viral infection by inducing an "antiviral state" within the cell. Using interferon, viral infection is blocked by at least two double-stranded RNA-dependent mechanisms. First, interferon induces a protein kinase which halts protein synthesis. Second, interferon activates 2′,5′ oligoadenylate synthetase, which ultimately leads to the activation of RNAse L (L for latent because it is normally inactive) which non-specifically cleaves viral and cellular single-stranded RNA. The lack of double-stranded RNA in the cell is often the limiting step in activating the antiviral state cascade.

HemispheRx's patents apply to two classes of molecules that stimulate the body's normal antiviral state. Ampligen drugs bind 2′,5′ oligoadenylate synthetase, helping to activate an antiviral cascade. Oragen drugs are 2′,5′ oligoadenylate derivatives that bypass the cascade and directly activate RNAse L. Ampligen is available in Canada and certain European countries for treating chronic fatigue syndrome, and is being tested in various clinical trials as a treatment for hepatitis B and AIDS.

HemispheRx's extensive patent portfolio has stemmed from its concerted focus on these compounds and on the antiviral cascade. Its structure/function studies have improved its understanding of the antiviral state cascade and the effectiveness of its nucleic acid analogs. Along the way, the company has diligently filed patents on all of the improvements. But is 300 patents overkill?

Even assuming that HemispheRx's original patent covers all of the later discovered improvements, its strategy of patenting all improvements has merit. Failure to patent improvements leaves the door open for competitors to patent them. Because a patent gives one the right to exclude others from practicing the invention, not the affirmative right to use the invention, a competitor may deprive you of using the patented improvement, even though it falls within the scope of, and infringes on your patent. This is particularly true in biotechnology, where minor improvements are generally considered patentable. By patenting all improvements, HemispheRx hopes to avoid being forced into licensing improvements, which naturally flow from its core research and patents, from its competitors.

Moreover, biotechnology patents are generally receiving narrow patent protection. The broad patents granted by the US Patent and Trademark Office (Washington, DC) are routinely being invalidated by the US Federal Circuit Court. It pays, therefore, to have overlapping patent coverage of varying scope. The "Achilles' heel" of the biotechnology industry, Carter says, is the paucity of patents. "You can't build a company on one patent because it will all come crumbling down like a house of cards if [the one patent] is invalidated," he adds.

"We have so many patents," Carter says, "that companies are encouraged to license [from HemispheRx], rather than risk infringement. That's how a small company gets a large multinational company to sit down and talk business."

It appears that the strategy is working. Ventures entered so far include one with Pharmacia & Upjohn (Kalamazoo, MI) and the industrial conglomerate South African Breweries (Sandown, South Africa). More announcements on the partnerships are expected later in the summer.

HemispheRx's patent strategy follows a much earlier model. "Perhaps few of us remember," says Carter, "that the most highly valued company in the world, General Electric [...] had its inception and growth because of the vast patent estate developed by one man, Thomas Edison." Edison considered that discoveries are fostered not by solitary geniuses, but by large, well-organized, well-financed groups. And toward that end, he obtained and vigorously enforcerd over 1,000 patents during his lifetime.

Ken Chahine

India fears patent and ethics abuses

One issue dominated a recent conference* in India on ethical issues surrounding the human genome: the fear that pharmaceutical companies would exploit Indian human diversity and inventiveness at great cost to the poorest of the peoples.

The Indian Genome Initiative (IGI) as described by Sunil K. Pandya of Mumbai's KEM Hospital, seemed an all-encompassing entity. Research under IGI, he said, should focus on India's genetic diversity, identifying loci of serious genetic disorders amenable to corrective intervention or therapy, and developing diagnostic tools and recombinant molecules to save lives and treat illnesses. But Pandya also recognized the need for parallel studies on the ethical, legal, and social implications (ELSI) of such research. He called for the provision of counseling, and on the procurement of guarantees that the confidentiality of genetic materials provided to other Indian laboratories will be maintained.

Participants at the conference expressed concern about the difficulty of obtaining voluntary first-person informed consent, given the education of the majority of Indian people. It was suggested that random tests to check whether research subjects actually understood what they were consenting to should be introduced. Protecting the economic interests of genetic donors was also a concern.

There was general agreement, at least among the Indian participants, that transfer of genetic material abroad should only take place in exceptional circumstances, and only to laboratories operating under similar legal constraints. This closed, protectionist attitude toward genetic information is part of a wider and, in India, hotly debated topic—intellectual property rights. The United Nations Development Program estimates that biological resources worth approximately $5.4 billion are being stolen from developing countries every year. Although India was a participant in the Uruguay round of GATT concluded last year, the Indian government has not yet ratified its intellectual property provisions. That, in effect, means both that India's own patents are not internationally recognized and that India does not recognize other nations' patents.

David Roberts of SmithKline Beecham (London) argues that India needs to change its intellectually property rights legislation. If its does not, he says, it will continue to lose out in the international competition for investments by the pharmaceutical industry. These arguments, however, failed to impress the conference participants. Some participants suggested that legislative changes would have no impact because there are not enough resources to enforce patent legislation in India. As an example of this laxity, they cited the wide flaunting of the ban on the use of amniocentesis and ultrasound for sex selection. Indeed, "genetic counseling" has become a euphemism for sex selection among certain service providers.

Vananda Shiva of New Delhi's Research Foundation for Science Technology and Natural Resources Policy, an internationally known activist, argued vehemently that India should retain sovereignty over its national resources and the creativity of its people. Patenting, she says, will prevent the poor from accessing potentially life-saving drugs because their prices will be controlled by transnational companies. Shiva claims that patents ultimately turn out to be a drain on public resources.

Udo Schüklenk

Udo Schüklenk is at the University of Central Lancashire, Centre for Professional Ethics, Preston, PR1 2HE, UK (u.schuklenk@uclan.ac.uk).

*Indian National Academy of Sciences bioethics symposium; May 22–25, Goa, India.