Using a virus against itself

With most pathogens, says David Leib, Ph.D., a professor of microbiology and immunology, “you either get better, or you die.”

But that paradigm doesn’t hold with the herpes simplex virus (HSV), which takes up residence in the host and usually remains for the host’s lifetime, a paradox that piqued Leib’s interest years ago. “How is it possible that a virus can outlive the host?” he wanted to know.

A study by Leib and postdoctoral researcher Philipe Gobeil, Ph.D., sheds some light on that question, but the results were so surprising that at first Leib didn’t believe them. “I told Gobeil he must have mislabeled his tubes or switched his samples,” Leib says. So Gobeil repeated the work, and then repeated it again, eventually convincing Leib. They found that one of the virus’s genes helps it defeat the immune system “in a very specific, very clever way,” as Leib puts it.

Leib has long studied an HSV protein called gamma-34.5. Early on, he discovered that this protein allows the virus to evade the host’s interferon response, a nonspecific activation of the immune system that is important in eliminating viruses. Leib kept investigating and eventually found that there was more to the protein’s action. “It also helps evade the more specific responses that our T cells make, the responses that are critical for us to remain permanently immune to an infection,” Leib says.

Leib and Gobeil discovered that gamma-34.5 prevents autophagy of HSV by dendritic cells. Autophagy translates literally as “self-eating,” and it is what cells do in response to starvation. They digest proteins within the cell, breaking them down into their constituent amino acids. It’s a fundamental process that occurs in organisms as simple as yeast and as complex as humans. The immune system also uses autophagy to break down invaders, such as viruses.

One way that dendritic cells stimulate immunity is by digesting a protein from the virus via autophagy and then presenting it as an antigen on the cell surface. This allows the immune system’s specific responders, the T cells, to make antibodies geared to the viral antigen. By shutting this process off, gamma-34.5 helps HSV survive indefinitely in the cell.

Leib engineered a herpes virus that lacks the gamma-34.5 protein and found that infected cells were more effective at presenting this version to T cells. The T cells, in turn, responded more robustly to the virus. One implication is the possibility that an HSV lacking the gamma-34.5 gene could be used as a vaccine against the virus, since it both weakens the virus and stimulates a stronger T-cell response. Leib says the next step is to see how well HSV can persist in the host without gamma-34.5, or if, in fact, it can be fully cleared from the system.

Lauren Ware

City health and country health

In her work as a nurse practitioner at the Maine-Dartmouth Family Medicine Center in the rural town of Fairfield, Maine, Alane O’Connor, D.N.P., noticed something about her patients. They seemed sicker and more likely to have a chronic disease than had her patients in Boston, where she had practiced previously. She began to wonder if what she had noticed reflected a real trend: Was there a higher prevalence of chronic disease in rural environments?

Research has shown that two of the most common chronic diseases in rural and urban areas are diabetes and coronary heart disease. Much work has been done looking at specific risk factors for both, such as obesity and smoking. But “nobody has looked at [the issue] from a rural-health perspective,” says O’Connor.

So O’Connor, who is a Geisel adjunct instructor of community and family medicine, studied data from a 2008 national survey conducted by the U.S. Centers for Disease Control and Prevention. People were asked about their chronic health conditions, socioeconomic status, weight, and other risk factors. O’Connor found that diabetes and coronary heart disease are more prevalent in rural locations than in cities. The prevalence of diabetes was 8.6% higher (9.7% versus 9.0%), and the prevalence of coronary heart disease was 38.8% higher (5.5% versus 4.0%).

O’Connor also wanted to know if the effect of income on the likelihood of disease was different between rural and urban areas. Were low-income people in rural areas sicker than people in the same socioeconomic bracket in urban areas? She found that this was true for coronary heart disease but not for diabetes. In rural areas there was also a higher percentage of current and former smokers, which is a risk factor for coronary heart disease, and a higher percentage of people who were overweight or obese, which is a risk factor for both diabetes and heart disease.

Overall, people living in rural environments, O’Connor found, are more likely to be diagnosed with diabetes and coronary heart disease than people living in urban areas. This difference, she wrote in an article on the research, “exacerbates many of the disparities already found in the rural U.S. health setting, including more difficulty obtaining health insurance and longer distances to reach health-care facilities.” Higher rates of poverty and less insurance coverage can mean that many rural residents cannot afford treatments such as smoking-cessation therapies, diabetic medications, and gastric bypass surgery. The shortage of primary-care physicians in rural areas makes the situation even more challenging.

This research is crucial to increasing people’s awareness of rural health issues—which is very much needed, O’Connor believes. “Folks are more aware of urban health issues,” she says. “We need more champions of rural health.”

Matthew C. Wiencke