Scholars develop new technology to decode gene transcription facilitating discovery of targeted therapy drugs

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A research team from the School of Chinese Medicine (SCM) of Hong Kong Baptist University (HKBU) has developed the world's first model framework and "LogicTRN" algorithm to accurately establish a gene regulatory route to analyse the genetic function and understand the biological processes that are responsible for the development of organs, progression of diseases and other complex biological events such as aging. Such a new mechanism could help efficiently locate the key regulatory route for complicated diseases, thereby facilitating the research and development of targeted therapy drugs. The research team has successfully applied the new integrative approach to analyse breast cancer and characterise the logical relations among transcription factors (TFs) in regulating biological processes. The work was recently published in the prestigious academic journal *Nature Communications*.

Professor Lyu Aiping, Dean of SCM, HKBU, Professor Zhang Ge, Director of Technology Development Division and Associate Director of Teaching and Research Division (CMTR), and Dr. Zhu Hailong, Assistant Professor of CMTR, are leading a bioinformatics team to investigate the gene regulatory mechanisms through computational modeling techniques and big data analytics.

Professor Lyu Aiping said that scientists have generated vast amounts and various types of biological big data; therefore, effective computational approaches must be developed to integrate and analyse

such data so as to generate useful information for understanding the core mechanism of biological processes. It was difficult in the past to develop a reliable relationship for gene regulation due to the lack of a theoretical model. "LogicTRN" is a model structure developed based on the biological process in which its parameters have significant meaning for the field of biology and its conclusion could be verified through experiments. Therefore, the application of LogicTRN has key implications on learning more about the gene regulatory mechanism during biological processes.

Dr. Zhu Hailong said that TFs are functional proteins that can bind to the promoter of genes to turn on/off the gene expression. To a great extent, the organism can conduct accurate regulation through the gene expression controlled by TFs in order to execute various functions. TFs on the other hand are regulated by its upstream gene, thus creating a very complicated regulatory route. This complicated and combinatorial nature of TF regulation is the core of various cellular processes; it also explains why 2,000 to 3,000 TFs are enough to control the complex spatio-temporal expression of over 30,000 genes in the right cell at the right time and in the right amount throughout the life of the cell and the organism.

Dr. Zhu said that "LogicTRN" is an open model framework which can be potentially extended to integrate the influences of various processes such as gene mutation, TF-DNA binding, miRNA regulation, protein translation, and protein-protein-interaction to decode the underlying mechanisms of gene transcription. With the acquisition and accumulation of biological data of more and more cellular processes, data analysis based on "LogicTRN" can enhance and contribute to a comprehensive understanding of molecular interactions in cells. He added that "LogicTRN" was successfully applied to analyse datasets representing the estrogen-induced breast cancer and human-induced pluripotent stem cell (hiPSC)-derived cardiomyocyte (CM)

development. The derived networks are consistent with existing knowledge and previous experiments.

Professor Zhang Ge explained that the major problem in the areas of disease research and drug discovery is how to cure targeted genes. Since the gene relationship is extremely complicated, it poses difficulties to the study of crucial genes. The biological informative method that is currently used seems to be a way to identify the correlation between genes, however, the accuracy is still unsatisfactory and yet to be verified. Professor Zhang added that "LogicTRN" provides researchers with a comparatively powerful analytic tool in unravelling the key pathways and new therapeutic targets of complicated diseases such as cancer.

More information: Bin Yan et al. An integrative method to decode regulatory logics in gene transcription, *Nature Communications* (2017). DOI: 10.1038/s41467-017-01193-0

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