LA JOLLA INSTITUTE for ALLERGY & IMMUNOLOGY

Overview of Scientific Research Achievements

In the 20 years since its establishment, the La Jolla Institute for Allergy & Immunology has emerged as a world leader in immunology research. Institute scientists have contributed profoundly to the study of the immune system and the Institute was recently ranked among the top five in the world in molecular biology and genetics. La Jolla Institute researchers have made many important findings that are moving science closer to new treatments or cures for type 1 diabetes, asthma, cancer, infectious diseases and many other debilitating disorders related to immune system function. Among their more notable recent achievements are:

Institute researchers provide critical data on H1N1 influenza. At the height of public concern about the spread of the H1N1 flu, Bjoern Peters, Ph.D., led a study which showed that previous seasonal flu infections may provide at least some level of immunity to the H1N1 flu. The study compared the H1N1 virus and seasonal flues dating back 20 years and found enough molecular similarities to suggest that the general population likely had some pre-existing immunity. The data was greeted by intense scientific and media interest and points to a possible reason that the H1N1 pandemic has not produced widespread death as originally feared. Dr. Peters' research also bore out the wisdom of being vaccinated, noting that the viral similarities could help reduce the severity of H1N1 infection, but would not prevent initially contracting the H1N1 flu.

Visionary concept earns Institute scientist one of top NIH awards. Hilde Cheroutre, Ph.D., received the 2009 NIH Director's Pioneer Award -- one of the NIH"s most prestigious awards – for her proposal to create a new way of detecting, treating and possibly preventing autoimmune diseases. She was one of 18 recipients selected from 2,300 applicants nationwide. The award was created by the NIH in 2004 to encourage distinguished scientists to pursue out-of-the-box ideas that have the potential to profoundly improve human health. Dr. Cheroutre will receive NIH funding of up to $4.7 million over five years to support her research.

Antibody breakthrough key to development of stronger, more effective vaccines. A research team led by Shane Crotty, Ph.D., has identified the specific gene which triggers the body to produce disease-fighting antibodies -- a seminal finding that has major implications for the development of new and more effective vaccines. The finding, published in the prestigious journal *Science*, is vitally important in terms of its long-term benefit to science and society because it illuminates a pivotal piece of the vaccine development puzzle. Researchers from Yale University contributed to the study.

Tumor suppressor discovery linked to certain blood cancers. Toshiaki Kawakami, M.D., Ph.D., who is internationally known for his allergy research, set out to explore an enzyme's possible role in allergies, and instead discovered a tumor suppressor mechanism that no one knew existed. Dr. Kawakami's finding, which continues to be explored, may have therapeutic implications for myeloproliferative diseases and some types of lymphoma and leukemia.

Mysterious and sometimes fatal reaction to smallpox vaccine unraveled. Toshiaki and Yuko Kawakami, M.D.s, Ph.D.s., a husband and wife scientific team, led the Institute's efforts to pinpoint the cellular defect that increases the likelihood, among eczema sufferers, of developing eczema vaccinatum, a severe and potentially fatal reaction to the smallpox vaccine. The research, conducted in mouse models, was funded under a special research network created by the National Institutes of Health in 2004.

Major asthma finding licensed for potential therapy. A discovery by Michael Croft, Ph.D., of a cellular mechanism to suppress asthma was licensed in 2008 for the potential development of a new asthma treatment. Dr. Croft 's finding, licensed by MedImmune, a leading biotechnology company, demonstrated in mouse models that the lung inflammation and accompanying symptoms of an asthma attack could be significantly suppressed by blocking the interaction of the OX40 ligand with its receptor. The finding is a major milestone in asthma research and has been cited as one of the recent breakthroughs in this area by the American Asthma Foundation. It offers the potential to control asthma for longer periods of time and with more specificity than current therapies.

