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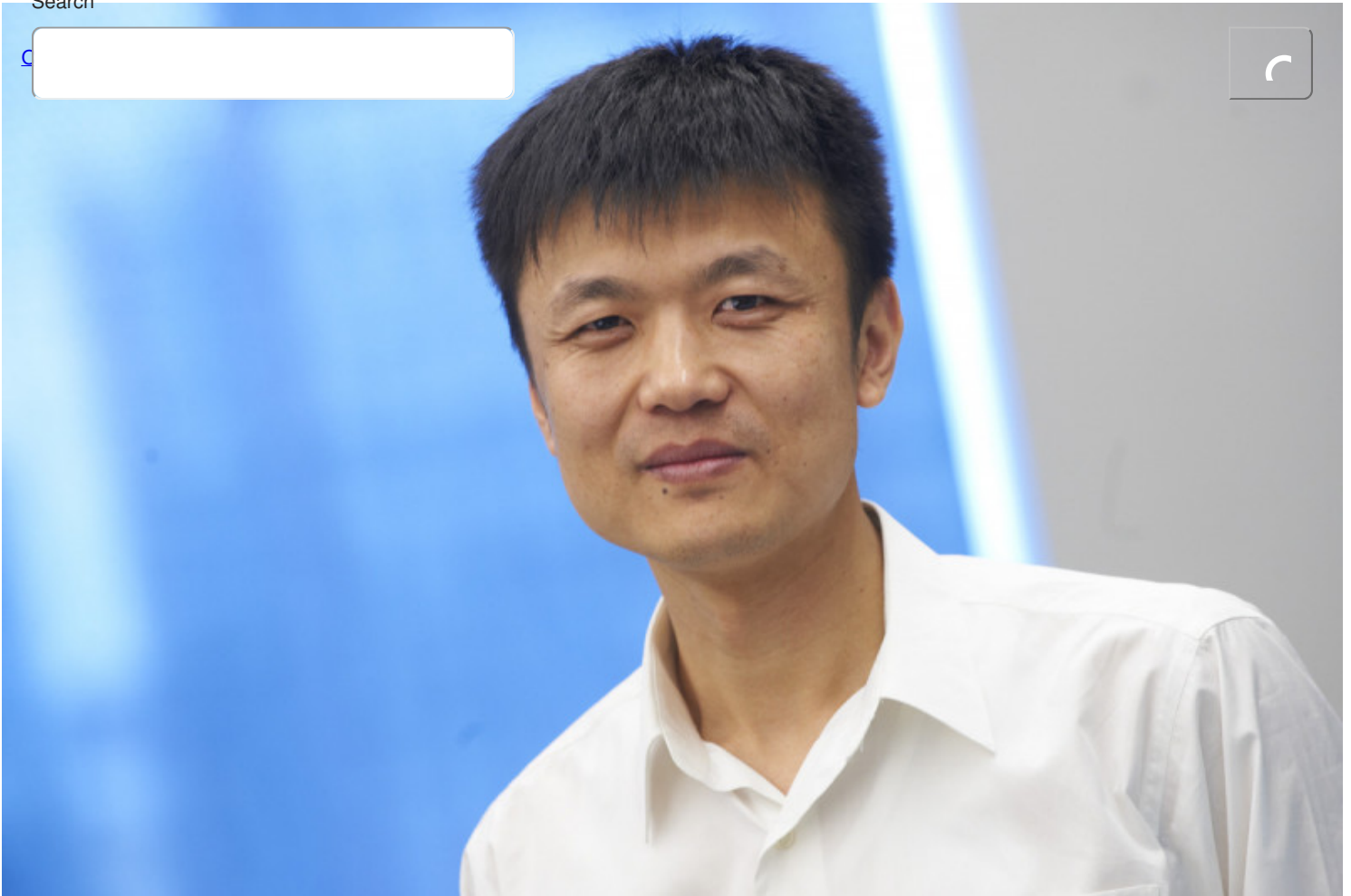
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## At Work: Immunologist Ming Li

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Ming Li

Immunologist Ming Li studies mechanisms of immune regulation and their relevance to diseases including cancer. We spoke with him soon after he joined Sloan Kettering Institute's Immunology Program in 2007.

Like many scientists, curiosity was my original motivation for entering the world of science. Being raised in a small town close to the Yangzi River and the East Ocean of China, my childhood was filled with wonderful outdoor adventures and an attachment to nature. Understanding the intricate beauty of nature has always fascinated me.

From very early on in my education, I showed great potential in mathematics. Resolving the logic behind the numbers is a fun thing for me to do. For some time, people thought I would grow up to be a mathematician or physicist. But biology has always been my favorite subject because for me it is

more interesting to study living objects than the inorganic world.

