China’s National Key Laboratory of Medical Immunology: Past, Present, and Future
At the western gate of the Second Military Medical University (SMMU) in Shanghai, there stands a five-story building. In 1999, when the Department of Immunology—the predecessor of the National Key Laboratory of Medical Immunology (LOMI)—moved into this building, Dr. Xuetao Cao, the director and founder, said to his colleagues, “It is our historical responsibility to establish a lab with an international reputation.” At that time, the Chinese economy was growing at an astonishing speed and attracting international attention; however, scientific research in China, especially the basic sciences, had yet to make a name in the world.

Fifteen years have now passed and Cao’s dream is beginning to come true. The Department of Immunology has blossomed from a small department to the only National Key Laboratory in the field of immunology in China. Focusing on basic research for the functional regulation of innate and adaptive immunity and on translational research for cancer immunotherapies, LOMI has been conducting innovative research and exploration, and is becoming a rising star in the international immunology community.

China’s National Key Laboratory of Medical Immunology

At the Forefront of Immunology Research

When the Institute of Immunology at SMMU won the title of National Key Laboratory of Medical Immunology in 2006, it was considered well deserved by Chinese colleagues. Though relatively young at just 15 years old, the institute has fast established itself at the forefront of immunology research worldwide.

This recognition is, in part, due to LOMI’s reputation for pioneering research. Director Cao has long followed the Chinese traditional philosophy of Yin-Yang while investigating immune regulation. For example, he has focused LOMI’s research not only on how the immune response is initiated to eliminate invading pathogens, but also on how immune responses are negatively regulated to avoid excessive activation that may cause damage. Such studies have resulted in the publication of over 250 peer-reviewed papers and China’s Ministry of Science and Technology choosing LOMI’s discovery of prognostic biomarkers for patients with cancer as one of the top ten scientific achievements of 2011.

The institute’s leadership has also worked hard to promote Chinese immunology research on the international stage, contributing greatly to its growing recognition. For example, LOMI has hosted several international immunology conferences in Shanghai to help its international colleagues learn more about Chinese research and scientists. Alongside such efforts to develop global relationships, Cao has been elected as the president of Global Alliance for Chronic Disease, president of the Federation of Immunological Societies of Asia-Oceania, and an editorial board member for the journals Annual Review of Immunology and Cell.

A unique history

Prior to being awarded its National Key Laboratory status in 2006, LOMI’s predecessor, the Department of Immunology, existed as part of the School of Basic Medical Sciences at SMMU. In 1990, Cao graduated from SMMU as the university’s youngest Ph.D. student. He turned down a postdoctoral training opportunity at Yale University to stay on at SMMU as a lecturer in the department to keep a promise to his mentor, Dr. Tianxing Ye, to grow the Department of Immunology into the most productive lab at SMMU. Cao quickly advanced, becoming the vice director of the department and full professor in 1992, and director in 1995. During that time, the department experienced its first round of rapid development and was focused on adoptive cellular immunotherapy for cancer.

However, in contrast to today’s funding climate, support for the basic sciences was limited at the time. Therefore, to create a better research environment, Cao sought out venture capital funding to set up a new building for his quickly expanding team. “I wished to establish a top-level lab. Inspired by my visits to top universities in Western countries, I worked with an architect to design a building with academic style for a new institute,” recalls Cao. In October 1999, he moved the lab into the five-story brick red building. One year later, he established a new institute, mainly from the Department of Immunology: the Institute of Immunology.

With the slow progress of cancer immunotherapy research, Cao was struggling to find ways to carry out basic research to develop new strategies for cancer treatment. Yu Yizhi, a professor at LOMI, recalls Cao’s astute decision regarding the department’s direction: “In the mid-1990s, Dr. Cao asked...
us to investigate antigen-presenting cells (APCs), particularly dendritic cells," says Yu. “During that time this field was not as popular, but Dr. Cao thought these cells could be important for the field of immunology, so we began researching them.”

This decision opened a new chapter for the institute. Starting in 1997, LOMI researchers began identifying novel genes from human immune cells (mainly dendritic cells) by random sequencing of cDNA libraries and bioinformatics analysis. Since then, 23 new gene names have been approved by the Human Genome Organization Gene Nomenclature Committee. These advances, along with studies on the functional regulation of dendritic cells, have led to a number of publications in high-impact journals—with the first Nature Immunology paper from China being published by LOMI researchers. LOMI underwent a second rapid growth period and was subsequently designated as China’s National Key Laboratory of Medical Immunology in 2006.

