus protects or deprotects individual features in the presence of adenine, cytosine, thymine or guanine. Usually several rounds of masking, light exposure and nucleotide addition are repeated until the oligos reach a length of 20 to 25 bp. To increase the specificity of *in-situ* synthesised microarrays, targets are probed with multiple oligos; typically 11 oligos are applied per 600 bases.

A slightly different approach to generate high density microarrays has been introduced by the US company NimbleGen (now Roche NimbleGen). NimbleGen's engineers have replaced Affymetrix' lithographic mask with a virtual or “digital” mask created by a micromirror device. Roche NimbleGen arrays are quite similar to GeneChip microarrays from Affymetrix with respect to density; however, the oligos are considerably longer (60 bp) and thus more specific than the short GeneChip oligos (20 to 25 bp).

*In situ* syntheses of microarray oligos is not necessarily bound to lithographic or digital masks and quartz wafers. Researchers at Agilent Technologies have developed

an *in situ* printing technique that enables inkjet printing of oligos directly on the glass slide surface. In the first round of the printing cycle a non-contact inkjet printer delivers a few picolitres of nucleotide solution to the activated microarray surface and the nucleotide is coupled to the surface through classical phosphoramidite chemistry. In the next round, the printer places a second nucleotide drop upon the first layer and the nucleotide is again coupled to the first nucleotide via standard phosphoramidite chemistry. The cycles are simply repeated 60 times to get the typical 60-mer-oligo of an Agilent microarray.

Similar to DNA microarrays, protein microarrays are prepared by spotting peptides or proteins on glass slides or other carriers via contact-splotters or non-contact microarrayers. To

immobilise the proteins, the slide surface is usually modified. Typical coatings for protein microarray slides are nitrocellulose, acrylamide, nickel (for affinity attachment of His-tagged proteins) or aldehyde and epoxy groups that covalently bind proteins.

### Different formats

Protein microarrays may be subdivided into three different categories: analytical, functional and reverse protein microarrays. Typical analytical protein microarrays are antibody arrays spotted with an antibody library and probed with a protein solution to measure, for example, binding affinities or protein expression levels. Functional protein microarrays in contrast are arrayed with functional proteins or protein domains to study protein interactions, while reverse arrays are spotted with lysed cells and are probed with antibodies against the proteins of interest.

HARALD ZÄHRINGER



Reminiscent of a microarray painting, however, Paul Klee's work “Ancient sounds” dates back to 1925.

