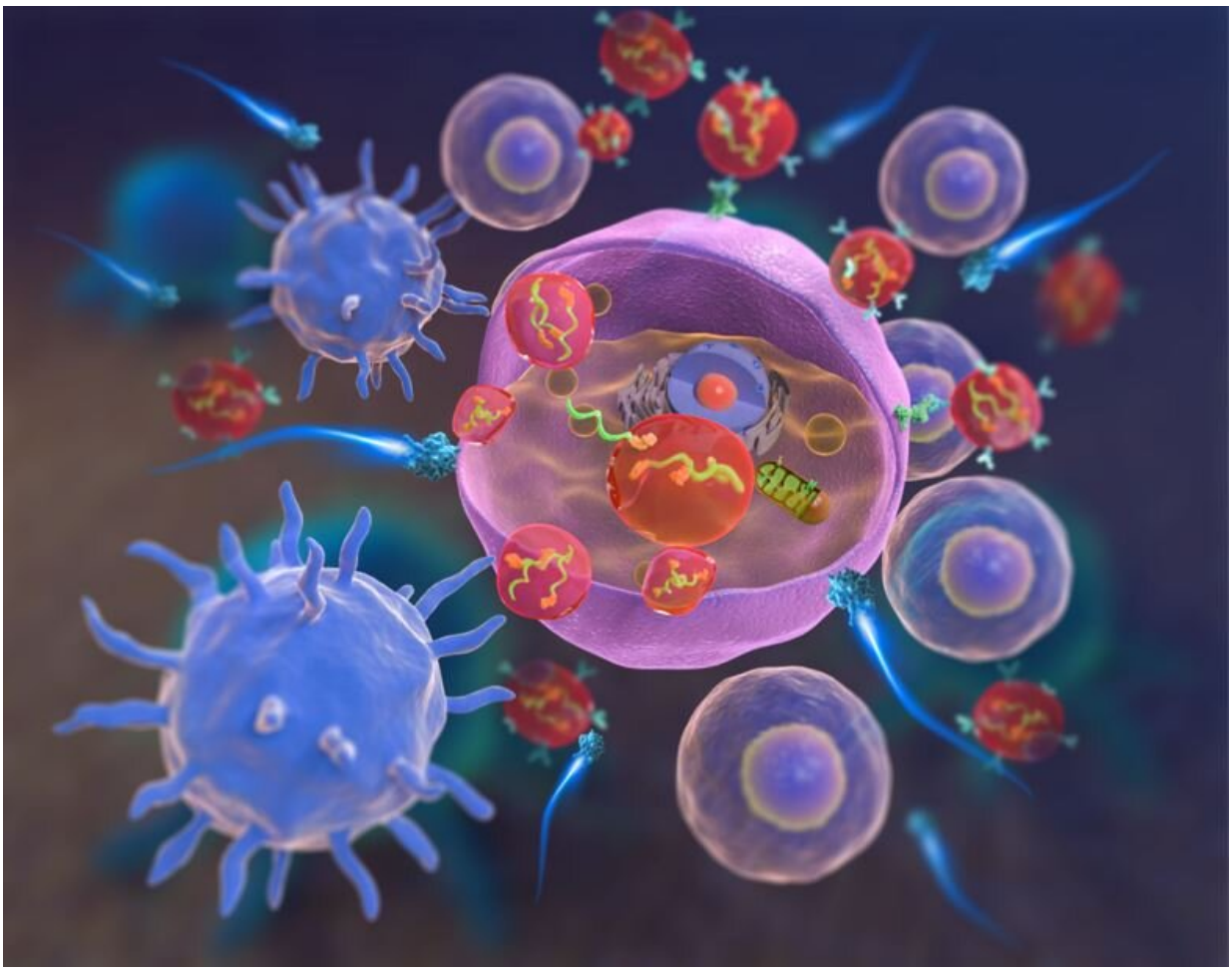
# Particles released by red blood cells are effective carriers for anti-cancer immunotherapy

