MEDIA RELEASE

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SCIENTISTS USE ARTIFICIAL INTELLIGENCE (AI) TO REVEAL HIDDEN LAYER OF INFORMATION ABOVE RNA

3D illustration of a RNA molecule. RNA molecules can be modified to impact their function.

SINGAPORE – A team of researchers from Agency for Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS) has developed xPore, a software that extracts RNA modifications (an additional layer of information above the genetic molecule RNA) from genomics data. Their research was published in *Nature Biotechnology* on 20 July 2021.

"When we speak, the same word can have very different meanings depending on the pronunciation and context. For RNAs, we have something similar as chemical molecules

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may change the function of the same RNA. These RNA modifications are widespread, but because they do not change the letters of the RNA. They are very difficult to identify," said Dr Jonathan Göke, Group Leader of Laboratory of Computational Transcriptomics at GIS. More than 100 RNA modifications are known to play different roles in cells. Some of these RNA modifications are associated with disease risk, while others are used in mRNA vaccines. One of the most common modifications is the m^6A methylation of the adenosine in RNAs. In the past, identifying RNA modifications required labour- and time-intensive bench-experiment assays that only very few laboratories can perform.

To overcome these limitations, the team utilised Nanopore direct RNA-sequencing, a new transcriptomic technology that sequences native RNA molecule with its modifications retained. To extract the hidden layer of RNA modifications, they developed xPore, a machine learning-based method that re-purposes tools from AI research to precisely detect differences in RNA modifications. A property employed in the method is the consistent data of the unmodified sites, and the existence of modifications disrupts this consistency.

"Similar problems occur in other data-rich areas such as finance or speech recognition that tap on machine learning. Here, we adopted an existing statistical model that is used frequently in data science, so that it can precisely identify these modified sites," explained Dr Ploy Pratanwanich, formerly a Postdoctoral Fellow, Epigenetics and Epitranscriptomics at GIS, current Lecturer at Chulalongkorn University (Thailand), and first author of the study. In their study, the authors demonstrated that xPore is highly accurate and is able to overcome many of the previous limitations in studying RNA modifications.

Collaborating with Prof Chng Wee Joo, Director of the National University Cancer Institute, Singapore (NCIS), the team successfully detected the m^6A RNA modification using xPore in multiple myeloma cancer patient samples, showing xPore's potential for large-scale clinical analyses. "We have been interested in studying m^6A modification in myeloma as this may have important clinical and therapeutic implications for patients with poor outcome. Now with xPore, we have an important tool to facilitate our studies," Prof Chng added.

Dr Sho Goh, Assistant Prof from Shenzhen Bay Laboratory who co-led the study, said, "The ability to map new RNA modifications is vital for determining their functions. Since xPore does not require specific reagents that specialise in identifying only a single RNA modification type, it can potentially detect other RNA modifications beyond m^6A. Therefore, xPore's flexibility can expedite our efforts to discover novel RNA modification functions."

Prof Patrick Tan, Executive Director of GIS, said, "This study introduces a computational method that enables the profiling of differential RNA modifications transcriptome wide, and provides a systematic resource of direct RNA-Seq data. It will be valuable as a benchmark data set for modification detection, with the potential to lead to better patient outcomes."

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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.

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<u>ANNEX A – NOTES TO EDITOR</u>

The research findings described in this media release can be found in the scientific journal *Nature Biotechnology*, under the title, "Identification of differential RNA modifications from nanopore direct RNA sequencing with xPore" by the following authors: Ploy N. Pratanwanich[1,2,3,*], Fei Yao[1,11], Ying Chen[1,11], Casslynn W. Q. Koh[1,11], Yuk Kei Wan[1,11], Christopher Hendra[1,4], Polly Poon[1], Yeek Teck Goh[1], Phoebe M. L. Yap[1], Chooi Jing Yuan[5], Wee Joo Chng[5,6,7], Sarah B. Ng[1], Alexandre Thiery[8], W. S. Sho Goh[1,9,*] and Jonathan Göke[1,10,*]

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