Microarrays					
Company/Distributor	Name of Product	Nature of Probe	Arrays per Slide / Probes per Array / Array Size	Miscellaneous, Specialities, Generally	Price [EUR]
<b>Active Motif</b> Belgium www.activemotif.com <b>Contact:</b> Phone +32 2-653-0001 eurotech@activemotif.com	Modified Histone Peptide Array	Novel peptide array to simplify histone modification screening: probes consist of 19mer histone H2A, H2B, H3 and H4 peptides which may contain as many as four modifications on each peptide to analyse the effects of neighbouring modifications on site recognition and binding	Array per Slide: 1 Probes per Array: 768 spots (384 peptide spots in duplicate) Array Size: standard microscope slide (26 x 76 mm)	Unique panel for histones and histone modifications – Up to 4 modifications per peptide – Study antibody, protein or enzyme interactions – Free analysis software available online	350.- (1 array) 1,400.- (5 arrays)
<b>Affymetrix</b> www.affymetrix.com	Genome-Wide Human SNP Array 6.0	--	--	Unbiased selection of 482,000 SNPs; historical SNPs from the SNP Array 5.0 – Selection of additional 424,000 SNPs – Tag SNPs – SNPs from chromosomes X and Y	On request
	DMET Plus Premier Pack DMET Plus Starter Pack	The DMET Plus Panel provides coverage of a wide range of genetic variations	--	1,936 drug metabolism markers in 225 genes – Markers in all FDA-validated genes – More than 90 percent of the ADME Core markers as defined by the PharmaADME group	On request
	GeneChip Human Mapping 250 K Nsp Array	--	--	Assessing loss of heterozygosity (LOH) and uniparental disomy (UPD) – Determining gross chromosomal breakpoints – Defining parent of origin for copy number change	On request
	Cytogenetics Whole-Genome 2.7 M Array	--	--	The Affymetrix Whole-Genome 2.7 M Array enables the detection of known and novel aberrations across the entire genome	On request
	GeneChip Human Mitochondrial Resequencing Array 2.0	--	--	Analysis of mitochondrial mutations is informative for a variety of applications from disease genetics to forensic identification	On request
	GeneChip Universal Tag Arrays	--	--	Available in 3 K and 5 K configurations	On request
<b>Agilent</b> www.genomics.agilent.com	Custom CGH Microarrays	Current content source databases include human, mouse, and rat	Multiple formats - High-Definition: 1 x 244 K, 2 x 105 K, 4 x 44 K, and 8 x 15 K; SurePrint G3: 1 x 1 M, 2 x 400K, 4 x 180 K, 8 x 60 K	Design your own custom microarrays at no cost with Agilent's eArray application – Printed using Agilent's 60-mer SurePrint technology – Customizable number of slides per kit	On request
	Human Genome CGH Microarrays	Coding/non-coding human sequences represented / Probes annotated against UCSC hg18	Slide format depends on microarray. Can be purchased as a kit of five or as a single slide	0.5 µg total genomic DNA input requirement – All slide formats printed using Agilent's 60-mer SurePrint technology	On request
	Model Organism CGH Microarrays	Probes annotated against indicated sources	--	Coding and non-coding sequences represented – Format-dependent overall median probe spacing – 0.5 µg total genomic DNA input requirement	On request
	Mouse Genome CGH Microarrays	--	Slide format depends on microarray. Can be purchased as a kit of three, five or as a single slide	0.5 µg total genomic DNA input requirement – Format-dependent overall median probe spacing – All slide formats printed using Agilent's 60-mer SurePrint technology	On request
	Rat Genome CGH Microarrays	--	Slide format depends on microarray	Format-dependent probe spacing – 0.5 µg total genomic DNA input requirement	On request
	Human Genome CGH + SNP Microarrays	--	Slide format depends on microarray	Detect copy number changes and LOH/UPD on a single microarray – Format-dependent overall median probe spacing	On request
	Human Encode ChIP-on-chip Microarray	Probes total represented within specific ENCODE regions of chromosomes 1-22	1 x 244 K slide format printed using Agilent's 60-mer SurePrint technology. Slide contains one 244 K microarray	Each Human Encode microarray is optimized using validated probes proven to deliver the robust hybridization and optimal binding critical to reliable data	On request
	Human Promoter Microarrays	Empirically validated probes of the highest quality	Slide can be G3-formatted with two 400 K or one 1 M microarrays or with high-definition format of one 244 K microarray	Human transcripts used based on RefSeq – Enriched content sourced from UCSC human genome (hg) databases – Available as a single slide or as a 5-slide kit	On request

