

BACTERIA RESEARCHER DARREN HIGGINS | MEETING THE MINDS

The Boston Globe

Pathogens are scientist's passion

By Keith O'Brien, Globe Correspondent | August 15, 2005

Darren Higgins was all set to be a doctor. It made sense. He had always liked science. And for the son of a career military man, medicine was a good match for Higgins. It was regimented, hard work, for the good of others.

There was just one problem.

Higgins loved bacteria.

Salmonella fascinated him. Shigella a turn on. He could spend hours thinking about pathogenic neisseria, the cause of bacterial meningitis. And then there was listeria, a deadly, but largely overlooked, food-borne pathogen that under the right circumstances can kill more people faster than anthrax.

As a student, Higgins saw them all under the microscope and got hooked on the detective work required to determine one from another. He scrapped medical school plans and devoted himself to learning how pathogens make a living, get inside cells, replicate, spread disease and sometimes death, and what scientists can do to stop them.

It worked out for him. Still just 38, Higgins is an assistant professor of microbiology and molecular genetics at Harvard Medical School. He is, according to colleagues, a rising star. And his latest work, recently published in the journal *Science*, has created something of a buzz among other bacteria lovers.

The study looked at how listeria infects the cells of a fruit fly. But instead of focusing on the pathogen, Higgins and his team decided to focus on the cell. They wanted to know what genes allow the infection to get inside in the first place.

"No one had ever done this before," Higgins said recently from his office overlooking the quad at Harvard Medical School. "We say it's a two-way street, a two-way interaction. The pathogen has to interact with the host -- has to get something from the host -- to be able to do these things. We wanted to know what the host was bringing to the table."

Higgins has been thinking differently ever since he was a child, moving from city to city and sometimes country to country, following his father and the call of the US Air Force. Constantly the new kid, Higgins learned early on that he couldn't wait for others to befriend him. He had to go to them.

"I was always the outsider," he said. But not for long. He learned to be outgoing, forced himself to talk to others, made friends, and these days he considers his nomadic childhood a good thing. He is a scientist, but not a wallflower. And although new acquaintances may not immediately understand what Higgins does for a living, he has a way of putting it just so.

"I love what I do," he said. "It's a profession and it's a hobby. Not that I'm so socially inept that I don't do other stuff. But routinely, I'd rather do stuff in the lab than sit around on the couch all day doing nothing."

On this, his colleagues agree. Vic DiRita, a microbiology professor at the University of Michigan and Higgins's mentor during his doctoral studies there, called Higgins one of the hardest working scientists he knows. "That trumps everything in science," DiRita said. And apparently, the hard work is paying off.

In his fruit fly study, Higgins and his team identified some 270 genes that cells don't need to survive and how the bacteria interacts with them. Now, with further studies, he hopes to isolate which genes allow the infection to actually get inside the cell and spread. If it's one of the genes not needed by the cell, it could be blocked, Higgins said, stopping the spread of listeria and, perhaps, other bacteria.

The work that could have far-reaching effects, he explained. Perhaps most importantly, it could reduce our reliance on antibiotics to stop bacteria. And while that may not make for the most exciting cocktail party conversation, it's making a name for Darren Higgins.

"It's immensely cool," he said.

Fact sheet

Home: Born on a military base in Michigan, raised in part in Izmir, Turkey, and now living in Jamaica Plain.

Family: His father was in the U.S. Air Force for 30 years and his older brother followed his footsteps into the military. Higgins chose science instead. He is single.

Education: Graduated from Texas A&M in 1988, and earned his doctorate in microbiology and immunology from the University of Michigan in 1995. Did post-doctoral fellowship work at University of Pennsylvania and University of California-Berkeley and came to Harvard as a professor in 1999.

What is listeria?: *Listeria monocytogenes* is a food-born pathogen similar to salmonella. In most cases, it causes stomach aches, fevers and other flu-like symptoms. But listeria is also a killer — the most lethal food-born pathogen in the world, according to Higgins. It kills one out of every four people it affects, and sometimes infects dozens in widespread outbreaks. The last major outbreak killed eight people in 2002 in several northeastern states.

His science: Higgins studies how bacteria get inside cells and replicate, and what scientists can do to prevent that. Most recently, he studied what the cells themselves bring to the table. As he explained, “The bacteria can’t get in without some help from the host cell.” It is his hope that he can isolate what genes give the infection access. If he can do that, it would then be possible for doctors to attack infection, not by using antibiotics, but by knocking out the cell proteins that make infection possible. ■