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Biotechnology: promises, promises, promises!

Perspective:

Clerk Maxwell worked out basic theory of the electromagnetic field in 1864. The electron was discovered around 1900.

Probably no one could have fantasized the final culmination of electronics in communications, computers, ... what we now call the electronic age, and the derivative industries of broadcast radio and TV. Perhaps we still can't.

Plenty of money was to be made at almost every step of the way. Not that the original inventors and investors garnered most of the fruit. In fact, so far as I know, neither Maxwell nor Kelvin got anything but scientific immortality as reward for their efforts.

For BIOTECH, 1864 translates to about 1944, with Avery's discovery at the Rockefeller Institute. (He never got a dime either). And 80 years after the electron, during the last decade did we begin to see the first practical fruits of these DNA discoveries. Of course the time frames are much compressed today, in large measure from the intensity of capital investment in technology; in part from the technical power of the electronic tools; in part from the enormous growth of the S&T research community.

So, looking ahead, a few words on the promise and the promises of biotechnology.

We've seen the first wave of commercialization -- using biotech to make things that we already knew were valuable, but did not know how to produce economically. Interferon and erythropoietin are good examples.

DNA research now is mostly focussed on discovering new things, products and processes we know little about. How cancer occurs. How viruses infect and can be blocked. How genes go bad and engender birth defects. How the embryo develops into a person. How we age.

This growth of understanding of intracellular process far outweighs the products that can be patented, commercialized and exploited by venture investment. When a product does emerge, it will be a new discovery -- with all the potential advantage of uniqueness, and all of the burdens of proof of safety and efficacy.

And so we are finding, with a sometimes bitter realization, that

a) the majority of exciting ideas on which so many companies are founded just don't pan out, and

b) many that are inherently sound will take years of humble and patient effort to get through the approval process. "humble and tedious" -- whose vocabulary do these words belong to?

What a contradiction in temperament with the gung ho, daring and impatience of original inventors, entrepreneurs and investors!
So of course we will see much disillusion and outright failure -- you know of a tragic example every month. And the public suffers too when the lifesaving potential of an interleukin-2 or a Centotoxin is held up by unrealistic and unhumble expectations.

So, there is a lesson, widely recognized. Lots of flaky ideas have attracted too many dollars; but even good ideas are just the first step. They need to be disciplined by a skilled management which must reconcile two contradictory mores:

1) the creative elan of R

2) the nose for everything that might go wrong in D.

But, it's not really that different in working out basic strategies

in the academic research lab. Our mistakes may be in 7 rather than 10 figures.

There is plenty of room to get rich in this setting. But not much to get rich quick, ~~except by the manipulation of Fortune or by selling paper to the greater fools, who may even find greater than themselves.~~ at least not on the fundamentals, and barring a few flukes of fortune and the playing out of the greater fools principle, one of the cosmic invariants of the financial game.

As the saying goes, my best friends are in this industry; there are few who can excel them at the top. And I have to record how much academic research is in debt to industry for such developments as PCR, which have truly revolutionized how we go about our business, and will surely do the same for diagnostics. I don't know a single basic biological research lab in the country that doesn't use PCR!

I have worked very closely with the biotech industry since it started in 1971, and for 20 years before that with pharm. and fermentation

Some final words, back to science.

1) We will see a larger proportion of biological interventions emerge from biotech, as opposed to products: cell transplants or infusions, often aided by new growth factors. Domesticated viruses for some kinds of somatic gene therapy. Diagnostic probes using cells in culture. Genetically engineering animals and their tissues. All this will shift the value added from the procedures, and the revenue taken, back to professional services rather than industrial vendors. Manufacturers of MRI machines hardly get the lion's share of the fees. And of course, the doctors write the prescriptions and have the greatest voice in these allocations.

From televisions pots to embryonic stem cells (like elephants)

2) The most exciting new technology I see emerging right now is "Antisense RNA". These are probes for specific segments of the genetic code that can, in principle, be used to home in on almost any target you wish to define in, say, a sick cell or an invading virus. They use the basic biological mechanism of strand pairing, of the

DNA double helix, as the source of their exquisite specificity. The applications are open-ended, including the stimulation as well as inhibition of stated biological functions. So we could enhance immunity or squelch a cancer. I have no doubt many examples of efficacy will be forthcoming; but we have hardly begun to think, hardly know how to think about the potential safety problems. Nor do we have much to go on in natural history to guess about those potentials. At the very minimum, we will have to be sure that one and only one target is there in the genome, the one we're after. And we have to look out for the same individual variability that we rely on for DNA fingerprinting; so testing one person's DNA will hardly be enough, nor will it just be a matter of looking up the DNA sequences on the master tape generated by the Human Genome Project.

3) Recall that there are at least 100,000 genes in the human, perhaps twice as many protein products (taking account of differential splicing and post-translational modifications). I'm sure that several percent, perhaps 10,000 of these will have significant applications. Can we foresee 10,000 biotech drugs in active development? FDA can hardly cope with 10 in one year. And where will the (modestly estimated) trillion dollars of capital come from (calculated at a mere 100MM per throw)? Well, I suppose $10B per year for a century is not altogether out of sight -- but that's the point, a century! Meanwhile, we have an enormous task of triage, to know that we're not merely pursuing good ideas, but only the best and the most feasible of them, from every standpoint: of scientific plausibility, of safety testing, of economic producibility, of the marketing at the far end of the cycle. New York is the great meeting place -- as this meeting shows -- of the crucial actors. I suggest we could go much further than we already do in harnessing the critical intelligence of our academic people with what you do in capital

Who is to do that weeding

must follow the seed + the fertilizer

allocation, and counterbalance the understandable enthusiasm of the interested proponents.