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La Jolla Institute-led consortium awarded up to \$35 million by NIH

The grant establishes the global Viral Immunotherapeutic Consortium to develop new treatments for Ebola, Lassa and other viral threats

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LA JOLLA—La Jolla Institute Professor <u>Erica Ollmann Saphire, Ph.D.</u>, will lead a five-year global effort totaling up to \$35 million that brings together experts from around the world to streamline and accelerate the development of immunotherapeutics against emerging and reemerging viral threats. The international consortium is funded through <u>the Centers of</u> <u>Excellence for Translational Research (CETR)</u> program at the <u>National Institute of Allergy and</u> <u>Infectious Disease</u>), part of the National Institutes of Health (NIH).

The <u>Viral Immunotherapeutic Consortium (VIC)</u> continues a tremendously successful international program that Dr. Saphire initiated and directed to bridge the gap between results obtained in the lab and effective treatments that can be deployed in the field. The consortium, now headquartered at La Jolla Institute for Immunology, pools the expertise of leading structural biologists, virologists, immunologists, clinicians and public health practitioners to understand which therapeutic monoclonal antibodies effectively combat disease in humans infected with Ebola or Lassa virus, and why.

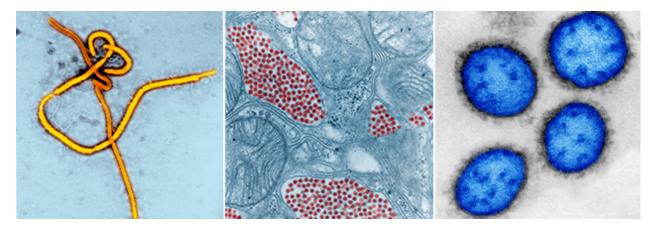
The program's effort will specifically focus on the clinical development of therapeutic candidates identified by the VIC for Ebola and other related filoviruses, arenaviruses, such as Lassa virus as well as a third major global threat, alphaviruses, which infect millions of people across the world.

"The recent resurgence of Lassa, the difficulties in containing Ebola outbreaks and the reemergence of alphaviruses in multiple locations including the United States, makes the development of therapies against these threats an urgent local and global concern," said Dr. Saphire.

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A key aspect of the previous rapid success of this consortium was how it uniquely united government, industry and academic laboratories across five continents to rapidly analyze viral infections and immunity from multiple perspectives and identify the fastest and best routes forward. In the course of their studies, the breadth of expertise and scale of the project allowed the team to uncover novel routes by which the immune response can clear viral infection, and to adapt to these new findings and revise the research pipeline.

"The first VIC was an excellent example of how we can make rapid progress when the best minds put their competing interests on the backburner and come together to work toward a common goal," said Dr. Saphire. "The new VIC expands our scope to include additional virus families while pushing new and improved immunotherapeutics for Ebola viruses and Lassa virus over the finish line and into the clinic."



The VIC focuses on the clinical development of immunotherapeutic treatments for Ebola (left), alphaviruse (middle) and Lassa virus (right) infections. Image: Courtesy of La Jolla Institute for Immunology.

With the support of the CETR grant, consortium members will study disease survivors to understand how their antibodies naturally fend off infection. They will then conduct detailed structural studies of interactions between virus proteins and these antibodies to determine which architectural features elicit the most robust protective immune response to guide development of treatments and vaccines.

The current Ebola virus outbreak in the Democratic Republic of the Congo is now the secondlargest in history and efforts to control the outbreak, including vaccination campaigns using an experimental vaccine, are hindered by violent conflict in the region. "There is an urgent need for therapeutics that can be administered after infection because of a lack of effective vaccines or challenges with vaccinating at-risk populations due to ongoing conflicts or resistance in the local population," says Dr. Sharon Schendel, Program Manager of the VIC.

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In addition to directing the overall effort, Dr. Saphire, whose pioneering research determined the molecular structure of the Ebola surface glycoprotein, will lead the Ebola project.

<u>Robert F. Garry, Ph.D.</u> (Tulane University School of Medicine in New Orleans, Louisiana) will guide the clinical development of first-in class human immunotherapeutics against multiple Lassa virus lineages. Although less well-known than Ebola, Lassa virus infects thousands of people in Africa annually. The young and women in late pregnancy are particularly vulnerable to Lassa virus infections, for which there are no vaccines or approved treatments.

The alphavirus project will also build upon available technologies and insights of the first VIC to identify broadly protective antibodies and rapidly translate those findings into human therapies to treat alphavirus infections. <u>Michael Diamond, M.D., Ph.D.</u>, (Washington University School of Medicine in St. Louis, Missouri) will lead this project.

Alphaviruses such as chikungunya and equine encephalitis viruses are largely transmitted by mosquitos and affect millions of people around the world. They can cause crippling pain and paralyzing encephalitis. Despite their epidemic potential, there are no existing therapies or licensed vaccines against any alphavirus.

A critical feature of the VIC is its scientific cores that tie together the projects on different pathogens. The Antibody Optimization Core, led by <u>Galit Alter, Ph.D.</u>, (Ragon Institute in Cambridge, Massachusetts) will explore how antibodies generated by the three projects can be tailored to harness the power of the immune system to lessen the severity of virus infections and prevent their associated diseases. <u>Doug Lauffenburger, Ph.D.</u>, (Massachusetts Institute of Technology in Cambridge, Massachusetts) will head the Computational Analysis and Modeling Core, which will develop algorithms that can predict which antibody features are most likely to confer protective activity.

The UCLA-DRC Health Research and Training Program, which is based at UCLA Fielding School of Public Health in Los Angeles and in the Democratic Republic of the Congo (DRC), will lead the sample collection in the DRC under the direction of <u>Anne Rimoin, Ph.D., M.P.H., (</u>UCLA and UCLA-DRC in Kinshasa).

The VIC will also engage industry partners to accelerate production of newly-developed therapeutics to the clinic.

Additional VIC consortium members include <u>Tom Geisbert, Ph.D.</u>, and <u>Alexander Bukreyev</u>, <u>Ph.D.</u>, (University of Texas Medical Branch), <u>Xiangguo Qiu, M.D.</u>, (Public Health Agency of Canada), <u>Daniel Streblow, Ph.D.</u>, (Oregon Health & Science University), <u>Richard Kuhn, Ph.D.</u>, (Purdue), <u>Daved Fremont, Ph.D.</u>, (Washington University), <u>Yoshihiro Kawaoka, Ph.D.</u>, (University of Wisconsin), <u>Carl Davis, M.D.</u>, <u>Ph.D</u>., (Emory University), <u>James Crowe, M.D.</u>, (Vanderbilt

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University School of Medicine), <u>Falk Nimmerjahn, Ph.D.</u>, (Erlangen), and <u>Boris Juelg, M.D.</u>, (Massachusetts General Hospital); industrial partners at <u>Zalgen, Inc.</u> (Luis Branco, Ph.D.), and <u>IDBiologics</u> (Charles Haines, M.D., Ph.D.); and collaborators Christos Kyratsous, Ph.D., (<u>Regeneron</u>), <u>Angela Rasmussen, Ph.D.</u>, (Columbia, Mailman School of Public Health), <u>Andrea</u> Marzi, Ph.D., and <u>Heinrich Feldmann, M.D., Ph.D.</u>, (Rocky Mountain Laboratories).

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About La Jolla Institute

The La Jolla Institute for Immunology is dedicated to understanding the intricacies and power of the immune system so that we may apply that knowledge to promote human health and prevent a wide range of diseases. Since its founding in 1988 as an independent, nonprofit research organization, the Institute has made numerous advances leading toward its goal: *life without disease*.

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