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Deformable and degradable nanozymes for inhaled viral pneumonia treatment

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The persistent threat of viral pneumonia to global health highlights the ongoing challenge facing the treatment for this infectious disease.[1] Conventional therapeutic strategies, including the use of antiviral drugs and supportive care, have demonstrated their limitations, especially against newly emerging viral strains. The time-consuming nature of developing vaccines for these variants restricts prompt responses to outbreaks. Therefore, there is an urgent need to establish a broad-spectrum treatment strategy for viral pneumonia.[2]

Viral pneumonia, frequently caused by viruses such as Influenza A (Flu A) or Sendai virus (SeV), is marked by an overactive inflammatory response and elevated levels of reactive oxygen species (ROS) within the lung tissues. This oxidative stress not only intensifies inflammation but also leads to tissue damage and compromised immune function. While natural enzymes play a crucial role in maintaining the redox balance in living organisms, they are prone to losing their activity under pathological conditions, leading to the secretion of nanozymes.[3,4] However, accurately delivering and concentrating nanozymes at the site of inflammation to treat viral pneumonia presents a significant challenge due to the complexity of internal inflammation.

In a recent work published in *Nature Materials*, Peng *et al.*[5] reported the development of an innovative nasal inhalable platform, CeTA-K_1tkP, for the treatment of viral pneumonia. This platform combines a degradable cerium-based tannic acid nanozyme with a self-assembling peptide (Figure 1A-C). In areas of inflammation with high ROS levels, CeTA-K_1tkP triggers the release of polyethylene glycol and forms a fibrous structure, effectively scavenging ROS and alleviating inflammation without systemic immune suppression. Notably, CeTA-K_1tkP demonstrated the ability to bind viral proteins, potentially neutralizing the virus and mitigating bacterial inflammation in pneumonia models. This nanoplatform offers a promising approach for managing severe inflammations such as pneumonia.

The CeTA nanozymes are synthesized from tannic acid and cerium nitrate, showing enhanced catalase-like and superoxide dismutase-like activities at higher concentrations. The CeTA-K_1tkP nanoplatform, integrating CeTA with a self-assembling peptide, exhibits reactive self-assembly in ROS-rich environments, forming β-sheet structures that boost its catalytic and ROS-scavenging capabilities. This nanoplatform also exhibits targeted accumulation in inflamed regions, effectively reducing ROS and inflammation, highlighting its potential for precise therapy in the treatment of inflammatory diseases.

The CeTA-K_1tkP nanoplatform has demonstrated potential in treating viral pneumonia by improving the over-oxidative environment. In a mouse model of H1N1-induced pneumonia, CeTA-K_1tkP inhalation therapy showed broad-spectrum therapeutic effects, reducing inflammation and viral load and restoring normal alveolar morphology. The treatment led to a significant decrease in inflammatory cytokines such as interleukin (IL)-6, tumor necrosis factor-alpha (TNF-α), and IL-1β in bronchoalveolar lavage fluid and serum. *In vitro* experiments confirmed CeTA-K_1tkP's neutralizing effect on the Flu A virus, with binding to the HA protein of H1N1 viruses. Molecular docking suggested that tannic acid in CeTA-K_1tkP interacts with HA proteins, forming hydrogen bonds and hydrophobic interactions. In a pulmonary virus infection model using SeV, CeTA-K_1tkP nasal administration attenuated inflammation and regulated the production of inflammatory cytokines (Figure 1D). The treatment increased the expression of the antioxidant gene *HO-1* and decreased the pro-oxidant gene *Nox2*, suggesting a rebalancing of redox homeostasis. CeTA-K_1tkP also reduced SeV viral load and showed neutralization ability *in vitro*. The treatment promoted the conversion of macrophages from pro-inflammatory M1 to anti-inflammatory M2 phenotypes, indicating the potential to inhibit viral-infection-related immunological disorders and lung damage. CeTA-K_1tkP also showed therapeutic efficacy in a model of viral pneumonia combined with

