MEDIA RELEASE

**17 NOVEMBER 2020**

SINGAPORE RESEARCHERS DEVELOP AI-BASED METHOD TO REVEAL MOLECULAR ARCHITECTURE OF RNA

Using cutting-edge technologies, researchers discover the link between the various complex RNA structures and how they govern the way our cells work
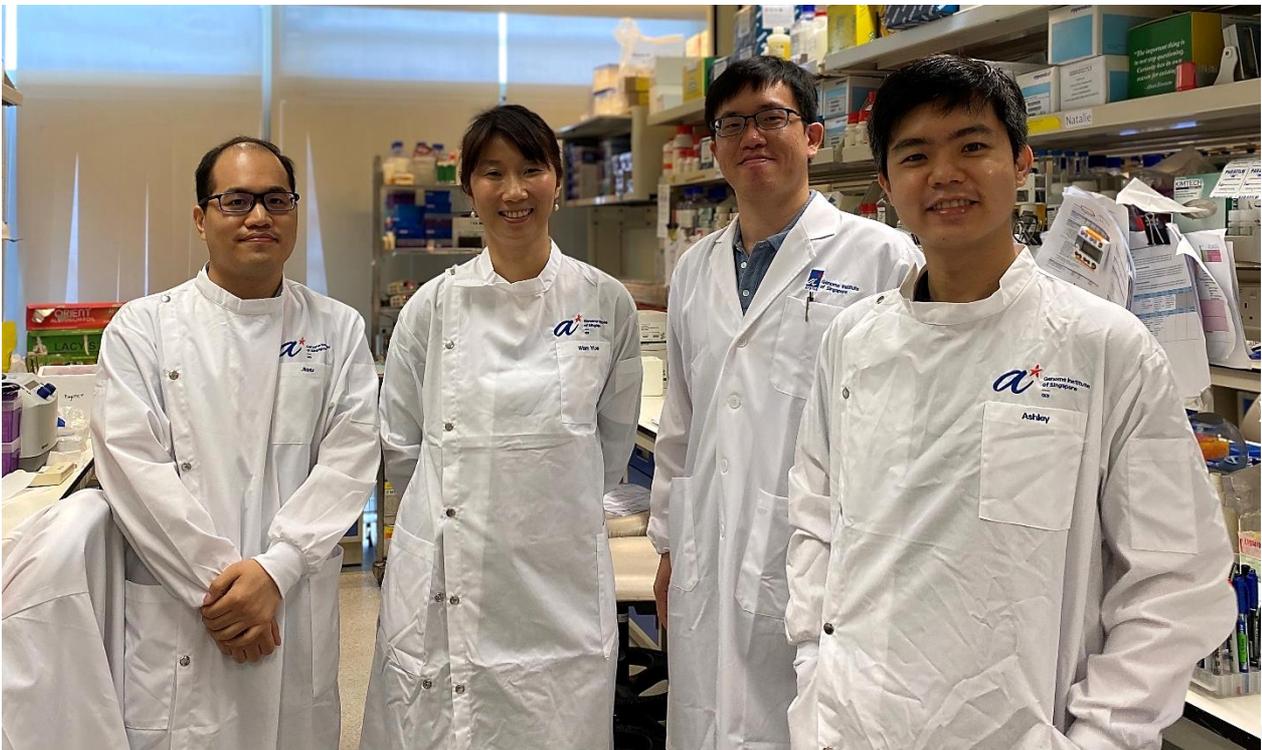
The team from the GIS' Laboratory of RNA Genomics and Structure, from left: Wang Jiaxu (Research Associate), Wan Yue (Group Leader), Shaun Lim (alumni), and Ashley Aw (Research Officer).

SINGAPORE – A team of researchers from Agency for Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS) has developed a new method to reveal ribonucleic acid (RNA) structures, and the way cells function. This is done by threading the RNA structures through protein pores and decoding the resulting signal. Using this novel method, the researchers have been able to shed light on the unique conformations that these molecules could adopt. They discovered that these molecules could have different structures despite being highly similar in sequence, and that these differences are

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associated with their unique function in the cell. Their research was recently published in Nature Biotechnology on 26 October 2020.

The human cell is extremely complex. One source of complexity comes from the fact that a single gene can be made into many different RNAs, which are then translated into different proteins. However, how these different RNAs are regulated remains to be understood. One of the long-standing puzzles in biology is whether RNAs arising from the same gene could have different functions, and whether different structures have a major role to play in their diverse fate even if they share highly similar sequences. In the past, it was not possible to discern individual structures in RNA populations with highly similar sequences, much less investigate the relationship between structure and function, because the technologies used for the readout of RNA structure can only generate short sequence reads[1].

