

ROS-triggered self-accelerating drug release nanosystem with charge conversion for enhanced cancer therapy

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SUBJECT AREAS

Nanoscience

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Doxorubicin, Reactive oxygen species, Charge-reversal, Lung cancer

Abstract

Background: The enhancement tumor retention and of cellular uptake of drugs are important factors in maximizing anticancer therapy and minimizing side effects of encapsulated drugs. Herein, a delivery nanoplatform with a pH-triggered charge-reversal capability and self-amplifiable reactive oxygen species (ROS) level inducing drug release pattern was constructed by encapsulating doxorubicin (DOX) in pH/ROS-responsive polymeric micelle.

Results: The surface charge of this system can be converted from negative to positive for enhanced tumor cell uptake in response to the weakly acidic tumor tissue. In addition, methionine-based system was dissociated in a ROS-rich intracellular environment, resulting in a phase transition and the release of DOX. Then, the exposed α -tocopheryl succinate (α -TOS) segments can be capable of producing ROS, which further induced the self-amplifiable disassembly of the micelles and drug release.

Conclusions: We confirmed efficient DOX delivery into cancer cells, upregulation of tumoral ROS level and induction of the apoptotic capability in vitro. The system exhibited outstanding tumor inhibition capability in vivo, indicating that dual stimuli nanosystem would be great potential as an anticancer drug delivery platform.

