

Gene expression profiling and p53 and Myc oncogenic pathways as biomarker and drug target in hematologic malignancies

Ken H. Young

The University of Texas MD Anderson Cancer Center, USA

Diffuse large B-cell lymphoma (DLBCL) is the most common and devastating form of non-Hodgkin lymphoma (NHL) in the world. The incidence of NHL and DLBCL, ranked fifth of all cancer types in the United States, has increased by at least 100% over the last twenty years. Majority of patients diagnosed with DLBCL are elderly (65 year-old) with poor survival. The objective of this study is to determine the impact of specific p53 and Myc genetic aberrations and altered genetic/phenotypic expression patterns in lymphoma patients. The present project is the initiation of a large-scale clinical attempt in our group to identify new molecular links between p53 or Myc genetic aberrations and clinical. Specifically, we analyze to address: (1) the distribution profile of p53 and Myc genetic aberrations (mutation and deletion) in a large cohort of 900 DLBCL patients; (2) whether any or subsets of p53 and Myc aberrations have predictive value for clinical outcome in DLBCL; (3) whether genetic subtypes of DLBCL with different clinical outcome will exhibit unique structural profiles of p53 and Myc gene aberrations; (4) the location of critical mutations on the p53 and Myc molecule that play significant roles as prognostic indicators in DLBCL by structural analysis, and finally (5) the correlation of the gene expression profiling and genetic data with the results obtained from functional study to determine if there are unique gene expression alterations associated with specific candidate genes or unique genetic pathway. The general approaches delineated in this study are used to expand our study for additional molecular targets, in the same signaling pathway that are responsible for cancer patients. We build a prognostic model combining both the genetic information obtained in this study and associated clinical data. The findings provide insight into the functional consequence of the p53 and Myc genetic lesions and targeted treatment regimens.

Biography

Ken H. Young upon completion of his doctorate in molecular hematology at the University of Lund School of Medicine in 1996 and fellowship at the University of Nebraska Medical Center, joined the faculty at the University of Wisconsin School of Medicine where he directed Clinical Hematology Laboratory and translational research in lymphoma program. This led to the development of international DLBCL consortium program composed of 29 medical centers in the world. The program allows extensive investigation by several novel technologies for high-resolution array comparative genomic hybridization, p53 and Myc pathway analysis, SNP array, microRNA profiling and methylation analysis. Since 2010, he joined the faculty at the University of Texas MD Anderson Cancer Center. At the MD Anderson Cancer Center, he is applying a whole genome analysis for structuring tumor genomes and transcriptomes. This technology will allow comprehensive analysis of tumor genome combined with gene expression profiling and other array profiles. The work will lead to development of novel therapeutic targets linked to predictive biomarkers, including p53 and Myc, and benefit for improved clinical management. Concurrently, he has applied novel approaches to the lymphoma patients who received most recent treatment regimens with the goal of stratifying patients based on unique genetic features.

khyoung@mdanderson.org