The researchers overcame this problem by leveraging the recent development of nanopore sequencing and the long-read advantage that came with it. By running biochemically-modified RNA molecules through protein pores and decoding the resulting current with artificial intelligence, the researchers are able to obtain RNA structures in a fast and direct way to tell what RNA molecules and structures are present in a cell.

As a proof of concept, the authors performed their studies on human embryonic stem cells and showed that many RNAs arising from the same gene contain different structures that can impact the amount of proteins that are made inside the cell. This technology has broad applications in diverse systems. Besides human cells, many pathogens (including RNA viruses such as dengue and Zika) also contain different transcripts with highly shared sequences. Application of this technology to studying RNA viruses in the future can elucidate how these pathogens function and serve as a basis for further research on how to target them.

Dr Wan Yue, Group Leader of Laboratory of RNA Genomics and Structure, and Associate Director of Epigenetic and Epitranscriptomic Systems at GIS, said, "Just like siblings are different from each other, RNAs made from the same gene can have very different shapes that govern their function. By using AI to convert current into structure in nanopore sequencing, we are able to study structure differences in RNA siblings to understand how each sibling work based on their shape."

Prof Patrick Tan, Executive Director of GIS, said, "This method revolutionises our understanding of RNA-based gene regulation, and adds another tool in the tool box for mapping RNA structures in a high-throughput manner. Understanding RNA at the level of structure will elucidate a new universe of disease biomarkers and drug targets"

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[1] Short sequence reads are typically reads shorter than 150 bases, generated by second generation high throughput sequencers.
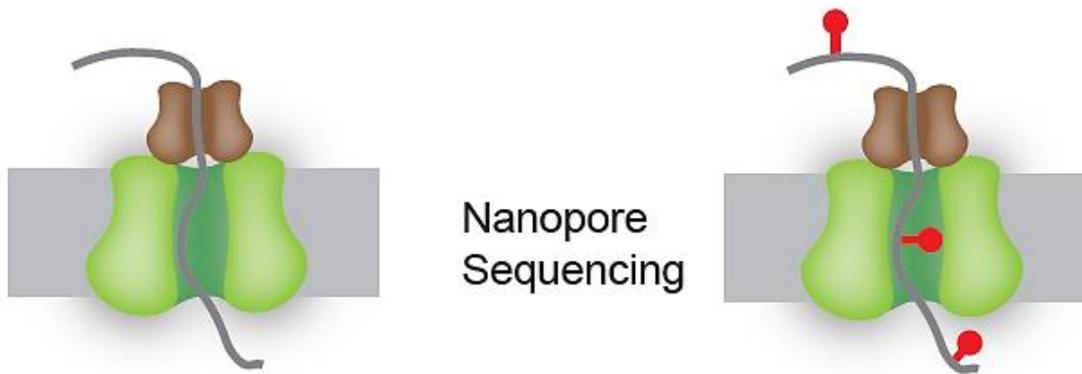
By coupling nanopore sequencing platform with artificial intelligence , the researchers were able to decode the structure of populations of RNA molecules.

– END –

Enclosed:

ANNEX A – Notes to Editor

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS pursues the integration of technology, genetics and biology towards academic, economic and societal impact, with a mission to "read, reveal and write DNA for a better Singapore and world".

Key research areas at the GIS include Precision Medicine & Population Genomics, Genome Informatics, Spatial & Single Cell Systems, Epigenetic & Epitranscriptomic Regulation, Genome Architecture & Design, and Sequencing Platforms. The genomics infrastructure at the GIS is also utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.a-star.edu.sg/gis.

About the Agency for Science, Technology and Research (A*STAR)

A*STAR is Singapore's lead public sector R&D agency. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit the economy and society. As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by improving societal outcomes in healthcare, urban living, and sustainability. A*STAR plays a key role in nurturing scientific talent and leaders for the wider research community and industry. A*STAR's R&D activities span biomedical sciences to physical sciences and engineering, with research entities primarily located in Biopolis and Fusionopolis. For ongoing news, visit www.a-star.edu.sg.

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ANNEX A – NOTES TO EDITOR

The research findings described in this media release can be found in the scientific journal Cell, under the title, "[Determination of isoform-specific RNA structure with nanopore long reads](#)" by Jong Ghut Ashley Aw[1*], Shaun W. Lim[1*], Jia Xu Wang[1*], Finnlay R.P. Lambert[1], Wen Ting Tan[1], Yang Shen[2], Yu Zhang[1], Pornchai Kaewsapsak[3], Chenhao Li[2], Sarah B Ng[4], Leah A. Vardy[5], Meng How Tan[3,6], Niranjan Nagarajan[‡2,7], Yue Wan[‡1,7,8]

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