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<b>Agilent</b> (continued)	Model Organism ChIP-on-chip Microarrays	Probe number depends on species	4 x 44 K and 1 x 244 K slide formats printed using Agilent's 60-mer SurePrint technology	Microarrays can be purchased as a 2-slide set or, in some cases, as a single slide	On request
	Mouse Promoter Microarrays	Empirically validated probes of the highest quality	Slide can be G3-formatted with two 400 K or one 1 M microarrays or with high-definition format of one 244 K microarray	Mouse transcripts used based on RefSeq - Enriched content sourced from UCSC Mus musculus (mm) databases - Available as a single slide or as a 5-slide kit	On request
	Human DNA Methylation Microarrays	Probes annotated against UCSC HG18	244 K slide format printed using Agilent's 60-mer SurePrint technology	27,627 expanded CpG islands and 5081 UMR regions - One slide per kit - Slide contains one 244 K microarray	On request
	Human Gene Expression Microarrays	Updated content providing full coverage of human genes and transcripts	Each slide contains eight 60 K microarrays or four 44 K microarrays, and can be purchased as a kit or as a single slide	Enriched content sourced from RefSeq, Ensembl, UniGene Human Genome, and GenBank databases	On request
	Model Organism Gene Expression Microarrays	5,208 or 43,803 probes depending on species	8 x 15 K or 4 x 44 K slide format printed using Agilent's 60-mer SurePrint technology	1 slide per kit. Slide contains either four 44 K or eight 15 K identical microarrays	On request
	Mouse Gene Expression Microarrays	Updated content providing full coverage of mouse genes and transcripts	Each slide contains eight 60K microarrays or four 44K microarrays, and can be purchased as a kit or as a single slide	Enriched content sourced from RefSeq, Ensembl, RIKEN, GenBank, and UniGene	On request
	Rat Gene Expression Microarrays	Updated content providing full coverage of rat genes and transcripts	Each slide contains eight 60K microarrays or four 44K microarrays, and can be purchased as a kit or as a single slide	Enriched content sourced from RefSeq and UniGene databases	On request
<b>ATG:biosynthetics</b> Merzhausen, Germany www.ATG-biosynthetics.com <b>Contact:</b> Lorenz Engel Phone +49 761-8889424 inquiry@ATG-biosynthetics.de	PepID - bioPeptides: for mapping and validating epitopes and identifying protein-protein interactions	Mono- and polyclonal serum antibodies and also protein fragments in case of protein-protein interaction analyses	Custom made MicroArray densities	Once generated biopeptides can be easily reproduced in constant quality in any amount - bioPeptide - Libraries are delivered tagged with carrier proteins like GST and/or GFP/YFP etc.	On request
<b>BadenBioTec</b> Denzlingen, Germany www.badenbiotec.com <b>Contact:</b> Patric Zeltz Phone +49 7666-884856-0 info@badenbiotec.com	Custom-made Protein Arrays	Recombinant proteins - Native proteins	ApS: 1/8/16/MTP-wells PpA: 10000/500/150/120 AS: 600 x 20 / 5 x 15 / 2 x 15 / 3.5 x 3.5 mm	Various surface chemistries - 8- or 16-chamber Slide Assemblies with 96/384-well MTP-Array-Holders - Standard 96-well MTP flat bottom plates - OEM production	On request
	Custom-made Nucleic Acid Arrays	DNA: Oligo to YACs RNA Various spacers	ApS: 1/8/16/MTP-wells PpA: 10000/500/150/120 AS: 600 x 20 / 5 x 15 / 2 x 15 / 3.5 x 3.5 mm	Various surfaces chemistries - 8- or 16-chamber Slide Assemblies with 96/384-well MTP-Array-Holders - Standard 96-well MTP flat bottom plates - OEM production	On request
	4096 Hexamer Array	Fully redundant Hexamer array	ApS: 1 PpA: 5000 AS: 52 x 16,5 mm	Inert 38-atom spacer - No additional nucleic acid stretches - Covalent coupling - Optimal probe accessibility - Ideal for protein-nucleic acid interaction studies	250.-
<b>BioCat</b> Heidelberg, Germany www.biocat.com <b>Contact:</b> Elke Gamer Phone +49 6221-7141516 gamer@biocat.com	GenoExplorer microRNA Chips (Human, Mouse, Rat, <i>C. elegans</i> , <i>Drosophila</i> , <i>Arabidopsis</i> )	DNA Oligos (30 nt average length), functionally validated, spotted in triplicates	Number varies depending on species - One chip contains oligos for all miRNAs (mature and precursor) as registered and annotated in the latest version of miRBase at the Wellcome Trust Sanger Institute for that particular species plus controls (5S rRNA, tRNAs, U6) - Also available as species-specific miRNA probe sets	Detection of less than 2-fold differential miRNA expression - Highly reproducible results with CV < 15% between experiments - High signal-to-noise ratio and subfemtomole sensitivity with only 1 µg total RNA input - Specificity of up to 94% - > 3 logs of dynamic range	1,390.- (4 chips, plus hybridization buffer) 1,530.- (Full kit, including 4 chips, labeling and detection reagents, hybridization & wash buffers)
	Biotin Label-based Antibody Arrays (Human, Mouse, Rat)	Antibodies	Human: 507 antibodies/array Mouse: 308 antibodies/array Rat: 90 antibodies/array Different formats available: 2 arrays/slide for processing 2 samples or 4 arrays/2 slides for processing 4 samples	Simultaneous detection of multiple target proteins including cytokines, chemokines, growth factors, angiogenic factors, proteases, soluble receptors in serum or cell culture supernatants - High detection sensitivity, as low as pg/ml level - Direct biotin labeling of proteins, no need for antibody pairs	Depending on antibody array selected

