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CPRC Update

'DESIGNER PROTEINS' MAY OFFSET NEED FOR ANTIBIOTICS

The issue of bacterial resistance to antibiotics is taken very seriously by the poultry industry. Further to encouraging prudent use, industry is supporting research into alternative measures that may offset the need for commonly used antibiotics. For example, a large research team including scientists from the University of Alberta, the National Research Council and Dow AgroSciences are looking at the prospect of engineering "designer proteins" that can combat specific diseases. The so-called field of Protein Therapeutics has changed the face of human medicine and has vast potential for novel disease treatments in agriculture as well.

Protein designed to fight Salmonella

One part of this research program, led by Dr. Christine Szymanski at the Alberta Glycomics Centre, University of Alberta and Dr. Jamshid Tanha at the National Research Council – Institute for Biological Sciences, are using bacteriophages to reduce Salmonella in chickens. Bacteriophages (phages for short) are a special class of virus that only infect specific bacteria. This specificity is conferred by phage proteins that bind surface structures on the bacterium; when the phage bumps up against a bacterium with the appropriate affinity, it attaches and infects the bacterium. Cellular machinery in the bacterium is then hijacked into making new copies of the phage, which then burst out of the cell killing the bacterium. Exploiting this specificity is an attractive prospect for scientists looking for alternative ways to target bacteria. Yet previous attempts have met with varying success; using intact phage in this manner is fraught with a number of technical problems. There is also an underlying risk that that the bacteria will develop resistance to the phage over time. To circumvent these problems, the researchers decided to use only a portion of the phage known as the tailspike protein (TSP); this is the piece of the phage that confers its specificity. They chose the TSP from a phage that is specific to *Salmonella enterica* serovar Typhimurium. Upon characterizing the TSP, the researchers recognized that, using modern protein engineering techniques, they could shorten the molecule without losing its specificity. The resulting protein resists digestion in the gastrointestinal tract of the bird (making it ideal for oral administration), can be produced in large quantities, avoids many of the technical issues and risks associated with intact phage, and is amenable to protein engineering for improved function. Properties like stability, binding strength, degree of specificity etc. can all be tailored to suit the application.

Does it work?

Lab tests showed the modified TSP does bind *S.* Typhimurium. The bacterium *Staphylococcus aureus* was unaffected during the same experiments, demonstrating the specificity of the protein. Bound TSP appears to impair the motility of *S.* Typhimurium, making it less able to colonize the chicken's gut. To see if this theory held true, Leghorn chicks were orally infected with varying amounts of Salmonella and fed varying doses of the modified TSP. Treatment with modified TSP resulted in significant reduction of Salmonella in the birds' ceca (part of the intestinal tract), liver and spleen (when birds are infected with Salmonella, the bacterium may also get in the blood stream and infect organs such as the liver and spleen). These results demonstrate the potential of designer proteins to reduce bacterial infection in the bird. This 'at source' approach to combating specific bacteria without affecting beneficial ones has tremendous potential for the industry.

What's next?

Next steps for this work are to further characterize exactly how the modified TSP reduces Salmonella colonization in the chicken gut. For example, is the protein affecting more than the bacterium's mobility?

The research group is also investigating ways to produce the proteins on a commercially viable scale. We'll tell you more about that in future updates.

Results of this work were published in the online journal PLoS ONE. Funding was provided by CPRC, the Alberta Ingenuity Fund and the National Research Council.

For more details on any CPRC activities, please contact The Canadian Poultry Research Council, 350 Sparks Street, Suite 1007, Ottawa, Ontario K1R 7S8, phone: (613) 566-5916, fax: (613) 241-5999, email: info@cp-rc.ca, or visit us at www.cp-rc.ca.

The membership of the CPRC consists of Chicken Farmers of Canada, Canadian Hatching Egg Producers, Turkey Farmers of Canada, Egg Farmers of Canada and the Canadian Poultry and Egg Processors' Council. CPRC's mission is to address its members' needs through dynamic leadership in the creation and implementation of programs for poultry research in Canada, which may also include societal concerns.