The global shift

Using machine learning in the search for antimicrobial alternatives

By Lilian Schaer

THERE'S A GLOBAL SHIFT away from the use of antimicrobials in livestock production, driven by growing concerns over resistance in both humans and animals.

Here in Canada, new rules governing the use of various types and classes of antimicrobials, including antibiotics, in livestock came into force in December 2018.

That means the hunt is on for alternatives; antimicrobial peptides – naturally occurring molecules that cells produce as a front-line defense against bacteria and viruses among other attackers – are one of the solutions being pursued.

Antimicrobial peptides have a different mechanism of action compared to traditional antibiotics – they directly attack the bacterial cell membranes, making bacteria less likely to develop resistance.

At the University of Guelph, researchers are looking at peptides as a way to control salmonella infection in pigs – in fact, they're searching for peptides they can use to design totally new peptides that will be both effective and safe, according to Prof. Chris Gray, Professor Emeritus in the Department of Physics.

"We've done computer simulations of model peptides and membranes to understand what makes specific peptides attack just the membrane of the bacteria directly and leave everything else alone," explains Gray. "Now, we are trying to design new ones that are more powerful and yet safe at the same time."

Gray, his postdoc Mostafa Nategh, and fellow researchers are using various computational tools – most notably machine learning – in their search for new, effective antimicrobial peptides that are active against salmonella.

They've partnered with experts at the Machine Learning Research Group at University of Guelph led by Prof. Graham Taylor to build neural network models that can associate peptides' potency with their chemical structure. According to Gray, the search for suitable peptides is so vast it can only be completed by using artificial intelligence and neural network computing.

"Artificial neural networks work like human brains – they link together neurons and teach them to recognize patterns the way a human brain does," he says, adding that the computer will learn to select "good" combinations of peptides that are active against salmonella and aren't toxic.

In order to teach the computer what to look for, though, the research team has also had to develop a database of examples of antimicrobial peptides that are active against various targets.

"What the computer methods do is produce a hundred potential candidates and we select the best 10 on paper to try," Gray says. "Then you have to try them in the lab to make sure they actually kill bugs in dishes before then doing those tests in animals. We further have to make sure they survive the biochemically harsh environment of the animal's gastrointestinal tract."

To that end, Gray's group collaborates with the Guelph food science labs of Prof. Michael Rogers and Prof. Alejandro Marangoni. Using a simulated digestive track apparatus, for example, researchers in Rogers' lab can measure how much of a given peptide survives in the gastrointestinal tract and hits the target at the infection site.

Key to bringing this technology to market will also be the ability to produce large quantities of the peptides at a low cost. Pigs and salmonella were the original target of this research - Prof. Bob Friendship of the Ontario Veterinary College has been advising the research team – but the work is very transferrable, and Gray says once the program to build and design the peptides is completed, it will be applicable to other infectious bacteria and other livestock species too.

"The industry as a whole, not just pork, would be very excited if we can make this viable," he says, although admitting that this is still a few years away from becoming reality.

The project, which will wrap up in early 2019, is supported by Ontario Pork and the Natural Sciences and Engineering Research Council of Canada.

This article is provided by Livestock Research Innovation Corporation as part of LRIC's ongoing efforts to report on Canadian livestock research developments and outcomes.