

A New Approach to Targeted Therapy

Discovery represents an exciting step toward developing new targeted medications for certain types of cancer.

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In cancer treatment, “targeted therapies” refer to drugs that identify and attack specific proteins in cancer cells that help them survive and grow, while leaving normal cells alone. Due to their specificity, targeted therapies tend to be less toxic than chemotherapy or radiation therapies. Often, they take the form of small molecule inhibitors, which bind to the cancer-promoting proteins and disable them. Unfortunately, however, small molecule inhibitors only work for a subset of cancers.

In his lab at Northwestern University, Damon Runyon-Dale F. Frey Breakthrough Scientist Xiaoyu Zhang, PhD, has been working on a new type of targeted therapy—a drug that, rather than inhibiting the problematic protein directly, chaperones it to the cell’s degradation machinery, like a bouncer escorting a troublemaker out instead of fighting them. This strategy, known as “targeted protein degradation” or TPD, could be used to treat those cancers for which small molecule inhibitors are not available. Additionally, because one “chaperone” can escort more than one protein, TPD may require a lower dosage than inhibitors to have a therapeutic impact.

The challenge has been finding molecular chaperones to get the job done. Recently, Dr. Zhang and his colleagues have had a breakthrough—their screening revealed two ligases, or enzymes capable of binding other proteins, that successfully targeted proteins associated with leukemia and breast cancer for degradation.

This discovery represents an exciting step toward developing a new targeted therapy for these cancers, and potentially others.

“We will be very interested in further exploring these ligases for their potential to degrade proteins in different disease contexts,” Dr. Zhang said.

Read more in [Nature Chemical Biology](#).

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