

Researchers discover gene that increases incidence of acute myelogenous leukaemia

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A novel study by the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore (NUS) found that an increase in a gene known as *Leo1* affects other genes that are directly implicated in acute myelogenous leukaemia (AML), increasing the incidence of cancer.

Led by Associate Professor Chng Wee Joo, Deputy Director and Senior Principal Investigator at CSI Singapore and Director of the National University Cancer Institute, Singapore, the scientists discovered that inhibition of *Leo1* and *Leo1* downstream signalling pathways provide an avenue for targeted treatment of AML. The findings were recently published in *Cancer Research*, the official journal of the American Association of Cancer Research.

In addition, this is the first study to suggest that the protein PRL-3 plays a role in the regulation of ribonucleic acid (RNA) related processes, a finding which advances the understanding of how the protein contributes to [cancer](#) progression. The team's work represents the first large-scale quantitative survey of proteins regulated by PRL-3 in leukaemia.

The elevated expression of PRL-3 has been implicated in the progression and metastasis of an array of cancer types, including gastric, ovarian, cervical, lung, liver, and breast. In particular, the protein PRL-3 is overexpressed in about half of AML patients and associated with poor survival. Assoc Prof Chng and his team were the first to report that elevated PRL-3 protein expression occurs in about 47 per cent of AML

cases while being absent from normal myeloid cells in bone marrow. As a result, PRL-3 is deemed as an attractive therapeutic target that spares normal tissues.

Previously, knowledge of the mechanisms of PRL-3 was limited. In this study, the researchers used a new, advanced SILAC-based mass spectrometry to identify all the [protein](#) changes induced by PRL-3 in a comprehensive manner. Using this approach, they discovered that the gene *Leo1* serves as a novel target of PRL-3 phosphatase, and inhibition of *Leo1* as well as *Leo1* downstream signalling pathways provide an avenue for PRL-3 targeted therapy for AML patients.

In the next phase of research, the team is validating several important proteins directly downstream of *Leo1* that can possibly be used as biomarkers and drug targets to improve treatment for leukaemia with PRL-3 overexpression.

Assoc Prof Chng said, "Our previous studies showed that PRL-3 is clinical and biologically important in acute myelogenous leukaemia, and may therefore be a useful treatment target. In the current study, we have taken the work further by understanding how PRL-3 confers cancer properties to the leukaemia cells. This now provides a framework for rational design of a treatment based on mechanistic understanding. In the process, we will also develop biomarkers to better select patients for the treatment and hence, progress towards personalising [treatment](#) for leukaemia patients."

More information: LEO1 Is Regulated by PRL-3 and Mediates Its Oncogenic Properties in Acute Myelogenous Leukemia, Published OnlineFirst March 31, 2014, [DOI: 10.1158/0008-5472.CAN-13-2321](https://doi.org/10.1158/0008-5472.CAN-13-2321), *Cancer Res* , June 1, 2014 vol. 74 no. 11 3043-3053

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