TUMOR IMMUNOLOGY
AND CANCER VACCINES
Cancer Treatment and Research
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TUMOR IMMUNOLOGY AND CANCER VACCINES

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It all started with an observation. Edward Jenner, an English physician, observed that milkmaids who contracted cowpox were rarely victims of smallpox epidemic, a disease that inflicted a heavy toll on humankind with an estimate of 500 million victims worldwide. In 1796, Jenner inoculated the extracted fluid from blisters on the hand of a milkmaid who was infected with cowpox into the arm of an 8 year old peasant boy. After the boy recovered from a mild illness caused by this inoculation, Jenner exposed him to smallpox and to his delight the boy did not develop the disease. He published his work in 1798 in three publications titled “Vaccination Against smallpox”, where the term vaccination is derived from the Latin word “vacca” meaning cow. Jenner was recognized to be the father of modern immunology, and his work marked the commencement of a new dawn in medicine that led to the 1979 declaration by the World Health Organization (WHO) of the global eradication of smallpox. By the beginning of the 20th century, vaccines for typhoid fever, rabies, polio, plaque and diphtherias were in use, and nowadays we are equipped with effective vaccines against more than 20 infectious diseases such as meningitis, rubella, whooping cough, rabies, and hepatitis B among others.

It is indisputable that the immune system plays a role in the natural history of cancer. This theory is supported in animal models by the fact that tumors develop earlier and more frequently in nude mice than in mice with normal immune systems. In humans, the principal evidence comes from many facts including that many ‘immunocompromized’ cancer patients have higher incidences of a number of tumor types, including those of the lung, colon, kidney and pancreas, as well as malignant
melanoma; immune response modifiers have been shown to be effective in treating
tumors and in some anecdotes; tumors are known to regress spontaneously; and
increased patient survival correlates with the presence of T cells (or tumor infiltrat-
ing lymphocytes, TIL) in a variety of tumors such as melanoma, neuroblastoma, and
breast, bladder, colon, prostate, ovary, and rectal cancers. This indicates that tumors
are amenable for immune recognition, and hence, are able to present antigens that are
recognized by the immune cells. These antigens are called tumor antigens. There-
fore, it is concluded that tumors develop due to the failure of the immune system to
recognize and reject cancer, this is called “Tumor immune escape”; we now under-
stand some of the factors that lead to tumor immune escape which will be discussed
along with the principle of tumor antigens in the chapters of this book.

Advances in both immunology and molecular biology in the past decade have
led to the identification and characterization of these tumor antigens. That in turn
led to the revival of immunotherapy as the fourth modality of treatment of cancer.
This treatment can be highly specific and an effective therapy based on the ability to
develop tumor-specific antigen directed vaccines. The concept of Immunotherapy
for cancer is over one hundred years old. The first reported “Cancer Vaccine” trial
was by W.B. Coley in 1894. Coley’s toxin’s, as it was called, was not so much a
vaccine as a non-specific immuno-stimulant. He used thirteen different preparations
of bacterial extracts, between 1892 and 1936, to treat patients with a variety of
malignancies with surprising success. He and others, including investigators at Mayo
Clinic, reported over 50% durable responses in patient populations where 10-15%
survival was historically expected. About the same time, in the early 1900’s, Paul
Ehrlich proposed the concept of “Immune Surveillance”. Ehrlich suggested that
tumors present unique antigens that could be recognized by the immune system,
leading to continuous identification and removal of transformed cells. It was another
fifty years before his theory could be proven. In the 1950’s, when inbred mouse
strains became available, Ehrlich’s theory was tested and proved the immunogenicity
of tumors. The tumor antigens were subsequently identified.

The new era of biotechnology is helping us rapidly progress in our efforts to
identify tumor antigens, compare their immunogenicity, and then design effective
delivery system to present the most powerful antigens to the immune system. With
the completion of the human genome project, new technologies such as microarray
analysis and proteomics have been added to our repertoire and have proved useful
in identifying antigens that produce the best immune response; a pivotal requisite
to the success of a cancer vaccine. Such a success is also dependent on how the
antigen is delivered to the patient, the vehicle used along with the choice of adjuvant
and cytokines. This wealthy “vaccine basket” provides researchers with tremendous
choices when planning clinical trials and emphasizes the need to compare different
strategies of vaccine design and delivery according to its efficacy in combating cancer
in clinical trials.

In lieu of the tremendous amount of knowledge in areas of tumor immunology and
cancer vaccines, we recognized the need to provide researchers and clinicians alike
with a comprehensive up-to-date book on tumor immunology and cancer vaccines.
The first section of the book includes in depth analysis of basic tumor immunology, both cellular and humoral. This section explains mechanisms of antigen presentation, as well as the molecular reasons why tumors evade the immune system. The second section includes six chapters encompassing different vaccine strategies with emphasis on their preclinical development and current clinical data. How to enhance the immune response to cancer vaccines is the question tackled by the third section of this book. It documents preclinical and clinical developments in cytokine therapy, peptide vaccines and adoptive cellular immunotherapy. Finally, the last section of the book emphasizes the different issues regarding clinical trials design and application in addition to the latest advances in immune monitoring.

*Tumor Immunology and Cancer Vaccines* is the fruit of tremendous cooperation between our knowledgeable and devoted authors and the commitment and foresight of our publisher. We worked hard to make this book an effective resource, which we hope will translate to discoveries in the field of tumor immunology and more effective treatments of patients with cancer.