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nanotube-mediated transfer of mitochondria from immune cells to cancer cells metabolically empowers the cancer cells and depletes the immune cells. Inhibiting the nanotube assembly machinery significantly reduced mitochondrial transfer and prevented the depletion of immune cells. Combining a farnesyltransferase and geranylgeranyltransferase 1 inhibitor, namely, L-778123, which partially inhibited nanotube formation and mitochondrial transfer, with a programmed cell death protein 1 immune checkpoint inhibitor improved the antitumour outcomes in an aggressive immunocompetent breast cancer model. Nanotube-mediated mitochondrial hijacking can emerge as a novel target for developing next-generation immunotherapy agents for cancer.

Fig. 2: Nanotubes mediate organelle transfer between immune cells and cancer cells.

Fig. 4: Mechanism underlying nanotube formation and mitochondrial transfer.

Fig. 5: Targeting nanotube-mediated mitochondrial hijacking augments antitumour immune

Data availability

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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Contributions

T.S. conceived the project, designed and executed the experiments, analysed the data, prepared the figures, and contributed to writing the manuscript. C.D. and R.J. helped in designing and executing the in vitro experiments. S.K. and J.M. helped in designing and executing the in vivo studies and analysed results. A.K. performed the genotyping experiment, analysed results and helped write the manuscript. K.K. helped with the Dendra2 mice and Seahorse studies. P.K.M. and A.B. helped with human tumour explant studies and contributed to the manuscript writing. H.L.J. and S.S. conceptualized and supervised the project, and guided the experimental design, data analysis and manuscript writing.

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Ethics declarations

Competing interests

S.S. is a co-founder and owns equity in Vyome Therapeutics, Akamara Therapeutics and Invictus Oncology, and receives fees from Famygen and Advamedica. H.L.J. is a founder and owns equity in Curer. A.B. is involved in the following consulting/advisory boards: Pfizer, Novartis, Genentech, Merck, Radius Health, Immunomedics, Taiho, Sanofi, Daiichi Pharma/AstraZeneca, Puma, Biotheranostics

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Supplementary information

Supplementary Information

Supplementary Figs. 1–29 and Table 1.

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