# Scientists wield plant viruses against deadly human disease

October 1 2014

Case Western Reserve University researchers hope to take a healthy salad up a level by growing a vaccine for an aggressive form of breast cancer in leafy greens.

"In the long run, one could think about administering the vaccine either by eating the salad or making a pill from the plant tissue," said Nicole Steinmetz, assistant professor of biomedical engineering at Case Western Reserve School of Medicine and leader of the project.

The Susan G. Komen breast cancer organization is funding the research with a three-year, $450,000 grant.

Steinmetz also received a $144,000 grant from the American Heart Association for a separate project: developing a transporter to deliver clot-busting drugs to the site of blood clots before they trigger heart attacks or strokes.

In both projects, researchers will manipulate plant viruses the size of nanoparticles to deliver protection from these killer diseases—but in very different ways.

## Aggressive cancer

About one in five cases of breast cancer are a form called HER2+ cancer. A mutation in the cancer cells causes an increase in production of the protein, human epidermal growth factor receptor 2 (HER2), which, in turn, promotes uncontrolled cancer cell reproduction.

The cancer is treated with chemotherapy and an antibody called trastuzumab. But the treatment doesn't work for all women, is costly and produces several unwanted side effects, including heart damage in some patients.

Steinmetz and colleagues propose to make a vaccine that would trick the body's immune system into attacking the HER2 proteins, thereby providing protection.

"It's complex to attack the disease," Steinmetz said. "Humans generate HER2 so the protein doesn't naturally trigger an immune response."

## Triggering immunity

The researchers plan to link HER2 epitopes, which are peptides they believe can elicit protective immunity against cancer, to potato virus X. Potato virus X is a non-toxic nanoparticle, but would be recognized as a foreign invader by the body.

Immune cells would steer the vaccine particles into the lymph system and spleen, which would produce antibodies to the virus and, more importantly, HER2 protein, thereby providing a long-lasting protective immunity to HER2+ cancer.

The scientists predict the vaccine would reduce the risk of cancer, its progression and recurrence, and metastasis.

The vaccine wouldn't necessarily be for general consumption, but for women with a family history of HER2+ breast cancer and to protect those who have just undergone surgery to remove an HER2+ tumor against metastasis.

"Metastatic disease is what kills most patients," Steinmetz said. "Before the doctor sees metastatic activity, this vaccine attacks."

Steinmetz grows the potato X virus in tobacco plants and will begin growing it in leaf lettuces and other plants. She is working with Case Western Reserve School of Medicine's Ruth Keri, professor of pharmacology; Alan Levine, professor of medicine, and Julian Kim, professor of surgery and Chief, Division of Surgical Oncology, Seidman Cancer Center. They plan to develop and test the vaccine in preclinical studies.

While this work focuses on HER2+ breast cancer, the researchers believe that, if successful, the technology could be used also to treat other HER2+ cancers: ovarian, pancreatic and prostate.

## Targeting trouble

In her second project, Steinmetz will use another of nature's nanoparticles—the tobacco mosaic virus—to deliver clot-busters directly to clots that cause a heart attack or stroke.

Currently, doctors inject medicines to dissolve clots, but the drugs circulate throughout the body and carry the risk of causing life-threatening bleeding in the brain.

Steinmetz is working with Daniel Simon, MD, chief of cardiovascular medicine at University Hospitals Case Medical Center and the Herman K. Hellerstein Professor of Cardiovascular Research at Case Western Reserve School of Medicine; Jonathan Pokorski, assistant professor of macromolecular science and engineering at Case School of Engineering; and Douglas E. Vaughan, MD, Irving S. Cutter Professor and Chairman of the Department of Medicine at Northwestern University Feinberg School of Medicine; to reduce the risk of bleeding and the cost of treatment.

Clotting is a complicated and essential process to stem bleeding from injury. But blood vessel damage from atherosclerosis and other forms of heart disease can also trigger the process, leading to heart attack, stroke or death.

The researchers are focused at a point in the process when a protein, called fibrinogen, is converted to fibrin—a mesh that holds blood platelets and other materials that form the clot together.

They will coat the elongated tobacco virus with peptides that seek and bond with a forming clot. The virus-based nanocarrier, due to its shape, will skim blood vessel walls rather than speed by in the main flow of blood, and will carry factors that promote the body's natural clot-dissolving process when it makes contact with the target.

By targeting clots, the rest of the body is not exposed to clot busters, thereby reducing both the amount of drug required and bleeding risk.

Provided by Case Western Reserve University