Full Text

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Figures

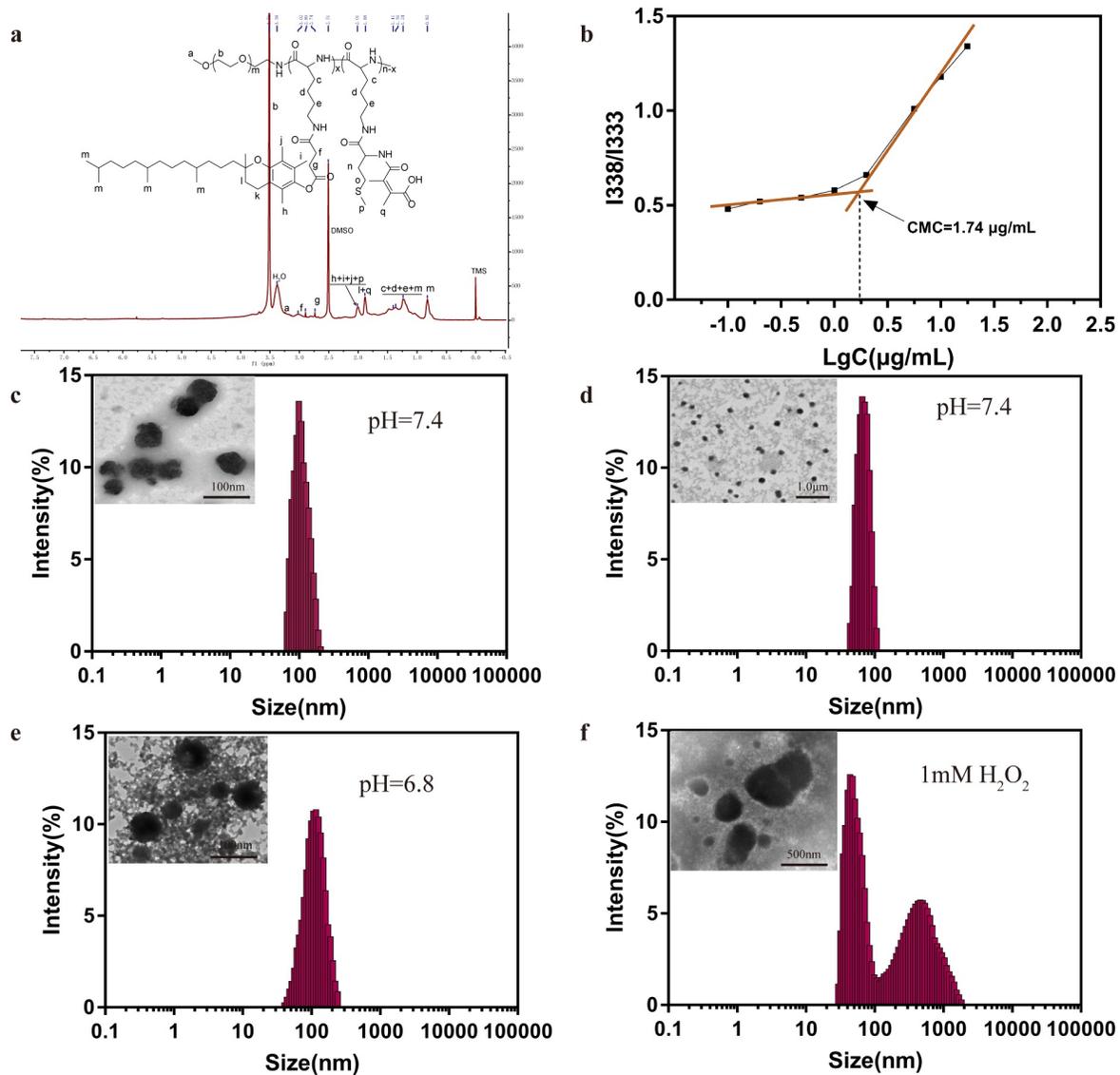


