Atlas
Effectors of Anti-Tumor Immunity
Atlas
Effectors of Anti-Tumor Immunity

Editor

Mikhail V. Kiselevsky
NN Blokhin Russian Cancer Research Center RAMS, Moscow, Russia
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preface</td>
<td>vii</td>
</tr>
<tr>
<td>List of Contributors</td>
<td>ix</td>
</tr>
<tr>
<td>1. Adoptive immunotherapy for human cancers: Flagmen signal first “open road” then “roadblocks.” A narrative synopsis</td>
<td>1</td>
</tr>
<tr>
<td>Joseph G. Sinkovics</td>
<td></td>
</tr>
<tr>
<td>2. Tumor microenvironment genesis and implications on cancer immune response</td>
<td>25</td>
</tr>
<tr>
<td>Gianfranco Baronzio and Isabel Freitas</td>
<td></td>
</tr>
<tr>
<td>3. Natural killer cells. Lymphokine-activated killers</td>
<td>45</td>
</tr>
<tr>
<td>Irina Zh. Shubina, Olga V. Lebedinskaya, Evgenia O. Khalturina, Irina O. Chikileva and Mikhail V. Kiselevsky</td>
<td></td>
</tr>
<tr>
<td>4. CD4(^+)/CD25(^+) T-regulatory cells</td>
<td>65</td>
</tr>
<tr>
<td>Irina Zh. Shubina, Nadezhda P. Velizheva and Mikhail V. Kiselevsky</td>
<td></td>
</tr>
<tr>
<td>5. CD8(^+) CD57(^+) T cells in tumor immunology</td>
<td>73</td>
</tr>
<tr>
<td>María I. Sada-Ovalle</td>
<td></td>
</tr>
<tr>
<td>6. Natural killer T (NKT) cells: Immunophenotype, functional characteristics and significance in clinical practice</td>
<td>81</td>
</tr>
<tr>
<td>Olga V. Lebedinskaya, Nelly K. Akchmatova, Irina O. Chikileva, Irina Zh. Shubina and Mikhail V. Kiselevsky</td>
<td></td>
</tr>
<tr>
<td>7. LAK immunotherapy in clinical studies</td>
<td>101</td>
</tr>
<tr>
<td>Irina Zh. Shubina, Lev V. Demidov, Irina O. Chikileva, Olga V. Lebedinskaya and Mikhail V. Kiselevsky</td>
<td></td>
</tr>
</tbody>
</table>
8. Major properties of dendritic cells and their actual and potential applications in cancer therapy and infectious disease prophylaxis
   Irina O. Chikileva, Natalia Yu. Anisimova, Olga V. Lebedinskaya, Mikhail V. Kiselevsky and Vyacheslav M. Abramov

Index

161
Traditional understanding of anti-tumor immunity is based on the theory of immunological surveillance and it suggests function of cytotoxic lymphocytes that can recognize tumor-specific antigens and lyse malig-nantly transformed cells. However tumor development is not the direct result of immune system disorders and even in case of marked immuno-deficiencies, in particular, in patients – transplant recipients, immune dysfunction does not always lead to higher cancer incidence comparing with total population. This phenomenon may be explained by the concept of immuno-editing, which suggests that anti-tumor immunity effectors can not only protect the organism from tumor development, but also select low immunogenic clones of transformed cells that can escape from immuno-biological surveillance. Mechanism of avoiding the immune attack is primarily due to the lack of specific antigens on tumor cell surface and loss or down-regulation of expression rate of molecules of major histocompatibility complex, which are necessary factors for initiation of adaptive immune response and generation of antigen-specific T-lymphocytes. Therefore recent data have more often given evidence in favor of innate immunity being the main weapon of immune surveillance over tumor development. And NKs play the crucial role as they can recognize and lyse transformed cells in MHC and antigen independent manner. An important part in realization of anti-tumor defense is assigned to other effectors of innate immunity as well, first of all, as potential NK activators, such as dendritic cells and natural killer T-cells. Along with the mentioned functions innate immunity effectors can have a negative regulatory effect on anti-tumor immuno-biological surveillance by secreting Th2 cytokines. Contemporary standpoints in understanding mechanisms of innate and adaptive immunity are the basis for development and improvement various methods of adoptive immunotherapy.

