Genome Institute of Singapore
A*STAR

MEDIA RELEASE
FOR IMMEDIATE RELEASE

5 MARCH 2015

SCIENTISTS DISCOVER NEW ROLES FOR VIRAL GENES IN THE HUMAN GENOME

Research on the expression of viral DNA within the human genome furthers our understanding of human evolution and embryonic development

Singapore – The human genome is the blueprint for human life, but much of this blueprint still remains a mystery. Researchers from A*STAR's Genome Institute of Singapore (GIS) have now discovered that sequences from old viruses that were thought to be useless, might contribute to the earliest cell types in the human life cycle. These newly discovered viral elements can be used to identify new types of embryonic stem cells, opening more possibilities to understanding human development and diseases.

The viral sequences that are the focus of the discovery are similar to retroviruses[1], but since they are a part of the human genome, they are known as endogenous retroviruses (ERV). ERVs are able to reinsert another copy of their own DNA into the human genome once they are activated. Since they mainly multiply their own DNA, they are sometimes referred to as 'selfish DNA'. Because of their 'selfishness', ERVs are potentially dangerous when they destroy genes that are essential to human life. In a study recently published in *Cell Stem Cell*, scientists describe that many ERVs are activated in cells from early embryos, but instead of being harmful, they might have become useful over the course of evolution.

Genes that are activated are transcribed into RNA to function. Therefore, scientists investigate the RNAs in the cell to identify active genes. "When we investigated public data from embryonic cells, we found that many RNAs originated from regions in the human genome that are ERVs," explained GIS Fellow Dr Jonathan Göke, who led the study. "We did not only observe isolated events, but systematic activation of these ERVs. Every cell type showed transcription of specific classes, something that is very unlikely to occur by chance".

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[1] A retrovirus is one which replicates in a host cell through a process known as reverse transcription, producing DNA from its RNA genome (a reverse of the usual replication pattern).

“Many ERV elements are only fragments of the full viruses,” added Dr Göke. “They maintain the activation sequence, but the RNA that they generate can be very different from the RNA that retroviruses generate”. In many cases, these ERV-RNAs are even parts of RNAs generated from other genes. This way, ERVs might have evolved to gain a new function; they might have become a part of the blueprint for human life.

ERVs have been shown to play a role in diseases such as cancer. Because many ERVs are not expressed in the most widely used cell models, and they do not exist in mouse, scientists do not yet fully understand their function. The researchers now showed that a part of the ERVs which functions as activator can be used to identify cells that show expression of these ERV families. Such cells might overcome the limitations of current cell models to study the role and function of ERVs in development and disease.

“These are fascinating findings as the embryonic cells that express these ERV-derived RNAs are fundamental to the human life cycle. Now the big question is what they are actually doing.” said Dr Guillaume Bourque, associate professor at the McGill University in Canada, who has worked on ERVs himself for many years. “From research with human embryonic stem cells, we know that ERVs have become essential, so it is quite likely that the ERVs described in this study contribute in a number of ways to human development.”

“This is a very exciting study,” said Prof Huck-Hui Ng, executive director of the GIS. “The results open up many new opportunities to better understand why and how embryonic cells are different from adult cells, and what role these newly discovered ERV-genes play. Some ERVs may even be involved in the formation of diseases, such as cancer.”

Dr Göke’s team at the GIS plans to take their research further. “We are now developing new algorithms that will help us identify additional ERVs in the human genome, and we try to isolate cells that express these ERV-RNAs. This way we will be able to study their function and how they contribute to human diseases”.

Notes to Editor:

The research findings described in the media release can be found in the *Cell Stem Cell* journal, under the title, “Dynamic Transcription of Distinct Classes of Endogenous Retroviral Elements Marks Specific Populations of Early Human Embryonic Cells” by Jonathan Göke,1,* Xinyi Lu,2 Yun-Shen Chan,2 Huck-Hui Ng,2,3,4,5 Lam-Ha Ly,1 Friedrich Sachs,2,3 and Iwona Szczerbinska2,3.

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About the 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 will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is 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.gis.a-star.edu.sg

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