Protein implicated in tumor growth found to be heavily associated with pancreatic cancer

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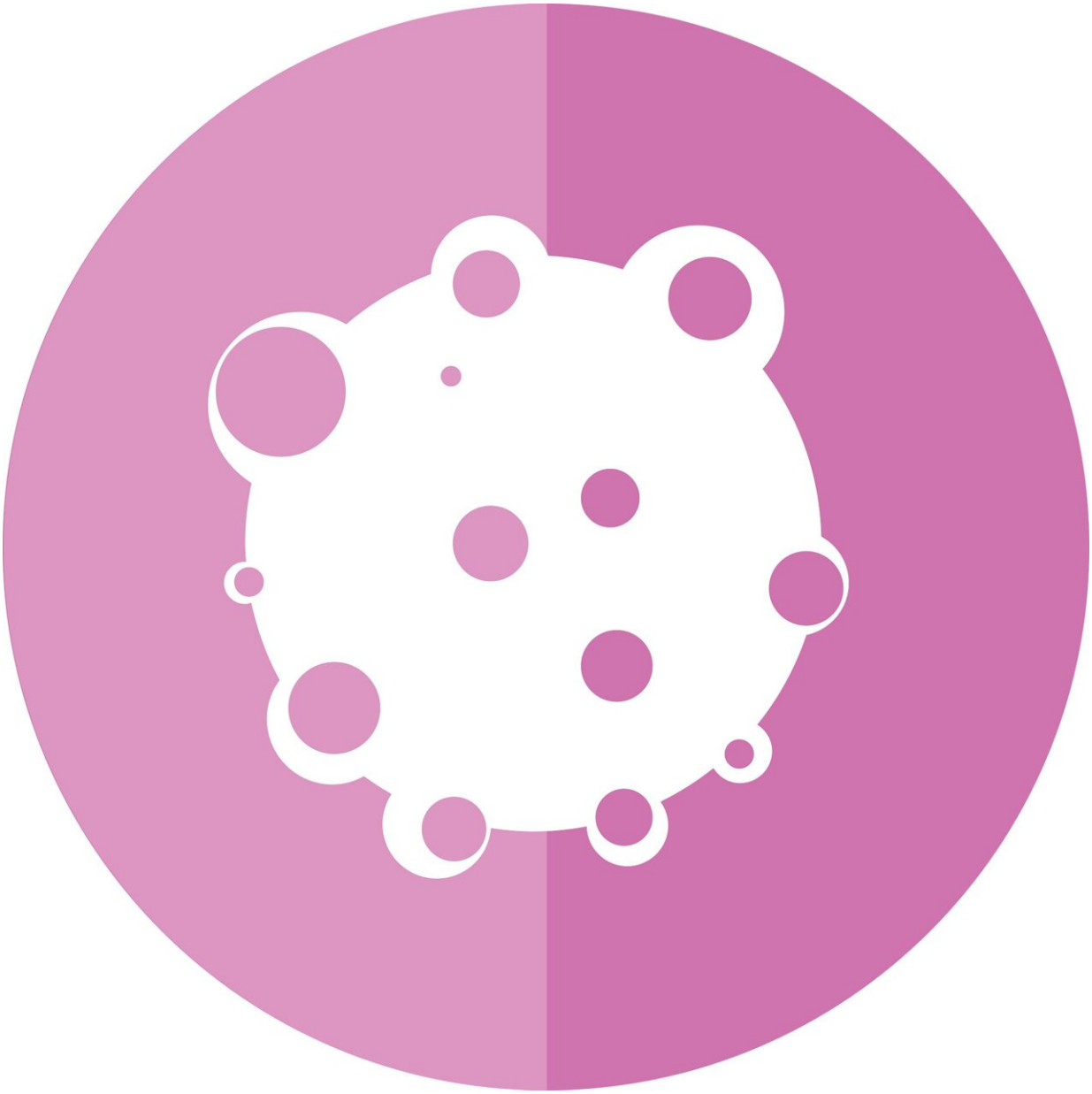

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When Nancy Klauber-DeMore, M.D., began studying secreted frizzled-related protein 2, or SFRP2, it was as a breast cancer researcher and surgeon. Since she first showed in 2008 that the protein is involved in tumor growth and angiogenesis—the growth of new blood vessels to feed the tumor—she's expanded her research to include osteosarcoma, a bone cancer that mostly affects children and young adults.

Now, in recent findings published in *Cancer Biomarkers*, the MUSC Hollings Cancer Center researcher shows that SFRP2 is especially abundant in pancreatic cancer—and the more that it shows up, the worse outcome the patient is likely to have.

However, the fact that so much SFRP2 is concentrated in the tumor, with very little in the surrounding normal tissue, also makes it a potential therapeutic target, Klauber-DeMore said.

"Our next steps will be to see if, by blocking SFRP2, we could affect the tumor," she said. "We could potentially affect tumor fibrosis. We could affect angiogenesis. We could kill the tumor cells themselves, and we could also affect the immune system as immunotherapy. So for those reasons, we have described SFRP 2 as a potential biomarker and a potential therapeutic target for pancreatic cancer."

Pancreatic cancer is especially difficult to treat, in part because it's most often diagnosed after it's already spread outside of the pancreas. A pancreatic cancer tumor grows within a thick stroma of connective tissue that not only prevents the effective delivery of chemotherapy but also interacts with the tumor to encourage its growth.

Pancreatic cancer is currently the third most common cause of cancer death and is on track to become the second most common by 2030.

Researchers have tried to attack the stroma, with mixed results. That shows that more research is needed into how all of the elements within the tumor microenvironment talk and influence each other, Klauber-DeMore said. Because SFRP2 has a role in stroma production, as well as preventing immune cells from springing into action, targeting SFRP2 could potentially have multiple effects on the tumor microenvironment, she said.

Klauber-DeMore came to pancreatic cancer after inputting SFRP2 into the Cancer Genome Atlas, a publicly available database of 33 cancers that have been molecularly characterized.

"You can look at expression of a gene in all different types of human cancer, and when we put SFRP2 in, the cancer that had the highest expression was pancreatic cancer," she said. "And so that's the reason that we started looking to see if SFRP2 was a target in pancreatic cancer."

She then saw that patients with high levels of SFRP2 had lower odds of survival. Her lab subsequently investigated how SFRP2 relates to KRAS, a gene that's heavily involved in pancreatic cancer when it mutates.

"When we silenced KRAS, it greatly reduced the expression of SFRP2. So what this is saying is that KRAS, which is known to be one of the main drivers of pancreatic cancer, drives the expression of SFRP2," Klauber-DeMore said.

More information: Julie B. Siegel et al, Secreted frizzled related-protein 2 is prognostic for human pancreatic cancer patient survival and is associated with fibrosis, *Cancer Biomarkers* (2023). DOI:

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