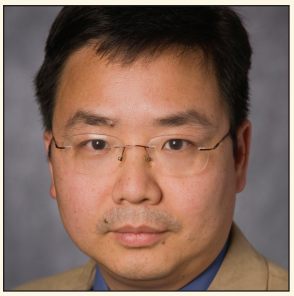
American Society of Clinical Oncology-ASP Junior Development Award in Geriatric Oncology



Award Recipient

William W. Tse, MD

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Project

"Biological and Clinical Study of AF1q Gene in AML"

Mentorship Team

Nathan A. Berger, MD
Scot Remick, MD
Stanton Gerson, MD
Kenneth P. Steinberg, MD

Acute myeloid leukemia (AML) is one of the most common forms of leukemia in adults. AML affects adults of all ages, but is especially common in older individuals. Approximately 12,000 new cases of AML are diagnosed each year in individuals with an average age range of 60 to 70 years. We expect that the incidence of AML will progressively increase as the population ages. Furthermore, the success of contemporary chemotherapy for different cancers is associated with significant marrow toxicity that can potentially increase the incidence of myelodysplastic syndrome and subsequently therapy-related AML. In contrast to younger AML patients, elderly AML patients generally have poor tolerance to intensive chemotherapy because the majority of elderly AML patients have pre-existing co-morbidities, poor performance status, and under-representation in clinical trials. The clinical outcome for elderly AML has shown little improvement over the last two decades. Therefore, there is a great sense of urgency to develop individualized risk-adaptive and minimally toxic treatment strategies for elderly AML patients.

My research interests focus on the molecular biology and pathophysiology of AML, with the goal of translating our laboratory findings into clinical practice by improving diagnosis, risk classification, targeted therapy, and therefore, clinical outcome for elderly AML patients. These studies can be divided into the following categories:

Developing Novel Molecular Markers to Improve Risk Stratification for AML

Traditional cytogenetics and contemporary FISH analysis are powerful tools to classify AML into different risk categories. However, more than 50 percent of AML patients do not have detectable cytogenetic or FISH abnormalities. These patients have a wide range of five-year survival rates between 24 and 42 percent. To date, there are few molecular markers available for risk stratifying adult AML patients with normal cytogenetics. Recently, we found that elevation of AF1q gene expression is an independent poor prognostic factor for pediatric AML and adult MDS. High AF1q expression is significantly associated with FLT3 mutations but is not associated with adverse cytogenetics. Therefore, we will determine whether high AF1q expression is a poor-prognosis marker for adult AML patients with normal cytogentics treated in the German AML Study Initiative AML-96. We will also try to understand the association of AF1q in leukemogenesis with other mutated leukemia associate genes, such as FLT3, in AML. These studies can help us to develop a risk-adaptive strategy to improve diagnosis and treatment of AML.

Bench-to-bedside Translational Focus on AF1q Signaling Pathways in AML

AML usually results in multiple aberrant signaling pathways. Since high AF1q expression is strongly associated with FLT3 mutations in AML, we will characterize how AF1q interacts with FLT3-ITD and the STAT5 signaling pathway. We will also try to develop both a pre-clinical and a clinical model based upon the molecular targeting of the AF1q, FLT3, and STAT signaling pathways in treatment of AML.

Thanks to the career development award generously supported by the American Society of Clinical Oncology and ASP, I will have a great opportunity to develop my clinical and translational research focus on improving the clinical outcome for elderly AML patients. In the meantime, this award will enhance my opportunity to develop an independent leukemia research program under the mentorship of Stanton Gerson, MD, and Kevin Bunting, PhD.