Systematic and Functional Interrogation of Tumor Genomes and Transcriptomes
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With a mission of identifying and applying biomarkers associated with different malignancies, Molecular Medicine Research Center at Chang Gung University has established comprehensive Omics platforms (genomics, transcriptomics, proteomics and metabolomics) to conduct in-depth profiling of tumor tissues of interest. With the global expansion of systems data, our goal is to complement this information by generating our own integrative biomarker databases specific to locally prevalent diseases. Despite the seemingly straightforward approach, we have frequently encountered technical challenges in providing an accurate account of tumor markers, primarily due to the insufficient quality of clinical samples – likely as a result of improper and/or prolonged storage. Here I will present our recent results on oral squamous cell carcinoma (OSCC) tissues. By integrating omics analyses in 50 matched samples, we uncovered in Taiwanese patients a predominant mutation signature associated with cytidine deaminase APOBEC, which correlates with the up-regulation of APOBEC3A expression in the APOBEC3 gene cluster at 22q13. High-level APOBEC3A expression is associated with better overall survival, especially among patients carrying APOBEC3B-deletion alleles. The frequency of APOBEC3B-deletion alleles is higher in OSCC-Taiwan samples as compared to the public OSCC data, therefore revealing an ethnic germline polymorphism with clinical prognostic relevance in oral cancer. Furthermore, with the aid of TruSeq RNA Access Library Prep Kit, which is originally intended for degraded RNA samples, we also identified several novel circular RNAs differentially represented in our dataset. We have performed series of experiments and designed analytical tools for interrogating their functional and pathological relevance. While this type of non-coding RNAs are normally undetectable by the traditional mRNA sequencing, we have established a new way of identification and provided strong evidence for their unique tumorigenic expression and potentially biomarker roles.