April 19 2022



Extracellular vesicles deliver RIG-I agonists to fire up cancer cells and trigger immune attack. Credit: NUS Yong Loo Lin School of Medicine

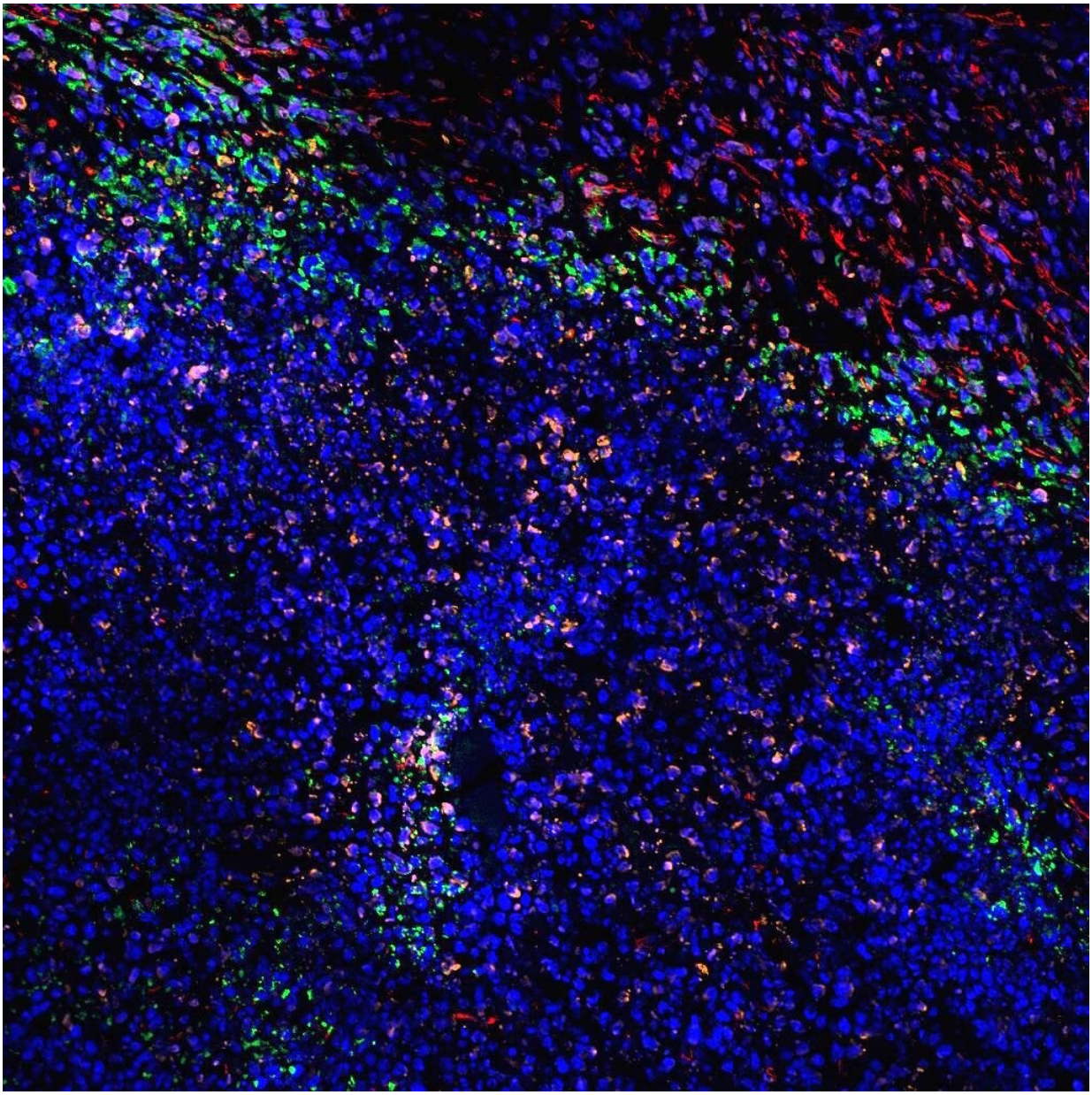
In the fight against cancer, the development of efficacious drugs is only half the battle; equally important is how drugs may be delivered efficiently and safely to the diseased sites in the body. The challenge of drug delivery is especially pertinent for RNA therapeutics which target an important immuno-modulatory receptor, RIG-I. When activated by certain types of RNAs, the receptor can initiate immune responses to kill cancer cells. As RNAs are unstable and fragile by nature, RNA-based drugs must be packaged in suitable carriers to prevent degradation, and promote efficient uptake by target cancer tissues.

