MEDIA RELEASE
FOR IMMEDIATE RELEASE

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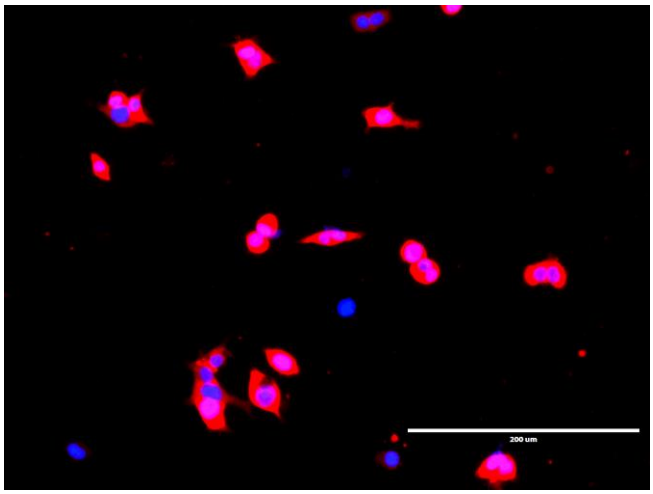
SINGAPORE SCIENTISTS DEVELOP DNA-ALTERING TECHNOLOGY TO TACKLE DISEASES

Finding could lead to new therapeutics for diseases

SINGAPORE – Researchers in Singapore have developed a new protein that can alter DNA in living cells with much higher precision than current methods.

The ability to alter DNA accurately will open more doors in the development of personalised medicine that could help to tackle human diseases that currently have few treatment options. Examples of diseases that have unmet therapeutic needs include neurodegenerative diseases like Huntington's disease, muscular dystrophies, and blood disorders like sickle cell anaemia.

This new protein, named iCas, can be easily controlled by an external chemical input and thus solves some of the problems with CRISPR-Cas[1], the existing gold-standard for DNA altering. For example, existing Cas enzymes may sometimes alter places in the DNA that result in dire consequences. With iCas, users now have the ability to control enzyme activity and thus minimize unintended DNA modifications in the cell.



Left: The iCas protein (stained in red) created by Singapore scientists is shown moving into the cells' nuclei to make changes to the DNA (stained in blue). The pink region indicates that iCas is positioned at the DNA to perform its function.

*Image source: A*STAR's Genome Institute of Singapore*

[1] The CRISPR-Cas (Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated proteins) system is a powerful technology that can be used to manipulate the DNA in living cells. For instance, it can be used to correct disease-causing mutations in humans or to engineer improved agricultural crops with desirable traits to ensure food security.

Developed by a collaboration between A*STAR's Genome Institute of Singapore (GIS) and Nanyang Technological University, Singapore (NTU Singapore), iCas was published in the peer reviewed scientific journal *Nature Chemical Biology* this week.

Leading the joint research team is Dr Tan Meng How, Senior Research Scientist of Stem Cell & Regenerative Biology at the GIS, and Assistant Professor at NTU's School of Chemical and Biomedical Engineering.

"DNA is like an instruction manual that tells living cells how to behave, so if we can rewrite the instructions in this manual, we will be able to gain control over what the cells are supposed to do," explained Dr Tan. "Our engineered iCas protein is like a light switch that can be readily turned on and off as desired. It also outperforms other existing methods in terms of response time and reliability."

How DNA altering works

To ensure that DNA is precisely altered, which is required in many biomedical and biotechnological applications, the activity of the Cas protein must be tightly regulated.

The chemical that switches the iCas protein on or off is tamoxifen, a drug commonly used to treat and prevent breast cancer. In its absence, iCas is switched off with no changes made to the DNA. When switched on with tamoxifen, iCas will then edit the target DNA site.

In the study, iCas was found to outperform other chemical-inducible CRISPR-Cas technologies, with a much faster response time and an ability to be switched on and off repeatedly.

The higher speed at which iCas reacts will enable tighter control over exactly where and when DNA editing takes place. This is useful in research or applications that demand precise control of DNA editing.

For example, in studies of cell signalling pathways or vertebrate development, iCas can precisely target a subset of cells within a tissue (spatial control) or to edit the DNA at a particular developmental stage (temporal control).

"The iCas technology developed by Dr Tan is an exciting addition to the growing CRISPR toolbox. It enables genome editing in a precisely controlled manner, thus opening new doors for applications of the CRISPR technology in basic and applied biological research," said Dr Huimin Zhao, the Steven L. Miller Chair

Professor of the Chemical and Biomolecular Engineering faculty at the University of Illinois at Urbana-Champaign (UIUC).

GIS Executive Director Prof Ng Huck Hui added, “This development allows the researchers to have precision control for more accurate DNA editing, and it can help researchers engineer cells with new properties or repair diseased cells with mutated DNA.”

Prof Teoh Swee Hin, Chair of NTU’s School of Chemical and Biomedical Engineering, said, “DNA editing is an exciting field with many potential uses in the treatment of diseases. NTU has been active in research in the area of gene sequencing and bioengineering over the past years and this work by Dr Tan and his Singapore team will add to the growing body of knowledge in cell engineering for medicine.”

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Chemical Biology,* under the title, “A chemical-inducible CRISPR–Cas9 system for rapid control of genome editing” by Kaiwen Ivy Liu[1], Muhammad Nadzim Bin Ramli[1], Cheok Wei Ariel Woo[1], Yuanming Wang[1,2], Tianyun Zhao[1], Xiujun Zhang[1,2], Guo Rong Daniel Yim[1], Bao Yi Chong[1,3], Ali Gowher[1], Mervyn Zi Hao Chua[1,4], Jonathan Jung[1], Jia Hui Jane Lee[1] & Meng How Tan[1,2*]

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The *Nature Chemical Biology* paper can be accessed online from: http://www.nature.com/nchembio/journal/vaop/ncurrent/full/nchembio.2179.html

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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.

For more information on A*STAR, please visit www.a-star.edu.sg

About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,500 undergraduate and postgraduate students in the colleges of Engineering, Business, Science, Humanities, Arts, & Social Sciences, and its Interdisciplinary Graduate School. It has a new medical school, the Lee Kong Chian School of Medicine, set up jointly with Imperial College London.

NTU is also home to world-class autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies, Earth Observatory of Singapore, and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Nanyang Environment & Water Research Institute (NEWRI), Energy Research Institute @ NTU (ERI@N) and the Institute on Asian Consumer Insight (ACI).

Ranked 13th in the world, NTU has also been ranked the world's top young university for the last two years running. The University's main campus has been named one of the Top 15 Most Beautiful in the World. NTU also has a campus in Novena, Singapore's medical district.

For more information, visit www.ntu.edu.sg