The following eight years brought stable financial support from the central government specifically for the National Key Laboratory, over 60 scientific publications, and a number of significant discoveries, including the unique function of long noncoding RNAs and the novel function of major histocompatibility complex class I and II molecules in toll-like receptor signaling. LOMI is now entering its third round of rapid expansion.

Research highlights

The institute’s success is largely due to the faculty’s creative research. The director’s office door bears the motto: “Time is precious, spend more time thinking.” It is in this spirit that Cao, who is also the past president of the Chinese Society for Immunology, leads his team of scientists and students. Cao says, “We are a young laboratory with great energy, and we focus on the frontiers of this field, which is why I think we have made some significant discoveries in the past years. Most importantly, our final goal is not only to produce publications, but also translate what we find into disease treatments.”

Understanding the regulation of immune system responses is one such frontier. Early on, Cao’s group discovered that the immune microenvironment could drive mature dendritic cells to differentiate into a unique type of regulatory dendritic cell, challenging the dogma that mature dendritic cells are terminally differentiated. This research became the cover story of a November 2004 issue of Nature Immunology. Cao’s team continues to study how immune system homeostasis is maintained and the role of the immune microenvironment.

LOMI researchers continue to cover novel immune cell-specific genes. Nan Li, who has been a professor at LOMI since 1996, has investigated the function of over 30 new proteins, including immune receptors, tumor antigens, and signaling molecules. “Most of these molecules have important roles in dendritic cell function, such as migration and activation of T cells,” she explains. “So they may be targets for the design of therapeutic approaches to infection and cancer.”

To investigate immune defenses against pathogen infections, Huazhang An, a professor who has worked at LOMI since 2000, explores the effects of innate immune receptors on inflammation. Invading pathogens can activate proinflammatory responses and cause tissue damage as well. “If we can find a way to inhibit inflammation but also enhance immunity against a virus, it would be much better for patients,” explains An. His group discovered that activating phosphatase SHP-1 inhibits inflammation while simultaneously increasing antiviral activity. This discovery could generate new treatments for antiviral infections.

Though such innate immune responses are key to combating foreign invaders, these cellular responses are disruptive when activated during organ transplantation. Professor Quanxing Wang explores ways to alter these responses. “We believe that the main limitation in organ transplantation is chronic rejection,” says Wang, “because it takes place over several months or years.” Wang’s team is searching for ways to treat chronic rejection by genetically modifying APCs, such as dendritic cells, to promote tolerance of transplanted tissue.

Translational research at LOMI also focuses on using basic research findings to develop new cancer therapeutics. For example, Professor Tao Wan’s team is trying to establish a new approach to chemoimmunotherapy. “Over the past ten years, we have been developing a new vaccine for colorectal cancer,” says Wan. This type of vaccine could greatly benefit these patients, who often show resistance to 5-fluorouracil, a major chemotherapy agent used to treat colorectal cancer.

A creative approach to research

Taoyong Chen, a young professor who also investigates the molecular mechanisms underlying host innate immune responses to pathogens, says that a unique and valued trait about the laboratory is that creativity is encouraged. Chen is developing strategies to enhance innate immune responses against infection and is searching for novel signaling mechanisms underlying inflammation in autoimmune diseases such as arthritis and multiple sclerosis. “If you are interested in a field, any field, you can research it,” he says. “The work time in our lab is very flexible, and I like to work in this style.”

This progressive work environment emanates from Cao’s leadership style. “If one of my faculty has a creative idea, I encourage them to go forward, even if it is not successful in the end,” says Cao. “Being a scientist means having an open mind and respecting the creativity of the individual. Coming from different directions with different views means we can collaborate. This is why our lab is so efficient.”

Collaboration is not only limited to the lab, but broadened to the global community. To facilitate such interactions, immunologists are invited from abroad to give lectures—and heated discussions often follow. Additionally, LOMI researchers are encouraged to study abroad. “They need to broaden their horizons,” says Cao. “We should pay attention to the frontiers in the field and learn new technologies, and then integrate what we learn into our own system.”

The institute has been successfully integrating basic immunology and translational research over the past decade and will continue to emphasize this strategy in the future. Cao believes that the challenges ahead lie in disseminating information to the medical community and forming new collaborations. “The future of LOMI lies in translating our scientific knowledge into clinical applications,” says Cao. “There’s a gap in communication between scientists and doctors, which we aim to fill by creating translational-focused projects.”

“We still have a long way to go before becoming a top-level lab; however, with the increasing support from the government, the timing is right for LOMI and its researchers to achieve our goals of contributing to the global understanding of immunology and developing new immunotherapeutic strategies to treat diseases,” says Cao.