Microarrays						
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<b>BioCat</b> (continued)	Antibody Arrays (Human, Mouse, Rat)	Antibodies	19-174 antibodies/assay Different formats available: 4 arrays/slide or 8 arrays/slide	As little as 10 µl of sample is needed for one array – Up to 8 samples/slide can be processed, much higher throughput than with membrane arrays – Antibody arrays available for many research areas, e.g. Adipokines, Angiogenesis, etc. – Arrays contain internal controls suitable for biomarker discovery – More economic than membrane-based arrays	Depending on antibody array selected	
	Tissue Microarrays (Paraffin & Frozen)	Different normal and/or malignant tissue cores	Hundreds of tissue cores per glass slide	Ideal for target validation and antibody characterization – Suitable for immunohistochemistry and <i>in situ</i> hybridization – Specimens selected to be highly representative for the tissues – Rigorous quality control ensures intact, valid and consistent cores – Normal frozen tissue arrays designed in close conformance with FDA guidelines also available	Depending on tissue microarray selected	
<b>Greiner Bio-One</b> Frickenhausen, Germany www.gbo.com/bioscience <b>Contact:</b> Dirk Leinberger (PapilloCheck) Phone +49 7022-948-0	PapilloCheck	DNA probes	ApS: 12 arrays per slide PpA: 24 different probes per array AS: Standard slide	Genotyping of 24 different HPV types – CE-IVD included control system – Automated analysis	On request	
	Cytolnspect	DNA probes	ApS: 12 arrays per slide PpA: 40 different probes per array AS: Standard slide	Detection of 40 mycoplasma species for quality control of cell culture based biologicals in pharma and biotech	On request	
	Björn Breth (Cytolnspect and CamoCheck) Phone +49 7022-948-0	CamoCheck	DNA probes	ApS: 12 arrays per slide PpA: 8 different probes per array AS: Standard slide	Detection of 8 animal species (pig, cow, chicken, turkey, sheep, goat, donkey, horse) in food and complex composition products	On request
	Bianca Priester (ParoCheck 10 and ParoCheck 20) Phone +49 7022-948-0	ParoCheck 10	DNA probes	ApS: 12 arrays per slide PpA: 10 different probes per array AS: Standard slide	Detection of 10 bacteria associated with periodontitis in human subgingival plaque samples	On request
	ParoCheck 20	DNA probes	ApS: 12 arrays per slide PpA: 20 different probes per array AS: Standard slide	Detection of 20 bacteria associated with periodontitis in human subgingival plaque samples	On request	
<b>Intavis</b> Köln/Heidelberg, Germany www.intavis.com <b>Contact:</b> Daniel Maisch Phone: +49 6221-6582553 maisch@intavis.com	CelluSpots Peptide Arrays, CelluSpots Kinase Substrate Arrays	Custom peptide arrays and pre-made kinase substrate arrays	Custom layout of arrays – Up to 768 peptides per slide – Arrays are spotted onto coated microscope slides	3-D structure for high peptide densities	Starting at 75.- (Custom array for 60 identical arrays)	
<b>Oxford Gene Technology</b> Oxford, United Kingdom www.ogt.co.uk <b>Contact:</b> Ruth Burton Phone +44 1865-856848 ruth.burton@ogt.co.uk	CytoSure ISCA UPD (4 x 180 k)	<i>In-situ</i>	ApS: 4 PpA: 180,000	Detects SNPs and CNVs	On request	
	CytoSure ISCA (4 x 44 k)	<i>In-situ</i>	ApS: 4 PpA: 44,000	Targeted ISCA design	On request	
	CytoSure ISCA v2 (8 x 60 k)	<i>In-situ</i>	ApS: 8 PpA: 60,000	Targeted ISCA design	On request	
	CytoSure ISCA v2 (4 x 180 k)	<i>In-situ</i>	ApS: 4 PpA: 180,000	Targeted ISCA design	On request	
	CytoSure Syndrome Plus v2 (2 x 105 k)	<i>In-situ</i>	ApS: 2 PpA: 105,000	Syndromes and whole genome	On request	
	CytoSure DMD (4 x 44 k)	<i>In-situ</i>	ApS: 4 PpA: 44,000	Targeted DMD array	On request	
	CytoSure Chromosome X (4 x 44 k)	<i>In-situ</i>	ApS: 4 PpA: 44,000	Chromosome X focussed	On request	
	CytoSure Chromosome X (2 x 105 k)	<i>In-situ</i>	ApS: 2 PpA: 105,000	Chromosome X focussed	On request	
<b>PEPperPRINT</b> Heidelberg, Germany www.pepperprint.com <b>Contact:</b> Volker Stadler Phone +49 6221-7264488 info@pepperprint.com	PEPperCHIP	Custom peptide microarrays – Representing proteins and stochastic sequences	Customized (1-8) – Up to 156,000 peptides – Custom and standard object slide	High content – Flexibility – Affordable – Proteomics – Serology	0,135.- (per peptide spot, 10-15mers)	

