Triggered Release of Vinorelbine from Thermosensitive Liposomes

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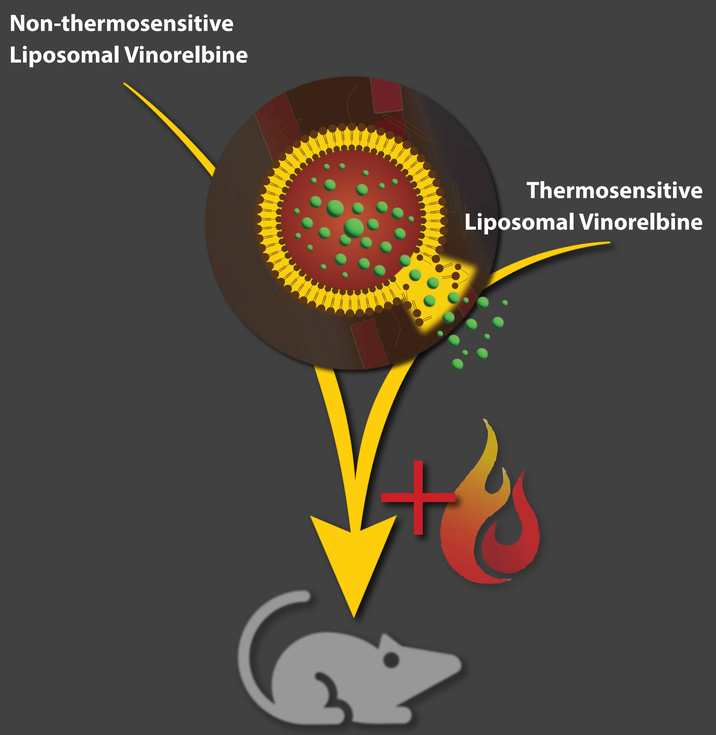
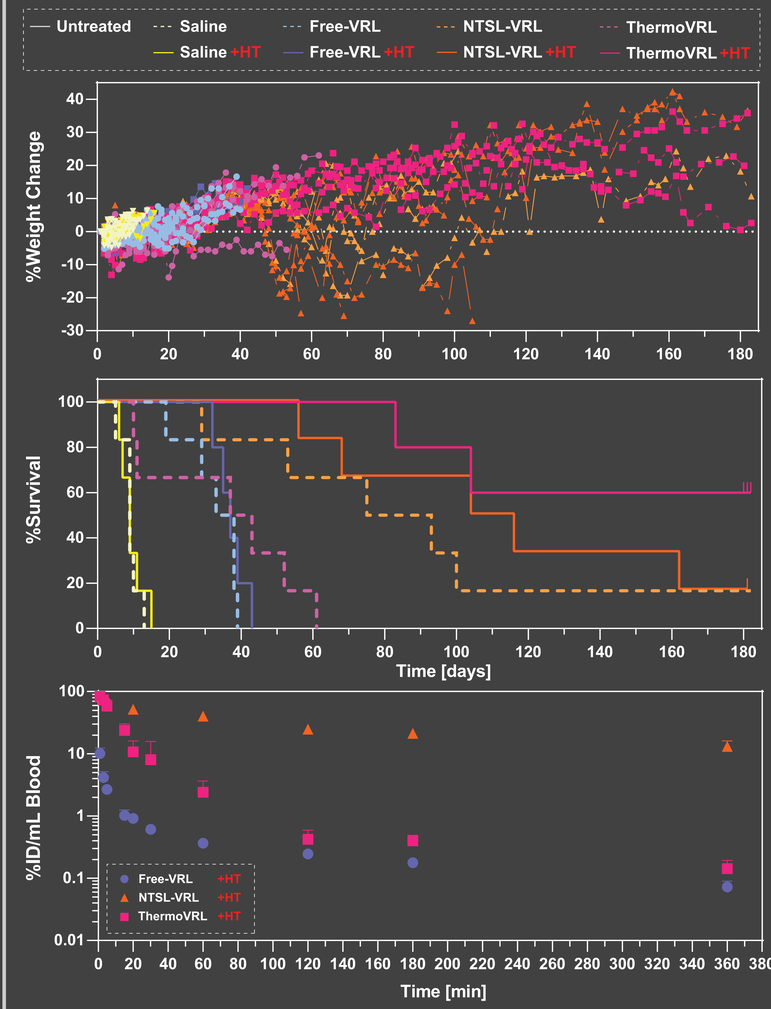
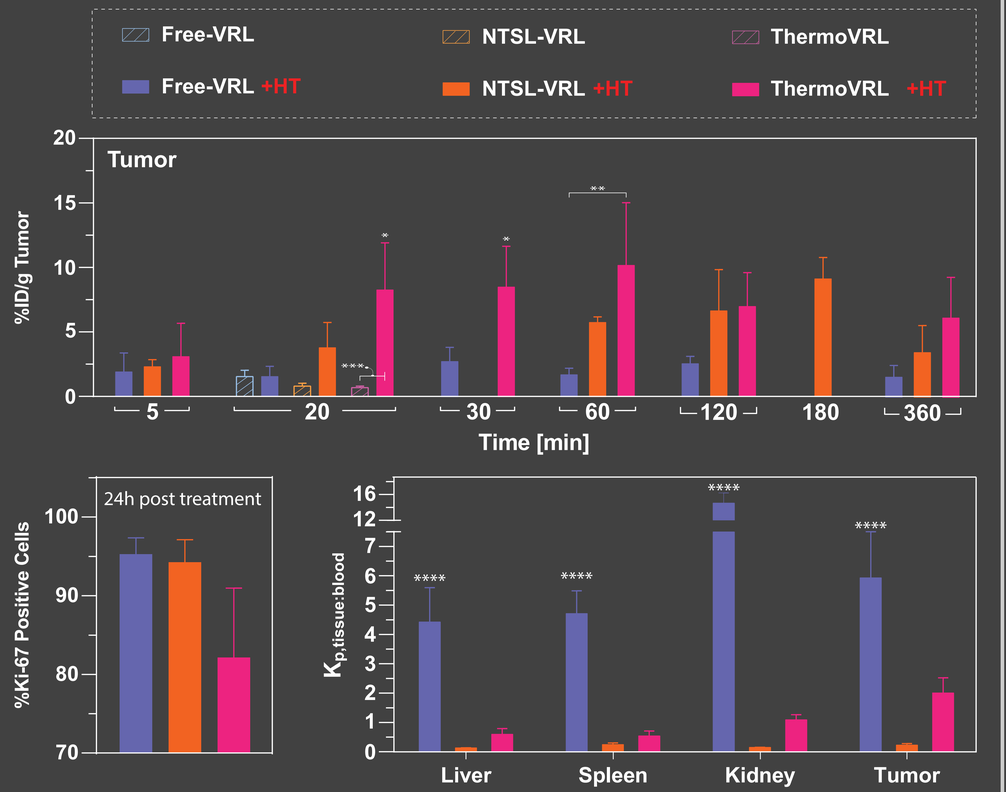
PURPOSE

