

MicroRNAco-regulation of TET2 associated genes

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Myeloproliferative neoplasms (MPNs) are a kind of bone marrow diseases and Ten-Eleven Transcription 2 (TET2) mutations are found in MPN patients. Located on 4q24, TET2 can catalyze the conversion from 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC) in DNA. TET2 mutations, such as nonsense mutations, out-of-frame insertions, deletions, and splice site mutations, alter catalytic activity and lead to low level of 5hmC. However, it was unclear why some MPN patients with wild type TET2 also revealed both low level of 5hmC. To explore other factors affecting the 5hmC level, we investigated the microRNAs' post-transcriptional regulation of TET2 and its associated genes using 11 bioinformatics resources in our previous study. It was found that TET2 is associated with eight genes and they are targets of miR-152 and miR-29b. Importantly, DNMT-1, an associated gene, is a DNA methyltransferase that catalyzes the methylation, in which a methyl group is added to cytosine and 5mC is formed. Involvement of microRNAs may explain the low 5hmC level in MPN patients with wild type TET2.

Microarray dataset of Chronic Myeloid Leukemia (CML) patients, a class of MPN, was downloaded from Gene Expression Omnibus (GEO). The expression profiles of TET2 and its associated genes were extracted from the microarray dataset, forming an "omic" expression matrix. We constructed the co-expression network of these nine genes and explained the regulatory roles of microRNAs in CML (and thus MPN) through the analysis of the gene co-expression levels and the network topology.

Biography

Dr. Lawrence Wing-Chi CHAN is currently Assistant Professor in the Department of Health Technology and Informatics at the Hong Kong Polytechnic University. His current research interests include gene regulation by microRNAs and transcription factors, ontological patient similarity and clinical decision support. Dr. Chan has published more than 12 SCI journal papers, one of which has been non-self cited for 29 times, and three book chapters, presented 23 conference papers or posters, granted or filed three patents, and received two international awards and one external research grant.