Figure 1

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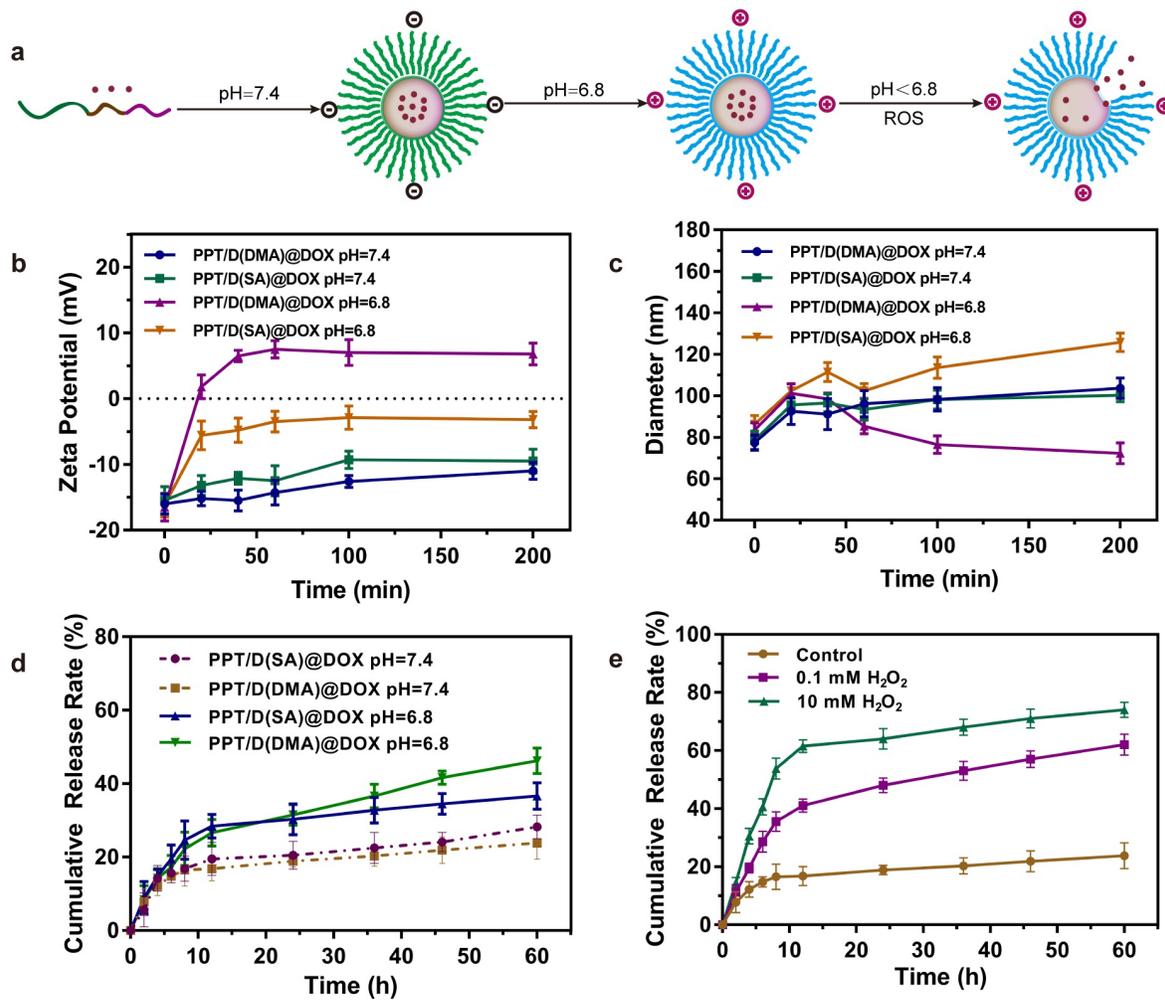


