With cancer so often presenting as a cunning enemy, scientists are working hard to develop therapies that can slip through its array of crafty defenses. These types of “Trojan horse” approaches use all kinds of trickery to sneak drugs into cancer cells to kill them off, but a team from Singapore’s Nanyang Technological University (NTU) is putting forward
another solution, demonstrating how a new drug-free nanoparticle can do all the heavy lifting on its own.

Cancer cells employ all kinds of methods to evade and overcome the body’s immune system, but they do have their weaknesses. Like many types of cells, they need amino acids to grow, and one they can’t do without is called L-phenylalanine, which is typically absorbed into the body from meat and dairy products.

The NTU researchers sought to take advantage of this dependency, by using L-phenylalanine as their Trojan horse. This peptide was used to coat a cancer-fighting nanoparticle 30,000 times smaller than a human hair, the idea being this disguise could help the nanoparticle sneak into the cancer cells and cause them to self-destruct.

Called Nanoscopic phenylalanine Porous Amino Acid Mimic, or Nano-pPAAM, this nanoparticle was put to the test against cancer cells in the lab through experiments in vitro and in mice. The researchers found the approach killed around 80 percent of breast, skin and gastric cancer cells, which they point out is similar to what you’d expect from standard chemotherapy drugs.

“Against conventional wisdom, our approach involved using the nanomaterial as a drug instead as a drug-carrier,” says lead author of the study Professor Dalton Tay. “Here, the cancer-selective and killing properties of Nano-pPAAM are intrinsic and do not need to be ‘activated’ by any external stimuli. The amino acid L-phenylalanine acts as a ‘trojan horse’ – a cloak to mask the nanotherapeutic on the inside.”
Called Nanoscopic phenylalanine Porous Amino Acid Mimic, or Nano-pPAAM, this nanoparticle was put to the test against cancer cells in mice. NTU Singapore

Nano-pPAAM works by entering the cancer cells through an amino acid transporter cell and, once inside, stimulates the production of molecules known as reactive oxygen species (ROS), which don't harm healthy cells, but do cause the cancer cells to self-destruct. The major benefit of the technique is that it could overcome common issues with cancer cells developing resistance to drugs, which often sees them gain the upper hand.

“This novel approach could hold much promise for cancer cells that have failed to respond to conventional treatment like chemotherapy,” says Associate Professor Tan Ern Yu, a breast cancer specialist at Tan Tock Seng Hospital, who was not involved with the study. “Such cancers often have evolved mechanisms of resistance to the drugs currently in use, rendering them ineffective. However, the cancer cells could potentially still be susceptible to the 'Trojan horse' approach since it acts through a completely different mechanism – one that the cells will not have adapted to.”

The team is now working to fine-tune the technique to improve its efficacy and enable it to better target certain cancer types. The researchers are also investigating how it could be combined with other therapies such as immunotherapy to act as a one-two punch.
The research was published in the journal *Small*, while the video below provides an overview of the study.

*NTU Singapore scientists devise ‘Trojan horse’ approach to kill cancer cells without using drugs*

Source: Nanyang Technological University