cows of 'high genetic value', and has recently teamed up with the American Red Cross and Pharming, of Leiden, the Netherlands, to clone animals that produce human proteins in their milk. The company is also working with Imutran of Cambridge, England, and the Swiss-based drugs giant Novartis, on cloning in xenotransplantation — the use of organs from animals in human transplantation.

Staking a claim

Infigen owns a suite of patents on the basic techniques of nuclear transfer, awarded before the Roslin team demonstrated that it is possible to clone mammals from differentiated cells. Last year, it sued ACT for breaching two US patents on cow cloning, one covering a specific culture medium, the other a method for activating bovine eggs after transferring the donor nucleus. Infigen also claimed that Stice, who had once worked for Infigen, stole its trade secrets. That complaint was rejected, but in June 1999, the US District Court in Wisconsin ruled that ACT had indeed infringed Infigen's patents — after which the two companies came to a confidential settlement.

Ominously, it seems that other cow cloners could soon be hearing from Infigen's lawyers. "We're taking steps right now to inform several parties about our patent estate," says Michael Bishop, the company's vice-president for research.

Infigen gained a further US patent in January this year, which is causing raised eyebrows. Again specific to cows, this patent covers cloning from fetal cells that have been developmentally 'reprogrammed' by treating them with specific biochemical growth factors. Given that the Roslin team and others have shown that nuclear transfer itself can reprogramme differentiated cells, most researchers cannot understand the relevance of the extra step.

Although the significance of Infigen's new patent remains unclear, everyone in the field is watching for the emergence of other patents that could alter the intellectual property landscape. "In my mind, there's no overarching patent out there," says Stice. "We are still all trying to find one technique that is efficient." Indeed, most cloning groups only get one or two live births for every hundred nuclear transfer procedures they perform.

Many observers are keeping a close watch on PPL Therapeutics, which in March announced that it had cloned five pigs from adult cells using a novel technique. Details have not yet been published, but Colman claims the method is "significantly different" from anything described previously. That could be important, as pigs have proved hard to clone, and are the animals of choice for xenotransplantation. An Australian company, Stem Cell Sciences of Melbourne, also claims to have developed an alternative method of cloning that similarly remains under wraps.

"The intellectual property situation in this field is very complex at the moment," says Emma O'Donovan, editorial analyst at Derwent Information, a company in London specializing in patent information. "The wording and scope of individual claims will have to be examined very carefully."

If the current confusion is not resolved, the danger is that the situation will restrict the flow of money needed to develop the technology. Investors like the ownership of the key intellectual property to be clear, explains Neal First of the University of Wisconsin in Madison, a cloning specialist who sits on the board of a venture capital company interested in the field.

But perversely, the confusion could have a stimulating effect in the short term. "There are scientists starting little companies without much regard to where the intellectual property lies," says First. "And they are increasing the pool of knowledge." But if the writs begin to fly, some of these scientists may wish they had been more circumspect. ■

Peter Aldhous is *Nature*'s Chief News and Features Editor.

PPL THERAPEUTICS/NEWSMAKERS

Quintuple vision: PPL Therapeutics has devised a new technique that has enabled it to clone five piglets.

Paradise lost in Hawaii

No discussion of cloning's landmark achievements would be complete without mentioning 'team Yana'. Working in the lab of Ryuzo Yanagimachi at the University of Hawaii in Honolulu, scientists led by Teruhiko Wakayama (below) stunned the world in 1998 by cloning scores of mice, some of them clones of clones[7].

Rather than fusing a donor cell with an egg, like other groups working in the field, Wakayama developed a technique in which he removed the donor cell's nucleus and injected it directly into the egg using a piezoelectric device. The university filed for a patent on the method, and granted an exclusive license to a local company called ProBio, headed by Australian businessman, Laith Reynolds.

But the story has since gone sour. ProBio is still waiting for the cloning patent to be granted, but 'team Yana' has broken up. Tony Perry (right), a member of the team, is suing the university over the rights to a transgenic technology, now licensed to ProBio, which was developed by him while he was a European Molecular Biology Organization research fellow in Yanagimachi's lab. Although Wakayama has not sued over the rights to his cloning technique, he is understood to be similarly unhappy. Both scientists have now left for Rockefeller University in New York, but declined to discuss the reasons for their move with *Nature*.

PROBIO AMERICA/NEWSMAKERS

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