splice arrays is now heating up, and companies such as ExonHit of Paris, France, and Jivan Biologics of Berkeley, California, are focused entirely in this area.

Most human genes are thought to undergo alternative splicing, the process by which individual genes can produce multiple messenger RNA and protein products. These so-called splice isoforms can have different, and even opposing, functions in the cell. With the recent commercial availability of splice-variant arrays, traditional gene-by-gene studies of alternative splicing are now taking a back seat to genome-wide methods. Further study in this area should provide a better — and more complete — understanding of the functional relevance of splice variants and of disease mechanisms.

ExonHit offers its SpliceArrays on a service basis, but from this September they can also be purchased directly from Agilent. Validation of the ExonHit approach, which involves the use of both exon- and junction-derived probes to follow every splice event associated with a given gene, was featured in a recent publication in *Nucleic Acids Research*.

The company offers both custom and catalogue SpliceArrays focused on specific gene families that are of particular therapeutic interest — cytokine and apoptosis pathways, nuclear receptors and co-regulators, G-protein-coupled receptors (GPCRs) and ion channels. "We are also in the process of expanding our line into mouse," says Laurent Bracco, ExonHit's vice-president of research and technology development, with products expected around the turn of the year.

COMBIMATRIX

Desktop DNA synthesis from CombiMatrix.

Jivan has been working in this area for the past four years and offers its suite of TransExpress splice-variant microarrays, which are manufactured by Agilent. The company's products include a genome-wide splice-variant array and a suite of arrays focused on gene families such as cytochrome P450, GPCRs, ion channels, kinases, phosphatases, phosphodiesterases, proteases and proteinases. Unlike ExonHit, Jivan's splice arrays do not include exon probes. "Exon probes are neither necessary nor sufficient to measure RNA splicing and so we do not include them in our Trans Express product line. Using junction probes, however, all splicing events can be detected," says Jonathan Bingham, Jivan's chief technology officer. The company also makes arrays to user specifications, and now offers a splice-variant microarray service through MOgene of St Louis, Missouri. "The next product will be an oncology array consisting of about 2,000 genes implicated in cancer along with their splice variants," says Bingham.

At the high-density end of the market, earlier this month Affymetrix rolled out its exon-only array with a million exons on a single chip. This Human Exon 1.0 ST (sense target) array offers whole-genome, exon-level expression profiling on a single array and includes all annotated exons, as well as computationally predicted and empirically identified exon content. As such, the company says, researchers will be able to study known splicing events, as well as discover novel splice variants. GeneChip mouse and rat exon arrays are planned for later this year.

Microarrays are now a widely used technology for studying gene expression and regulation on a global scale and at high-throughput. Other applications for this technology include single-nucleotide polymorphism discovery and validation (see *Nature*, 422, 917–922; 2003) and comparative genome sequencing. The use of microarrays is also moving downstream as the first microarray-based diagnostic tests begin to trickle into the marketplace (see 'Microarrays move downstream', page 1196). The future indeed looks bright. Has it really been only ten years? ■

Diane Gershon is assistant editor, *Nature Medicine*, Technical Reports

ON THE HARDWARE FRONT

Researchers interested in printing their own microarrays in-house now have an array of options — from contact (pin or split pin) and non-contact printing methods (bubblejet or piezoelectric inkjet) to *in situ* array synthesis.

Bio-Rad Laboratories of Hercules, California, launched the BioOdyssey Calligrapher miniarrayer last month, which prints oligos, proteins or cell lysates onto slides, membranes or 96-well plates. This bench-top instrument has an eight-pin print head and prints up to 16 slides at a time. Optional extras include humidity and temperature controls. Telechem International of Sunnyvale, California, has also added humidity controls to its NanoPrint microarrayer.

A plate-arraying option is now available on the BioRobotics MicroGrid ii and GeneMachines OmniGrid Accent platforms from Genomics Solutions of Holliston, Massachusetts. This enables DNA and protein microarrays of up to 1,000 features per well to be printed in 96- and 384-well microplates, providing high-throughput, multiplexing capabilities for diagnostic, ELISA and protein–protein interaction applications.

Non-contact printers may have got a bad rap in the early days but Arrayjet of Mayfield, UK, hopes to win over researchers with its new Aj120 piezoelectric inkjet printer, which it launched in July. "Contact printing can affect the quality of the data you get because it introduces surface-based artefacts into the microarray," says Duncan Hall, sales and marketing director for Arrayjet. Pin printers can also be very susceptible to atmospheric conditions, he says, particularly when hygroscopic printing buffers are used. "We carry our sample inside the print head so there isn't any evaporation from the print head."

ARRAYJET

Arrayjet makes non-contact printing high-throughput.

The Aj120 includes a microplate stacker and lid lifter, which enables walk-away printing of microarrays from up to 48 (96- or 384-well) microtitre plates. With the standard 12-sample connector block, 100 slides (samples and replicates side-by-side) can be printed in 90 seconds, says Hall. Additional replicates can be printed on the fly in no extra time. The Aj120 prints DNA, proteins and intact cells with a 100-μm spot diameter. PerkinElmer Life and Analytical Sciences of Boston, Massachusetts, also offers contact and piezoelectric non-contact systems.

For those with deeper pockets, CombiMatrix sells a CustomArray desktop DNA synthesizer for the *in situ* synthesis of oligonucleotides on microarrays with up to 12,000 features. Synthesis occurs on a blank CombiMatrix semiconductor chip using standard phosphoramidite chemistry methods. D.G.