Anti-tumor immunity has been subject of most thorough interest and detailed investigation over the last decades. Nowadays more and more specialists in medicine and adjacent areas face the problem of immuno-biological surveillance function. Research data on this issue are diverse and extensive. In numerous monographs, educational books and scientific papers a keen reader can find practically any material concerning the questions of interest. The purpose of the present publication is to convey considerably full and up-to-date information to the reader in a reasonably comprehensible format. To make the material easy for perception the Atlas has a large number of illustrative pictures, which also help to track interrelations between morphological features of anti-tumor immunity effectors and their phenotype and functional characteristics. The Atlas is aimed at a wide audience of students and teachers of medical and biology faculties, specialists
of research laboratories and diagnostics centers, practicing oncologists and immunologists, as well as physicians of different specializations.

The Atlas comprises over 200 figures and schemes referring to effectors of anti-tumor immunity and methods of anti-cancer adoptive immunotherapy.
List of Contributors

Vyacheslav M. Abramov  
Institute Immunological Engineering Moscow Region, Russia

Nelly K. Akchmatova  
II Metchnikov Research Institute of Vaccines and Serums, Laboratory of Therapeutic Vaccines, Moscow, Russia

Natalie Yu. Anisimova  
NN Blokhin Russian Cancer Research Center RAMS, Laboratory of Cell Immunity, Moscow, Russia

Gianfranco Baronzio  
Family Medicine Area ASL1 Legnano (Mi) and Radiotherapy, Hyperthermia Service, Policlinico di Monza, Monza, Italy

Irina O. Chikileva  
NN Blokhin Russian Cancer Research Center RAMS, Laboratory of Cell Immunity, Moscow, Russia

Lev V. Demidov  
NN Blokhin Russian Cancer Research Center RAMS, Department of Biotherapy, Moscow, Russia

Isabel Freitas  
University of Pavia, Department of Animal Biology and IGM-CNR Center for Histochemistry and Cytometry, Pavia, Italy

Evgenia O. Khalturina  
I.M. Setchenov Medical Academy, Department of Microbiology, Virusology and Immunology Moscow, Russia

Mikhail V. Kiselevsky  
NN Blokhin Russian Cancer Research Center RAMS, Laboratory of Cell Immunity, Moscow, Russia

Olga V. Lebedinskaya  
EAVagner Perm Medical Academy, Department of Histology, Embryology and Cytology Perm, Russia

María I. Sada-Ovalle  
Research Unit, Biochemistry Department, National Institute of Respiratory Diseases, Calzada de Tlalpan 4502, Col. Sección XVI, Delegación Tlalpan, México D.F., Mexico

Irina Zh. Shubina  
NN Blokhin Russian Cancer Research Center RAMS, Moscow, Russia

Joseph G. Sinkovics  
St. Joseph’s Hospital’s Cancer Institute Affiliated with the H. L. Moffitt Comprehensive Cancer Center at the University of South Florida College of Medicine; Department of Medical Microbiology & Immunology, the University of South Florida College of Medicine, Tampa FL, USA

Nadezhda P. Velizheva  
NN Blokhin Russian Cancer Research Center RAMS, Moscow, Russia
The *Atlas Effectors of Anti-Tumor Immunity* was published with the financial support of The International Science and Technology Center (ISTC). Chapters 3–8 have been written by the participants of ISTC-supported projects. This publication has been produced with the financial assistance of the European Union as a Funding Party to the Agreement establishing the ISTC.

The International Science and Technology Center is an intergovernmental organization holding diplomatic status, created to prevent nuclear weapons proliferation, contribute to global security, and to link the demands of international markets with the exceptional pool of scientific talent available in Russian and other Commonwealth of Independent States (CIS) institutes. The ISTC was established in 1992 by the European Union, Japan, the Russian Federation, and the United States of America on the basis of a multinational agreement. Canada joined as a full Governing Board member in 2004. The ISTC’s core activity is associated with the development of international science projects. Since 1994, the ISTC has managed financial support exceeding USD 769M to 2500 projects, encompassing over 70,000 scientists and technicians at more than 700 institutes in Russia and CIS. The ISTC also provides a tax and customs-duty exempt mechanism for its 370 commercial and governmental agency Partners to fund research with ISTC beneficiary institutes. Biotechnology is the most dynamically evolving direction of the ISTC activity, with over 640 projects totaling USD 202M.

The ISTC has established strategic partnerships with Russian and CIS innovation foundations and organizations, has engaged in technology transfer using its internationally agreed procedures, and has assisted a broad range of other international institutions, government organizations, universities, and the scientific community as a whole, to deliver their R&D and commercialization objectives.

*Contact details*

Steve Bourne
Communications Manager
Krasnoproletarskaya ul. 32-34, ISTC
P.O. Box 20, 127473 Moscow,
Russian Federation
Email: bourne@istc.ru
Office: (7-495) 982 3141
Web site www.istc.ru