I was a “bookworm” in high school and college. I read many books of different disciplines, including those of the Belgian Nobel Prize-winning chemist Ilya Prigogine. His theory of nonlinear nonequilibrium thermodynamics has been used to explain the structures in organized systems. His books, especially *Order Out of Chaos*, inspired me to believe that there are fundamental principles underlying highly complex living beings, and I wanted to uncover some of those principles myself.

I majored in biochemistry when I studied at Fudan University in China. My curiosity about the control of biological responses made me interested in the transcriptional regulation of gene expression. I did my college thesis with a famous Chinese biochemist, Yonglian Zhang, during my senior year. I was exposed to various techniques for looking at the binding of transcription factors to promoter regions. That was my first real introduction to biology at the molecular level.

To continue what I had started, I went to Shanghai Institute of Biochemistry for my master's degree. My three years of training there was a great experience. I became more scientifically mature and technically capable. Meanwhile, I decided to pursue a PhD degree in biology.

## Coming to New York City

I chose to go to Columbia University for my PhD because its biological sciences department offered diverse topics of research. In the same year, an immunologist named Amer Beg finished his training with David Baltimore at MIT and joined the Columbia faculty. When Amer was at MIT, he generated a “knock-out” mouse model for the transcription factor NF- $\kappa$ B and discovered a critical function for NF- $\kappa$ B in regulating cell survival.

After my rotation in Amer's lab, I was drawn to the power of mouse reverse genetics. Indeed, the 2007 Nobel Prize went to Mario Capecchi, Martin Evans, and Oliver Smithies, who together made the original contribution of introducing specific gene modifications in mice.

I felt that a combination of biochemistry and genetics would be an ideal approach to study mammalian physiology. In Amer's lab, I was also introduced to the fascinating world of immunology, a field in which the intricate network of cells and molecules involved in the body's defense responses is studied. Amer was a great mentor who gave me freedom to conceive and pursue projects. This was a rich experience for a graduate student, and it prepared me for more independent research after graduation.

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## Going to New Haven

When it was time to pursue my postdoc training, I wanted to find a place where I could use mouse genetics as a tool to study biology. Meanwhile, I was looking for more training in the field of immunology. I decided to join Richard Flavell's lab at Yale. Richard pioneered the use of genetically modified mouse models in immunology research. His diverse interests created a uniquely rich environment in his lab, and he was extremely supportive of independent thinking.

During my stay at Yale, I was able to pursue my scientific interests with great freedom, while at the same time getting exposure to various topics of cutting-edge research from my labmates.

Increasingly, more studies reveal that cancer develops as a consequence of sophisticated interactions between tumor cells and their environment, including the immune system.

Ming Li  
Immunologist

I was most interested in learning how the immune system is regulated to allow it to discern foreign pathogens from self-tissues and to mount an effective immune response. I was particularly attracted to the regulatory cytokine TGF- $\beta$  that has diverse functions in a broad range of cell types.

To study the precise function and mechanism of TGF- $\beta$  control of immune responses, we used a tissue-specific gene-targeting technique to inactivate TGF- $\beta$  and TGF- $\beta$  receptor in various cell types in mice. These studies revealed TGF- $\beta$  as a critical regulator of T lymphocyte development, homeostasis, tolerance to self-antigens, and differentiation during the immune responses.

T cells are key components of the adaptive immune system. We were amazed by such a remarkably potent and pleiotropic function of TGF-beta in the control of T cell responses. As in most scientific research, interesting observations invite more intriguing questions. I felt it was time for me to start my own laboratory.

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## Coming Back to New York and Joining SKI

Coming back to New York City and joining the Sloan Kettering Institute was an easy decision for me. The [immunology program at SKI](#) is attracting the top scientists and is still growing. SKI also has the most amazing support resources to facilitate research. And cancer biology has always been one of my favorite topics of research.

My lab got off to a great start. I am a lucky receiver of two career development awards. I have also recently been selected as a Rita Allan Foundation Scholar. It is an honor for me to know that my work and ideas are recognized by my peers. Some terrific people have also joined my lab.

The focus of our research at this point is two-fold. One is in the general area of immune regulation. We are interested in dissecting the molecular and cellular mechanisms of T cell regulation, with an emphasis on the TGF-beta pathway. The second is on the topic of immune control of tumor development. Cancer researchers have focused on the genetic programs intrinsic to tumor cells.

Increasingly, more studies reveal that cancer develops as a consequence of sophisticated interactions between tumor cells and their environment, including the immune system. Gaining insights into these processes will not only help us understand cancer mechanisms but will also facilitate the harnessing of the immune system for the therapy of cancer. I believe that, with our hard work and the superb support from SKI, we will make interesting findings in the field of immune regulation and cancer immunity in the years to come.

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