Researchers publish whole genome map of key biomarker for detecting cancer

December 3 2020

Credit: CC0 Public Domain

Bluestar Genomics and University of Chicago have published a genome-wide 5-hydroxymethylcytosine (5hmC) map across multiple human tissue types. The study, published in the peer-reviewed journal *Nature*

Communications, demonstrated the robust performance of 5hmC as a global biomarker for the detection of multiple serious illnesses, such as cancer and various chronic diseases. Unlike 5mC which is a gene repression mark, 5hmC is a gene activation mark representing one of the most prevalent pathways involved in the regulation of embryogenesis, neurological processes, and carcinogenesis. The new map advances the understanding of diverse biological drivers in various diseases, which is necessary for the development of next-generation diagnostic tests.

"While previous studies have shown that 5hmC can serve as an excellent biomarker for the diagnosis and prognosis of human diseases including cancer, the lack of a whole-body tissue map limits our global understanding of this mark and its potential tissue specificity," says Dr. Chuan He, Professor of Chemistry at the University of Chicago and the senior author of the study. "Through this collaboration with Bluestar Genomics, the new publication significantly expands our understanding of this global biomarker, delivering what we believe is the broadest reported human tissue map that catalogs 5hmC modifications. The new map confirms 5hmC as a prevalent gene activation mark for both gene bodies and enhancers with superb tissue and cell type specificity, which is key to future early diagnosis of human cancer and monitoring of human chronic diseases."

In this study, the University of Chicago scientists collaborated with Bluestar Genomics to evaluate the performance and reproducibility of 5hmC as a biomarker across 19 tissue types from multiple male and female organs. The published results demonstrate that the 5hmC profiles identified in the new map provide an unprecedented database of potential diagnostic development, specifically in cancer.

Based on a study of 96 samples representing ten major organ systems: nervous, cardiovascular, digestive, reproductive, endocrine, respiratory, urinary, integumentary, skeletal, and lymphatic, the map represents the

most comprehensive examination of 5hmC as a biomarker for cancer detection. The data confirms the profiling accuracy (Spearman r = 0.82 compared with gold standard TAB-seq profiles) and reproducibility (Spearman r = 0.974) of the genome-wide 5hmC profiles obtained in various tissues, which underscores its clinical relevance and provides a unique resource to study distributions of 5hmC in the human genome.

Building on Bluestar Genomics' previously published work, the new publication highlights that 5hmC reveals known biology in human tissues by enabling the measurement of gene transcriptional and gene regulation activity with the same assay. The published map, which characterizes the genomic distributions of 5hmC in 19 human tissues derived from ten organ systems lays the foundation for the future development of diagnostic tests.

"With the ultimate goal of developing a robust cancer screening test, this map brings us a step closer to enhancing our ability to accurately read and interpret cancer signals coming from tumor tissues in cell-free DNA," says Samuel Levy, Ph.D., Chief Executive and Chief Scientific Officer at Bluestar Genomics, co-senior author of the study. "I'm proud that our work will also contribute to the broader scientific community by deepening scientists' precise understanding of the breadth of biology through the utilization of 5hmC."

More information: Xiao-Long Cui et al, A human tissue map of 5-hydroxymethylcytosines exhibits tissue specificity through gene and enhancer modulation, *Nature Communications* (2020). DOI: 10.1038/s41467-020-20001-w

Provided by Bluestar Genomics