Nanomedicines can enable tumor-specific drug delivery. This targeted treatment approach has enormous potential to mitigate many of the side effects associated with long-term systemic exposure to chemotherapeutics. This is particularity important in childhood cancer patients who often develop treatment related adverse effects later in life. However, several challenges have prohibited the widespread success of these treatment strategies, including limited drug release as well as heterogeneous drug distribution at the target site. Heat-triggered drug delivery via thermosensitive liposomes has been proposed as an approach to address these challenges. Our lab has previously developed a thermosensitive liposome formulation of the commonly used vinca-alkaloid vinorelbine (ThermoVRL) [1]. Here we demonstrate the in vivo efficacy of this triggered drug delivery approach in a murine model of rhabdomyosarcoma.





RESULTS



Treatment with ThermoVRL or non-thermosensitive liposomal VRL (NTSL-VRL) in combination with localized mild hyperthermia (HT) increased median survival times nearly five- and three-fold respectively, compared to treatment with free VRL. Drug distribution studies revealed that liposomal encapsulation significantly increased the amount of VRL delivered to the tumor. Specifically, when administered as ThermoVRL, VRL partitioning into tumor tissue was increased nearly two-fold compared to other organs. When administered as free VRL or NTSL-VRL no such improvements in tumor specific delivery were noted.

CONCLUSIONS

Triggered-drug release of VRL from ThermoVRL offers a targeted delivery approach that increases the amount of bioavailable drug delivered specifically to the tumor compared to the administration of free drug or drug in non-thermosensitive (i.e., traditional) liposomes. Thus, this study highlights this externally triggered drug delivery strategy as an approach to repurpose conventional chemotherapy drugs and achieve improved targetability.

ACKNOWLEDGEMENTS

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[1] M. Regenold et al., J. Controlled Release. (2020). https://doi.org/10.1016/j.jconrel.2020.08.059.