New vulnerability revealed in blood cancer development

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Walter and Eliza Hall Institute leukemia researchers have pinpointed a protein that allows blood cancers to develop. Credit: Walter and Eliza Hall Institute

Walter and Eliza Hall Institute researchers have uncovered a protein that is key to the development of blood cancers caused by a common genetic error.

The discovery is a missing piece in the puzzle of understanding how high levels of a protein called MYC drive cancer development, and may to lead to future strategies for early treatment or possibly even prevention of these cancers.

Seventy per cent of human cancers have abnormally high levels of MYC, which forces cells into unusually rapid growth.

Dr Stephanie Grabow, Dr Brandon Aubrey, Professor Andreas Strasser and colleagues at the Walter and Eliza Hall Institute discovered that blood cancers driven by MYC could be prevented by lowering the levels of another protein, called MCL-1.The research was published today in the journal *Cell Reports*.

Dr Grabow said the developing cancer cells were dependent on MCL-1, a protein that keeps stressed cells alive by preventing programmed cell death (apoptosis). "No one had realised just how vulnerable cells undergoing cancerous changes are to a relatively minor reduction in the levels of MCL-1," she said. "We found that MCL-1 is critical for keeping developing cancer cells alive through the stressful events that cause the transformation of a healthy cell into a cancerous cell.

"This result is particularly exciting because MCL-1 inhibitors are already in development as anti-cancer drugs," Dr Grabow said. "Our colleagues had previously discovered that reducing the activity of MCL-1 is a promising strategy to treat malignant MYC-driven cancers. We have now shown that the same approach might be able to prevent those cancers from forming in the first place."

Dr Aubrey, who is also a clinical haematologist at The Royal Melbourne Hospital, said the research could inform future strategies to prevent cancer.

"Early treatment or even cancer prevention are likely to be a more effective way to fight cancer than treating an established cancer after it has already formed and made a person sick," he said.

"Cancer researchers are building a better picture of who is at risk of developing cancer, and enhancing how we can detect early stage cancer in people before it has grown to the point of causing illness. Our research has suggested that dependency on MCL-1 could be a key vulnerability of many developing cancers. In the future MCL-1 inhibitors might have potential benefit for treating the very early stages of MYC-driven cancers, or we may even be able use these agents to prevent people from getting cancer in the first place," Dr Aubrey said.

More information: "Loss of a Single Mcl-1 Allele Inhibits MYC-Driven Lymphomagenesis by

Sensitizing Pro-B Cells to Apoptosis," *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.02.039

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