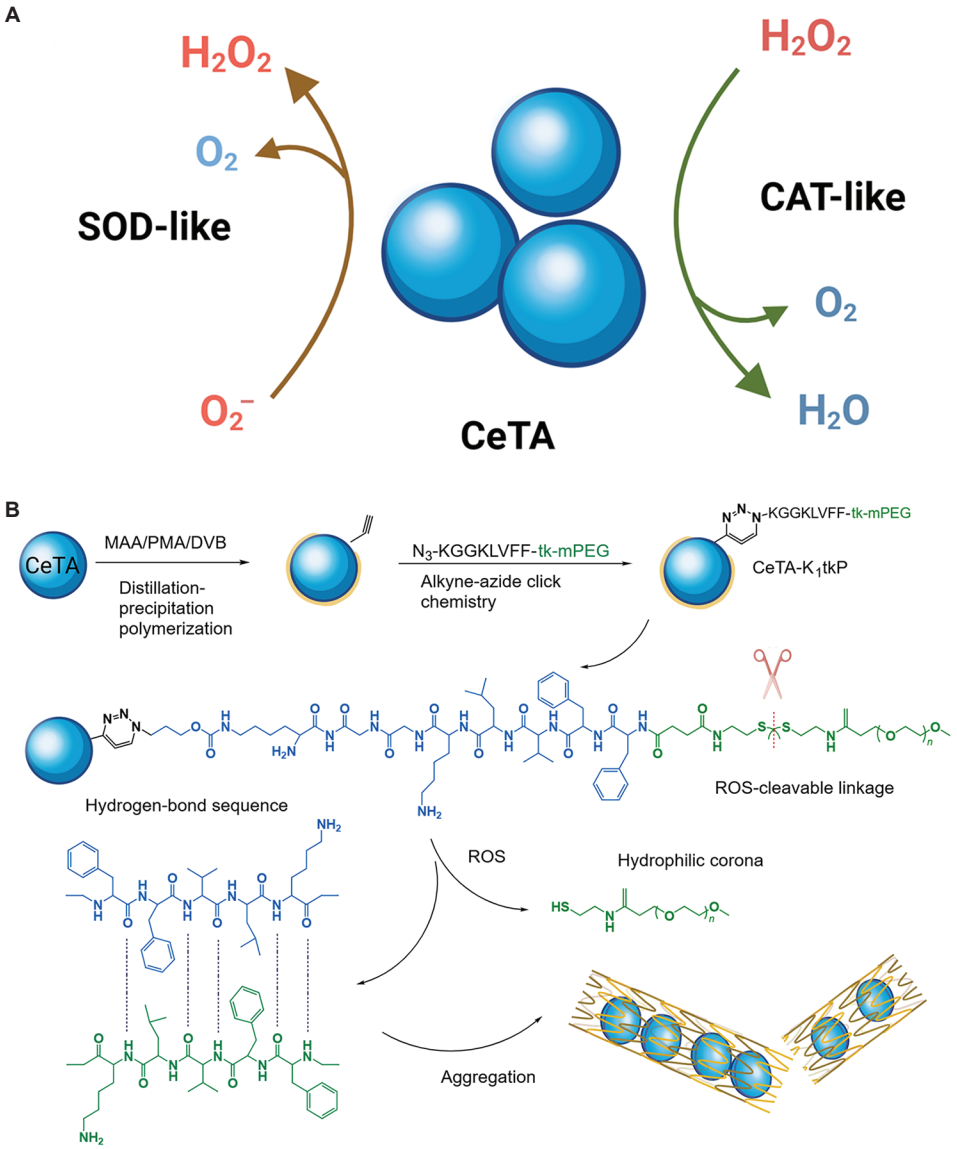

Figure 1. (A) Schematic presentation of the enzyme-like activities of CeTA nanozyme. (B) Schematic illustration of the self-assembly performance of the CeTA-K1tkP nanoplatform. Created with Biorender.com.

bacterial infection. The treatment minimized secondary bacterial lung damage, reduced the expression of inflammatory cytokines, and effectively regulated macrophage polarization in the inflammatory environment.

In summary, this work has developed a novel degradable and safe inhalable CeTA nanozyme based on peptide-based biological self-assembly for the treatment of viral pneumonia. Building upon the design that enables the material to respond to the deformation of the inflammatory microenvironment, this work also provides a detailed characterization of the material's ability to alleviate the microenvironment of viral pneumonia. It is an excellent work that balances the dual innovation of material design and preparation with biomedical effects, opening up new directions for smart biomaterials. Inhalable formulations have always been of great interest due to their simple administration methods and specific targeting pathways.[6,7] However, due to the fragile environment of the lungs and the weak metabolic capacity, the development of nanomaterials, especially inorganic materials, in the field of inhalable formulations has not been entirely satisfactory.[8] The degradable nanoenzymes developed in this work have also been thoroughly validated for their biosafety and *in vivo* metabolic pathways, potentially paving the way for a new direction in inhalable bio-nanomaterials.

Author contributions

Conceptualization: TZ; *Writing – original draft:* JS; *Writing – review & editing:* TZ. All authors read and approved the final manuscript.

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Conflicts of interest statement

The authors declare no conflicts of interest.

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Not applicable.

Consent for publication

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Availability of data

Not applicable.

References

1. Ruuskanen O, Lahti E, Jennings L, Murdoch D. Viral pneumonia. *Lancet.* 2011;377:1264-1275. doi: 10.1016/S0140-6736(10)61459-6
2. Vigant F, Santos N, Lee B. Broad-spectrum antivirals against viral fusion. *Nat Rev Microbiol.* 2015;13:426-437. doi: 10.1038/nrmicro3475
3. Jiang D, Ni D, Rosenkrans Z, Huang P, Yan X, Cai W. Nanozyme: New horizons for responsive biomedical applications. *Chem Soc Rev.* 2019;48:3683-3704.
4. Wang H, Wan K, Shi X. Recent advances in nanozyme research. *Adv Mater.* 2019;31:e1805368. doi: 10.1002/adma.201805368
5. Peng W, Tai W, Li B, *et al.* Inhalable nanocatalytic therapeutics for viral pneumonia. *Nat Mater.* 2024. doi: 10.1038/s41563-024-02041-5
6. Bai X, Chen Q, Li F, *et al.* Optimized inhaled LNP formulation for enhanced treatment of idiopathic pulmonary fibrosis via mRNA-mediated antibody therapy. *Nat Commun.* 2024;15:6844. doi: 10.1038/s41467-024-51056-8
7. Ye T, Jiao Z, Li X, *et al.* Inhaled SARS-CoV-2 vaccine for single-dose dry powder aerosol immunization. *Nature.* 2023;624:630-638. doi: 10.1038/s41586-023-06809-8
8. Li J, Wu S, Guo X, *et al.* Safety and immunogenicity of heterologous boost immunisation with an orally administered aerosolised Ad5-nCoV after two-dose priming with an inactivated SARS-CoV-2 vaccine in Chinese adults: A randomised, open-label, single-centre trial. *Lancet Respir Med.* 2022;10:739-748. doi: 10.1016/S2213-2600(22)00087-X

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