Figure 2

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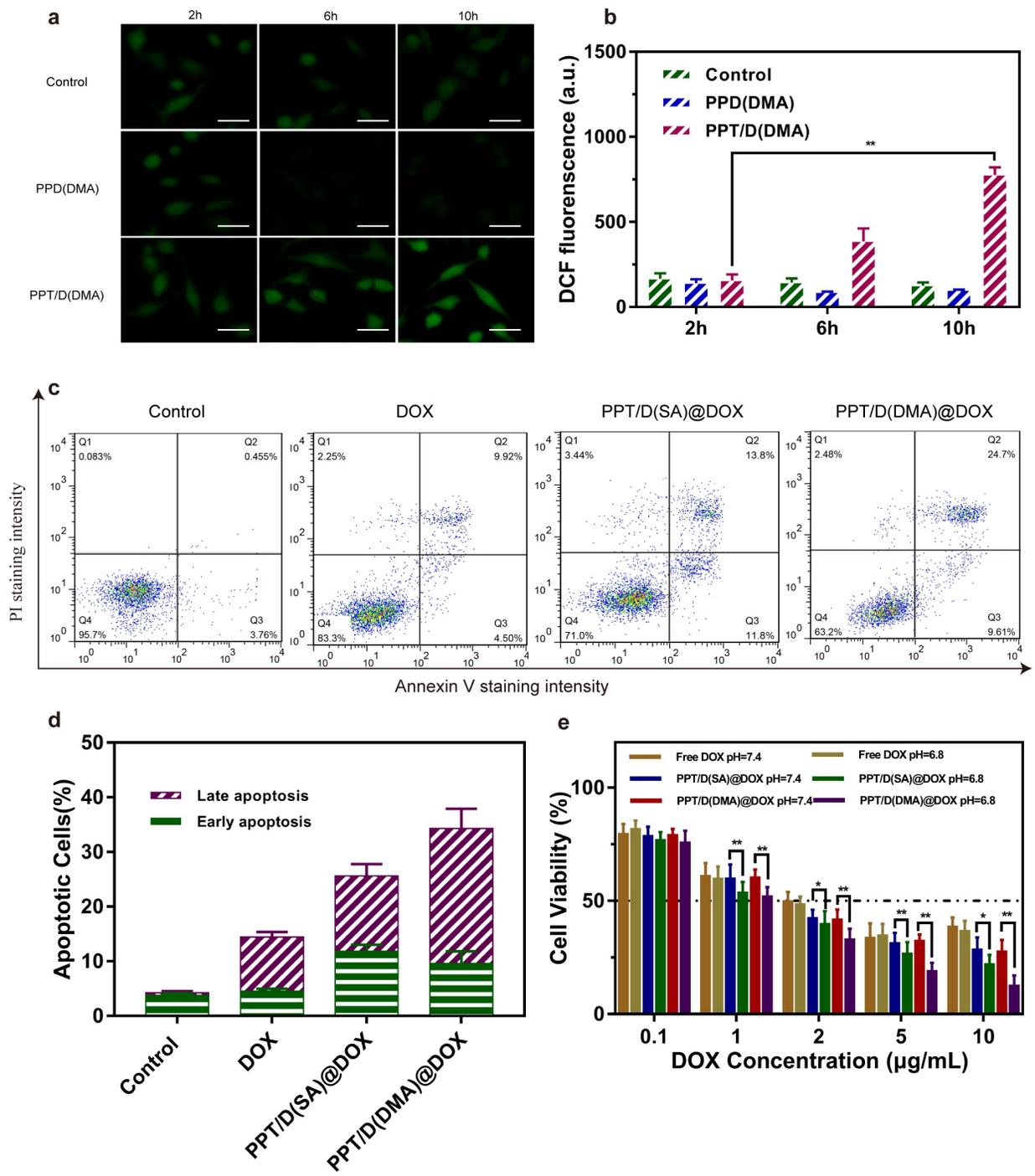


