Protein called FAIM could help doctors to parse which cancer patients will respond to multiple myeloma therapy

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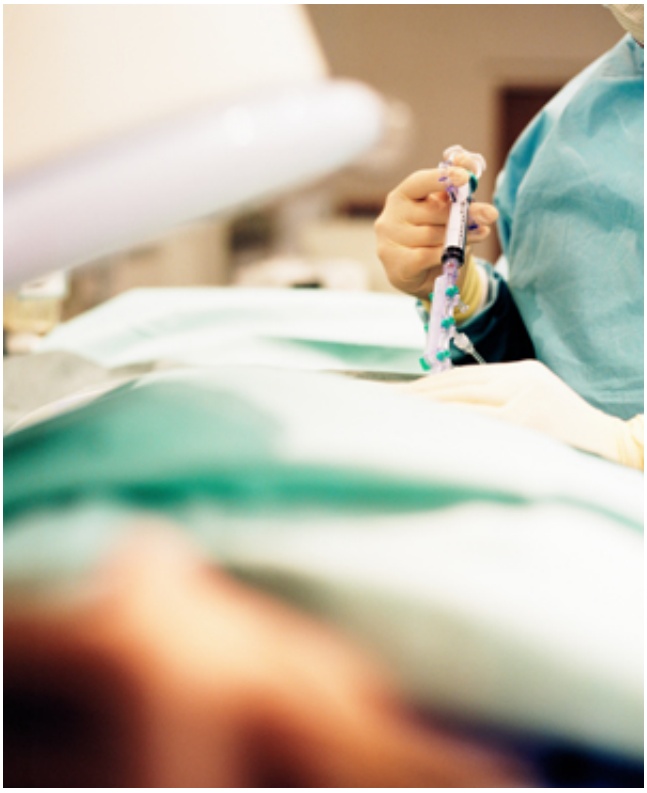

Discovery of a biomarker for multiple myeloma may improve treatments for newly diagnosed and relapsed patients. Credit: Jupiterimages/Photos.com/Thinkstock

A number of drugs exist that can extend the lifespan of people with multiple myeloma (MM), but none of these medicines are curative.

Thus, medical researchers continue to search for targets for new drug therapies as well as new ways to predict which particular patients will be most responsive to existing treatment options.

A protein called FAIM—newly implicated in multiple myeloma by a team of A*STAR scientists—could help to achieve both of these goals. "As FAIM is important to keep MM cells alive, it could be a useful and novel target for the development of novel therapeutic interventions," says Lam Kong Peng from the A*STAR Bioprocessing Technology Institute in Singapore, who led the work. "Concurrently, the significant association of elevated FAIM expression with poorer survival outcomes of MM patients suggests that FAIM can also be used as a poor-risk marker for selection of patients for more targeted therapy."

FAIM, short for 'Fas apoptosis inhibitory molecule', is a protein activated by IRF4, a key driver of the blood cell differentiation that gives rise to MM. Although scientists had previously implicated FAIM expression in the survival of pancreatic tumor cells, the protein's role in other types of cancer was unknown.

Lam's group charted the role of FAIM in MM. Through a series of cell-based studies, they demonstrated that the protein is overexpressed by known myeloma growth factors such as IGF1. FAIM then acts through a signaling axis involving Akt, an important signaling protein, and IRF4. By genetically disrupting FAIM or its signaling partners, the researchers could induce MM cell death in the laboratory. They now hope to achieve the same effect in the body by making a safe and effective drug. "Our next step will be to design and screen for specific inhibitors to inhibit the expression or function of FAIM protein," Lam says.

In addition, the researchers studied clinical specimens, showing that people with symptomatic MM had higher FAIM levels than either healthy individuals or patients with premalignant conditions. They also

analyzed biopsies taken from two clinical cohorts: one included people newly diagnosed with MM and treated quickly and aggressively with both high-dose chemotherapy and stem cell transplantation; the other included a set of relapsed patients and those treated in clinical trials with a proteasome inhibitor drug called bortezomib. In both cases, Lam and co-workers found that FAIM expression correlated with worse overall survival rates, demonstrating the prognostic value of the biomarker.

More information: Huo, J., et al. Fas apoptosis inhibitory molecule is upregulated by IGF-1 signaling and modulates Akt activation and IRF4 expression in multiple myeloma. *Leukemia* 27, 1165–1171 (2013). www.nature.com/leu/journal/v27 … abs/leu2012326a.html

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