New nanoinducer of interferons found for cancer immunotherapy

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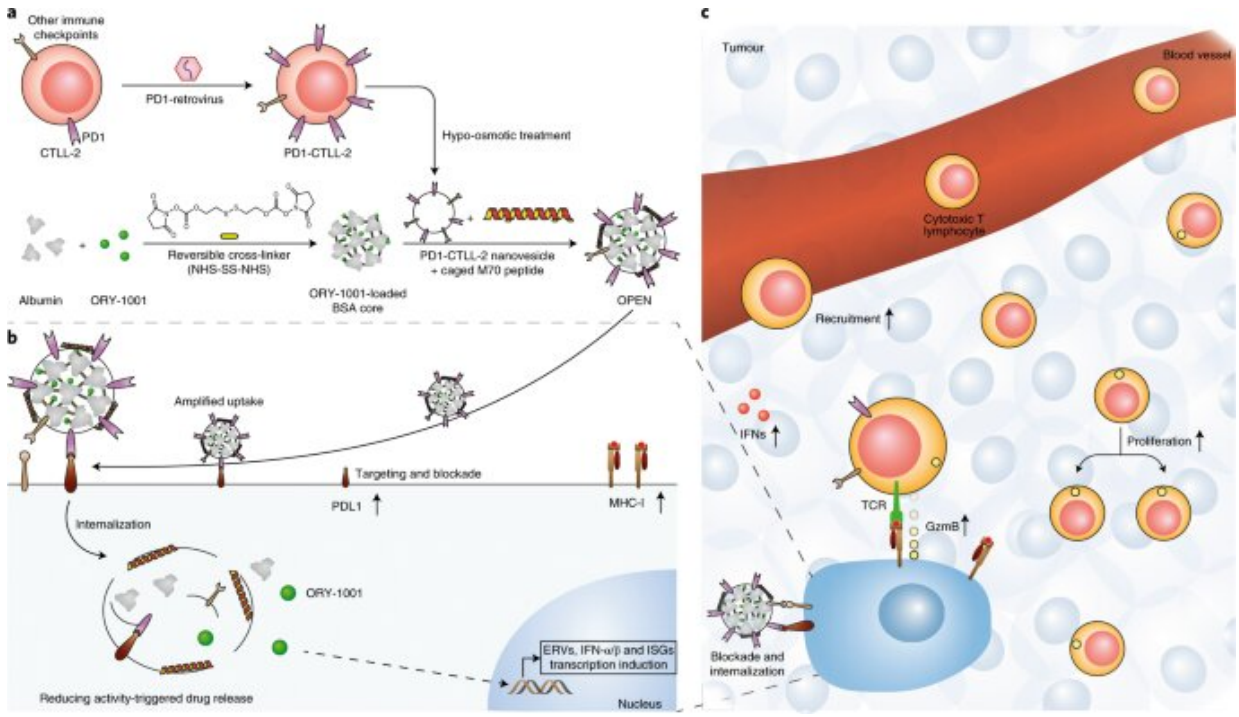

Fig. 1: Schematic illustration of the preparation and mechanism of action of OPEN. Credit: DOI: 10.1038/s41565-021-00972-7

Cancer immunotherapy such as immune checkpoint blockade (ICB) is a revolutionary treatment against tumors by re-enforcing immune surveillance and even inducing long-term disease control.

Type I interferons (IFNs) are key coordinators of tumor-immune system

interaction. Impaired IFN signaling is associated with poor prognosis in patients with colon cancer, melanoma, triple-negative breast cancer, etc. Current IFN supplementary therapy sometimes brings severe side effects and IFN-induced multigenic resistance program to ICB.

In a study published in *Nature Nanotechnology*, a research team led by Li Yaping and Zhang Pengcheng from Shanghai Institute of Materia Medica of the Chinese Academy of Sciences (CAS) demonstrated that the paradoxical effects of IFN supplementary therapy could be addressed using a T lymphocyte membrane-decorated epigenetic nanoinducer of IFNs (OPEN).

The researchers first genetically engineered a programmed death receptor 1 (PD1)-overexpressing cytotoxic T cell line, and then used the membrane of these cells to envelope protein nanoparticle loaded with ORY-1001, an inhibitor of lysine-specific histone demethylase 1 (LSD1), to create OPEN.

They revealed that the OPEN improved the intratumoral accumulation of ORY-1001 and local production of IFNs after intravenous administration, and demonstrated that the IFNs increased tumor infiltration, proliferation and activity of tumor-specific cytotoxic T cells and antigen display of tumor cells.

Besides, they proved that the IFN-induced programmed death ligand 1 (PDL1) and other immune checkpoint molecules were readily neutralized by subsequent OPEN. This sequential process specifically replenished intratumoral IFNs and alleviated IFN-induced immune evasion, and thus retarding tumor growth in multiple tumor models.

"The study demonstrates an elegant strategy to solve the paradoxical effects of IFN supplementary therapy using epigenetic nanoinducer of IFNs. It is a milestone in the field of nanomedicine for safer and more

effective cancer immunotherapy," said Prof. Zhao Yuliang, an academician of CAS.

"This is the first research that elaborates the great potential of epigenetic nanomedicine in cancer immunotherapy. The nanomedicine has significant clinical translation value due to its advantages in tumor targeted delivery and immune checkpoint blockade," said Prof. Hao Xishan, an academician of Chinese Academy of Engineering (CAE).

More information: Yihui Zhai et al, T lymphocyte membrane-decorated epigenetic nanoinducer of interferons for cancer immunotherapy, *Nature Nanotechnology* (2021). DOI: 10.1038/s41565-021-00972-7

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