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IBBR Awarded NIH Grant to Investigate T Cell Biology Toward Development of Biotherapeutics

Findings may show how immune checkpoint LAG3 can be exploited to fight disease

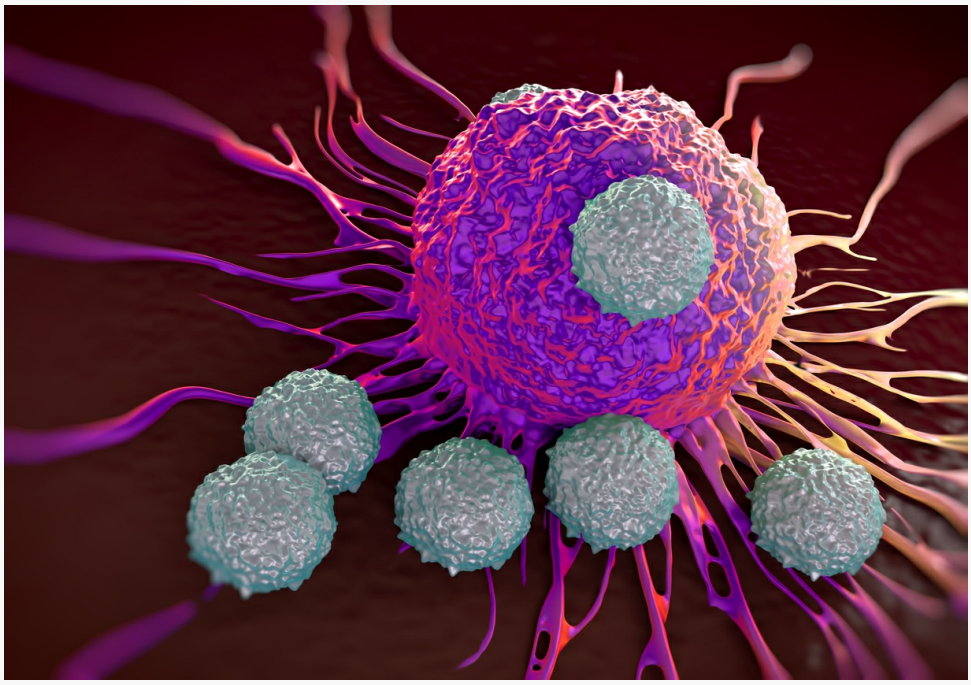

Illustration of T cells attacking a cancer cell

(Rockville, MD, January 31, 2019) A team of investigators from the Institute for Bioscience and Biotechnology Research (IBBR) and the University of Pittsburgh recently received a $3.6M National Institutes of Health award to expand the scope of their T cell research. IBBR Fellow Dr. Roy Mariuzza (Professor, UMCP Department of Cell Biology & Molecular Genetics) and collaborator Dr. Dario Vignali, Professor and Vice Chair of the Immunology Department at the University of Pittsburgh, will work to further characterize LAG3 -- a well-known inhibitory receptor on T cells. LAG3 activity has been implicated in various cancers, as well as in the chronic infections associated with malaria and HIV.

The human immune system fights infectious agents and protects us from cancer. But, this powerful system requires many mechanisms of self-regulation to minimize damage to our own tissues through autoimmune diseases and excessive inflammation. An important part of the checks and balances of the immune system involves “immune

checkpoint molecules," receptors on immune cells that turn down the immune response.

Pathogens and tumor cells thrive, in part, by engaging these immune checkpoint molecules, making them important drug targets in the fight against infectious disease and cancer. However, "the immune system is famously complicated and intricate," says Dr. Mariuzza, "so blocking a single checkpoint is unlikely to be effective for all applications." LAG3 is emerging as an important member of the immune checkpoint family of proteins with potential as drug targets.

Dr. Mariuzza is an expert in the structural biology of immune system proteins, including T cell receptors (TCR), antibodies, and MHC proteins. His group will determine the 3D structure of LAG3 bound to various molecules. This will provide structural insight into the function of LAG3, to support the development of new biotherapeutics that might inhibit, or activate, this important immune checkpoint molecule. Pharmaceutical companies with anti-LAG3 therapies in their development pipelines include Bristol-Myers Squibb, Boehringer Ingelheim, Regeneron, and Novartis.

The LAG3 project complements IBBR's growing T cell program which, in addition to integrating multiple state-of-the-art structural biology methods, also includes development and application of computational modeling tools for predicting how T cell receptors recognize and bind to their targets.

"An increased focus on T cells and TCR-based therapies supports IBBR's mission of pursuing breakthrough research and its translation to important solutions to scientific and medical challenges. We thank the NIH for their continued support of this exciting area of research," said Dr. Thomas Fuerst, IBBR Director.

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 sits at the nexus of academic research and commercial application, bringing together critical elements necessary inspire transformative discoveries in the field of biotechnology that provide innovative solutions to major scientific and engineering challenges important to society. IBBR researchers seek to advance the fields of disease pathways and biomolecular targets, biomolecular measurements sciences, and biomolecular engineering including structure-based design of vaccines and therapeutics. The Institute also serves to expand the economic base of science and technology in the State of Maryland and at the national level. For more information, visit https://www.ibbr.umd.edu/.

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