DDT Vol. 8, No. 19 October 2003

Mark Chandler discusses Rules-Based Medicine and multi-analyte profiling

Interview by Stephen L. Carney

Mark Chandler, CEO and Chairman of the Board, Rules-Based Medicine

Mark Chandler founded Rules-Based Medicine (RBM) in 2002 and serves as Chief Executive Officer and Chairman of the Board. Before heading RBM, he founded Luminex Corporation in May 1995, serving as Chairman of the Board and Chief Executive Officer. In 1982, he founded Inland Laboratories, which provides plant and bacterial toxins to the medical research community. As President and CEO of Inland, he received the KPMG Peat Marwick High Technology Entrepreneur of the Year award in 1987. Dr Chandler established the Foundation for a Healthier World in 2003 to apply the large-scale multi-analyte profiles created by RBM to health care issues in the developing world. Supported by Dr Chandler and major corporate contributors, the foundation will also undertake disease surveillance and epidemiological studies to further the understanding of infectious disease worldwide. Dr Chandler received his PhD in immunology from the University of Texas Southwestern Medical School in Dallas in 1981. He is a fellow of the Explorer's Club and serves on the board of the EastWest Institute.

Could you describe the early defining events that shaped your development as an entrepreneurial scientist?

When I was getting my doctorate, there was a fortuitous convergence of interest and opportunity in that I was working on a group of toxins, such as ricin, that were just achieving commercial potential. Developing a market for these toxins involved discovering new toxins with novel properties. Because these compounds are primarily found in the leaves, seeds or roots of plants from equatorial jungles, I was able to build a successful business, Inland Laboratories, while indulging a long-held wanderlust.

Did you have a particular role model in this respect?

Everybody who started a biotechnology business in the early 1980s looked to the founders of Genentech. When I was getting my doctorate at Southwestern Medical School, entrepreneurial activities in the biotechnology business were not considered an option. One would either teach at a medical school or university, or go into research at a pharmaceutical company. The people at Genentech started with an idea and built it into a great company. They are the role models for anyone in biotechnology. Amgen came along a few years later to reinforce the concept.

You have a long history of recognised entrepreneurial success, for example the KPMG Peat Marwick High Technology Entrepreneur of the Year award in 1987. What factors have been key to your success?

Interestingly, I shared that award in 1987 with an obscure fellow named Michael Dell. Since then he has left me far behind, but I'm still doing things that I find interesting.

I have been fairly successful at looking ahead and seeing how things might change if new technology could be brought to bear on a particular problem. That has happened throughout my career in a logical progression. Luminex Corporation's Multi-Analyte Profiling (MAP) technology evolved from a need to very accurately detect multiple, potentially deadly contaminants in the toxin products worked on at Inland Laboratories. Rules-Based Medicine, my current company, has developed the ultimate application of the Luminex technology in the form of comprehensive screens of hundreds of blood biochemicals from a very small sample. RBM MAPs are now used throughout the pharmaceutical and biotechnology industries.

What advice would you give to a young scientist who has an idea that they would like to develop commercially?

It is becoming increasingly difficult for a small company to take a single idea and make it a success without corporate partners. Even financing is different than it was three years ago. Today I would advise any young scientist with a great idea to find angel investors who understand the industry. Friends and family are good sources of start-up funds for many businesses, but they are probably not the best source of funds for a biotechnology venture. Additionally, you need board members who are experienced in the industry. They can be a tremendous resource for the entrepreneur as he or she begins to build a network of customers and collaborators.

Your most recent companies have dealt with multi-analyte testing. Where do you think this technology will be in the next five to ten years?

There are obvious applications now for MAPs. One that has already achieved commercial success is in the area of tissue matching for organ transplantation. Additionally, many companies are bringing to market tests for the mutations of cystic fibrosis based on Luminex technology. However, neither of these applications approach the market potential of comprehensive biochemical imaging. The ability to accurately measure hundreds, and eventually thousands, of serum analytes will redefine the definition of many diseases and allow a more thorough look at the action of therapeutic drugs on a broad range of biochemical systems.

In your opinion, what will be the defining factors that will allow the wider uptake of your technology – from target validation to lead identification and optimisation, in clinical trials and in diagnostics and prognostics?

Impacting the time-to-market for pharmaceutical companies that are using our product, or improving the detection of early safety problems with a drug, will drive adoption of the technology. If we can prevent a Baycol from happening again, the whole pharmaceutical industry will

  PII: S1359-6446(03)02861-7

move very quickly to large-scale biochemical imaging. This is true in the diagnostics field as well, as we demonstrate significant improvement in diagnosis and prognosis from the analysis of multiple markers, compared with the one or perhaps two markers used today. The clinical relevance and cost savings of this approach, by identifying disease early and treating more or less aggressively based on the prognosis, will be a critical factor in the acceptance of our technology.

