

nature biotechnology

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Why buy biotech?

Biotechnology companies are no longer able to turn heads with the winds of a gassy idea as they once did, and as Internet stocks are for the moment doing. For all the stern talk about biotechnology's poor business plans and scarcity of products, is it really possible to say with a straight face that Internet companies and their valuations are grounded in reality, are more concrete? The simple fact is that people who want to make a quick buck are following the latest craze. When it ends, the Internet stock implosion ought to make biotech consolidation look like a Sunday picnic.

Many biotech companies are now in the mezzanine stage, the middle years, and for many the timing of their arrival at this financial point could not be more unfortunate (see "Will investors return to biotechnology?", p.128). According to Burrill & Company, the top 20 publicly traded biotech companies accounted for approximately two-thirds of the total biotech industry market capitalization in 1998. Capital markets are for the moment investing in profitable companies and leaving the rest behind. Period.

But the timing of this flight-from-biotechnology could not be more unfortunate for investors too. For while there is still a surfeit of hair-brained biotech company schemes, there is everywhere evidence

of a mature industry coming into focus, with biotech companies that understand that IPOs are not MacArthur Foundation grants. These companies recognize their responsibilities and have products to sell and market share to claim (with 14 new drugs approved in 1998 and more on the way). Some of biotechnology's current problems are certainly of its own making—and the journal does not endorse the wild-eyed boosterism that often accompanies any scientific advance, whether incremental or earth-shattering—but there is now a significant group of companies that understand how to use the tools of the new biology to make useful, and commercially successful, products.

When confronted by the new investor litany "why should I buy biotech when I can buy Internet and make a 400% return on my investment in 3 hours?", one Wildean wag at the Hambrecht & Quist 17th Annual Healthcare Conference held last month in San Francisco said, "Well then, the next time one of your relatives gets cancer, you can send her a book from Amazon.com."

Bitter, but true. Biotechnology's financial attributes are not the only things about it that are at the moment undervalued. The smartest investors know that this will not remain so for long. There is too much of real concern and of real value up ahead.

Signal transduction 2000

Signal transduction is in some sense like the great arduous physical feats of exploration and mapping: What at first sight appears to be a straight passage across the Rockies or the Alps turns out to be an endless expedition that in some instances finds itself back where it began. The cell's signaling pathways turn out to be more reminiscent of the massively redundant, overlapping neural networks of the brain than neat Manhattan traffic grids of interacting streets and vehicles. Understanding the interactions between these pathways is intrinsic to understanding how all cellular activities are regulated.

Biotechnology took up signal transduction as a drug discovery platform 15 years ago when Stanley Crooke and George Poste organized the first pharmaceutical symposium devoted to cell signaling in the context of the new recombinant genetic technologies at Smith Kline and Beecham in 1984. It was a marvelous and seductive first sighting: All physiological functions and malfunctions depend on signal transduction. Figure out what happens at the cell surface when a cell receives a signal, and then map out how it transmits that information to the various cellular machines controlling gene expression, and you will succeed in identifying any number of drug targets and points of therapeutic intervention. Too much or too little signaling should also reveal therapeutic endpoints. But then the signal transduction expedition turned into the new particle physics expedition—a blizzard of entities with whimsical names and acronyms blew up, the hoped-for linear pathways turned out not to be linear, and many different potential targets turned out to use very similar or overlapping pathways, making accurate target selection difficult, and the development of a "big picture" even more so.

Despite the difficulties it presents, and despite the insurgence of upstart genomics, signal transduction is still in many quarters the royal road to the New World of Therapeutics. Every major pharmaceutical company has a signal transduction drug discovery program, and more than 30 smaller biotechnology companies are pursuing discovery research via this route (see *Nat. Biotechnol.* 16:1082, November 1998). The research coming out of this area is copious and rich (see, for example, Redfern et al., p. 163), and several promising signal-transduction-based compounds are in clinical trials. The fact that more than 800 delegates plan to attend the *Nature Biotechnology* Miami Winter Symposium on signal transduction and therapeutic strategies this month is testimony to the interest in all things transductive.

But what's clear from all of signal transduction's hard work is that a single field of research will not likely turn out to be the "ideal" drug discovery platform on its own. The application of powerful high-throughput genomic and proteomic approaches to signal transduction will yield more satisfying results (see *Nat. Biotechnol.* 16:1329, December 1998). Indeed, the integration of biochemical and molecular approaches, genomics, proteomics, and bioinformatics will be needed to fully illuminate the complex interactions in and between these pathways and to analyze regulation at many levels simultaneously—so there is plenty of opportunity for collaboration on all sides. It also seems clear that sophisticated computer modeling of these networks will be needed to successfully develop the "big" picture. Advances in computation should allow us to see how the system is put together in the broadest sense—where else and how quickly might the intrepid cartographers of yesterday have gone with a computer and a satellite to extend their already formidable senses!