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T-cell leukaemia: Cancer cells take advantage of 'survival protein'

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The overproduction of the BCL-2 protein is due to a defect in the ribosome, the protein factory of the cell. This defect is found in 10% of the pediatric patients with T-cell leukaemia.

"In the past couple of years, it has become clear that ribosome defects play a role in different types of cancer," explains Professor Kim De Keersmaecker, head of the Laboratory for Disease Mechanisms in Cancer at KU Leuven. "In the case of a ribosome defect, the cells still produce proteins but the balance between their quantities is slightly off, which leads to cancer."

Professor De Keersmaecker and Dr. Kim R. Kampen, a postdoc in her lab, were able to delineate the cancer promoting function of a specific ribosome defect that has a severe impact on pediatric patients with T-cell leukaemia. The impact of this ribosome defect on T-cell leukaemia has never been elucidated before.

If a cell is too damaged due to ageing or disease, a specific signal induces cell death. But some proteins—including the protein known as BCL-2—can put a stop to cell death. Due to a ribosomal defect, some T-cell leukaemia patients produce too much of this cell death preventing protein.

The overproduction of BCL-2 has detrimental effects, says Professor De Keersmaecker. "Cancer cells take advantage of the BCL-2 protein: it helps them to survive under difficult circumstances, including

chemotherapy."

A drug that suppresses BCL-2 is already used to treat another type of leukaemia.

"Clinicians use this drug to treat chronic lymphocytic leukaemia. But our research in mice shows that it also suppresses T-cell leukaemia with a specific ribosome defect."

But it's too soon to talk about cure, De Keersmaecker warns. "This hasn't been tested on human beings yet."

"Patients with leukaemia often get a drug cocktail, while our study only tested the BCL-2 inhibitor. That's why our follow-up study will focus on a cocktail of this BCL-2 inhibitor and other drugs. For patients with the ribosome defect analyzed in our study, this avenue is definitely worth examining in greater detail."

More information: Kim R. Kampen et al, The ribosomal RPL10 R98S mutation drives IRES-dependent BCL-2 translation in T-ALL, *Leukemia* (2018). DOI: 10.1038/s41375-018-0176-z

Provided by KU Leuven