Preface: Natural Killer Cells in Cancer: Surveillance, Progression, and Therapy

This special issue is dedicated to the memory of Dr. Ronald B. Herberman (1940–2013). It is meant to celebrate his years of mentorship and scientific and clinical contributions focused on natural killer (NK) cells. For those of us who participated in creating this special issue, it has been a trip down memory lane, reestablishing old friendships and revisiting old times. Above all, however, this endeavor has served to trace the history of NK cell biology from its very beginning to the present. Today, NK cells are more popular than ever, and their considerable biological and clinical importance is illustrated by a steadily increasing volume of scientific reports in prominent peer-reviewed journals, as well as clinical trials utilizing these cells for therapies.

This special issue is an amalgamation of historical and memorial papers, as well as scientific and technical submissions. The overall intent is to show how, from rather humble beginnings, the field of NK cells has progressed via numerous mechanistic *in vitro* and *in vivo* studies to the clinic. The beginnings of NK cell research are described in the submission by Drs. Ortaldo, Wiltrout, and Reynolds, who, with Ron, were experimenting with natural cytotoxic cells, as NK cells were then known. We think you will enjoy this paper, particularly if you are "of an age," and you may be reminded of various interactions, controversies, and, of course, meetings, all of which were triggered by Dr. Herberman. The submission by Dr. Kiessling is a similar overview, but from a European perspective concerning the origin of NK cells and their early functional attributes. Some of the controversial aspects of NK cell identity and activities that emerge from these two accounts contribute to an interesting historical perspective.

The manuscript by Dr. Bonavida attempts to fuse the American and European camps, in addition to discussing the phenotype and functional heterogeneities of NK cells. These insights are extended by Drs. Butterfield and Whiteside, who address the phenotypic and functional assessment of NK cells, predominantly of human cells. Their discussion incorporates current technology, as well as an overview of historical assays.

The submission by Drs. Sungur and Murphy surveys the regulatory activities of NK cells emphasizing dendritic cells (DCs), T cells, as well as B cells, in addition to NK cell control of immunologic responses to neoplasia and chronic infectious diseases. Their theme focuses on NK cell regulation of DCs is extended by Drs. Ferlazzo and Moretta, who discuss the selective editing by NK cells of DCs during immune responses. They emphasize the fact that, as recognized today by many current researchers, DC–NK cell interactions are critical to optimizing adaptive immune responses in DC-based anti-cancer vaccine therapies. NK-cell–tumor interactions are a focal point of the paper Drs. Gao and Basse, who examine the interactions between the microenvironment and NK cells. In addition, Drs. Bernadini and Santoni focus on the role of chemokines in tissue homing, retention, and NK cell activation, as well as the effect of NK cells on tumor growth and metastasis. Their investigations have extended to not only malignancies but also infectious diseases and inflammation. In a parallel series of studies, Drs. Larson, Gao, and Basse discuss NK cell infiltration into tumors and the resultant prognostic and diagnostic implications. In addition, they discuss mechanisms whereby NK cells home to tumors and potentially regulate tumor growth and metastasis.

In their paper, Drs. Mishra, Welsh, and Szomolanyi-Tsuda discuss both historical and more recent studies examining NK cell-mediated regulation of virus-related tumors. Specifically, their discussion concerns clinically related viruses that may have an oncogenic potential and, more importantly, NK cell regulation of viral growth and induction of neoplasia. Dr. Rooney and her collaborators have brought the art of NK cell culture for human therapy to new heights. Their manuscript provides a concise, practical narrative of methodologies for NK cell purification and expansion under good manufacturing practices and their application to the treatment of neoplasia.

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Studies by Drs. Bachanova and Miller profile the use of NK cells for therapy of patients with neoplastic growths. The paper by Dr. Basse's group also addresses the clinical utility of NK cells, but from a more prognostic and diagnostic perspective. These authors address not only NK cell homing to sites of infection but also their infiltration to tumor sites, as well as prognostic correlations with NK cell density.

As editors of this special issue, we wish to express our gratitude to our colleagues for making our task possible. We hope that readers will benefit from this broadly sketched perspective into the NK cell world. To this world Dr. Herberman significantly contributed most of his career. We hope that this special issue will provide an enduring recognition of his efforts and his dedication to research. Taken together, this memorial to Ron by his colleagues, students, and "scientific descendants" is a fitting tribute to a man who remains our role model and our inspiration for conducting future studies into the clinical utility of NK cells to treat human disease.

Guest Editors:
James E. Talmadge, Ph.D.
University of Nebraska Medical Center
Omaha, NE

Theresa L. Whiteside, Ph.D., M.D.H.C.
University of Pittsburgh Cancer Institute
Pittsburgh, PA