Indian Institute of Technology Hyderabad

भारतीय प्रौद्योगिकी संस्थान हैदराबाद
Indian Institute of Technology Hyderabad

Dr. Aravind Kumar Rengan *M.B.B.S, M.Tech, Ph.D*

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29th Aug 2024,
Hyderabad.

Research work – Sun Pharma Science Foundation Fellowship (Pharmaceutical Sciences)

Dear Sir,

I would like to submit the research work titled "Nano transformable Hydrogel for the treatment of metastatic cancers" for availing the Sun Pharma Science Foundation Fellowship – Pharmaceutical Sciences category. Metastasis is one of the predisposing factors for cancer-related mortalities worldwide. Patients with advanced cancers (stage IV) receive palliative care with minimal possibility of achieving complete remission. Antibody-based therapeutic modalities are capable of targeting tumors that are confined to a particular location but are ineffective in targeting distant secondary tumors. In the current study, we have developed a smart nanotransforming hydrogel (NTG) that transforms in situ to polymeric nanoparticles (PA NPs) of 100−150 nm when injected subcutaneously. These nanoparticles targeted the primary and secondary metastatic tumors for up to ∼5 and ∼3 days, respectively. The in situ-formed PA NPs also demonstrated a pH-responsive drug release resulting in about ∼80% release within 100 h at 5.8 pH. When tested in vivo, substantial inhibition of lung metastases was observed compared to chemotherapy, thus demonstrating the efficiency of nanotransforming hydrogels in targeting and inhibiting primary and secondary metastatic tumors.

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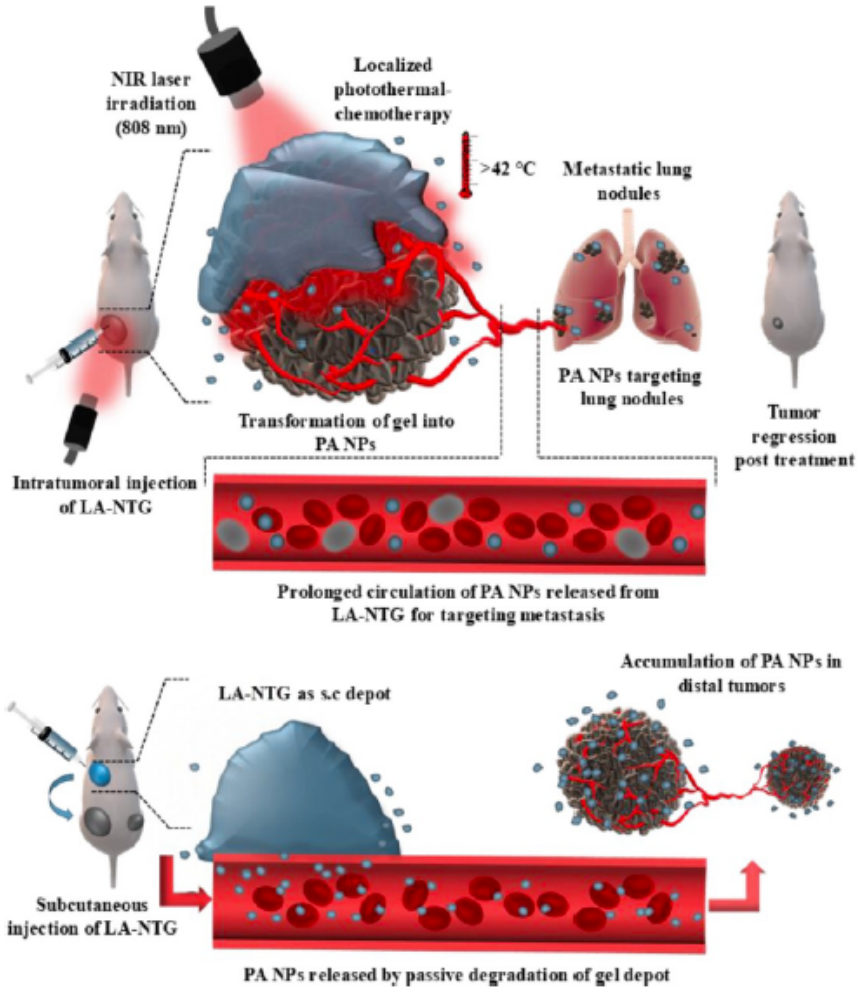
Scheme 1. *In Vivo*-Localized Chemo-PTT by LA-NTG and the Inhibition of Metastatic Foci by PA NPs[a]



[a]The passive degradation of the subcutaneously administered LA-NTG depot into PA NPs targeting multiple distant tumors by EPR.

