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Commentary

Cancer Vaccines 2005: Closing remarks

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The first thing I want to do is thank the organizing committee of this program for putting together an outstanding program with speakers from diverse backgrounds, giving an overview of some of the emerging concepts in the field of tumor immunology.

Secondly, I want to thank CRI for these meetings. They are now a little over ten years old. More importantly, the person who has been behind this extensive organization is Jill O'Donnell-Tormey, and I would like us to just recognize her contributions. [Applause]

As you are all aware, this meeting has covered several aspects of tumor immunology from innate immunity to adaptive anti-tumor immune responses. I have tried to capture some of the key elements from the different sessions.

The first session dealt extensively with innate immunity. New pathways of Toll-like receptor signaling were presented. Clearly, a greater understanding of this pathway should facilitate the development of more effective adjuvants for cancer immunotherapy. There was also information about the important role of NKG2D in controlling tumor progression and editing. Evidence was also provided that expression of NKG2D ligands is related to DNA damage response and this in turn, may lead to the generation of an anti-tumor response. For example, it is possible that chemotherapy and radiation therapy may enhance NKG2D ligand expression and thereby increase tumor sensitivity to NK cells.

In the second session, we saw a series of talks on *in vivo* tumor imaging. These series of talks are very fascinating, and, as a clinical investigator, one of the hopes is that this perhaps can be translated into human clinical trials in the future.

In session three, there were a series of talks on laboratory monitoring of the anti-tumor immune response, and a number of controversies were raised in this area. The concept of the cancer/trophoblast gene was introduced as perhaps more appropriate than cancer/testis (CT) genes. The notion was also raised that CT antigens are expressed on cancer stem cells, making these antigens even more attractive as targets for cancer immunotherapy. In that session, clinical trials coordinated through the Cancer Vaccine Collaborative of CRI and the LICR were presented. In these trials, it was clear that immune responses could be induced, and there was even a hint of clinical efficacy from the Australian trial of NY-ESO-1 plus ISCOMATRIX. Data was presented on lympho-depleting therapies, followed by adoptive transfer of tumor-reactive T cells along with treatment with low-dose IL-2. In some patients, clinical responses measured according to RECIST criteria were demonstrable.

The session on barriers and checkpoints was also very fascinating. The family of molecules involved in co-stimulation and co-blockade are expanding and the potential to harness this area in enhancing anti-tumor immune response was presented. Clinical trials of anti-CTLA4 antibody in several human cancers were presented with some promising results. I was particularly fascinated by the transgenic goat that is able to produce human monoclonal antibody for human clinical trials.

The fourth session on regulatory T cells (T-regs) really brought home the question of how to deal with this population of cells in human tumor immunotherapy. Data was presented on how immunization with SEREX-defined antigens led to the generation of T-regs. Therefore it will be important to recognize the potential of expanding an undesirable population of cells in immunotherapy trials. Importantly, in ovarian cancer, data from a clinical trial was presented and indicated that treating patients with an anti-CD25 antibody, the Ontak antibody, may lead to enhanced anti-tumor immunity in patients. The identification of ligands for T-regs was also very fascinating and the finding that specific ligands can be utilized to suppress these suppressor cells is of considerable interest.

The last two lectures were also very revealing. Data on the ability to expand NK T cells using α-gal-ceramide was presented. This was shown to lead to the generation of a better adaptive immune response. Finally, data on the need for T-cell help in programming fitness of CD8+ effector T cells, especially for their capacity for secondary expansion was presented. Robust expansion of both CD8+ and CD4+ T cells appears to be critical for an effective anti-tumor immune response.

Taking all of these areas together, it is clear that the sessions were very stimulating and very engaging, but the question is: where do we go from here? Again, as a clinical investigator myself, I would like to see the rapid translation of some of these findings into human clinical trials. In other words, there is a need for efforts to harness all the components of all of our basic understanding of all of the anti-tumor immune responses for effective immunotherapy. In my opinion, this meeting clearly demonstrates that there has been significant progress in the field, and it is hoped that this time next year, we will see even further progress in the application of some of these findings in human clinical trials.

Once again, I would like to thank everyone for their participation, and wish you all safe journey back to your different destinations. Thank you. [Applause]

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