Genome Institute of Singapore
A*STAR

MEDIA RELEASE
FOR IMMEDIATE RELEASE

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NOVEL GENOMIC SEQUENCING REVEALS POTENTIAL CAUSES OF AUTISM

Finding could lead to new treatments which include development of drugs

SINGAPORE – Scientists studying autism have applied a novel epigenomic sequencing approach to find possible causes of the disorder, discovering that thousands of gene control regions are consistently altered in autism patients. The epigenome refers to the layer of molecular features that allows cells in the body to have diverse properties, despite having the same genomic DNA. Although autism is generally believed to be a heterogeneous collection of distinct diseases, the scientists found that epigenomic aberrations in the brain cells of autistic individuals were surprisingly homogeneous, thus opening up new avenues for treatment. This finding is published in the scientific journal *Cell*.

Autism is an umbrella term for several brain disorders that have three symptoms in common: altered thought and imagination processes, social impairment and communication deficits. Despite massive worldwide DNA sequencing of autism patients, the causes of this disorder are still poorly understood due to its complexity. With no common disease mechanism known, it has been difficult to develop effective drugs that could treat the majority of autism patients.

In this study, the researchers used a method, known as “epigenome profiling”, to characterise thousands of gene control elements across the genome in both healthy individuals and autism patients. Uniquely, they focussed on epigenomic changes to DNA packaging molecules in specific regions of the brain. By comparing these two groups, the team discovered for the first time that thousands of control regions behave differently from those of healthy subjects. These elements act as an autism-specific signature and could explain how autism develops in the majority of patients. Importantly, this finding opens up the possibility of treating autistic individuals with “epigenetic drugs” that alter the epigenomic profiles of cells.

“We now have a method with which we can basically investigate any disease, and find the aberrant gene control regions. This development took six years,”

said one of the study's lead authors Dr Sun Wenjie, Research Associate, Computational & Systems Biology at A*STAR's Genome Institute of Singapore (GIS).

Led by GIS, this multi-national, multi-institutional project also involved researchers at the University of California at Los Angeles (UCLA, US), the University of Exeter (UK) and King's College London (UK). The US team was led by Prof Daniel Geschwind, Director of the UCLA Center for Autism Research and Treatment, and the UK team was led by Jonathan Mill, Professor of Epigenetics at the University of Exeter.

"We could not have done this without our collaborators. For this study, we had to combine deep knowledge of the biology of autism with cutting edge experimental techniques and highly precise data analysis methods," added Dr Shyam Prabhakar, the study's senior author and Associate Director of Integrative Genomics at the GIS.

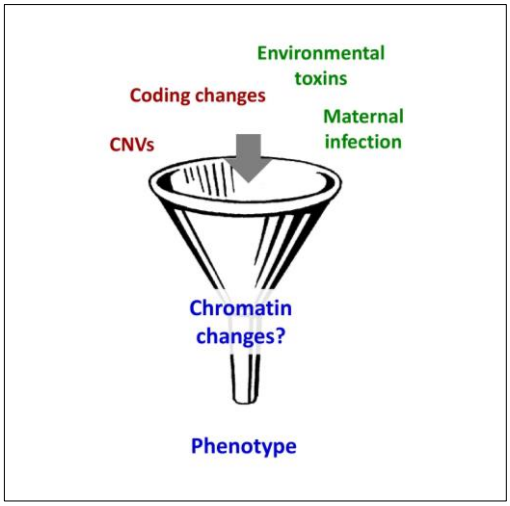
GIS Executive Director Prof Ng Huck Hui said, "This is a major breakthrough for the research community because the method can now also be applied to other diseases. This work on epigenomics clearly illustrates the importance of epigenetic signatures in linking the critical genome regulatory loci to disease states."