Figure 3

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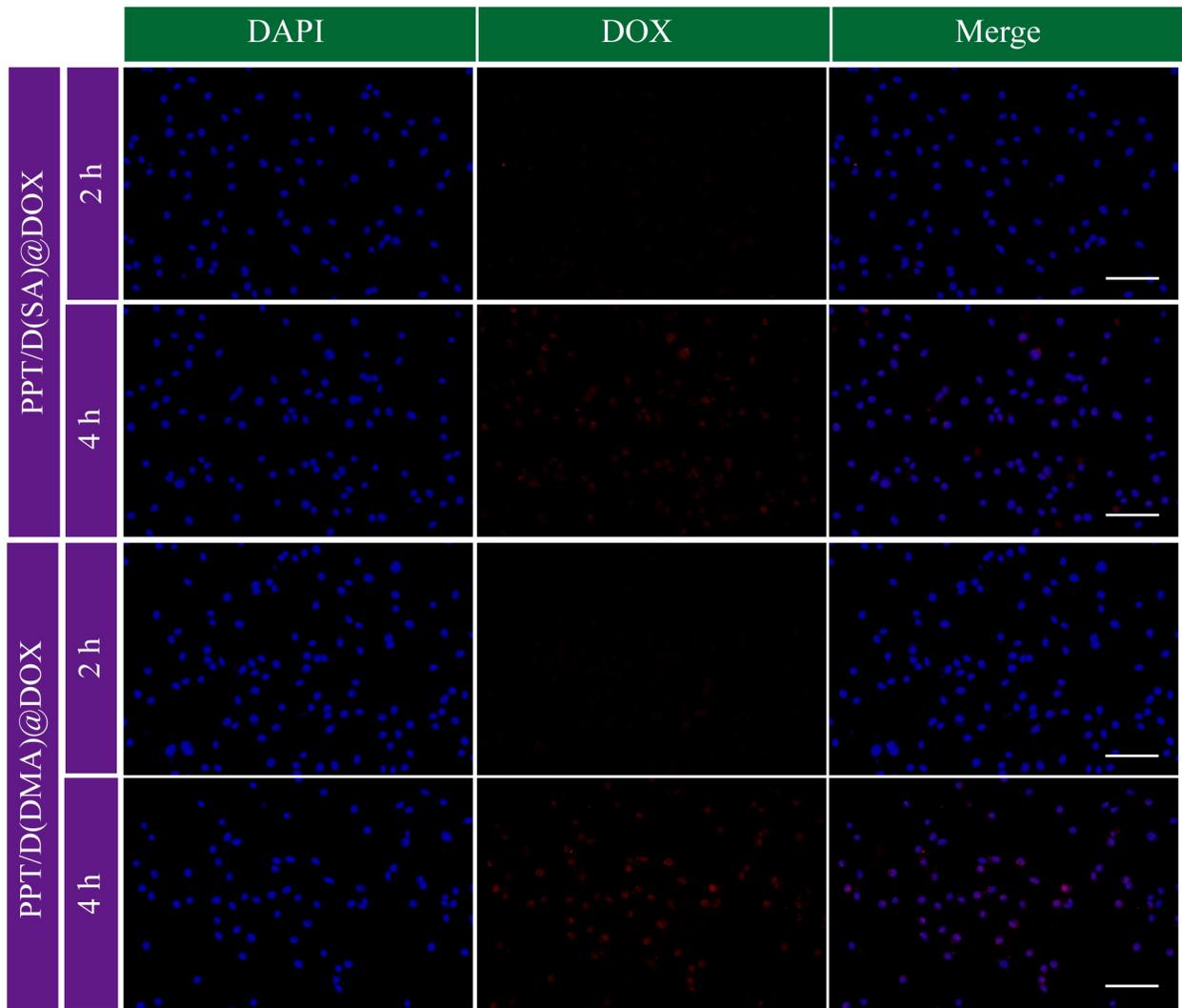
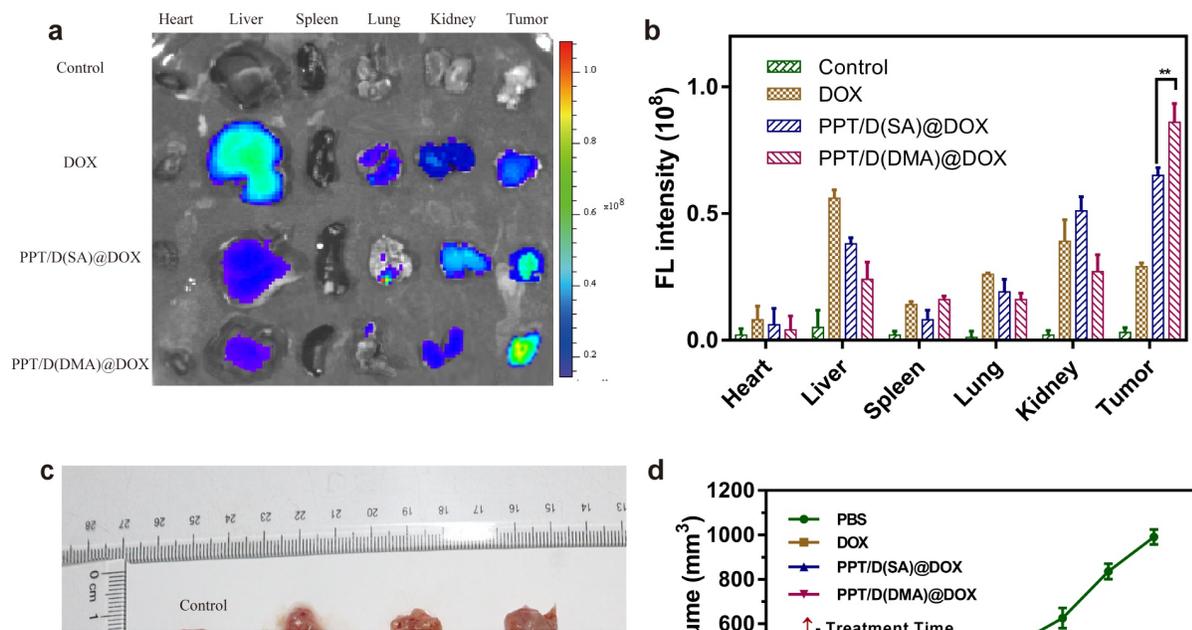


