The Magic of Comparative Genomics

Shih-Feng Tsai
Institute of Molecular and Genomic Medicine,
National Health Research Institutes, Zhunan, Taiwan

Genomic technology has made significant progress and impact in biology and medicine. In our laboratory, we have established high-throughput genome sequencing technology and applied it to the fields of microbial genomics and cancer genomics, taking a comparative approach. For microbial genomics, we have studied *Vibrio vulnificus*, *Enterobactericiae* and *Acinetobacter* species. To date, genome sequences representing three biotypes of *V. vulnificus* has been determined, and the ongoing comparative analysis should generate new insights regarding the different diseases caused by this marine bacterium in human and eels. We have developed protocols for genomic analysis of common bacterial pathogens and focused on studying the molecular evolution, pathogenesis, and drug resistance mechanisms, aiming at improving the diagnosis and treatment of the bacterial infection. For cancer genomics, we have taken a transethnic comparative approach in investigating liver cancer (hepatocellular carcinoma, HCC). HCC is a multifactorial disease involving both genetic and environmental factors, and it is characterized by prominent genomic instability, as revealed by loss of heterozygosity (LOH) analysis or comparative genomic hybridization, and most recently, by whole-genome sequence analysis. Several etiological factors have been implicated in causing HCC in different geographical regions of the world, and it is well known that viral infection, both hepatitis B virus (HBV) and hepatitis C virus (HCV) plays a significant role in HCC pathogenesis in our country. Besides, environmental factors, such as alfatoxin exposure, and behavior and life style, reflecting in diabetes and hypertriglycidemia, are also important risk factors for HCC. To implement preventive medicine and precision medicine for HCC, we propose to conduct detailed analysis of the genomic lesions of HCC by conducting whole-genome sequence analysis on HCC tumor specimens collected by the Taiwan Liver Cancer Network (TLCN). In a preliminary analysis, we have characterized the clinical features of four groups of HCC cases with a history of HBV or HCV infection, with dual HBV and HCV infection, and with neither of them. Based on this classification, we conducted whole genome sequencing on 100 HCC cases and compiled the genomic data of 25 from each group. In the current application, we propose to conduct detailed analysis to determine mutational profile, including: 1. functional gene mutations in known pathways; 2. tumor mutation load; 3. mutational signatures, to determine the unique genomic features associated with the major types of HCC.