

UC San Diego Researcher Named 2007 Hartwell Fellow

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Douglas A. Mitchell, Ph.D., a postdoctoral fellow in the Department of Pharmacology at the University of California, San Diego School of Medicine, thinks that it might be a more diplomatic strategy to disarm bacteria rather than kill them. His efforts have uncovered a wealth of potential targets for novel antibiotics to fight childhood disease, which led to his recent selection by UC San Diego to receive a Hartwell Fellowship, which provides support of his research for two years at \$50,000 per year. The support is made possible by The Hartwell Foundation to enable scientists in the early stages of biomedical research careers to pursue further specialized training as part of their career development.

Mitchell - who works in the research laboratory of Jack Dixon, Ph.D., professor of pharmacology, cellular and molecular medicine, and chemistry and biochemistry at UC San Diego - is among the 2007 class of ten Hartwell Fellows announced by the Foundation. UC San Diego was named as one of The Hartwell Foundation's Top Ten Biomedical Research Centers in 2007. This designation allows UC San Diego to participate in The Hartwell Foundation's nomination process in support of competitive research awards, including the opportunity for the university to select one postdoctoral researcher - who exemplifies the values of the Foundation - to receive a Hartwell Fellowship.

The Hartwell Foundation seeks to stimulate discovery in early-stage biomedical research that it hopes will benefit children. Mitchell is working to develop a new therapeutic strategy to combat the notorious pathogen, *Streptococcus pyogenes*, which causes strep throat, among other diseases. Children are especially prone to strep infections, as indicated by 2.5 million visits to pediatricians annually in the United States alone.

Strep produces a complex polypeptide known as streptolysin S (SLS), a toxin also linked to diseases such as toxic shock, a skin infection called impetigo, and necrotizing fasciitis, better known as the "flesh-eating disease." Mitchell is studying how this toxin is produced by bacteria, in hopes of discovering how to take out a critical component and render it ineffective. In these efforts, Mitchell and colleagues have discovered that many bacterial pathogens biosynthesize toxins structurally related to SLS, leading to the belief that many diseases could be treated by targeting toxin production.

"All antibiotics now in clinical use or in development target essential life processes of the bacteria," said Mitchell. He added that the bacteria are pressured into developing drug resistance if such a vital process is inhibited, so a more thoughtful strategy is to target virulence and remove the bacteria's ability to cause disease in its host, or, as he puts it, "Let them live, but make them incapable of infecting humans."

Mitchell and colleagues have devised a way to attenuate the SLS toxin, a finding that could potentially lead to a strep vaccine, which stands to benefit more than just humans. A highly related bacterium, *Streptococcus iniae*, infects fish and devastates the food supply in countries that rely on fish as the cornerstone of their dietary needs. "Children living in poverty pay the price of malnourishment or even worse," Mitchell said.

The fish-infecting strep bacteria produce a toxin nearly identical to that which infects humans. In addition, a plant pathogen produces a similar toxin that wipes out entire crops, costing farmers in Europe and the United

States billions of dollars each year. Financial support from the Hartwell Fellowship paves the way for continued research into these important areas.

UC San Diego Vice Chancellor for Research, Arthur B. Ellis, noted "Douglas Mitchell is a superb choice for UC San Diego's first Hartwell Fellow. We are honored as an institution to be recognized by The Hartwell Foundation as one of the nation's leading centers for biomedical research. Douglas's project exemplifies our commitment to improving children's health, and we are extremely grateful for the support that The Hartwell Foundation is providing for this project and for Douglas's professional development."

Mitchell came to UC San Diego in fall 2006 after receiving his Ph.D. in Chemistry from UC Berkeley. A native of Pennsylvania, he received a B.S. degree in chemistry from Carnegie Mellon University in Pittsburgh.

The other institutions named as 2007 Top Ten Biomedical Research Centers by The Hartwell Foundation are Duke University, Johns Hopkins University, University of Texas Southwestern Medical Center, University of Pittsburgh, St. Jude Children's Research Hospital, University of Michigan, University of Wisconsin-Madison, Cornell University and University of Virginia.

More information about The Hartwell Foundation may be found on its web site at www.thehartwellfoundation.org.

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