Figure 4

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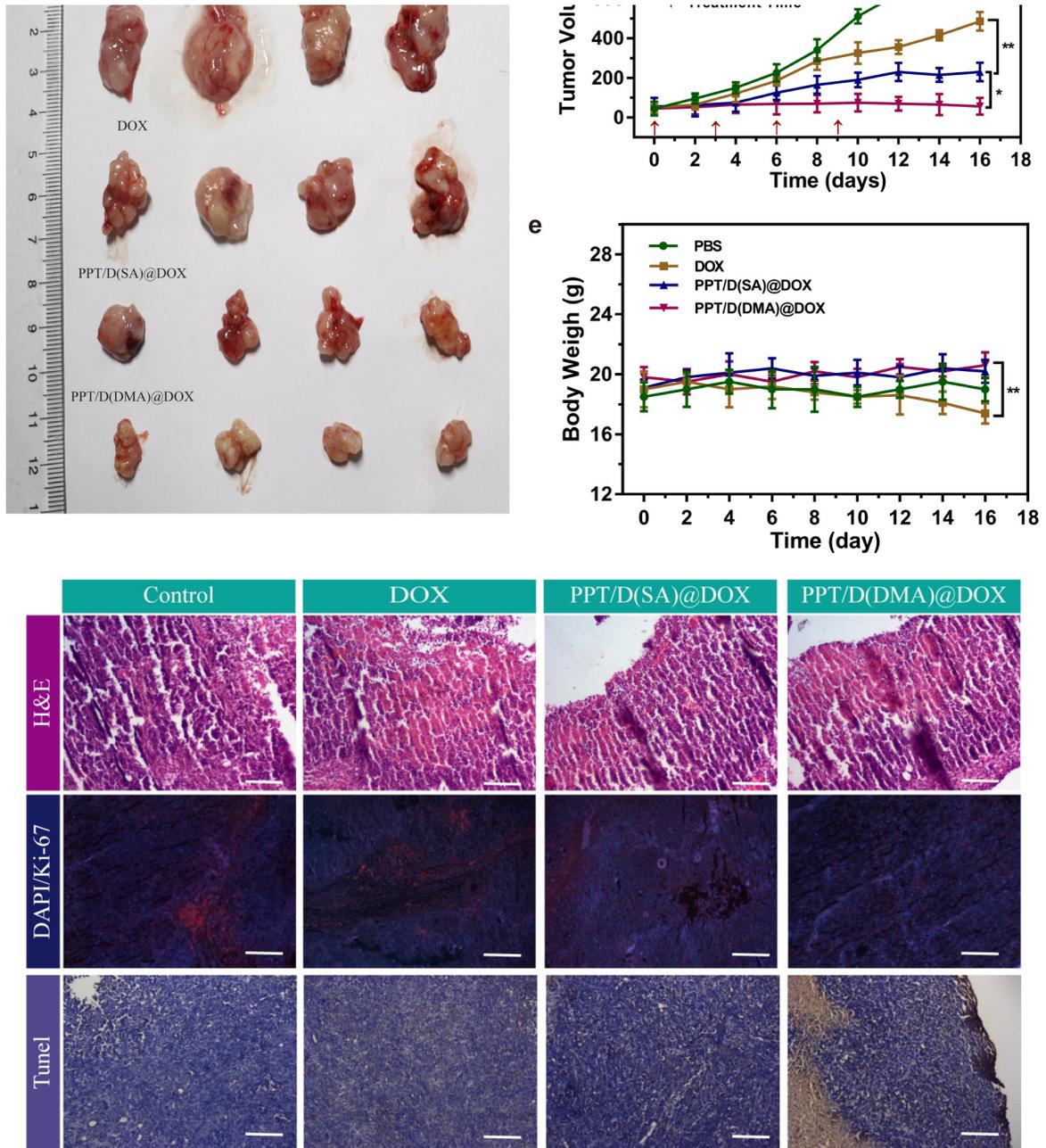


Figure 5

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