Going viral

Victor Bethencourt & Christopher Scott

Affymetrix was an early mover in the DNA microarray space that came to dominate the market, overcoming criticism from its users and a slew of cutthroat competitors. How did it do it?

Today, Affymetrix (Santa Clara, CA, USA) has more than 1,000 employees and can boast over 24,000 publications citing its technology. From 1995 on, it weathered criticism and defections from its primary user base, patent battles, and competition in a crowded market to expand a sector-leading customer list and dominate the research market. Last year, revenue topped $311 million, of which $69 million was ploughed back into discovery. Affymetrix now owns an estimated one-third share of a $1 billion biochip market, according to several data services. How did the company achieve its position as a market leader?

In 1989, after consultations with federal officials at the US National Institutes of Health (NIH), serial entrepreneur Alex Zaffaroni hired Stanford University's (Stanford, CA, USA) Steve Fodor to develop the first microarray at Affymax (Palo Alto, CA, USA). Borrowing approaches from the semiconductor industry, Fodor and Zaffaroni spun out Affymetrix in 1992, launching their first chip two years later. With federal and private money, the company started a series of successful R&D collaborations and consortia that were deeply rooted in the Stanford and Silicon Valley intellectual networks. The strategy used a base of NIH-funded academic researchers to fine-tune and validate its photolithographically synthesized oligonucleotide microarrays (termed 'GeneChips').

From the outset, Affymetrix targeted users in academic laboratories to generate an efficient viral marketing campaign. But using researchers to spread usage didn't always sit well with its academic customer base.

One problem was the company's approach to licensing. Many of its deals with universities sought reach-through rights to discoveries made with the GeneChips, allowing Affymetrix to capitalize on future products not containing the original technology. Because universities engage in basic, not applied, research, often leading to translational research in completely unanticipated directions, academic users were loathe to sign such agreements with restrictive intellectual property (IP) clauses. Another problem was the high price of Affymetrix scanner machines, GeneChips and reagents (starting in the region of $135,000). This restricted technology access to bigger research laboratories with bigger budgets. Lastly, the user community began to question whether longer cDNAs were better for certain applications than the short oligonucleotides used in GeneChips and grumbled about the lack of flexibility and customization in the gene sets offered by Affymetrix.

These issues opened the door to competitors. In a 1995 paper in *Science*, Stanford's Mark Schena, Dari Shalon, Ron Davis and Pat Brown described a robotic method to print 30,000 cDNA arrays. Shalon subsequently left Brown's laboratory to form Synteni (Fremont, CA, USA; later bought by Palo Alto–based Incyte Genomics) and Schena started Arrayit (Sunnyvale, CA, USA) in 1996, with a view to create more affordable microarray platforms. Several other companies also entered the crowded space, including Hyseq (Sunnyvale), Agilent (which first made scanners for GeneChips and then went on to develop its own 60-mer platform), NimbleGen (which was eventually snapped up by Basel-based Roche), Nanogen (San Diego), Caliper (Mountain View, CA, USA) and the UK's Oxford Gene Technology. But the player that eventually emerged as Affymetrix's chief competitor was Illumina (San Diego). Started in 1998, it built a competing technology that attaches oligonucleotide sequences to beads, which are then bundled into very high density arrays.

Affymetrix responded by building its patent portfolio and going after competitors with aggressive litigation. The company established a dominant patent position (now >200 patents) covering its GeneChip, scanner, detector technology and associated microfluidics as well as broader IP on the use of beads to measure nucleic acid or peptide binding for genomic analysis. At the same time, it countersued Hyseq and filed numerous lawsuits against (among others) Incyte and Oxford Gene Technology and later Illumina, alleging infringement of its IP, most of which were upheld in the courts.

Overall, Affymetrix's success can be attributed to its ability to create inertia through its network of academic users. The network created a snowball effect: those thousands of publications using GeneChips drove further use of the technology, which reinforced the brand. Many of the early, high-impact studies using microarrays sprang from authors who had some sort of affiliation to the Santa Clara–based firm, and those early studies led other researchers to duplicate the work, right down to the tools and reagents. New technologies repeated in the scientific literature gives comfort to researchers gambling their scarce resources on high-risk, discovery-based projects.

The company also dodged a bullet with its early, highly aggressive business approach, which spurred competition. By building a strong patent portfolio and pursuing aggressive litigation, however, Affymetrix quickly smacked down market interlopers that competed on price and performance. Whereas other array companies relied on big money and up-and-out business plans, Affymetrix combined its entrepreneurial vision and scientific aptitude into a mélange of strengths, even in the face of competition from possible eclipsing technologies.

Networking and collaborating within the scientific community and federal agencies were fundamental to success. Interestingly, Illumina has followed a similar approach. At the beginning of the last decade, heavy promotion of its single nucleotide polymorphism genotyping system to researchers at major genome centers in the International HapMap project drove publications and ultimately galvanized adoption of their technology by the academic community, creating a $288 million business. For these companies, finding an early market share and building and maintaining inertia translates to a tough game of catch-up for everyone else.

Victor Bethencourt is Associate Business Editor & Christopher Scott is Contributing Editor.