'The ability to accurately measure hundreds, and eventually thousands, of serum analytes will redefine the definition of many diseases…'

This approach can be highly successful for diseases where there is a clear relationship between the presence of a particular analyte and disease progression. For more complex diseases, especially psychiatric disorders, do you think you will make such rapid progress?
I doubt it. I think the more complex diseases will become elucidated as our panel grows much larger, but I don't think that psychiatric disorders will be resistant to this approach when you realise that even one's thoughts can be detected by blood markers. For example, fear causes compounds like cortisol, adrenaline and a corticotrophin-releasing hormone surge into the blood. And when one is in love, endorphins and enkephalins appear. So I do think that psychiatric disorders can be detected in the blood and pharmaceutical companies might be interested in evidence of that.

How do you view the approach to disease profiling adopted by RBM – intuitive or empirical?
It is much more empirical. We do not know enough to be effectively intuitive. For example, C-reactive protein was previously considered a marker only of inflammation, not cardiovascular risk. Similarly, studies coming out of the University of California, San Francisco, have suggested that high titers of antibodies against varicella zoster are protective against the most common form of brain cancer. The Rules-Based Medicine approach should uncover many more such associations.

Once you have identified the key analytes for a particular disease, would you offer their analysis alone as a service? Could such a strategy drive mass acceptance of the assay format at a lower cost?
To answer the second question first, certainly, this would drive mass acceptance. However, we would not be the company offering this single analysis. The large clinical labs and clinical research organizations are designed to handle such testing. Our approach is very clear. We will use our screen of hundreds, and someday thousands, of blood analytes to discover new biomarkers of disease and to more fully understand the beneficial and harmful effects of therapeutic drugs.

How significant do you believe the announcement of the partnership between Charles River Laboratories and RBM will be in the establishment of your technology in the wider drug discovery arena?
We think the partnership is going to be crucial to the development of our technology in the pharmaceutical space. Charles River is one of the most highly respected companies serving this industry.

One of the most talked about developments in therapy in the near to mid future is that of personalised medicine. How is RBM positioning itself to react to developments in this area?
In the near term, only the RBM approach will deliver on the promise of personalized medicine. Everything that goes on in the body manifests itself in blood. Genes may be your destiny, but blood proteins are manifest destiny. Furthermore, the pharmaceutical industry is skilled at developing drugs that act on proteins. Intervention at the genetic level has been much less successful. Personalized medicine will be much more about the precise evaluation of the condition of a patient rather than their SNP profile.

'Genes may be your destiny, but blood proteins are manifest destiny.'

How critical do you think it will be for companies involved in genotypic analysis of disease to back this up with phenotypic measures?
There is nothing more critical.

You currently offer 214 analytes in humans and almost 100 for rodents. What is your strategy for increasing this list? Will you add antibodies at random; or will you target those with particular relevance for disease platforms?
We will do both. Several of our customers have asked that we add new analytes, of their choice, to our panel. Of course we do that, but we are also growing the panel with our original randomness.

How many antibody tests do you think will be required to adopt a shotgun approach to profiling various diseases?
I do not know if we will ever reach a number that does a perfect job of it. There are literally thousands of blood proteins that might ultimately be important. However, the algorithms become more and more refined with the addition of each new analyte,. It is also crucial to understand that proteins exert their effect through their concentrations. Small changes in the levels of most proteins can have a very large impact. For this reason, detecting just the presence or absence of a protein is essentially useless.

Do you view your partnership with Charles River as key to driving acceptance of your technology?
Absolutely. It is not quite as crucial in the diagnostic industry, but in the preclinical segment of the pharmaceutical industry, we are depending upon them to drive acceptance. We are not going to move into that market ourselves.

Would you outline the aims and works of the Foundation for a Healthier World, which you have personally established?
The foundation is bringing RBM technology to medically underserved areas of the world, including those areas that I first explored years ago in my search for novel toxins. Infectious disease is the biggest problem facing people in these areas. Our tests will be used diagnostically to detect exposure to almost 50 bacteria, viruses and parasites. Furthermore, the comprehensive imaging of the blood that will also be performed could contribute significantly to our understanding of disease susceptibility and resistance.

Mark Chandler
CEO and Chairman of the Board
Rules-Based Medicine
3300 Duval Road
Austin, Texas 78759, USA
e-mail: markc@rulesbasedmedicine.com