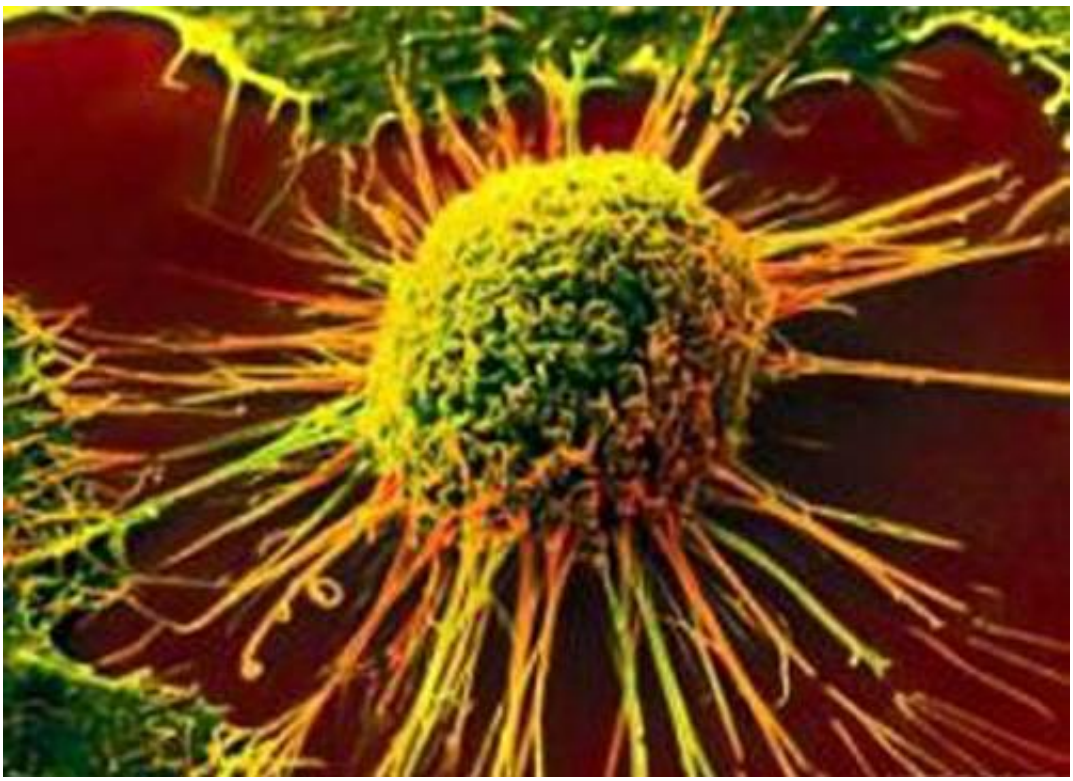
Discovery of key protein behind cancer relapse and progression can lead to new therapies

June 30 2020, by James L. Manley



Reports show that cancer is the second-highest leading cause of death globally, with the possibility that every one in four to five people in Singapore may develop cancer in their lifetime. A recent study by scientists from Duke-NUS Medical School provides new evidence

supporting the presence of a key mechanism behind progression and relapse in cancer. The study, published in *Proceedings of the National Academy of Sciences* (*PNAS*), discusses the role of MBNL1 protein as a biomarker for cancer prognosis, which can lead to the development of new treatment strategies for cancer.

Cancer cases have been rising over the years and according to the statistics, the number of people living with cancer will continue to increase. Despite decades of research, cancer treatments are still inefficient and have unacceptable side effects that continue to prompt an urgent need for new approaches to prevention and treatment. Uncovering novel mechanisms associated with cancer would fill current knowledge gaps and help meet this need.

"We discovered a mechanism involving MBNL1 protein that predicts several characteristics of cancer such as progression and relapse," said Dr. Debleena Ray, Senior Research Fellow at Duke-NUS' Cancer and Stem Cell Biology (CSCB) program, the lead author of this study. "We found that MBNL1 protein is present in low amounts in many of the common cancers in the world, including breast, colorectal, stomach, lung and prostate cancers, which when combined account for about 49 percent of all cancers diagnosed in 2018. This can cause poor overall survival in many of these commonly-occurring cancers."

The team also found that this mechanism can be reversed by blocking the JNK protein, a well-known target in cancer treatment, in cancer cells with low levels of MBNL1.

"While JNK inhibitors have been tested as a cancer drug previously, currently there are no clinical trials for the same. However, if in the future there is a JNK inhibitor against cancer, MBNL1 could be used as a biomarker to select patients for the treatment," said Adjunct Associate Professor David Epstein at the Duke-NUS' CSCB program and the co-

corresponding author of this study.

"Cancer is a global health challenge and Singapore is no exception. This study provides important information about novel targets and biomarkers that are implicated in several major cancers, which could lead to the development of new treatment strategies that can improve the lives of patients," said Prof Patrick Casey, Senior Vice Dean for Research at Duke-NUS.

Over the next year, the team will be investigating the role of MBNL1 in colorectal cancer and exploring the potential of anti-JNK therapeutic for cancer using antisense technology, a tool that is used for the inhibition of gene expression.

More information: Debleena Ray el al., "A tumor-associated splice-isoform of MAP2K7 drives dedifferentiation in MBNL1-low cancers via JNK activation," *PNAS* (2020). www.pnas.org/cgi/doi/10.1073/pnas.2002499117

Provided by Duke-NUS Medical School