Milestones in Cancer Immunology

2013 AACR-Cancer Research Institute
Lloyd J. Old Award in Cancer Immunology

Dr. Lloyd J. Old (1933–2011) was the founding scientific and medical director of the Cancer Research Institute (CRI) and was elected as an honorary member of the American Association for Cancer Research (AACR) in 1995. He was recognized as the founder of modern tumor immunology and the standard-bearer in the field of cancer immunotherapy. With steadfast vision and leadership, the late Dr. Old shepherded basic discovery in tumor immunity from the bench and animal models into clinical research, with the goal of discovering immune-based solutions to cancer.

"Dr. Old's prescient vision for the future of cancer treatment was rooted in his unwavering belief that the study of the immune system would ultimately yield the key to providing cancer patients with new and lifesaving treatment options," said Jill O'Donnell-Tormey, PhD, Chief Executive Officer and Director of Scientific Affairs at CRI. "Many of Dr. Old's own important discoveries laid the foundation for today's successes in clinical cancer immunotherapy, and it is fitting that the AACR and CRI have so named an award that celebrates others who are unlocking the cancer-fighting secrets of our own immune system."

The AACR-CRI Lloyd J. Old Award in Cancer Immunology was established to honor Dr. Old's legacy. The award is intended to recognize an active cancer immunologist who has done outstanding and innovative research in cancer immunology that has had a far-reaching impact on the field. Dr. James (Jim) P. Allison, Chairman and Professor of the Department of Immunology at The University of Texas MD Anderson Cancer Center, is the recipient of the first annual AACR-CRI Lloyd J. Old Award. Dr. Allison's work beautifully illustrates Dr. Old's vision of how basic science discoveries can lead to the development of new therapies that ultimately benefit the lives of cancer patients.

Dr. Allison received his BS in microbiology and PhD in biological sciences from the University of Texas, Austin. In 1982, as Assistant Professor of Biochemistry at The University of Texas System Cancer Center in Smithville, Texas, Dr. Allison was one of the first to discover and characterize the protein structure of the T-cell receptor (TCR), the targeting moiety that confers on T cells the exquisite specificity of target recognition. The activation of T cells required more than simply triggering the TCR. In 1992, as Head of the Division of Immunology and Director of the Cancer Research Laboratory at the University of California, Berkeley, Dr. Allison elucidated the function of a second T-cell molecule, CD28, which proved to be a critical costimulator for T-cell activation. He went on to show that CTLA-4, a T-cell molecule identified based on homology to CD28, was actually an inhibitor of T-cell function. These additional signals, collectively known as T-cell costimulators, became checkpoints modulating T-cell immune responses.

Dr. Allison realized that developing a drug that could block the negative signal mediated through CTLA-4 might result in more powerful T-cell responses. Together with his students and fellows, he developed an antibody/drug that blocked the function of CTLA-4. They tested the anti-CTLA-4 antibody in mouse models and showed that it could safely enhance the function of T cells and promote immune-mediated tumor destruction. He then forged collaborations with industry to develop fully human versions of this anti-CTLA-4 antibody that were suitable for testing in cancer patients.

Dr. Allison played a key role in the clinical development of the anti-CTLA-4 antibodies. This work culminated in two large randomized clinical trials, which demonstrated that CTLA-4 blockade increased the survival of patients with advanced malignant melanoma, the most common lethal skin cancer. This was the first time that any treatment was shown to prolong survival in this deadly cancer. Remarkably, about

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20% of the patients who received this drug achieve long-term survival, some ongoing now at more than 10 years. Based on these striking results, the FDA approved the use of anti-CTLA-4 antibody as a treatment for melanoma, and now many thousands of patients are receiving this drug worldwide. To improve the outcome of CTLA-4 blockade, Dr. Allison has elucidated some of the mechanisms that limit the activity of anti-CTLA-4, and these studies have given rise to new combination treatments involving other immunomodulators and cancer therapies. It seems likely that anti-CTLA-4 antibodies will become a critical part of curative treatment for many different kinds of cancer in the near future.

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