How Hyaluronic Acid Fuels Pancreatic Cancer Growth

The discovery that pancreatic cancers can be sustained by hyaluronic acid is challenging to translate into therapies. Here's why.

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New research indicates that hyaluronic acid (HA), a sugar-based compound naturally produced by the body and a popular ingredient in skincare products, also plays a role in fueling pancreatic cancer growth. Former Damon Runyon Fellow and Breakthrough Scientist Costas A. Lyssiotis, PhD, at the University of Michigan explains this finding in a recent paper published in eLife.

Because cancer cells grow and divide at a higher rate than normal cells, they require more energy than normal cells, and thus need to rewire the cell's energy-producing processes to meet this excessive demand.

Pancreatic cancers face the additional challenge of growing in a low-nutrient environment due to the pancreatic tumor's relative lack of blood circulation. In order to survive in these conditions, pancreatic cancer cells adjust their metabolism to derive fuel from the nutrients available—namely, HA, abundant in the tumor environment.

In normal cells, an enzyme called GFAT1 converts glucose and other nutrients into molecules that are necessary for cell structure, signaling, and survival. Cells cannot grow in vitro (i.e., in a dish) without GFAT1. When the researchers inactivated GFAT1 in pancreatic tumors, however, the cells survived; the molecules normally produced by GFAT1 were being made by other means. The researchers also noticed that HA was entering the cells from the surrounding environment. These observations allowed them to conclude that, like a vending machine when you forget your lunch, HA sustains cancer cells in a pinch.

How to translate this discovery into a therapeutic approach is complicated. As mentioned above, the dense HA matrix that surrounds pancreatic tumors limits blood circulation, which impairs both nutrient and drug delivery to the tumor. Therapies that break down this matrix would make the tumor susceptible to drug (and immune cell) invasion, but may also enhance tumor metabolism and growth. Given these conflicting roles of HA—guarding and suppressing the tumor, causing and circumventing its limited nutrient supply—researchers say "considerable work remains" to exploit this intriguing feature of pancreatic tumors.

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