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First roadmap of stomach cancer super-enhancers paves the way for new treatments

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A*STAR researchers have homed in on a potential new way to diagnose and treat stomach cancer, through the mapping of an unprecedented catalog of almost 3,800 super-enhancers from stomach cancer tumor cells.

Gastric or stomach cancer is the world's fifth most common cancer and the third leading cause of cancer death globally, according to Patrick Tan, the Deputy Executive Director of A*STAR's Biomedical Research Council (BMRC).

Tan led the A*STAR Genome Institute of Singapore research team that mapped more than 100 epigenomic profiles from stomach tumors, surgically removed from patients in Singapore, and compared them to normal stomach cells. They validated these profiles using gastric cancer data from scientific institutions in Japan, the United States and South Korea.

Tan says the study is yielding new insights into gastric cancer that have been overlooked by previous approaches.

The epigenome consists of chemical tags that attach to the DNA and instruct it. Tan says, "what makes each cell type different—one cancerous and one not, is really which genes are turned on or off. This is a process we refer to as gene expression."

Tan explains that enhancers are "control circuits in the genome which

determine which elements are switched on or off".

Recently, researchers have discovered super-enhancers: clusters of enhancers localized to specific regions of the genome. They have broad and powerful effects on gene expression, and are pivotal to cancer and other disease processes.

Tan says: "When one looks at the gene expression patterns controlled by the super-enhancers, the function of these genes are all related to different traits of cancer, including resistance to cell death and uncontrolled proliferation."

Analyzing stomach cancer and matched normal samples, the research team investigated almost 37,000 enhancers and found 3,759 predicted super-enhancers. The active super-enhancers are recognized by a special DNA tag, known as H3K27ac.

They also studied 848 gastric cancer patients and showed that those with a high level of super-enhancer associated genes had a worse survival rate than other patients.

The research team will now focus on cancer therapies that target factors that allow the super-enhancers to promote gastric cancer growth. They want to develop a method of early diagnosis for stomach cancer by testing for these gastric cancer-specific super-enhancers.

The team plans to open a laboratory that will offer the epigenomic profiling platform they developed, to collaborators investigating other cancers and diseases.

More information: Wen Fong Ooi et al. Epigenomic profiling of primary gastric adenocarcinoma reveals super-enhancer heterogeneity, *Nature Communications* (2016). DOI: 10.1038/ncomms12983

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