

Scientists to study genetic changes in cancer through fruit flies

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Singapore: By studying fruit flies, scientists at A*STAR's Institute of Molecular and Cell Biology (IMCB) have successfully devised a fast and cost-saving way to uncover genetic changes that have a higher potential to cause cancer. With this new approach, researchers will now be able to rapidly distinguish the range of genetic changes that are causally linked to cancer (i.e. "driver" mutations) versus those with limited impact on cancer progression.

This research paves the way for doctors to design more targeted treatment against the different cancer types, based on the specific cancer-linked mutations present in the patient. This study published in the prestigious journal *Genes & Development* could help advance the development of personalised medicine in cancer care and treatment.

The era of genomic sequencing has generated an unparalleled wealth of information on the complexity of genetic changes that occur as cancer develops and progresses. "Many genetic changes arise in cancer cells and changes continue to accumulate during the progression of disease to metastatic cancer. The current challenge is to understand which of the many genetic changes are important drivers of disease progression," said Dr Stephen Cohen, principal investigator at IMCB and team leader of this paper.

Though very different in many ways, fruit flies and humans share similarities in a remarkable two-thirds of their genomes. That is to say, many of the genes found in humans are also present in the flies. Similarly, various signalling pathways involved in tumor formation are also well conserved from fruit flies to humans. In fact, previous studies have shown that about 75 percent of known human disease genes have a recognisable match in the genome of fruit flies.

Leveraging on their genetic similarities, Dr Héctor Herranz, a post-doctorate from the Dr Cohen's team developed an innovative strategy to genetically screen the whole fly genome for "cooperating" cancer genes. On their own, these are the genes that appear to be harmless and have little or no impact on cancer. But in fact, they cooperate with other cancer genes, so that the combination causes aggressive cancer, which neither would cause alone.

In this study, the team was specifically looking for genes that could cooperate with EGFR "driver" mutation, a genetic change

commonly associated with breast and lung cancers in humans. SOCS5, reported in this paper, is one of the several new "cooperating" cancer genes to be identified through this innovative approach. Most of these new-found genes have yet to be identified as cancer genes in human or mouse models.

Mr Xin Hong, a PhD student and the co-first author of this paper, said, "We were very surprised by our finding because this is the first time that the Socs gene family is found to be linked to cancer. Previously it has only been associated with immunological disorders."

Dr Cohen added, "Though these studies are in the early stages, they are very promising. Already, there are indications that levels of SOCS5 expression are reduced in breast cancer, and patients with low levels of SOCS5 have poor prognosis."

The IMCB team is preparing to explore the use of SOCS5 as a biomarker in diagnosis for cancer.

Professor Wanjin Hong, executive director of IMCB, said, "This study sheds light on the complexities of cancer genetics and paves the way to accelerate development of personalised medicine in cancer care. It is a fine example of how powerful genetic approach using the fly model can reveal molecular mechanisms underlying human cancer. More importantly, it shows how fundamental research can have far-reaching applications for potential clinical benefits."