Don't let the bad bugs win: Team seeks to outsmart C. difficile with $9.2 million effort

March 9 2016

Single cell of *C. difficile*, a strain of bacteria responsible for the deaths of more

than 14,000 Americans each year. Credit: Centers for Disease Control and Prevention

If you want to beat a fearsome enemy, you must first learn to think like them. If you do, you can predict their next move - and block it.

This advice may work on the battlefield. But scientists also think it will work in humankind's battle against one of the most dangerous bacteria our bodies can face: *Clostridium difficile*. *C. difficile* infection has been identified by the CDC as an urgent threat requiring immediate and aggressive action.

Now, University of Michigan researchers have launched a $9.2 million assault against *C. difficile*, sometimes pronounced "see-diff" for short. They're doing it thanks to a new grant from the National Institutes of Health—part of the U.S. government's $1.2 billion effort for a multi-agency attack on antibiotic-resistant bacteria.

Over the next five years, they'll use the money to accelerate their existing work on this "bad bug", which causes diarrhea, hospitalization and even death if it infects the gut.

Using data from their lab and from actual *C. difficile* patients, they'll create computational models that will help them understand this tiny enemy, predict its next move, and generate tools that can help medical teams fight back against it.

"This should help us lay the groundwork for both short- and long-term solutions to the *C. difficile* crisis, by understanding what puts patients at risk for *C. difficile* infection, and how we can best protect and cure them," says team leader Vincent Young, M.D., Ph.D., a professor in the

Department of Internal Medicine's Division of Infectious Disease at the U-M Medical School who has studied *C. difficile* for years and treats patients with it.

A wily foe

C. difficile sickens half a million Americans each year, causing diarrhea and dangerous colon inflammation. It kills more than 14,000 directly while playing a role in the deaths of 15,000 more. Caring for its victims costs the U.S. nearly $5 billion a year.

And because *C. difficile* often strikes people who have taken antibiotics for other conditions, the front lines in the battle against it are in every hospital and nursing home in America.

The over-use of antibiotics for many conditions has actually made patients more vulnerable to *C. difficile* than they need to be. Antibiotics upset the natural mix of healthy bacteria in the gut, allowing *C. difficile* to "colonize" and grow out of control. Over time, the bacteria have evolved to take advantage of the altered landscape of the human gut in the age of antibiotics.

Battle plan

The U-M team's new grant from the National Institute of Allergy and Infectious Diseases takes a system biology approach. It will use information from *C. difficile* patient records, blood samples and detailed studies of the mix of microbes living in patients' guts, to create computational models of the diseases.

This will allow the researchers to get a better, more nuanced understanding of how a patient's underlying health status and natural

microbe population, and his or her treatment with antibiotics, combine to make *C. difficile* colonization and infection possible, and affect the odds of successful treatment.

Depending on what those models show, the scientists will then test their new knowledge about human *C. difficile* infections by trying to get the same thing to happen in mice in the laboratory.

They'll try to figure out what risk factors make a patient most vulnerable to *C. difficile* infections - either a first-time illness or a recurrent one in someone who has survived a first bout. They'll also work to understand what factors make someone most likely to get colonized with *C. difficile* in the first place.

The team, co-led by Patrick Schloss, Ph.D., from the U-M Department of Microbiology & Immunology, will try to produce specific data that medical teams could use to prevent *C. difficile* infections in healthcare settings, and to plan the treatment of those who get ill.

U-M work on *C. difficile* has been under way for nearly a decade, thanks to previous NIH grants and funding from the Medical School's self-funded Host Microbiome Initiative.

Working in mice, the team has detailed the organism's natural life cycle in the gut. They've also made strides in understanding the mechanisms by which the "village" of normal gut bacteria can interfere with *C. difficile* colonization. And they've even shown a connection between depression and increased risk of *C. difficile* infection.

Provided by University of Michigan Health System