

KEYNOTE TALK

Wednesday, October 16, 2019 at 9am
(Emerald Bay 123)

Recognition of non-synonymous somatic mutations by Tumor Infiltrating Lymphocytes (TIL) in metastatic Breast Cancer

Nikos Zacharakis
National Cancer Institute
USA

Abstract: Adoptive transfer of tumor infiltrating lymphocytes (TIL) can mediate long-term durable regression in patients with metastatic melanoma, a type of cancer which is characterized by a high number of mutated genes and pronounced lymphocytic infiltrate. Common epithelial cancers, including breast cancer, express far fewer somatic mutations than melanoma and the level of reactive TIL is limited. This pilot study investigated the ability to identify personalized non-synonymous somatic mutations in metastatic breast cancer lesions, to grow TIL that recognize the products of these mutations, and to adoptively transfer these TIL into patients with metastatic breast cancer, refractory to other treatments. Metastatic and primary tumor lesions from thirty one patients with breast cancer were studied in the Surgery branch, NCI, NIH and all of them were found to contain and express mutated genes (range: 4-1788 , median: 99). TIL recognized at least one (range: 1-10, median: 3) mutated product in 21 of 32 the patients (66%). Five evaluable patients with metastatic breast cancer, refractory to prior multiple lines of treatment, were treated with enriched mutation-reactive TIL in our ongoing pilot clinical trial. The immunogenicity of mutations in the majority of the patients with metastatic breast cancer can be the platform for an adoptive T cell transfer therapeutic approach targeting those mutated genes.



Speaker Bio-Sketch: Nikolaos Zacharakis received his bachelor degree in Chemistry, from the University of Patras, Greece, followed by a Master of Science degree in Medicinal Chemistry from the same university. He earned his Ph.D. in Microbiology and Immunology from Temple University in Philadelphia, USA. In 2015, he joined Dr. Steven Rosenberg's group in Surgery Branch, NCI, NIH, where he remains until today. Dr. Zacharakis recently received the 2019 Federal Technology Transfer award by the Center of Cancer Research, NCI. The immune system and in particular, the biology of T lymphocytes has been in the center of Dr. Zacharakis research interests. In the earlier stages of his career, he investigated the T cell involvement in autoimmune diseases like Multiple Sclerosis and Scleroderma, whereas, in the recent years, the focus of his research is on the tumor immunology of Breast cancer. Dr. Zacharakis examines

the potential of tumor infiltrating T cells to fight metastatic lesions in advanced stages of the disease. Specifically, he is investigating the presence of immunogenic somatic mutations in patients with metastatic breast cancer and whether these mutations can be a sufficient target of T cells, aiming to the tumor killing. To ultimately evaluate the potential of those T cells, they are adoptively transferred into patients with breast cancer, as part of the clinical trials conducted in the NCI. Dr. Zacharakis believes that fully harnessing the powers of the immune system will be the key element in the fight against the disease and that immunotherapy can be in the frontline of therapy in cancer.