IBBR awarded NIH grant to investigate body’s T-cell mechanism of attack

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New approaches hope to give researchers a glimpse into the cell’s “alert system” to fight tumors and viruses

(Rockville, MD, December 13, 2017) A new research initiative by the University of Maryland’s Institute for Bioscience and Biotechnology Research (IBBR) and the University of Pittsburgh could finally uncover how T-cells—the “killer cells” that defend the body from microbes—are alerted to hazardous invaders in the body. Funded by a $3.7 million grant from the National Institutes of Health (NIH), the research will be the first to combine X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy for a unique view of the cell’s alert system, which could lead to innovative therapeutics to fight viruses and tumors.

T-cells defend the body by recognizing and attacking a foreign invader, such as a virus, through a receptor on its surface (TCR). When viruses infect cells, they are broken up into pieces (peptides) that move to the cell surface where they are recognized by TCR’s. This causes the T-cell to activate and kill the infected cell, allowing the immune system to stop the spread of the virus.

“We have long known about the process of T-cell recognition, but not how the receptors signal to the T-cell that this recognition has taken place,” says Dr. Roy Mariuzza, who, along with Dr. John Orban, are IBBR’s principal investigators on the project. “Understanding the TCR signaling mechanism may allow researchers to develop new, targeted immunotherapies, such as those used in immuno-oncology to control or eliminate tumors.”

The team will apply a new approach, combining X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, two complementary techniques used for determining the structure and dynamics of proteins. “Proteins transmit signals by undergoing changes in their structure and dynamics,” says Dr. Orban. “When the viral peptide binds to the TCR, there may be perturbations in the TCR that trigger signaling. Our goal is to shed light on this process using our combined approach.”

Mariuzza and Orban will analyze and present hypotheses about the structural changes to Dr. Dario Vignali, a prominent molecular immunologist from the University of Pittsburgh and the third principal investigator. Vignali will test these theories by making mutations in the TCR and analyzing the effect of the mutations in biological systems.
“This research is an excellent example of fundamental science conducted at the institute that may lead to new therapeutic products. The Institute facilitates application of groundbreaking, basic scientific research to address significant unmet medical needs. We thank the NIH for their support of this promising area of research.” said Dr. Thomas Fuerst, IBBR Director.

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About IBBR
IBBR is a joint research enterprise of the University of Maryland, College Park, the University of Maryland, Baltimore, and the National Institute of Standards and Technology. The Institute serves as the nexus between academic research and commercial application, bringing together all of the critical elements necessary to pursue solutions for major scientific and medical challenges. Through collaboration and interaction among academia, government and industry, IBBR focuses on structure-based design, characterization and testing of proteins and nucleic acids, and conducting groundbreaking research to develop innovative translational applications. IBBR’s leverages its unique infrastructure and capabilities to advance projects and innovations towards commercialization in real world applications. The Institute also serves to expand the economic base of science and technology in the state of Maryland and at the national level.