Life Sciences

# New Strategy to Develop an mRNA Vaccine for Durable Cancer Immunotherapy

Messenger RNA (mRNA) vaccine is a promising candidate in cancer immunotherapy as it can encode tumor-associated antigens with an excellent safety profile. Unfortunately, the inherent instability of RNA and translational efficiency are major limitations of RNA vaccine.

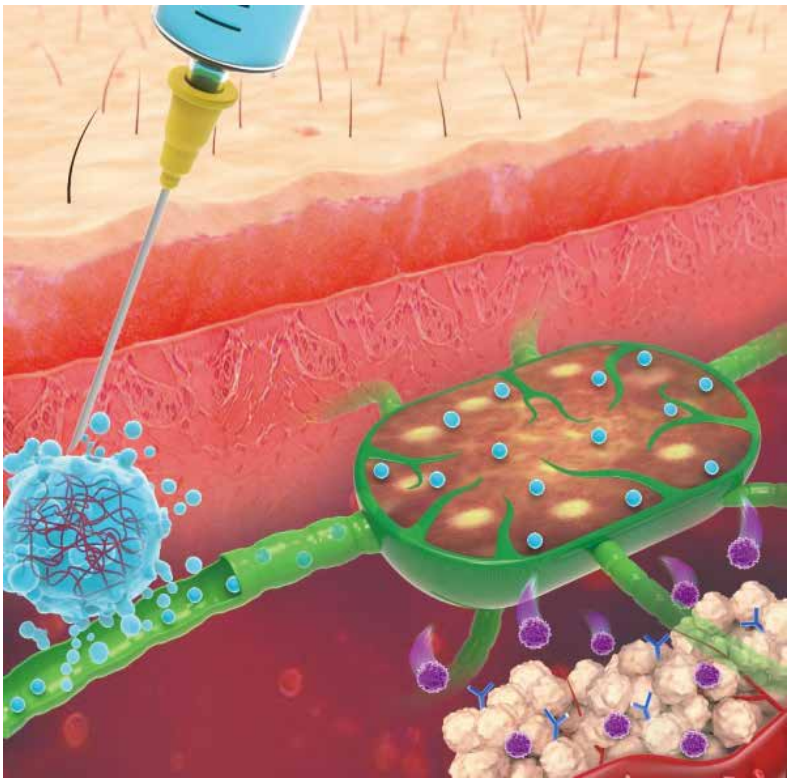
During cancer progression, the functions of cytotoxic T lymphocytes (CTLs) are disturbed and exhausted because of the immunosuppression or tolerance induction in the tumor microenvironment (TME).

It is important to stimulate the innate immune response to generate $CD8^+$ T cells for durable and efficient antitumor immune responses. Immune adjuvants can enhance the immune response to the administrated antigens, and therefore have been exploited in the past several decades.

Recently, a research team led by Prof. WANG Hai and Prof. NIE Guangjun from the National Center for Nanoscience and Technology (NCNST) of the Chinese Academy of Sciences (CAS), reported an injectable hydrogel formed with graphene oxide (GO) and polyethylenimine (PEI), which can generate mRNA (ovalbumin, a model antigen) and adjuvants (R848)-laden nanovaccines for at least 30 days after subcutaneous injection.

This work was published in *Nano Letter* on March 10, 2021, entitled "*In situ* transforming RNA nanovaccines from polyethylenimine functionalized graphene oxide hydrogel for durable cancer immunotherapy."

The *in vivo* results show that the mRNA (mOVA) and R484-laden nanoparticles (GLP-RO) can be slowly released from GLP-RO Gel after injected into subcutaneous layers, delivering R848 and mOVA to lymph node for at least 30 days.



A schematic illustration for the transforming RNA nanovaccines from injectable hydrogel to durable cancer immunotherapy. (Image by NCNST)

After subcutaneously injected for only one time, GLP-RO Gel can significantly increase the number of antigen-specific $CD8^+IFN^-\gamma^+$ T cells and efficiently inhibit the tumor growth compared with other control groups. Meanwhile, GLP-RO Gel can generate antigen specific antibody in the serum which in turn induce a potent anti-metastasis effect, significantly preventing the formation of lung metastases.

Collectively, this study indicates the injectable

and transformable GLP-RO Gel is a valuable strategy to achieve durable and efficient antitumor immune responses for cancer immunotherapy.

The novel strategy may lay the foundation of developing a promising method for RNA vaccines delivery and have a significant impact on the field of vaccine and cancer immunotherapy.

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(NCNST)

**Reference**

Yue Yin, Xiaoyang Li, Haixia Ma, Jie Zhang, Di Yu, Ruifang Zhao, . . . Hai Wang, (2021) *In situ* transforming RNA nanovaccines from polyethylenimine functionalized graphene oxide hydrogel for durable cancer immunotherapy. *Nano Letters* 21, 2224. doi: 10.1021/acs.nanolett.0c05039.