UNIVERSITY OF Southampton

The fight against parasitic worms: understanding a new resistance-breaking drug

A 15 year collaboration between biological scientists at the University of Southampton and Bayer AnimalHealth has broken new ground in the battle against parasitic worms, that cause many diseases in animals and humans. Researchers have demonstrated that a new class of compounds, the cyclooctadepsipeptides, paralyses them in an entirely new way.

This knowledge has underpinned the registration and marketing of three new veterinary medicines starting with the award winning Profender Spot-on for cats in 2005. They have improved veterinary care for dogs and cats around the world, and enabled a world-leading animal health company to develop a new range of valuable drugs.

Parasitic nematode worms infect humans, livestock and pets. This is a global problem affecting human health, animal welfare and food production. One particularly distressing condition is river blindness which affects people who live near rivers in sub-Saharan Africa. Human and animal infections have been treated with anthelmintic (anti-worm) drugs, such as Ivermectin which was developed in the 1980s. However, over the last two decades, such drugs are losing their effectiveness due to the emergence of drug resistant nematodes.

In 1993, Fujisawa Pharmaceutical Co Ltd in Japan filed a patent for a new chemical class of anthelmintic drugs called cyclooctadepsipeptides. They had potential to act against many types of gastrointestinal nematodes, including parasitic worms that attack livestock and pets. One drug in particular, the cyclooctadepsipeptide called emodepside was taken up by Bayer AnimalHealth for its potential as a veterinary product.

Biological scientists at the University of Southampton were approached by the global pharmaceutical company in 1999 to lead research into how cylooctadepsipeptide drugs work against parasitic worms. Bayer AnimalHealth made the contact because of Southampton's international reputation in nematode neurobiology. The initial collaboration was between Professors Lindy Holden-Dye and Robert Walker with Professor Dr Achim Harder of Bayer AnimalHealth and later included Southampton colleagues, Professors Vincent O'Connor and Dr Neil Hopper. In 2002, Professor Harder from Bayer AnimalHealth reported that emodepside was effective against parasitic worms, which were resistant to all other anthelmintic drugs, and that it could form the basis of a powerful new drug

Southampton researchers provided the pharmaceutical company with the findings of their work on the effects of emodepside on the microscopic worm C. elegans which explained the molecular basis of its resistance-breaking properties. This research supported the licensing of the veterinary medicines Profender® tablets and Procox®, by the EMA and FDA in the review period. These added to the earlier successful licensing of Profender® Spot-on. Bayer AnimalHealth has confirmed that Southampton's explanation of emodepside's mode of action was critical in bringing all three drugs to market.

The discovery of a drug to counter parasitic worms has influenced international debate concerning the treatment of human infections. The World Health Organisation is interested

in emodepside as a treatment for neglected tropical diseases such as river blindness; these filarial conditions afflict one sixth of people in the world.