WORLD WAR III?

PATENTING IL-6

LONDON—Interleukin-6 (IL-6) looks like the battleground for the next major patent dispute in biotechnology. While Ares-Serono (A-S, Geneva, Switzerland) appears to have a dominant position in Europe, the picture in the U.S. is less clear. There, Genetics Institute (GI, Cambridge, MA) may have at least a blocking position, possibly something stronger. Ajinomoto (Tokyo) may also enter the fray.

IL-6, also known as beta$_2$-interferon, has major potential indications as a platelet-growth stimulator in cancer-therapy-related thrombocytopenia, as an antiproliferative in breast cancer, colon cancer, and melanoma, and as a vaccine adjuvant worth, in total, an estimated $2-4 billion a year. Yet with IL-6 still in the preclinical phase (A-S's human studies are scheduled to start in the second quarter of 1992), talk of markets is premature—especially since ownership issues are undecided.

A-S's work on IL-6 started when the Weizmann Institute (Rehovot, Israel) isolated two antiviral compounds which they named beta$_1$- and beta$_2$-interferon. They filed patents, for which A-S is now the exclusive worldwide licensee, in 1979. The claims on beta$_1$ have now been disallowed because of prior disclosure by a Japanese inventor but, according to Mario Vannini, head of A-S innovative research, the company has heard unofficially that the claims of the 1979 patent relating to beta$_2$ have been allowed.

In 1985, following the cloning of the IL-6 (beta$_2$-interferon) gene, A-S filed further patents with broad claims for DNA sequences, vectors, host cells, formulations, and product by process. With "technical completion" in Europe and a "notice of allowance" in the U.S. Vannini anticipates that the patents will issue in the next three months. "This dominates any other company's position," he says. "IL-6 is the exclusive property of Ares-Serono." Despite this confidence, he expects to have to fight interference proceedings in the U.S. from GI and its exclusive licensee, Sandoz (Basel, Switzerland).

Bruce Eisen, GI's chief patent counsel, expects that, too. GI's patents on an rDNA, non-glycosylated form of IL-6 produced in *Escherichia coli* were filed shortly after the 1985 A-S patents on cloned material. Eisen believes that GI will be granted rights on the non-glycosylated form of the molecule and, importantly, on IL-6 uses in blood-cell stimulation, the activity most likely to be commercialized first and an activity which Eisen says A-S didn't claim until later.

With the U.S. interference procedure stacked against A-S—inventions made outside the U.S. (e.g., in Israel) are dated from patent filings whereas those made inside can date from other documentation such as laboratory notebooks—Eisen is confident that GI will not be excluded. "We're not going to say what the dates of documented discovery are, but there are reasons to believe we will be successful because of A-S's legal inability to back up their claims," says Eisen. He also believes that the 1979 A-S filing, which clearly predates all others, is deficient: specifically, the anti-viral activity claimed for beta$_2$-interferon (IL-6) has proved difficult to reproduce, raising questions about the purity of the substance isolated in 1979.

The most likely outcome of interference proceeding would be that A-S will be granted claims for the DNA sequence, vectors, and expression systems, while GI will get claims relating to lymphokine activities. Anticipating a need to cross-license, principals of the two companies have already met.

If the earlier Ares-Serono patent is brought into question, that might open doors for Ajinomoto. Their 1984 filing describes IL-6 activities in the stimulation of immunoglobulin production. Much may depend, therefore, on which of IL-6's many activities prove the most useful clinically.

—John Hodgson