The changing face of bioinformatics

'As legal and technical barriers are overcome, the commercialization of personalized medicine will grow'.

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Not long ago bioinformatics was touted as the 'next thing'. Market research firms pegged the potential annual market at anywhere from US$2–40 billion. Bioinformatics, the information technology infrastructure, databases, and software for the life science market, held promise to provide great value for drug development companies. The promise was that bioinformatics could speed the identification and validation of drug targets and possibly shorten the time to market for new drugs. This promise has not yet been fully realized and the initial estimates may never be achieved. Does this mean that bioinformatics is dead? Certainly not.

The future of bioinformatics companies

While bioinformatics is necessary for biotechnology research and does provide important benefits, the number of stand-alone companies that will survive based solely on selling bioinformatics software or licensing databases for drug discovery will be limited. As successful companies often must do, many bioinformatics companies have morphed, at least partially, into drug research companies. Rather than just licensing bioinformatics data or tools, some of these companies have added internal research capability and now use their own data and tools to identify drug targets. For example, Celera (http://www.celera.com/), Incyte (http://www.incyte.com/) and Variagenics (http://www.variagenics.com/) have all diversified in this way.

Obvious upsides to this business model are that the results of the research can lead to patentable inventions and facilitate partnership with big Pharma. The successful identification and patenting of one drug candidate can generate more revenue for a bioinformatics company than dozens of software licenses combined. For many of these companies, software or data licensing continues to provide short-term revenue, while the hope of drug discovery provides potentially larger long-term returns. After all, in the biotech and pharmaceutical world it is all about who owns the patents. To the extent there is any doubt about this, consider the recent lawsuit between City of Hope and Genentech (http://www.gene.com/). Genentech was ordered to pay a half-billion dollars in patent license fees to City of Hope. The dispute revolved around a patented method for making protein-based drugs that City of Hope developed and licensed to Genentech in 1976.

The role of bioinformatics in 'personalized medicine'

Bioinformatics is changing in another way. To date, the primary focus of bioinformatics has been in the drug discovery market. Not an illogical approach, given that roughly 80% of the health care dollars in the US are spent on treating diseases, not preventing them. But there is another face to bioinformatics — for use in preventing disease. This area, often termed 'personalized medicine' or 'lifestyle management' has seen steady growth. Although not yet mainstream, personalized medicine also holds great promise.

A confluence of factors is helping to make this promise more of a reality. These include the successful mapping of the human genome, the relatively low cost of individual genetic screening, the FDA's endorsement of pharmacogenomics in connection with clinical trials, and the insurance industry's push to make genetic screening more wide spread. Here is a quick look at how each of these factors is relevant.

Mapping the human genome facilitated identification of the gene (or genes) or markers associated with various diseases. Although all humans have many similar genetic characteristics, the reality is that each person's genome differs slightly. Even slight genetic differences can have a significant impact on an individual's susceptibility to disease and response to treatment.

In addition, owing to advances in information technology (bioinformatics) the cost of individual genetic screening has decreased and the speed with which individuals can be screened for known genetic conditions or variations has increased. Personal genetic screening is now a practical reality.

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These two factors have paved the way for the third factor — pharmacogenomics. Simply put, pharmacogenomics is the study of how an individual's genetic inheritance affects the body's response to drugs. Some drugs are safe for 95% or more of the population, but fail to make it through clinical trials due to genetic differences in 5% or less of the population that cause those individuals to experience adverse effects. As a result, the vast majority of the population is denied the benefits of these drugs to protect a relatively small percentage of the population. And drug companies lose out too.

How can bioinformatics help in this situation? By using bioinformatics tools, companies can determine in advance of clinical trials those patients likely to experience adverse reactions based on genetic variations. By excluding those people with certain genetic conditions from clinical trials, more drugs can be approved by the FDA subject to genetic exclusions. The FDA recently took its first step to encourage the use of pharmacogenomics in the drug approval process. It published an article entitled, '*Pharmacogenomic-guided drug development: regulatory perspective*' (http://www.fda.org). The FDA also plans to establish educational programs and public workshops to raise awareness of pharmacogenomics and its use in drug development.

In practice, implementing pharmacogenomics requires that patients submit to genetic screening; however, this requires someone to pay for the screening. This leads to the fourth factor — insurance companies — which typically are expected to pay these costs. Will insurance companies agree to pay? Apparently at least one will.

Aetna (http://www.aetna.com/) recently announced it is in favor of individual genetic testing. In June 2002, John W Roe, CEO of Aetna, announced the insurer's commitment to work on establishing national guidelines to promote genetic testing as a tool for disease prevention and management. Whether this development is good or bad remains to be seen. A host of ethical and privacy-related issues are automatically raised when insurance companies become involved with such sensitive personal data.

While this confluence of factors points towards an increase in personalized medicine, as with all 'new' technologies, certain legal issues must be considered. As mentioned above, a major obstacle to genetic screening is ensuring the privacy of an individual's genetic data. Patients will need to be assured that submitting to screening will not lead to adverse consequences. Would a genetic condition that signals a propensity for a disease be considered a 'pre-existing condition?' Will insurers deny coverage for people with a genetic high-risk profile? If employers get access to this information, will hiring or firing decisions be made based on genetic propensities? In at least one case, these concerns were real, but were promptly addressed.

In February 2002, the Equal Employment Opportunity Commission (EEOC) sued Burlington Northern Santa Fe Railroad (BNSF) alleging it had violated the Americans with Disabilities Act by secretly running genetic tests on employees claiming to have developed carpal tunnel syndrome. Apparently, it was screening employees for a genetic trait called chromosome 17, which may lead to carpal tunnel syndrome. According to the EEOC, BNSF maintained a nationwide policy of requiring employees who had submitted claims of work-related carpal tunnel syndrome to provide blood samples for genetic testing.

Even worse, the EEOC charged BNSF with failing to disclose the purpose of the blood samples taken to do the testing in the first place and with threatening to fire at least one employee if he refused to submit a blood sample. Three days after the EEOC filed suit, BNSF publicly announced that it had reviewed its genetic screening policy and agreed to stop it. Hopefully these situations will be limited, but these and a host of other legal and ethical issues need to be resolved for personalized medicine to achieve its potential.

Conclusions

As legal and technical barriers are overcome, the commercialization of personalized medicine will grow. Forward-looking companies are devoting significant resources to develop the technology and business methods necessary to enable personalized medicine to become mainstream. These pioneers are filing system and business method patents at an increasing pace. Many of these applications will probably become issued patents over the next couple of years, just as personalized medicine hits its commercial stride. For those that come to the game later, navigating the patent minefield of the commercial pioneers will pose another challenge. In some respects, personalized medicine in 2003 is like the Internet in 1994. Many people with foresight know it will be big and ubiquitous, but finding the right business model to capitalize on it and to control key intellectual property for these business methods will be critical.

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