Groundbreaking discovery on potential autoimmune disease treatment. Hilde Cheroutre, Ph.D., and her team found that retinoic acid, a vitamin A derivative, can play a critical role in controlling inflammation in the body, which is the chief cause of inflammatory bowel disease, rheumatoid arthritis and several other autoimmune diseases. The finding, initially published in the prestigious journal *Science*, opened a new frontier in inflammatory disease research and was later named as one of the key biomedical research advances of 2007 by *Nature Medicine,* an internationally renowned research journal. Already used to treat some leukemias, Dr. Cheroutre's discovery demonstrated -- for the first time -- that retinoic acid also may have the potential for treating a host of autoimmune diseases.

Potential cure for recent-onset type 1 diabetes. Matthias von Herrath, M.D., and his research team have developed a combination therapy that is showing significant promise at stopping type 1 (insulin-dependent) juvenile diabetes, when caught in the early stages. Dr. von Herrath's study used a combination of a vaccine and an immunosuppressant drug in mice, and found it reversed recent onset type 1 diabetes in the majority of animals tested. Particularly exciting -- the diabetes never reoccurred in the lifespan of the mice. Human clinical trials of the combined treatment are planned in the next few years, once FDA approval of the two drugs individually is received.

Development of world's largest infectious disease database. The Institute developed and now hosts the National Institute of Health's Immune Epitope Database (IEDB), the world's largest database on how the body responds to infectious diseases. The database is a public health tool designed to accelerate vaccine-development on a global scale and was funded under the U.S. biodefense program. The NIH chose the Institute to develop the database in a competitive process in which its international experience in vaccine development and that of epitope expert Alessandro Sette, Ph.D., figured prominently. The database is now available freely to scientists worldwide at www.iedb.org

Institute discoveries advance fight against IBD; potential treatment advances. Major findings by President & Chief Scientific Officer Mitchell Kronenberg, Ph.D., and Carl Ware, Ph.D., are moving science closer to new ways to combat Crohn's disease and colitis, two chronic intestinal disorders collectively known as inflammatory bowel disease (IBD). Dr. Ware's discovery of a molecule, known as LIGHT, is now in pharmaceutical research for use in the creation of a potential new antibody therapy for IBD. Dr. Kronenberg, meanwhile, recently found new information about the possible molecular causes of IBD. His finding on regulatory T cells (TREGs) was recently published in the prestigious journal *Nature Immunology and* may explain why TREGs sometimes fail and cause the inflammation leading to IBD

Researcher fights bioterrorism concerns with potential smallpox treatment. Shane Crotty, Ph.D., has identified an antibody that could become the nation's first line of defense in protecting against a terrorist-sponsored smallpox outbreak. This is vital since the younger portion of the U.S. population is not vaccinated, and up to 10 percent of Americans cannot tolerate the current vaccine. Even though the smallpox virus is officially eradicated in the U.S., it has been the subject of intense research interest worldwide in the last several years, prompted by bioterrorism concerns. The U.S. government is considering stockpiling Dr. Crotty's antibody treatment alongside the smallpox vaccine and recently awarded Dr. Crotty a $7.1 million NIH grant to further his research.

Major allergy study could revolutionize treatment. Allergies are the subject of a major five-year project being conducted by the Institute, with funding from the National Institutes of Health. Led by faculty member Alessandro Sette, Ph.D., the project will map down to the level of molecules and atoms the chemical structures recognized by the immune system which initiate allergic reactions. This study could lead to revolutionary new approaches for treating allergies, which affect as many as 40 to 50 million people in the United States alone.

The role of NK T cells in asthma, Lyme disease and other bacterial infections. Mitchell Kronenberg, Ph.D., Institute president & scientific director, is drawing international interest due to his novel finding of an apparent connection between NKT cells, which are powerful disease-fighting cells, and Lyme disease, a serious tick-borne disorder. Dr. Kronenberg's finding that a glycolipid in the bacteria that causes Lyme disease triggers an immune attack by the NKT cells has led to hope for a new vaccine. He also co-authored a study published in the *New England Journal of Medicine* that found high concentrations of NKT cells in the lungs of asthma patients, opening the door to possible new asthma therapies based on controlling NKT cells.

###