Aggressive form of leukemia linked to defective 'protein factory'

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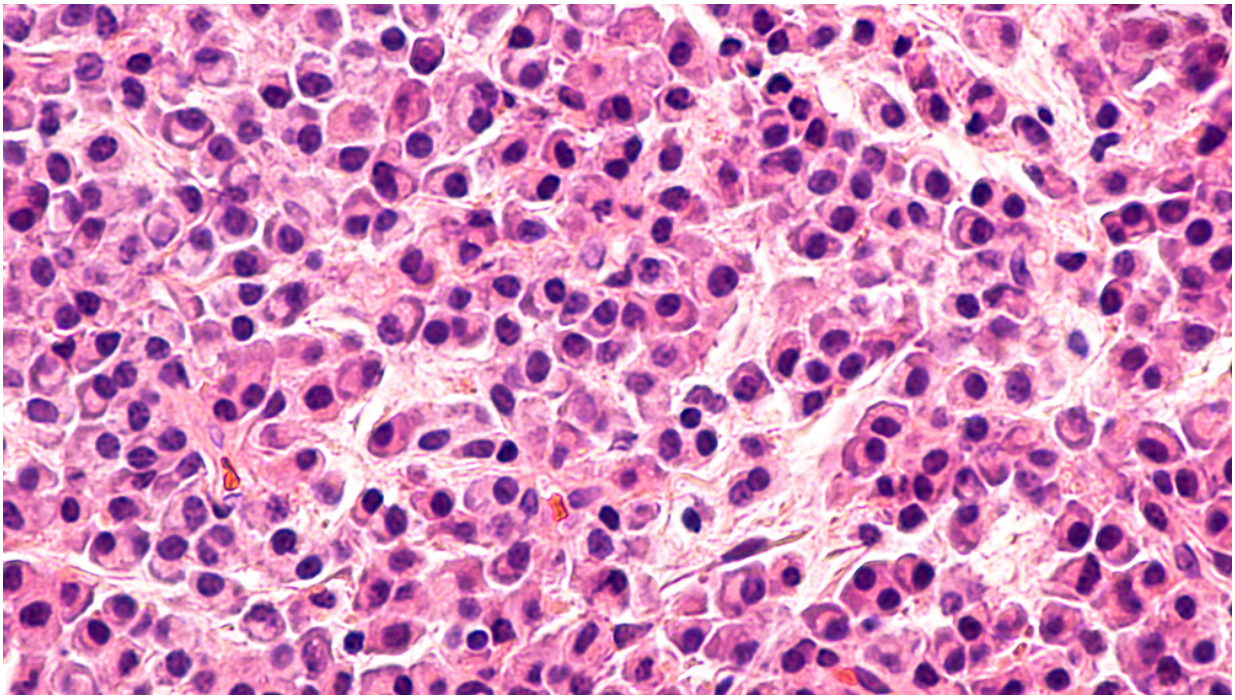


In patients with multiple myeloma, the plasma cells in the bone marrow start proliferating malignantly. Credit: KU Leuven

