Red light-triggered anti-angiogenic and photodynamic combination therapy of age-related macular degeneration

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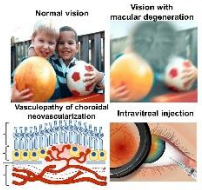
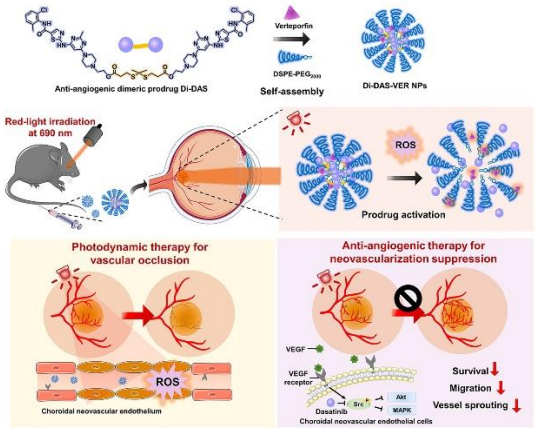
BACKGROUND

Exudative age-related macular degeneration (wAMD) is a leading cause of irreversible vision loss in the elderly, which is characterized by choroidal neovascularization (CNV).

The limitations of the current standard therapy with anti-vascular endothelial growth factor (VEGF) agents included the safety concerns of invasive intravitreal administration and insufficient efficacy for neovascular occlusion.



ABSTRACT SUMMARY



In this study, we report a novel and minimally invasive approach to achieve anti-angiogenic and photodynamic combination therapy of wAMD by intravenous administration of photoactivatable nanoparticles (Di-DAS-VER NPs).

NANOPARTICLE CHARACTERIZATION

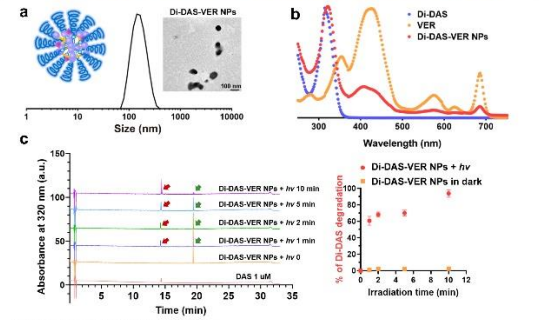


Fig.1 Characterization of Di-DAS-VER NPs.
(a). Hydrodynamic size distribution and transmission electron microscope image of Di-DAS-VER NPs.
(b). UV-Vis absorption spectra of free Di-DAS, verteporfin (VER) and Di-DAS-VER NPs.
(c). Representative HPLC chromatograms of Di-DAS-VER NPs upon 690 nm laser irradiation (100 mW/cm^2) and quantitative analysis of Di-DAS degradation rates.

IN VITRO THERAPEUTIC EVALUATION

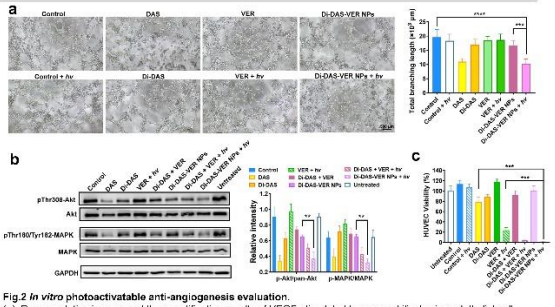


Fig.2 *In vitro* photoactivatable anti-angiogenesis evaluation.
(a). Representative images and the quantification results of VEGF-stimulated human umbilical vein endothelial cell (HUVEC) tube formation assay of Di-DAS-VER NPs at 4 h post-treatment.
(b). Representative images and the quantification results of Western blot analysis of pro-angiogenic signaling proteins.
(c). Quantitative HUVEC cell viability of Di-DAS-VER NPs by MTT assay.

IN VIVO CNV SUPPRESSION

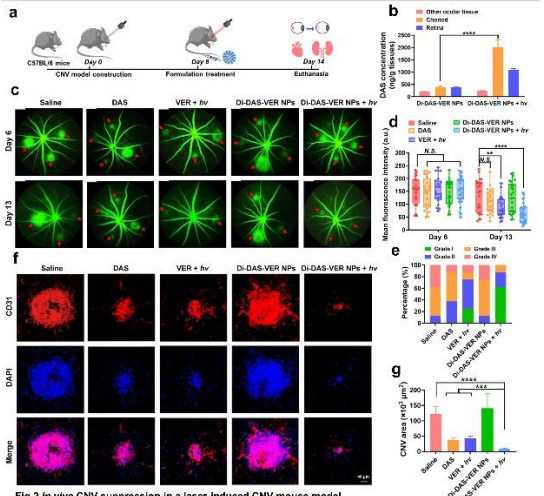


Fig.2 *In vivo* CNV suppression in a laser-induced CNV mouse model.
(a). Schematic illustration of the treatment process with Di-DAS-VER NPs in CNV mice.
(b). LC-MS/MS quantitative analysis of ocular DAS concentration of CNV mice at 2 h post-intravenous injection of Di-DAS-VER NPs with or without 690 nm light irradiation.
(c-d). Representative fundus fluorescein angiography images and the quantification results of CNV regions on days 6 and 13.
(e). Clinical grading of the fluorescein leakage degree on day 13.
(f-g). Representative confocal images of anti-CD31 immunofluorescence-stained vessels of RPE-choroid flat-mounts and the corresponding quantification results of the CNV areas.

CONCLUSION

- ✓ Red light-triggered intraocular drug release strategy was applied to achieve anti-angiogenic and PDT combination treatment of wAMD via intravenous administration.
- ✓ We have confirmed photoactivatable anti-angiogenic ability and efficient intraocular DAS release from Di-DAS-VER NPs upon light irradiation.
- ✓ Di-DAS-VER NPs strengthened CNV suppression effect compared with anti-angiogenic or PDT monotherapy *in vivo*.

ACKNOWLEDGMENTS: This work was supported by the National Natural Science Foundation of China Excellent Young Scientists Fund (82222903) and the National Natural Science Foundation of China (82271099).

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