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Dr. Miguel Valvano, Department of Microbiology and Immunology at the University of Western Ontario

Peeling Back the Layers

Researcher fights opportunistic infection in cystic fibrosis patients

By Matt Teeter

Burkholderia cepacia is a type of bacteria commonly found in soil and water that has negligible effects for most humans, but it can be deadly for people with cystic fibrosis (CF), a hereditary disease affecting one in 2,000 Canadian babies characterized by persistent lung infections. CF patients with weakened lungs and immune systems are unable to fight off the bacteria that when inhaled, invade and colonize in the lungs, deteriorating function. Now, a University of Western Ontario researcher is using a multi-pronged approach to help CF patients fight the bacteria.

Prof. Miguel Valvano says patients with CF have a decreased ability to eliminate inhaled environmental organisms such as *Burkholderia*. This leads to chronic lung infections which are difficult to treat, particularly because of increased antibiotic resistance.

“*Burkholderia* is a very damaging organism,” says Valvano. “It’s not the frequency of infected patients, but that once established in a patient it is very hard to eliminate. The increased inflammation due to infection can rapidly lead to death.”

Valvano is the Chair of the Department of Microbiology and Immunology at University of Western Ontario, and is a Canada Research Chair in infectious disease and microbial pathogenesis. He completed medical studies in his native Argentina before immigrating to Canada in 1988. It was his residency in paediatrics, where he specialized in infectious disease, which led him to study CF.

His research has since evolved to consider three themes related to *Burkholderia* infection.

The first is to understand how the organism becomes resistant to antibiotics. Valvano is finding the resistance is due in part to the structure of the envelope that surrounds and protects the bacteria. He’s looking for ways to inhibit the synthesis of envelope components and create new ways for antibiotics to penetrate it.

Already, the synthesis pathway of one envelope component has been identified. Inhibiting this pathway kills the bacteria. This is the first time the pathway has been identified as critical to the organism’s survival, Valvano says, and it could be used to develop new antibiotics that will fight infection.

The second theme of the research examines how *Burkholderia* can survive inside macrophages (the white blood cells that engulf and kill bacteria). Valvano wants to find ways to make the macrophages more capable of killing the bacteria, or make the bacteria more susceptible to the macrophages.

The third research theme seeks strategies to prevent the bacteria colonization in the airways of CF patients.

A vaccine has been developed for use in young people, since most who acquire the organism are in their late teens to early 20s. Valvano hopes to use it to provide early immunity to delay or prevent infection and prolong life.

Valvano says the success of his research is made possible through the excellence of his students and research fellows and he highlights five in particular. Karen Keith and Julie Lamothe have studied the nature of interactions between the bacteria and macrophages. Sylvia Cardona and Ximena Ortega identified the critical genes needed for the survival of *Burkholderia*. Finally, Ron Flannagan created genetic tools to allow the manipulation of the organism.

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