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<b>Protagen</b> Dortmund, Germany www.protagen.de <b>Contact:</b> Phone +49 231-9742-6300 info@protagen.de	UNichip Protein Microarrays	Recombinant human proteins	ApS: 1 PpA: 384 Human proteins in quadruplicate + 320 control proteins in quadruplicate  2816 Protein spots	Characterization of biotherapeutics – Ranking of specificity and pharmacokinetic – Optimization of downstream-processing	On request
	Discovery and validation services  Companion diagnostics development		For research applications custom made microarrays with up to 10,000 proteins spots are available		
<b>Roche Nimblegen</b> www.nimblegen.com	Sequence Capture Arrays	> 60 bp probes	2.1 M and 385,000 features per array	The latest genomic build from UCSC for human (HG18) – Optimized, empirically tested design algorithm (version 2.0) used for all designs	On request
	Cytogenetics (CGX) Arrays	For genome-wide analysis of DNA copy number changes with a subset of probes focused in disease-associated regions	--	Roche NimbleGen offers several types of CGH/CNV arrays for a variety of organisms to meet your specific research needs	On request
	CNV Arrays	For high-resolution CNV discovery and association studies	--	See above	On request
	CGH Whole-Genome Exon-Focused Arrays	For genome-wide analysis of DNA copy number changes with a subset of probes focused in exon regions	--	See above	On request
	ChIP-chip (chromatin immunoprecipitation on chip) microarrays and services	--	Roche NimbleGen has a wide range of ChIP-chip 2.1 M, 3 x 720 K, 385 K and 4 x 72 K designs to choose from, or you can customize the array probe set to your specifications	The existing designs include whole genome survey sets, consisting of uniform tiling arrays covering all unique regions of the human genome, and promoter array designs aimed at known promoter regions	On request
	DNA methylation microarrays	--	Roche NimbleGen offers a wide range of 2.1 M, 3 x 720 K, 385 K and 4 x 72 K DNA methylation array designs	--	On request
	Eukaryotic Gene Expression Microarrays	Broad range of eukaryotic arrays represent the latest builds for human and model genomes, incl. rat, mouse, zebrafish, <i>Drosophila</i> , <i>C. elegans</i> , yeast, and more	Roche NimbleGen offers three array formats for Gene Expression products: 12 x 135 K, 12 x 135 K and 385 K	NimbleGen microarrays enable accurate, sensitive, and specific interrogation of genome-wide expression for any sequenced and annotated genome	On request
	Prokaryotic Gene Expression Microarrays	Each expression microarray contains up to 385,000 probes per array with our 385K format and 72,000 probes per array with our 4 x 72K format	--	Roche NimbleGen offers the most comprehensive set of prokaryotic gene expression designs in the industry, covering over two hundred Class I, II, and III organisms and growing as new genomes become available	On request
	Custom designed Gene Expression Microarrays	Custom-designed arrays may be ordered for delivery (for hybridization in your own lab) for any organism	--	Custom designs may also be ordered for full service analysis	On request
	Comparative Genome Sequencing (CGS) Microarrays	29mer to 39mer	--	Efficient, high-throughput, cost-effective method for rapid, genome-wide analysis	On request
<b>Scienion</b> Berlin/Dortmund, Germany www.scienion.com <b>Contact:</b> Phone +49 30-63921700 support@scienion.com	Microarraying Service – Contract Development & Manufacturing	DNA, proteins, peptides, antibodies, antigens, glycans, cells, polymers	Tailor-made solutions: Up to 200 arrays per slide Up to 384 probes per array Up to 10000 spots per cm <sup>2</sup>	Non-contact spotting – Arrays in microtiter plates, biosensors, microfluidic chips – Tailored surface coating	On request