nature biotechnology

Animal attraction

Zoonoses have dominated the headlines in recent months, and for good reason. After the emergence of a highly contagious and virulent strain of avian flu in Asia and the discovery of bovine spongiform encephalopathy (BSE) in the western United States, tens of millions of birds have been slaughtered and hundreds of cattle killed. Similar culls occurred in Hong Kong during avian influenza outbreaks in 1997 and 1999. Whereas BSE may have been a temporary economic disaster for the US beef industry, the economic and human catastrophe that has accompanied the culls in Asia remains incalculable and curiously under-reported.

One reason that there are no practical alternatives to brute-force culls of diseased and healthy animals is that veterinary biotechnology—which might produce the vaccines, drugs and diagnostics capable of protecting the animals—remains in its infancy. Growth of the sector has been slow because most food animals are commodity products. The low margins of agricultural businesses mean they cannot afford the premium prices charged by biotech companies to recoup money invested in R&D. Paltry public investment in basic research on animals compared with biomedical and plant research has also stymied the area: the US government currently spends twice as much on boll weevil research than on research into animal influenza. And a side effect of the lack of investment is a paucity researchers with the requisite expertise. Perhaps most important, regulators continue to drag their feet in providing guidance on how to generate animal biotech products. As *Nature Biotechnology* went to press, the FDA still had not introduced its draft risk assessment of animal cloning, and guidelines for genetically modified animals raised for the dinner table or to produce drugs remains far off. Without clear and transparent guidelines, there is little hope that investors will risk ploughing much money into animal biotech enterprises.

Current sales of biotech-based products for use in animal health generate $2.8 billion (out of a total market for products of $18 billion), a figure expected to double in the coming year. To put this in perspective, just one biopharmaceutical protein, erythropoietin—marketed by Johnson & Johnson, Amgen, and Kirin Pharmaceuticals—collected $7.1 billion in global sales in 2002 alone. Thus, although around 70 biotech companies are active in the animal health sector (including emerging companies like Anigenics, AviGenics, Gala Design, Genetics Savings & Clone, Infigen, Iogen, Metamorphix, Nexia Biotechnologies and Prolinia), the market for animal biotech remains a tiny fraction of that for human biopharmaceuticals. With little economic incentive to develop innovative drugs and vaccines and diagnostics for animals, and the dominance of the sector by existing large 'animal health companies,' some may presume a bleak future for veterinary biotech. They would be wrong.

The future of veterinary biotech lies not in its application to food animals, but in its application to companion animals. The reasons for this are twofold. According to an article in the *New Yorker* magazine from last year, pet lovers in the United States spend $19 billion a year on veterinary care, up from $11 billion in 1996 (single-digit billion dollar markets also exist in Europe and Australia). This figure is the same ballpark as the entire R&D budget for the US National Institutes of Health. Second, in tandem with the money being lavished on furry companions, veterinary care is ramping up and rapidly increasing in sophistication. Thus, pet owners are no longer content to take Fido or Mr. Tiddles to a general practitioner. Today, they want consultations with veterinary oncologists, veterinary orthopediatricians, veterinary ophthalmologists—you name it; indeed, 7,000 such specialists are now listed by the American Veterinary Association.

With the influx of money into research on companion animals, traditional fields of animal biotech such as marker-assisted breeding programs, genetic engineering of disease resistance, enhancement of meat quality and flavor traits, expression of transgenic pharmaceutical and industrial proteins, and xenotransplantation research are likely to be increasingly joined by more exotic applications in pets. For example, Jerry Yang of the University of Connecticut has been working to create cats missing the allergen gene *Fel d1* to benefit feline-friendly people with cat hair allergies. And Genetic Savings & Clone is offering to preserve DNA from pampered pets until such time they can offer 'commercial cloning of dogs and cats.'

One might even imagine companies developing embryonic stem (ES) cell therapies for cats with kidney damage or immunotherapies for Alsatians crippled with arthritis. It is conceivable that reproductive cloning, ES cell treatments or xenotransplants—areas that have traditionally presented ethical and moral barriers in human research—may be more permissible in the context of animals, allowing companies to sidestep regulatory and legislative restrictions on human work that currently stymie progress. This could reap immediate benefits not only for veterinary medicine but also for human healthcare, particularly if the freedom to refine treatments in animal subjects enables the kinks to be ironed out of procedures under development involving nuclear transplantation, ES cells or xenografts.

Clearly animal and human health are intrinsically linked. In the case of influenza, we need to study the ways in which viruses infect animals to anticipate problems if they cross into humans. New sources of funding for this type of biotech can come indirectly from tapping into the enormous market for therapies for pampered pets. And if regulators and legislators allow animal biotech to proceed with rational oversight, the influx of companies into animal biotech may very well propel experimental veterinary treatments to the point where *not* applying them to human subjects becomes the ethically untenable issue.