Theresa L. Whiteside: if you believe you are correct, stay with it even if no one initially believes you

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Editor's note

Immunotherapy has been showing impressive outcomes for some cancer patients. However, due to the heterogeneity of cancers, some malignant cells are able to evade immune elimination, which is known as the tumor-escape mechanisms. To make things more complex, each tumor develops its own way of escape, and thus these mechanisms are highly dependent on the host-tumor interactions. Nowadays, it remains a challenge for clinicians to select patients who are most likely to respond to immunotherapy. Therefore, enhancing the efficacy of immunotherapy is of utmost importance in improving patient selection and developing rational combination therapies for these patients.

As the Professor of Pathology, Immunology and Otolaryngology at the University of Pittsburgh School of Medicine, UPMC Hillman Cancer Center, Pittsburgh, USA, Prof. Theresa L. Whiteside has been studying cellular and molecular cancer immunology for many years, with a special interest in tumor-mediated escape mechanisms and surrogate immunologic markers of prognosis and response to therapy in patients with cancer. *Translational Cancer Research (TCR)* is pleased to interview her this time with a focus on the current understanding about the tumor-escape mechanisms, her recent NIH-funded research, the NIH Career Development Program (CDP) that she is involved in, and some special moments throughout her research.

Figure 1 Prof. Theresa L. Whiteside.

Expert introduction

Theresa L. Whiteside, PhD, currently serves as the Professor of Pathology, Immunology and Otolaryngology at the University of Pittsburgh School of Medicine, UPMC Hillman Cancer Center, Pittsburgh, USA (*Figure 1*). She is a clinical immunologist with extensive experience in evaluating human immune-mediated diseases. She directed several laboratories performing a broad spectrum of immunodiagnostic assays and serial testing of patients with cancer. Her research has been focused on tumor immunology and immunotherapy, especially on mechanisms of tumor-induced immunosuppression, cytokine networks, development of anticancer vaccines, immunology of human head and neck cancer and the role of natural immunity in the control of cancer progression.

Prof. Whiteside is well-known for her studies of immune monitoring in patients with cancer. Since 2002, she has served on numerous National Institutes of Health (NIH) and Department of Defense (DOD) study sections, and is a past member of the Board of Scientific Counselors for National Institute of Dental and Craniofacial Research (NIDCR). She is a member of numerous journal editorial boards and has authored over 600 peer-reviewed publications in scientific journals, and over 110 chapters and review articles. Over the years, she has trained more than 90 post-doctoral fellows from the United States and abroad.

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Interview

TCR: What is the current understanding about the tumor-escape mechanisms?

Prof. Whiteside: There are numerous tumor-escape mechanisms. Many have been identified and studied, but equally many remain poorly defined. The problem is complex because each tumor develops and uses its own unique escape mechanisms, and these mechanisms are dependent on the host-tumor interactions. This is a personal relationship that has to be unraveled at an individual basis. The role of tumor-derived exosomes in tumor escape and in modulating of responses to immunotherapy in cancer is not yet understood, but it emerges as one of the most important aspects of tumor progression as well as resistance to therapy.

To enhance the efficacy of immunotherapy, the rational way is to identify the escape mechanisms used by the given tumor and then devise the strategy for eliminating or blocking these mechanisms by immunological or pharmacological interventions.

TCR: Would you introduce us to a recent NIH-funded research that you are involved in?

Prof. Whiteside: I am just completing a 5-year NIH-funded project in which we are focusing on plasma-derived exosomes in patients with head and neck cancers (HNC) and the role of these exosomes as biomarkers of tumor progression and also as biomarkers of immune responses to conventional cancer therapies and to immune therapies. Patients with HNC in the Pittsburgh area serve as donors of plasma or tumor tissues for these studies. The objective is to show that tumor-derived exosomes are potentially valuable biomarkers for cancer and for evaluation of the patients' anti-tumor immune responses. In the future, we hope to be able to eliminate or silence immunosuppressive tumor-derived exosomes and take advantage of exosomes that could be engineered to promote anti-tumor immunity.

TCR: We realize you are also helping NIH to lead a CDP that recruits new and established investigators to carry out research in HNC. What is the mission of this program? And what role do you play in it?

Prof. Whiteside: The mission of the program is to prepare medical students, postdoctoral fellows or young physicians' scientists for future academic research in medical fields. These young individuals need special training in doing translational research and by being engaged for a year or two in supervised bench research in the sponsor's laboratory. This allows them to acquire experience and build confidence in their own ability to function as translational scientists. I have served as a sponsor to a 4th year medical student who has just completed the year of research in my lab and is currently in the medical residency training.

TCR: Are there any interesting stories/challenges met during the recruitment and mentoring of these investigators?

Prof. Whiteside: The students or postdocs who select to enter this program are very bright and highly motivated. It is a wonderful opportunity for them to entirely focus on research and evaluate their potential for a research career. The challenge is to take advantage of as many opportunities for collaboration and interaction with other researchers as possible. I find that most of the participants are very interactive and tend to do too many things. So, the challenge is to keep them focused on the project they are funded to perform.

TCR: Out of the broad spectrum of medicine, why are you particularly interested in pathology and immunology? And what would be your advice to young investigators to further develop and grow in the field?

Prof. Whiteside: I am a cancer immunologist dedicated to studies of immune therapy of cancer. My special interest and expertise are in tumor immune escape. I have identified and worked with several different mechanisms of tumor escape and the challenges of discovery and clinical significance of these discoveries drive my desire to work harder and better. Currently, tumor-derived exosomes are my passion!

Having taught students and mentored young investigators for years, my advice to them would be: Choose what you want to do and why (the choices are always many and varied). Test your hypothesis as best you can and if you believe that you are correct stay with it even if initially no one believes you. Hard work, creativity and perseverance always win.

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