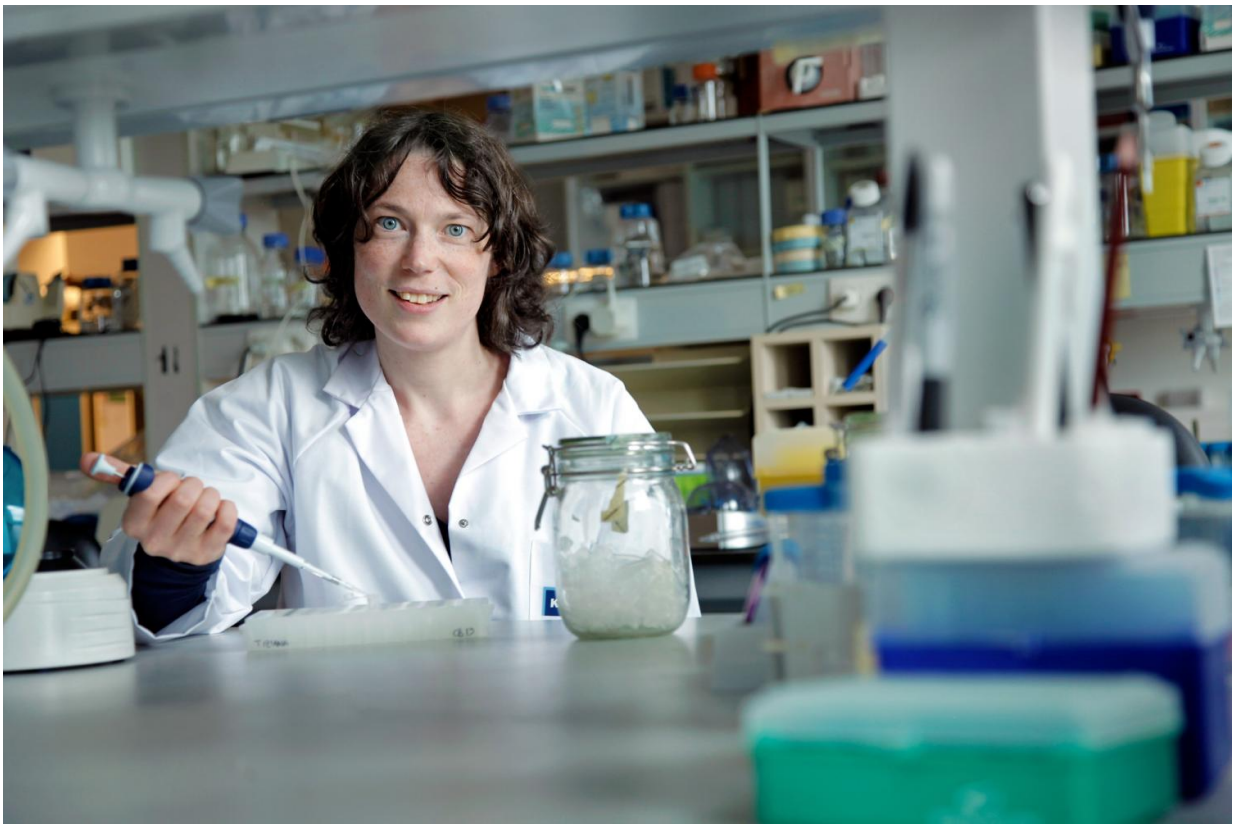
Twenty to forty percent of the patients with the type of leukaemia known as multiple myeloma have a defect in the 'protein factory' of the cell: the ribosome. These patients have a poorer prognosis than patients with intact ribosomes. At the same time, they respond better to a drug that already exists. These are the findings of a study by the KU Leuven

Laboratory for Disease Mechanisms in Cancer, led by Professor Kim De Keersmaecker.

Multiple myeloma (MM, also known as Kahler's disease) is a blood cancer whereby the plasma cells in the bone marrow start proliferating malignantly. MM cannot be cured and is most common among older people. Various treatments exist to temporarily suppress the disease, but the challenge is determining to which treatment the patient will respond best.

Doctoral student Isabel Hofman (KU Leuven) discovered defects in the ribosome of MM patients. "The ribosome is the protein factory of a cell. In MM patients, one part of the ribosome is produced less in 20 to 40 percent of the patients, depending on how aggressive the cancer is. We suspect that their cells are still producing protein, but that the balance is somewhat disrupted. In any case, we found that these people have a poorer prognosis than MM patients with an intact ribosome," explains Professor Kim De Keersmaecker, head of the KU Leuven Laboratory for Disease Mechanisms in Cancer.

One possible treatment for MM is the use of proteasome inhibitors. "The proteasome is the protein demolition machine in a cell. There's a type of drugs, including Bortezomib, that inhibits its functioning. How the defects in the ribosome influence the proteasome is not quite clear yet. But we discovered that patients with a defective ribosome respond better to Bortezomib. In other words, their poorer prognosis can be offset by this treatment. On the basis of these findings, we can now develop tests to identify defects in the ribosome and thus determine which therapy will have most effect in a specific patient."



Professor Kim De Keersmaecker (KU Leuven, Belgium) . Credit: KU Leuven - Rob Stevens

The notion that cancer is related to ribosome defects is a relatively new concept in science. "A few years ago, we discovered defects in the ribosome of patients with acute lymphatic leukaemia. Now we know that the same applies to MM. In all likelihood, this will also hold true for other types of cancer. Our next research goal is finding out for which cancers this is the case, how the link between ribosome and proteasome works, and what the possibilities are of drugs that target the ribosome itself."

More information: I J F Hofman et al, RPL5 on 1p22.1 is recurrently deleted in multiple myeloma and its expression is linked to bortezomib

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