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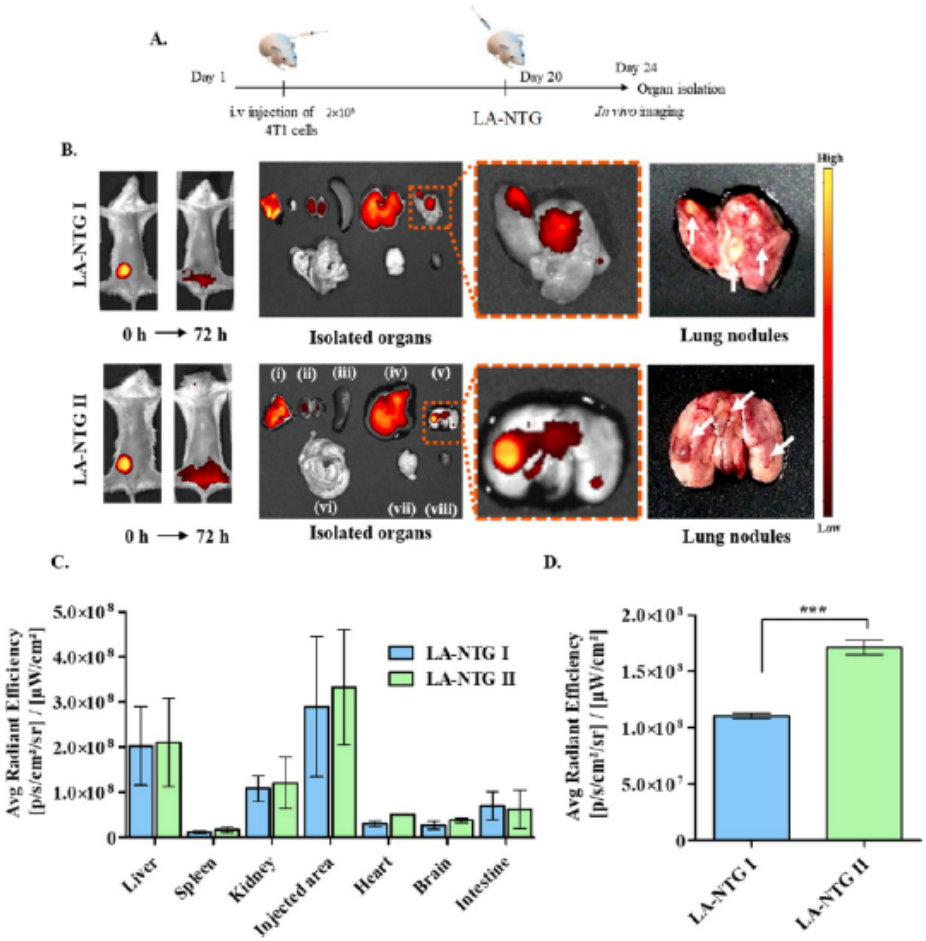

Figure 11. (A) Schematic representation of lung metastasis induction and LA NTG administration. (B) Metastatic lung nodule targeting by LA-NTG I and LA-NTG II. (i) Skin, (ii) kidneys, (iii) spleen, (iv) liver, (v) lungs, (vi) intestines, (vii) brain, and (viii) heart. (C) Biodistribution of LA NPs and PA NPs different organs. (D) Quantification of the fluorescent signal from isolated lung nodules (images were acquired from stage B of *in vivo* imaging system). Data are represented as mean ± SEM ($n = 3$), and unpaired t-test was performed (***$P < 0.001$).

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In this study, we report a biocompatible and biodegradable NIRresponsive smart in situ nanotransforming gel. The injected hydrogel depot degrades into self-stabilized polymeric albumin nanoparticles (PA NPs), exhibiting prolonged systemic circulation and accumulation in distant tumors by the EPR effect. These PA NPs were also able to accumulate within the secondary metastatic lung nodules selectively for a prolonged time. When tested in vivo on melanoma-bearing mice, a single dose of hydrogel inhibited the tumor growth by demonstrating sustained chemo-PTT. It was also able to prevent splenomegaly, thereby reducing cancer burden. When tested in vivo, spontaneous metastasis model LA-NTG was also able to suppress the formation of metastatic lung nodules, outperforming chemotherapy. Thus, the protein-polymer-based nanotransforming gels hold immense potential for clinical translation and can offer a better therapeutic effect in treating aggressive cancers.

Thanking you,

Best regards,

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