Recent Advances in Vaccination Therapies of Hematological Malignancies

Essay

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List of Abbreviations

Ags .....Antigens

Allo SCT .....Allogeneic stem cell transplantation

AML.....Acute myeloid leukemia

APC .....Antigen presenting cell

BAGE.....B-Melanoma antigen gene

BCG .....bacilli calmette-Guérin

BCL٢ .....B-cell chronic lymphocytic leukemia/lymphoma ٢

BCR-ABL .....Breakpoint cluster region-Abelson

BMT.....Bone marrow transplant

CD .....Cluster of differentiation

cDNA..... Complementary deoxyribonucleic acid

CG .....Cancer/germ line antigen

CLL.....Chronic lymphocytic leukemia

CML.....Chronic myeloid leukemia

CMV.....Cytomegalovirus

CR .....Complete response

Cru .....Complete response unconfirmed

CT-antigen ....Cancer/Testis-antigen

CTL.....Cytotoxic T-lymphocyte

CVP .....Cyclophosphamide, vincristine, and prednisone

DC .....Dendritic cell

DKK١ .....Dickkopf-١

List of Abbreviations (Cont.)

DLI .....Donor lymphocyte infusion

DNA .....Deoxyribonucleic acid

FL.....Follicular lymphoma

FLT٣ .....FMS-like tyrosine kinase ٣

GM-CSF.....Granulocyte-macrophage colony-stimulating factor

GVHD .....Graft versus host disease

GVL .....Graft-versus-leukemia

Hib .....Haemophilus influenza type B

HIV .....Human immunodeficiency virus

HL٦٠..... Human promyelocytic leukemia cells ٦٠

HLA .....Human leukocyte antigen

HSCT.....Hematopoietic stem cell transplantation

hTERT.....Human telomerase reverse transcriptase

Id.....Idiotype

IFN .....Interferon

Ig.....Immunoglobulin

IL.....Interleukin

ITD .....Internal tandem duplications

KLH.....Keyhole limpet hemocyanin

LAAs.....Leukemia-associated antigens

LSCs.....Leukemic stem cells

MAPK .....Mitogen-activated protein kinases

List of Abbreviations (Cont.)

MDS.....Myelodysplastic syndrome

MHC .....Major histocompatibility complex

MM .....Multiple myeloma

MRD .....Minimal residual disease

mRNA.....Messenger Ribonucleic acid

MUGS .....Monoclonal gammopathy of undetermined significance

NHL .....Non Hodgkin lymphoma

NK .....Natural Killer cell

PACE .....Prednisone, doxorubicin, cyclophosphamide, etoposide

PBMCs.....Peripheral blood mononuclear cells

PCR .....Polymerase chain reaction

PFS.....Progression-free survival

Ph١ .....Philadelphia chromosome

PR.....Partial response

PR٣ .....Proteinase ٣

PRAME .....Preferentially expressed Ag of melanoma

PRR.....Pattern recognition receptors

RAR.....Retinoic acid receptor

R-CHOP.....Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

RHAMM.....Hyaluronic acid–mediated motility

RNA.....Ribonucleic Acid

S.C.....Subcutaneous

List of Abbreviations (Cont.)

SD.....Stable disease

SPAG٩ .....Sperm-associated antigen ٩

TCR .....T-cell receptors

Th١ .....T helper ١ cell

Th٢ .....T helper ٢ cell

TKIs .....Tyrosine kinase inhibitors

TNF .....Tumor necrosis factor

TSA.....Tumor specific antigens

WT١ .....Wilm's tumor type ١ gene

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INTRODUCTION

Hematological malignancies include the acute and chronic myeloid and lymphocytic leukemia, multiple myeloma, the Hodgkin's lymphoma and the non-Hodgkin's lymphomas. Most are of B-cell origin (acute and chronic lymphocytic leukemia, multiple myeloma, and B-cell lymphomas) ***(Bae, ٢٠٠٨).***