A study led by researchers at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)—in collaboration with the Lee Kong Chian School of Medicine, Nanyang Technology University, Singapore (LKCMedicine, NTU Singapore) and A*STAR's Genome Institute of Singapore (GIS)—demonstrated that nano-sized vesicles released by red blood cells are a viable platform for delivering immunotherapeutic RNA molecules to suppress breast cancer growth and metastasis.

Published in the *Journal of Extracellular Vesicles*, the study successfully delivered RIG-I-activating RNAs using small, lipid membrane-bound particles released by red blood cells, called red blood cell extracellular vesicles (RBCEVs), to suppress cancer progression. The team had also discovered in earlier studies that these vesicles are ideal therapeutic carriers with a natural ability to deliver bioactive molecules to many cell types.

Assistant Professor Minh Le from the Institute for Digital Medicine (WisDM) and Department of Pharmacology at NUS Medicine, who led the study, explained, "With the discovery of these vesicles' ability to deliver therapeutics effectively to targeted receptors, we hope that our research can lead to better treatment outcomes for cancer patients. The correct homing of the therapeutics to diseased cells is also critical in

minimizing off-target effects that can result in toxicity."



“Killer T cells seeking out and attacking tumor cells"(Nuclei in blue; Cancer-associated fibroblasts (the most abundant stromal cells) in red; Apoptotic tumor cells in tangerine; CD8+ T cells in green). Credit: NUS Yong Loo Lin School of Medicine

For the study, two novel RNA molecules were developed at LKCMedicine, and packaged into RBCEVs to activate the RIG-I pathway, induce cell death in breast cancer cell cultures, and suppress tumor growth in laboratory models with breast cancer. The team also engineered RBCEVs to improve their specificity of homing towards metastatic cells that took hold in the lungs. Associate Professor Luo Dahai, Associate Professor of Infection and Immunity at LKCMedicine, said, "Asst Prof Le's RBCEV technology can overcome several hurdles related to therapeutic RNA delivery and unleash the anticancer potential of our immunomodulatory RNA (immRNA). I am thrilled to see the success of our collaboration."

Dr. Tam Wai Leong, Group Leader and Associate Director at GIS, one of the collaborators of the study, added, "The promising results highlight two key strengths of this innovative platform—the capacity for efficient delivery of different therapeutic cargoes, as well as the possibility for genetic modifications to enhance targeting to more cancer types."

To further examine the function of RBCEVs in carrying a broader range of therapeutics to more cancer cell types, the team plans to conduct further research in collaboration with the National University Cancer Institute and Cancer Science Institute of Singapore. Concurrently, RBCEV technologies are under intensive research at Carmine Therapeutics, an EVX Ventures company which aims to develop the next generation of gene therapy based on RBCEVs for treatments of rare diseases and cancer. "We hope to expand the therapeutic value of the RBCEV platform to more cancer types and increase the reach of such novel forms of therapy to benefit more cancer patients," said Asst Prof Minh Le, who is also one of the co-founders of the company.

**More information:** Boya Peng et al, Robust delivery of RIG-I agonists using extracellular vesicles for anti-cancer immunotherapy, *Journal of Extracellular Vesicles* (2022). DOI: 10.1002/jev2.12187

Provided by National University of Singapore