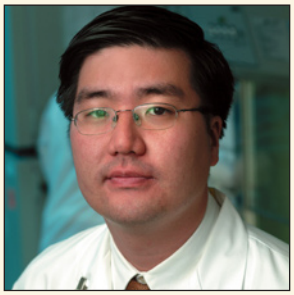
American Society of Clinical Oncology-ASP Junior Development Award in Geriatric Oncology



AWARD RECIPIENT

Allen S. Yang, MD, PhD

Keck School of Medicine at the University of Southern California

PROJECT

"Clinical Applications of DNA Methylation Changes in Myelodysplastic Syndrome"

MENTORSHIP TEAM

Roger Jelliffe, MD Peter Jones, PhD
Alexandra Levine, MD

There are an estimated 20,000 new cases of myelodysplastic syndrome (MDS) in the United States each year; however, as this disease is more prevalent in the elderly, this number is expected to increase with the aging of the US population. MDS is a heterogenous collection of hematologic malignancies, with a highly variable clinical course. About one third of patients with MDS will develop acute myeloid leukemia (AML). Treatment options for older patients with AML are poor. The current standard of care with cytarabine-based regimens produce a long-term survival rate of less than 10 percent and has a treatment associated mortality of 25 percent for patients older than 60 years of age. MDS patients who do not develop leukemia are still at high risk and usually succumb to infectious and bleeding complications of their disease. There is an immediate need to improve clinical management and treatment of MDS. Classification systems for MDS are based on pathological features, clinical features, or cytogenetic abnormalities.

Current classification systems (French-American-British, World Health Organization) are inadequate and are supplemented by the International Prognostic Scoring System, but improved methods of MDS classification would improve the clinical management of the disease. DNA methylation is a chemical modification of DNA that is associated with gene silencing. DNA methylation is part of a rapidly growing field, epigenetics, that studies gene regulation. Aberrant DNA methylation changes have been described in most cancers, including MDS. These methylation changes are accompanied with aberrant gene silencing, abnormal gene function, and the cancer phenotype. The importance of these changes is highlighted by the use of drugs that inhibit DNA methylation in MDS. It has been shown that these drugs inhibit DNA methylation in patients with MDS and other myeloid leukemias. We hypothesize that aberrant DNA methylation in MDS can be used as a classification and prognostic tool for MDS.

My research interests focus on the study of DNA methylation to improve the classification and treatment of MDS. We will use previously identified DNA methylation markers as well as established techniques to identify new DNA methylation markers for MDS. We will use these DNA methylation markers in an attempt to classify subtypes of MDS. In addition, we believe the use of DNA methylation inhibitors, as treatment for MDS, will lead to reversal of these aberrant DNA methylation changes. Finally, we believe these aberrant DNA methylation markers can be used to help predict the development of MDS in patients at risk of developing the disease either due to benzene exposure or previous treatment with chemotherapy.

With the generous support of the American Society of Clinical Oncology and ASP, my clinical and translational research work will be greatly enhanced. In addition, I will continue my career development under the mentorship of Alexandra Levine, MD, Peter Jones, PhD, and Roger Jelliffe MD, to gain further expertise in the fields of hematology, DNA methylation, and geriatric medicine. It is our ultimate goal to improve the lives of older patients with MDS.