# Researchers identify molecule that blocks immune cells from entering and killing breast tumors

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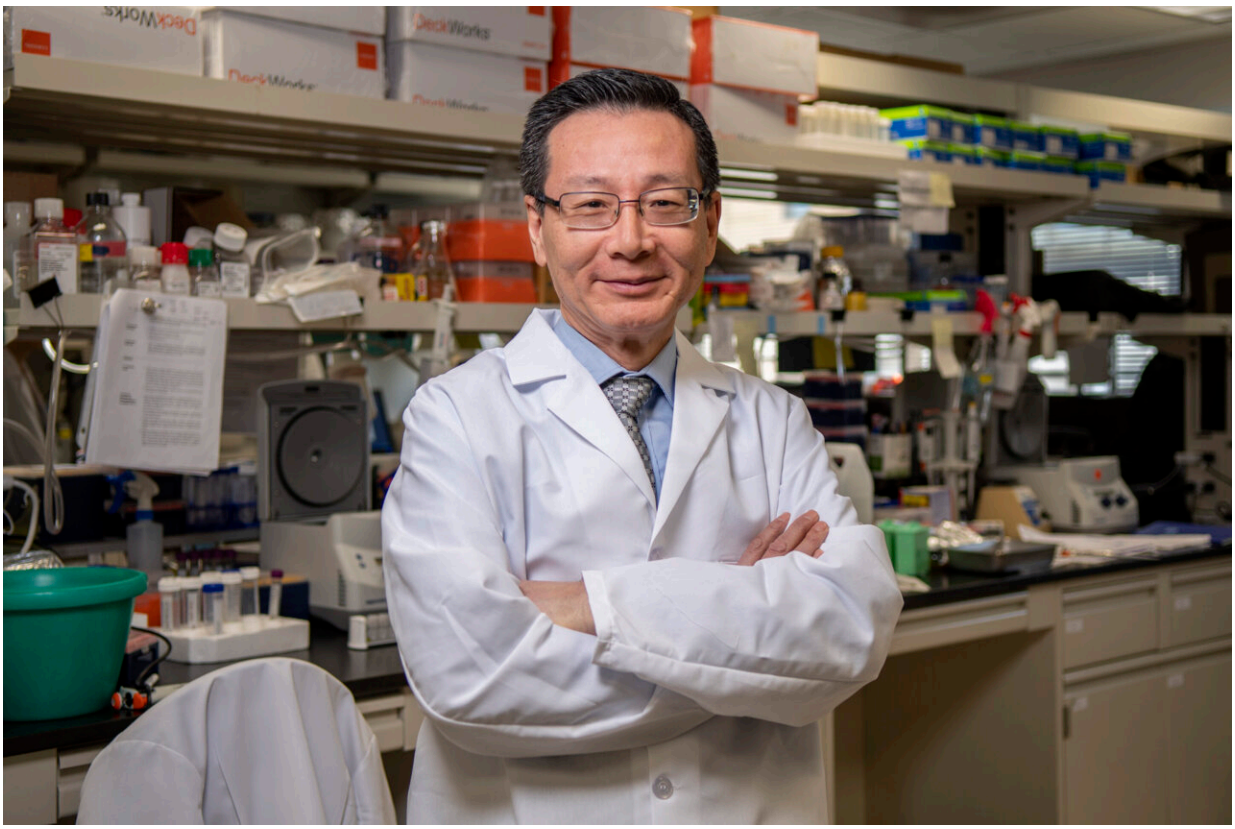

Dr. Rong Li, the Ross Professor of Basic Science Research at GW. Credit: GW

George Washington University researchers have identified a key molecule in certain kinds of breast cancers that prevent immune cells

from entering tumors and killing the cancer cells inside. The paper and its findings, published today in *Nature*, could pave the way toward a new treatment for certain kinds of aggressive breast cancer.

"During cancer progression, this molecule, known as DDR1, organizes a high-order extracellular matrix that acts like barbed wire around the boundary of a tumor to prevent immune cells from entering the tumor," Rong Li, the Ross Professor of Basic Science Research at GW and lead author of the paper, said. "Knowing that the DDR1 molecule creates a protective boundary around tumors, we were able to use pre-clinical models to show that the moment you deactivate DDR1, immune cells can infiltrate the tumor and kill the cells inside."

Li and his colleagues studied triple-negative breast cancer, an aggressive form of cancer that accounts for about 15% of all breast cancer cases. This type of cancer, according to the Centers for Disease Control and Prevention, lacks the receptors commonly used in targeted cancer therapies, making it difficult to target the tumor cells. Immunotherapy is designed to activate immune cells when they can get to the center of a tumor, but the DDR1 molecule puts up a physical barrier to anti-tumor immune cells. Identifying the underlying mechanism could provide a new way of looking for novel therapeutic agents for this hard-to-treat cancer, Li said.

In the *Nature* study, the researchers assessed the impact of removing DDR1 in multiple pre-clinical models. They determined that knocking out DDR1 not only halts tumor growth, but it also may protect the body from future tumors.

In conjunction with the new findings, co-corresponding author Zhiqiang An has developed a therapeutic DDR1-targeting antibody that breaks down that line of defense and helps tumor-killing immune cells cross.

"The discovery of the important role of DDR1 in cancer resistance is a significant advance that can potentially transform treatment pathways," said An, who serves as director of the Texas Therapeutics Institute and a professor of molecular medicine at The University of Texas Health Science Center at Houston (UTHealth Houston). "I'm delighted by the collaboration between researchers and academic labs, excited by synergies of basic and translational research, and encouraged by the rapid translation from discovery to therapeutic candidates for the benefit of people living with cancer."

With this more comprehensive understanding of DDR1, researchers also hope to identify additional molecules like DDR1 and use the same approach to fight other cancers.

"Tumour DDR1 Promotes Collagen Fibre Alignment to Instigate Immune Exclusion" appears online Nov. 3 in the journal *Nature*.

**More information:** Rong Li, Tumour DDR1 promotes collagen fibre alignment to instigate immune exclusion, *Nature* (2021). DOI: 10.1038/s41586-021-04057-2.
www.nature.com/articles/s41586-021-04057-2

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