The past several years have witnessed a significant progress in the treatment of hematologic malignancies. This improvement has been largely the result of newer and more effective combination chemotherapy, improved radiation delivery, and the major impact conferred by bone marrow transplantation (BMT). In spite of these successes, a significant portion of patients with hematologic tumors will ultimately die of their disease ***(Borrello and Sotomayor, ٢٠٠٣).***

The use of immune-based strategies in the treatment of tumors of hematologic origin is now paving the road to a better cancer treatment. During the past several years, the critical role of the immune system in the treatment of hematologic malignancies has been highlighted in a variety of settings ***(Sotomayor and Loughran, ٢٠٠٣).***

Cancer immunotherapy attempts to increase power and specificity of the immune system for the treatment of malignancy ***(June, ٢٠١١).***

A growing body of evidence suggests that immune mediated mechanisms may aid in the killing of malignant cells in patients with hematologic malignancies ***(Borrelloand Sotomayor, ٢٠٠٣).***

The identification of tumor specific antigens derived from hematological malignancies has facilitated the development of cancer vaccine strategies ***(Avigan, ٢٠٠١).***

An ideal tumor vaccine should be able to generate an active systemic immune response in the cancer bearing host, leading not only to specifically reject disseminated malignant cells, but also, and more importantly, to provide long-lived immunologic memory capable of protecting the vaccinated host against relapse ***(Borrello and Sotomayor, ٢٠٠٣).***

Tumor cells evade host immunity through a variety of mechanisms that suppress the function of antigen presenting and effector cells and inhibit anti-tumor immunity creating an immuno-privileged site at the tumor bed. Research in cancer immunotherapy has focused on the reversal of this phenomenon through the enhancement of antigen presentation, augmentation of T-cell function and memory responses, and the circumvention of tumor mediated immune suppression ***(Avigan, ٢٠٠١).***

Immunotherapy may be passive and active which is more effective ***(Neelapu and Kwak, ٢٠٠٧).***

AIM OF THE WORK

To highlight the future of vaccination therapy and its promising role in curative treatment of hematological malignancies.

IMMUNE SYSTEM

The Latin "immunis", meaning free from burden, has provided the English term immunity; it is often used in non-scientific contexts such as diplomatic immunity, crown immunity and so on. In biology, the burden is disease caused by a variety of viruses, fungi, bacteria, protozoa, worms and toxins and the physiological role of the immune system is to keep it at bay ***(Peakman and Vergani, ٢٠٠٩).***

"Immunity" refers to the global ability of the host to resist the predation of microbes that would otherwise destroy it ***(Hoebe et al., ٢٠٠٤).***

The complex and challenging task of the mammalian immune system is to detect and defeat host-threatening 'non-self' such as pathogens while avoiding damage to the host by uncontrolled immune activation in response to 'self'. The immune system of vertebrates can be roughly divided into two major branches – innate and adaptive immunity – to fulfill this task. Adaptive immune responses occur at later stages of infections and are characterized by the activation of highly antigen-specific lymphocytes and contribute to immunological memory. In contrast, the innate immune system provides components specialized on early and rapid sensing of invading

microorganism such as bacteria, fungi and viruses and act as first line of defense ***(Volz et al., ٢٠١١).***

History of immunology:

The earliest known reference to immunity was during the plague of Athens in ٤٣٠ BC. Thucydides noted that people who had recovered from a previous bout of the disease could nurse the sick without contracting the illness a second time ***(Retief and Cilliers, ١٩٩٨).***

In the ١٨th century, Pierre-Louis Moreau de Maupertuis made experiments with scorpion venom and observed that certain dogs and mice were immune to this venom ***(Ostoya, ١٩٥٤).***

This and other observations of acquired immunity were later exploited by Louis Pasteur in his development of vaccination and his proposed germ theory of disease ***(Plotkin, ٢٠٠٥).***