Cornell University
College of Veterinary Medicine

Baker Institute for Animal Health

DEDICATED TO THE STUDY OF VETERINARY INFECTIOUS DISEASES, IMMUNOLOGY, GENETICS, AND REPRODUCTION

Sialic acids: The key to understanding influenza infections

For many viruses, the first step to invading a cell is finding and attaching to just the right variety of sialic acid, a type of sugar molecule that is found on the surface of most animal cells, including those of humans. To understand the roles that sialic acids play in viral infections, Dr. Colin Parrish's group at the Baker Institute for Animal Health are using new techniques to explore the variation, diversity of expression, and evolution of sialic acid molecules in different animals.

Sialic acids have numerous modifications, resulting in a variety of different structures. In healthy cells sialic acids play many important roles, including controlling communications between cells and the development of many tissues and organs, including those in the nervous and immune systems. All vertebrate animals, and even some plants and microbes, have sialic acids on their cells, but the collection of different modified forms vary greatly between species.

Perhaps because sialic acids are so widespread in different animals, viruses such as influenza use them to enter cells. The group in Dr. Parrish's laboratory is interested in the differences in the sialic acid types in humans, dogs, and other animals that come down with the flu. The differences and similarities in their sialic acid profiles may help to explain why some influenza viruses infect one species and not others, and why some virus strains can jump between species. "There is lots of flu in birds, for example, but most strains are not able to move to humans or other animals," said Dr. Brian Wasik, a research associate in the Parrish group.

Studying the variation in the expression of sialic acid variants can also inform other studies relating to human health. "Understanding how the structure of sialic acids and its chemical modifications can change how the virus interacts with them could have applications for [developing new] antivirals," said Karen Barnard, a graduate student working on the project.

Sialic acids are difficult to study because sugars aren't encoded in the genome, so scientists can't directly edit or delete their genetic blueprints to see how those changes impact the cell. Instead, they must manipulate the enzymes that make and modify these sialic acids. Wasik, Barnard, and Brynn Lawrence, a technician in the laboratory, have succeeded in using the new gene editing technology named CRISPR/Cas9 to alter the activity of these enzymes, and have been looking for changes in how influenza viruses interact with the cells.

They are also working with colleagues at the University of California, San Diego, to find ways to use viral proteins to tag and identify specific types of sialic acids. "Because we're still developing tools, we go down a lot of weird side roads," said Lawrence. "There's a lot of trial and error."

Access to clinical samples from different animal species through the College of Veterinary Medicine has helped expand the scope of their work. "Being at the Baker Institute and the [College of Veterinary Medicine] is really helpful when we're thinking about influenza across species," said Wasik. "The resources here are really what helps drive this research in a way that you probably couldn't accomplish at a lot of other places."