Stopping germs from ganging up on humans

November 20 2008

Keeping germs from cooperating can delay the evolution of drug resistance more effectively than killing germs one by one with traditional drugs such as antibiotics, according to new research from The University of Arizona in Tucson.

John W. Pepper proposes a new strategy in the arms race between humans and germs-- targeting the teamwork within gangs of germs.

Most drugs used to fight infections kill the vulnerable disease-causing organisms, or pathogens, but the resistant ones survive. The next generation will all carry the resistance to the drug.

"We know that the pathogen is causing the disease. The obvious solution is to kill the pathogen. It makes perfect sense, and that's what we've always done," said Pepper, a UA assistant professor of ecology and evolutionary biology. "But there's one big flaw with that -- and that is the evolution of resistance."

Pepper's mathematical models show it takes longer for a group of cells to develop resistance to drugs that attack the teamwork factors than for individual cells to become resistant to a traditional antibiotic.

He advocates developing drugs that attack the pathogens' methods and resources for cooperation. Pepper said once the teamwork is disrupted, the immune system can combat any remaining infection.

He said this new approach will work against "old enemies and some new

ones" that are becoming drug resistant, including methicillin-resistant Staphylococcus aureus bacteria (MRSA), HIV, malaria, tuberculosis, avian influenza and cancer.

Pepper is also a member of UA's BIO5 Institute and an external professor at the Sante Fe Institute in New Mexico. His paper, "Defeating Pathogen Drug Resistance: Guidance from Evolutionary Theory," is scheduled for publication in the December issue of the journal Evolution.

Pepper began investigating cooperation by studying parrots and dolphins. Now he studies cooperation among individual cells.

Most cells such as a bacterium produce materials that ensure their own survival and maintain infections by helping both themselves and their fellows.

For pathogens, there's strength in numbers. As they form groups, they become a greater threat.

For example, MRSA produce more than 50 resources essential for the group.

Where others may see an unconquerable defense, Pepper sees 50 opportunities.

The number and type of materials produced within a gang of pathogens varies. However, if one material is eliminated, none of the cells will survive. Neither will the infection.

He is currently collaborating with cancer biologists to attack chemicals that allow cancer cells to gang up on normal cells.

One type of chemical, the angiogenesis factor, is secreted by cancerous cells to stimulate the growth of blood vessels into tumors. Blood vessels carry oxygen and nutrients to the cells in the tumor.

Some doctors currently use angiogenesis blockers, such as the anti-cancer drug Avastin, to inhibit the signal. Without blood vessels, tumors suffocate and starve.

As opposed to toxic drugs that poison and kill cancer cells, Pepper said these new types of anti-cancer drugs will stay potent longer.

"The basic point I'm making is in order to save the patient, we don't have to have a drug that kills the cancer cells," Pepper said.

If drug development continues to focus on killing individual cells, he said, "We're always going to keep running on the same treadmill.

"We're going to be in this situation where we desperately need a new antibiotic by tomorrow, or maybe by yesterday," Pepper said. "That's not going to be a temporary emergency -- it's going to be a permanent emergency, unless we take a new approach."

Source: University of Arizona