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National Science Award

Dr. Ruan Yijun

Dr. Wei Chia Lin

Dr. Patrick Ng

Dr. Sung Wing Kin

Genome Institute of Singapore

"For their innovative work in developing the Paired End diTag sequencing technology for comprehensive characterisation of the human genome and transcriptome"

The human genome sequence, which was completed in 2004, provides a framework of the entire genetic information in Homo sapiens. However the vast functional content within the genome is not well-defined. In order to fully understand human genetics, it is necessary to identify all the functional elements and analyze how these elements interact with each other to deliver biological outcomes.

The research focus of the Genome Technology and Biology group at Genome Institute of Singapore, led by Dr. Ruan Yijun and Dr. Wei Chia Lin, is to elucidate the structure of all functional DNA elements in the human genome with a focus on transcriptome characterization and transcriptional regulation. To achieve their goals, they assembled a team that includes Dr. Patrick Ng of the group and Dr. Sung Wing Kin with computational skills from the Informatics group, and developed an innovative DNA sequencing strategy for studying the human genome.

The concept behind this technology is to extract short 5'-end and 3'-end signatures from each of many fractionated DNA segments to form the Paired End diTags (PET) structure for efficient sequencing analysis. Based on this PET strategy, the team devised Gene Identification Signature (GIS) analysis to precisely demarcate the boundaries of gene coding regions in the genome. GIS analysis has proved to be 30-fold more efficient than conventional sequencing approaches for transcript annotation, and possesses the unique capability of identifying unconventional transcripts derived from trans-splicing and chromosomal rearrangements. Leveraging on this new capability, the team invented the ChIP-PET (chromatin immuno-precipitation coupled with paired-end ditagging) analysis method for highly accurate, robust and unbiased genome-wide identification of transcription factor binding sites.

The team achieved a further 100-fold efficiency improvement over the conventional sequencing methods for PET experiments by developing the multiplex sequencing for paired end ditag (MS-PET) analysis technique, which utilises a new parallel pyrosequencing method. The team has also developed total computational solutions, including an ultra-fast tag-to-genome mapping algorithm (SAT2G), a complete software suite (PET-Tool), and a graphical browser (T2G) to accommodate and process the high volume of data generated from each PET experiment. Collectively, this team has established an integrated, high throughput and high precision technology platform that has been demonstrated to be effective for the comprehensive characterization of the human genome and transcriptome.

The team has numerous publications on their invention of these technologies and exciting biological discoveries in prestigious journals including Proceedings of the National Academy of Sciences, Nature Methods, Nature Genetics, and Cell. The team has been also awarded a USD$1 million grant by US National Institutes of Health to further develop their technology. It is anticipated that the PET technology can be widely applied to many aspects of genome interrogation, and it is emerging to become a

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premium technology in the post-genomic era. Its application to addressing biological questions is expected to provide insights into normal and diseased genomes and transcriptomes for years to come.

For their innovative work in developing the Paired End diTag technology for comprehensive characterisation of the human genome and transcriptomes, Dr. Ruan Yijun, Dr. Wei Chia Lin, Dr. Patrick Ng and Dr. Sung Wing Kin from the Genome Institute of Singapore are awarded the National Science Award 2006.

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