RESEARCHER TAKES NEW APPROACH TO ANTIBIOTIC TOLERANCE

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Wins National Award to Further Research

With a perfect score on his research proposal, chemical and biomolecular engineering researcher Mehmet Orman received the National Institute of Allergy and Infectious Diseases (NIAID) Career Transition Award, meant to help initiate a successful bioengineering career as an independent research scientist. Orman will use the $250,000 prize to investigate cells that are resistant to antibiotics.

“A small fraction of cells in bacterial populations enter a dormant state. Once these cells become dormant, they intrinsically become tolerant to extraordinary levels of antibiotics,” said Orman. Conventional antibiotics function by targeting the mechanisms that enable the rapid growth of bacterial cell populations, but since the cells don’t grow while dormant, the antibiotics have little chance to work.

Eventually, these persister cells, as they are called, wake up and regain their ability to proliferate. Because of this, persister cells are thought to facilitate the recurrence of infections, and they serve as a reservoir for the emergence of drug resistant mutants. Recurrent infections are generally associated with biofilms, a slimy bacterial film in which persister cells are significantly enriched and can evade the host immune system. Biofilm infections, such as airway infections in cystic fibrosis patients, chronic obstructive pulmonary diseases, chronic wound infections, or infections caused by medical devices or prostheses, pose a significant health care problem in the United States.

Using E. coli as a model organism, Orman is aiming to identify and explore the mechanisms in bacterial cells that lead to dormant cell formation to discover new therapeutic strategies that eliminate bacterial persisters.

“I’m going to perform a high-throughput screening to identify candidate genes that regulate the cell dormancy in
bacteria,? said Orman. ?Then, I can focus on those genes individually and see how they impact the persister levels of the bacterial cells.? The high-throughput screening process allows Orman to screen a large number of genes rapidly.

Orman has been dogged in the study of these stubborn cells. Previously he developed the first methods to directly measure the metabolism of these rare and transient persister cells. He has also developed cell sorting strategies to segregate persisters from highly heterogeneous bacterial cell populations. He will be using these methods in his current research project.

?The physiology of persisters has remained elusive and hindered progress toward eliminating them,? said Orman.

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