Antibody targets mechanism that enables lung cancer to grow and spread

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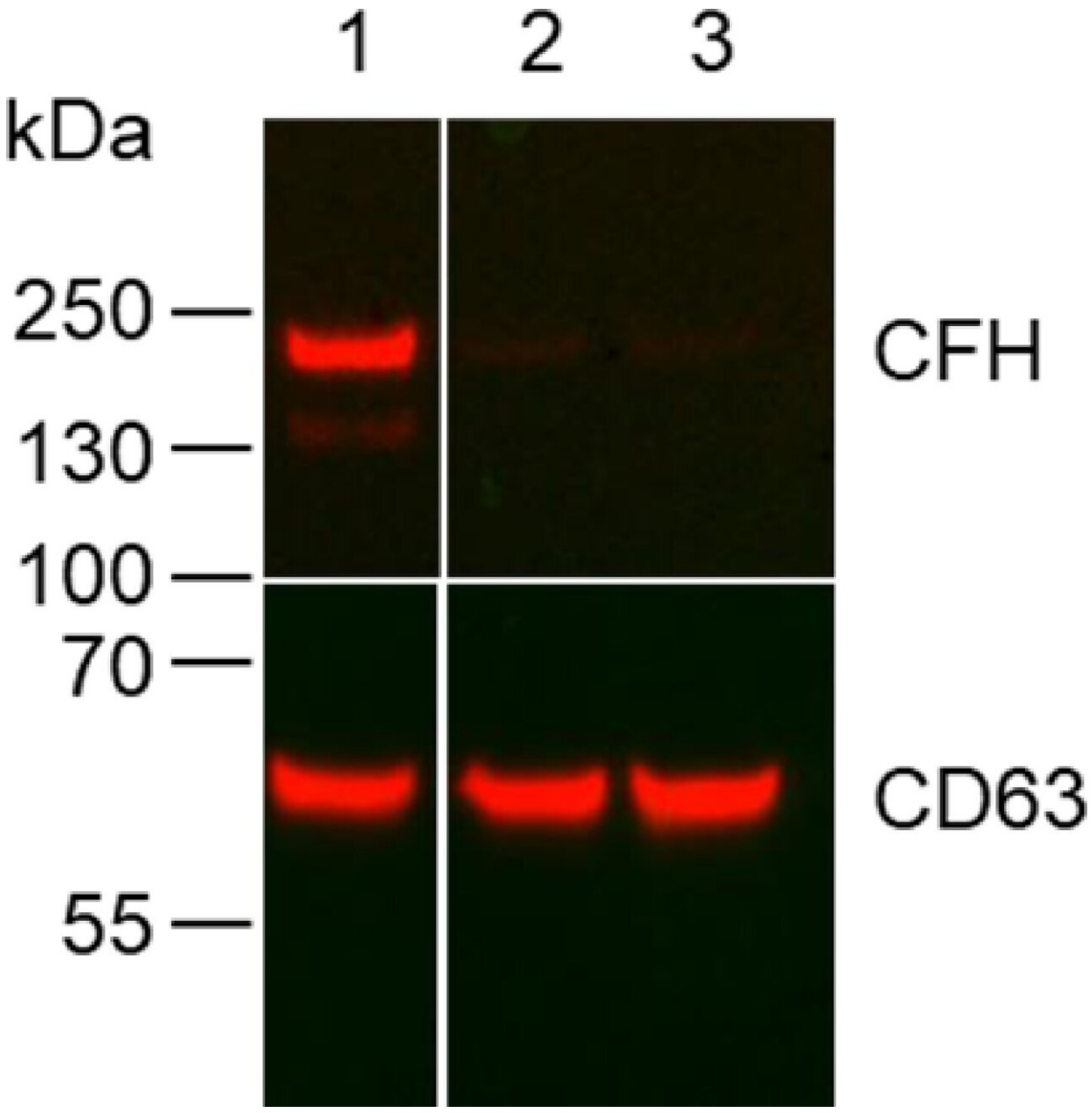

Fig 1. CFH in EVs from CMT167 wild type vs. CFH knockout lung cancer cell lines. EVs were isolated from cell line conditioned media and 7.5 μg protein were western blotted and probed with GT103 and an anti-human IgG-HRP, then stripped and probed with anti-CD63 (SBI Biosystems) and a goat-anti-rabbit-HRP conjugate. A composite of the two images is shown. Lanes contain EV protein from 1, wild type CMT167; 2 and 3, two different CFH-CRISPR/Cas9 knockout cell lines.

An investigational antibody in clinical trials for lung cancer appears to disrupt a mechanism that tumor cells exploit to avoid being destroyed by the body's innate immune system, researchers at Duke Health report.

In a study appearing online June 16 in the journal *PLOS ONE*, the researchers describe a mechanism by which the investigational antibody may potentially inhibit the growth and spread of cancer cells. The antibody, which was identified by Duke scientists, is currently being tested in a Phase 1 clinical trial among advanced non-small-cell lung cancer patients.

"These findings are an important insight to understand the mechanism of action for this antibody, which will help us select who are the most appropriate patients to receive it as a line of treatment," said senior author Edward F. Patz, M.D., professor in the departments of Radiology and Pharmacology & Cancer Biology and member of the Duke Cancer Institute.

Patz and his laboratory, in collaboration with investigators at the Duke Human Vaccine Institute, isolated the antibody. Patz has co-founded a spin-out company, Grid Therapeutics, to advance its development.

He said the antibody works against a regulator called complement factor

H (CFH), which protects host cells from attack and destruction by the body's own immune system. Tumor cells use this same method to protect themselves from destruction by the immune system.

Notably, CFH also protects a type of tiny sac called an extra-cellular vesicle that is secreted by tumor cells. These bubble-like vesicles contain proteins and information-carrying molecules that they transport between cells. Lung cancer tumors have an abundance of CFH, which results in greater numbers of extracellular vesicles. Protected from immune attack, the vesicles transfer their cargo into other cells, enabling the cancer to grow and spread.

"This is a way that tumors promote growth and metastasize," Patz said. "Our antibody targets this by shutting down CFH, inhibiting the tumor growth. This was an unexpected but interesting finding, which helps us understand a complicated process. If we can better understand the mechanism of the antibody, we can use it more effectively."

Patz said the antibody therapy will move to a Phase 2 clinical trial shortly, with patients enrolled at multiple sites. The study will combine the antibody with the current immunotherapy, pembrolizumab.

More information: Ryan T. Bushey et al, Complement factor H protects tumor cell-derived exosomes from complement-dependent lysis and phagocytosis, *PLOS ONE* (2021). DOI: 10.1371/journal.pone.0252577

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