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Counteracting tumor evasion of antibody immunity by a novel therapeutic strategy

The natural immune responses that patients develop to their own tumors, as well as therapeutic regimens employing the latest anti-cancer monoclonal antibodies, would reasonably be expected to suppress tumor growth. Yet, a perplexing resistance to both is widespread. The ineffectiveness of the immune system to prevail in these situations suggests that cancers possess tactics to evade antibodies that could otherwise eradicate them. With a clinical context in mind, we observed that tumor-associated protein-degrading enzymes can diminish, and in some cases negate, cell killing functions by inducing a single clip in a small part of the antibody structure. The structural modification is so subtle that it had not been previously recognized and would not have been anticipated to so profoundly impair the antibody. To be able to visualize and establish if such cleavage occurred in cancer, we had to develop innovative antibodies for that exact purpose. Indeed, the new antibodies readily enabled the visualization of antibody damage when incubated with cancer cells in the laboratory or within tumor tissues obtained from animals or human patients. More importantly, the same antibody tools possessed the additional and remarkable property of restoring the lost functions to the damaged antibodies. The rescue of lost function suggested that this could be exploited as a therapy in cases where tumors cause antibody damage in order to evade our immune system. This novel therapeutic strategy represents a potentially new direction in cancer immunotherapy.

Biography

Zhiqiang An is a Professor of Molecular Medicine, the Robert A Welch Distinguished University Chair in Chemistry and the Director of the Texas Therapeutics Institute at the UT Health Science Center at Houston. His laboratory focuses on breast cancer antibody drug resistance mechanisms and cancer antibody drug discovery. Previously, he was the Director of Biologics Research at Merck Research Laboratories. He has received his PhD degree from the University of Kentucky and his Postdoctoral training at the University of Wisconsin-Madison. He is an elected Fellow of Society for Industrial Microbiology and Biotechnology and the American Academy of Microbiology.

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