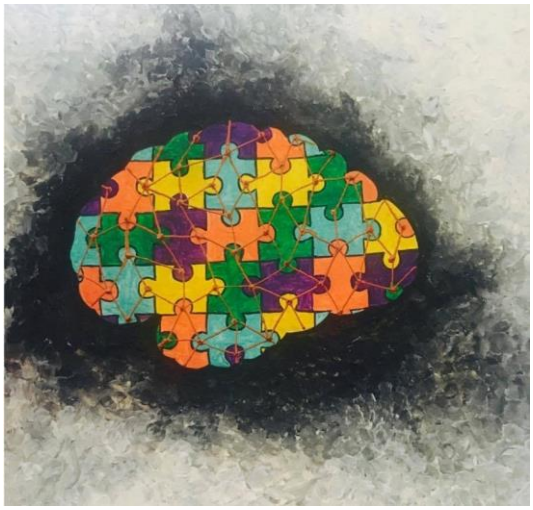
This international collaboration was funded by the PsychENCODE program of the US National Institutes Health and Singapore's A*STAR. Furthermore, this study was performed as part of the International Human Epigenome Consortium (IHEC).

"Being part of such multi-national consortia enables us to significantly impact on research while sharing our findings with scientists throughout the world," noted joint lead author Dr Jeremie Poschmann, Research Fellow, University of Exeter.

This is part of a collection of 41 publications in Cell, Cell Press-associated and other high-impact journals by IHEC scientists[#].

Images





Left:
*Image source: A*STAR's Genome Institute of Singapore*
Autism spectrum disorder (ASD) is defined by a shared set of symptoms, but has diverse causes, both genetic (red) and environmental/external (green). We propose that the multifarious primary causes of ASD converge upon a common set of chromatin aberrations, which in turn contribute to disease.

Right:
"Making connections in the puzzle of autism" by Sonish Azam
A graphical representation of the brain puzzle piece, a historic logo signifying the complexity and the lack of understanding about autism.

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Cell,* under the title, "Histone Acetylome-wide Association Study of Autism Spectrum Disorder" by Wenjie Sun[1,6], Jeremie Poschmann[1,6], Ricardo Cruz-Herrera del Rosario[2], Neelroop N. Parikshak[3], Hajira Shreen Hajan[1], Vibhor Kumar[1], Ramalakshmi Ramasamy[1], T. Grant Belgard[3], Bavani Elanggovan[1], Chloe Chung Yi Wong[4], Jonathan Mill[4,5], Daniel H. Geschwind[3,*], Shyam Prabhakar[1,7,*]

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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 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

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

The Agency for Science, Technology and Research (A*STAR) is Singapore's lead public sector agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit 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 contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

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#International Human Epigenome Consortium (IHEC) celebrates major coordinated paper release

One of the great mysteries in biology is how the many different cell types that make up our bodies are derived from a single cell and from one DNA sequence, or genome. We have learned a lot from studying the human genome, but have only partially unveiled the processes underlying cell determination. The identity of each cell type is largely defined by an instructive layer of molecular annotations on top of the genome – the epigenome – which acts as a blueprint unique to each cell type and developmental stage. Unlike the genome the epigenome changes as cells develop and in response to changes in the environment. Defects in the factors that read, write and erase the epigenetic blueprint are involved in many diseases. The comprehensive analysis of the epigenomes of healthy and abnormal cells will facilitate new ways to diagnose and treat various diseases, and ultimately lead to improved health outcomes.

A collection of 41 coordinated papers now published by scientists from across the International Human Epigenome Consortium (IHEC) sheds light on these processes, taking global research in the field of epigenomics a major step forward. A set of 24 manuscripts has been released as a package in Cell and Cell Press-associated journals, and an additional 17 papers have been published in other high-impact journals.

These papers represent the most recent work of IHEC member projects from Canada, the European Union, Germany, Japan, Singapore, and the United States. The collection of publications showcases the achievements and scientific progress made by IHEC in core areas of current epigenetic investigations.

For more information, please visit http://ihec-epigenomes.org/news-events/coordinated-paper-release