

**MEDIA RELEASE  
FOR IMMEDIATE RELEASE**

**7 OCTOBER 2016**

**UNMASKING NEW DRIVERS OF STOMACH CANCER**

*Study advances understanding of stomach cancer progression and could lead to new therapeutic targets and improved clinical outcomes*

**SINGAPORE** – Scientists have uncovered a new class of master control elements in stomach cancer called “super-enhancers”, which control critical cancer genes and proteins required for stomach tumours to survive and grow.

The team’s generation of this unprecedented and comprehensive catalogue of stomach cancer super-enhancers is an important milestone for the community. Currently, stomach cancer is the fifth most common cancer worldwide and the third leading cause of global cancer death<sup>1</sup>. Most gastric cancers are diagnosed late, and the disease is often resistant to current clinical treatments.

By studying super-enhancers in stomach tumours, the team was able to shed light on how these elements impact the risk of stomach cancer development and progression of the disease. For example, stomach cancer patients whose tumours exhibited high numbers of super-enhancers exhibited a significantly poorer survival rate. Selective activation of these super-enhancers could explain why certain groups of people are at risk of developing the disease.

These tissue-specific super-enhancers also represent a previously untapped reservoir of cancer vulnerability, acting to bridge oncogenic signalling to tissue-specific features of malignancy. Thus, studying the mechanisms driving the development of super-enhancers in stomach cancer may lead to novel therapies. Specifically, the team also identified two DNA-binding proteins as drivers for the formation of tumour-specific super-enhancers. These may serve as potential drug targets for stomach cancer.

The researchers were able to make this finding using a highly sensitive, “made-in-Singapore” technology, called Nano-ChIPseq. Developed at A\*STAR’s Genome Institute of Singapore (GIS), Nano-ChIPseq enables the study of epigenomic changes in clinical samples obtained directly from stomach cancer patients, rather than laboratory cultured cell lines. Unlike DNA which is stable

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<sup>1</sup>World Health Organization: <http://www.who.int/mediacentre/factsheets/fs297/en/>

and unchanging, epigenomic instructions are strongly influenced by factors such as food, infectious agents, and chemicals, suggesting that they can be modified by environmental risk factors.

The team is now working to commercialise the technology and develop data technologies, which will enable scientists to revolutionise cancer therapeutics.

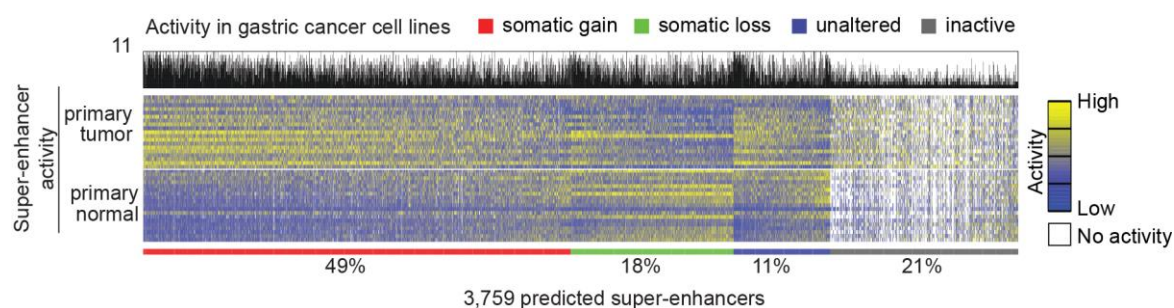
“Future work in our lab will investigate how such super-enhancers can be disrupted by drugs, which will open up new avenues for cancer therapy,” said the study’s corresponding author Prof Patrick Tan, Deputy Executive Director of A\*STAR’s Biomedical Research Council and an associate faculty member at the GIS. “We hope that our findings will encourage the scientific community to embrace our technology as a means to rapidly uncover master control elements that are highly relevant to diseases and clinical outcomes. This effort may eventually change the way stomach and other cancers are managed, which will enhance the clinical outcomes of cancer patients.”

Published in scientific journal *Nature Communications*, this study was led by GIS, in collaboration with Duke-NUS Medical School, Cancer Science Institute of Singapore at the National University of Singapore (NUS), Singapore General Hospital (SGH), Weatherall Institute of Molecular Medicine at Oxford University, and the Singapore Gastric Cancer Consortium (SGCC). Commercialisation of the Nano-ChIPseq platform is currently supported through gap funding awarded by ETPL Pte Ltd, the commercialisation arm of A\*STAR.

"I felt something awesome will be coming when I heard about the new method, Nano-ChIPseq. The study suggests that extensive alterations in gene regulation, and not genes themselves, explain deep mysteries of gastric cancer, which are known to exhibit small numbers of mutations and deep involvement of bacterial infection, an environmental factor. Naturally, development of novel therapeutic strategies must take account of these findings," said Dr Toshikazu Ushijima, Chief of Division of Epigenomics at the National Cancer Center Research Institute in Japan, and a member of the SGCC Scientific Advisory Board.

GIS Executive Director Prof Ng Huck Hui added, “This is a remarkable technological breakthrough for the community. As we constantly work to find better treatments for cancer, it is also important that we find more efficient ways to study how epigenomic changes can drive the formation of cancerous cells from healthy cells. A greater understanding about molecular changes in diseases can potentially lead to early therapeutic intervention and improved care for the patients.”

## IMAGE



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

Activity of super-enhancers in stomach cancer *in-vivo* and *in-vitro*.

### Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Communications*, under the title, "Epigenomic profiling of primary gastric adenocarcinoma reveals super-enhancer heterogeneity" by Wen Fong Ooi<sup>1,\*</sup>, Manjie Xing<sup>2,3,\*</sup>, Chang Xu<sup>2,4,\*</sup>, Xiaosai Yao<sup>1</sup>, Muhammad Khairul Ramlee<sup>2</sup>, Mei Chee Lim<sup>4</sup>, Fan Cao<sup>4</sup>, Kevin Lim<sup>2</sup>, Deepak Babu<sup>4</sup>, Lai-Fong Poon<sup>2</sup>, Joyce Lin Suling<sup>1</sup>, Aditi Qamra<sup>1,5</sup>, Astrid Irwanto<sup>6</sup>, James Qu Zhengzhong<sup>1</sup>, Tannistha Nandi<sup>1</sup>, Ai Ping Lee-Lim<sup>1</sup>, Yang Sun Chan<sup>1</sup>, Su Ting Tay<sup>2</sup>, Ming Hui Lee<sup>2</sup>, James O.J. Davies<sup>7</sup>, Wai Keong Wong<sup>8</sup>, Khee Chee Soo<sup>9</sup>, Weng Hoong Chan<sup>8</sup>, Hock Soo Ong<sup>8</sup>, Pierce Chow<sup>9,10</sup>, Chow Yin Wong<sup>10</sup>, Sun Young Rha<sup>11</sup>, Jianjun Liu<sup>6</sup>, Axel M. Hillmer<sup>1</sup>, Jim R. Hughes<sup>7</sup>, Steve Rozen<sup>2,12</sup>, Bin Tean Teh<sup>2,4,12,13</sup>, Melissa Jane Fullwood<sup>4,14</sup>, Shang Li<sup>2</sup> & Patrick Tan<sup>1,2,4,12,15</sup>

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The *Nature Communications* paper can be accessed online from:  
<http://www.nature.com/ncomms/2016/160928/ncomms12983/full/ncomms12983.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](http://www.gis.a-star.edu.sg)

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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](http://www.a-star.edu.sg)