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# Supporting Information

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Ligustrazine Nanoparticle Hitchhiking on Neutrophils for Enhanced Therapy of Cerebral Ischemia-Reperfusion Injury

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Supporting Information

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## Supplementary figures

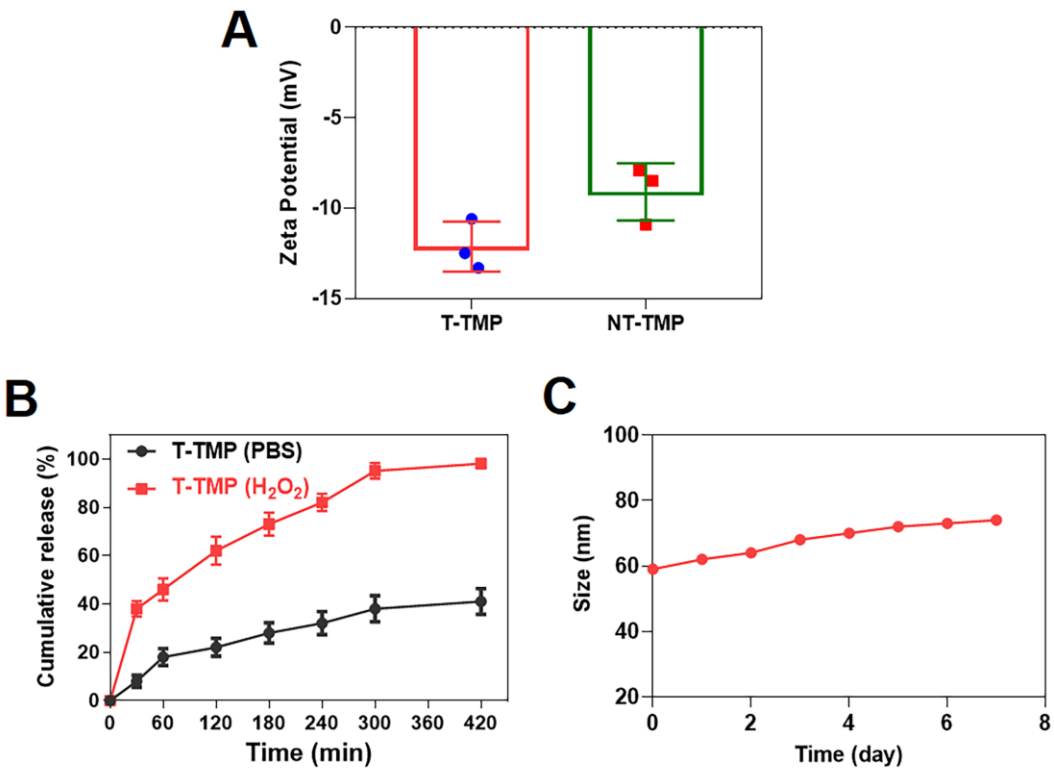

**Figure S1.** T-TMP Materials Characterization. (A) The zeta potential of NT-TMP and T-TMP nanoparticles. (B) Cumulative release of TMP from NPs in PBS (7.4 pH) and $H_2O_2$ (1 mM). (C) Stability of T-TMP nanoparticles (NPs) after a week storage in aqueous solution under 4 ℃.

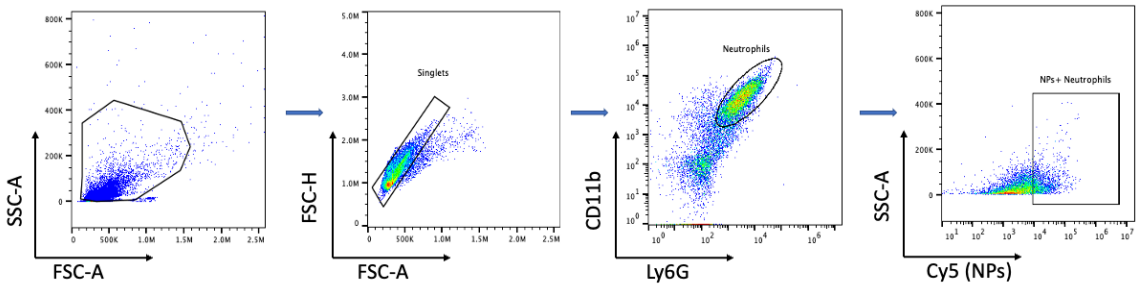


**Figure S2**. Flowcytometry results of the nanoparticles targeting neutrophils.

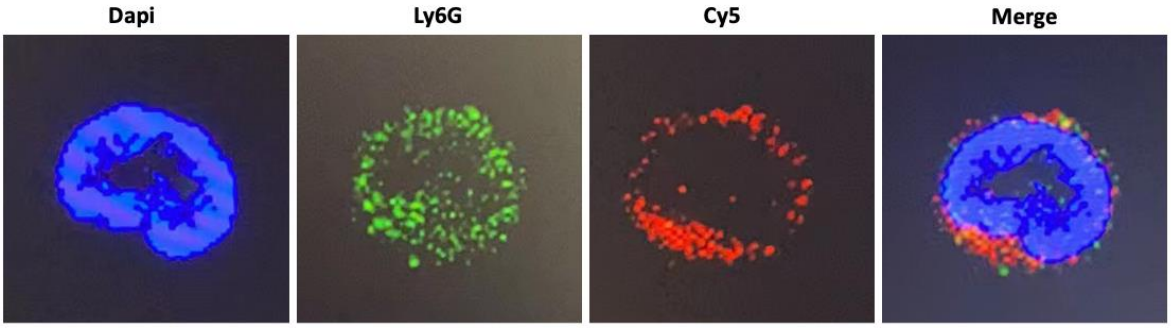


**Figure S3.** Representative confocal images showing the surface binding of nanoparticles (Cy5) on the surface of neutrophils (Ly6G).

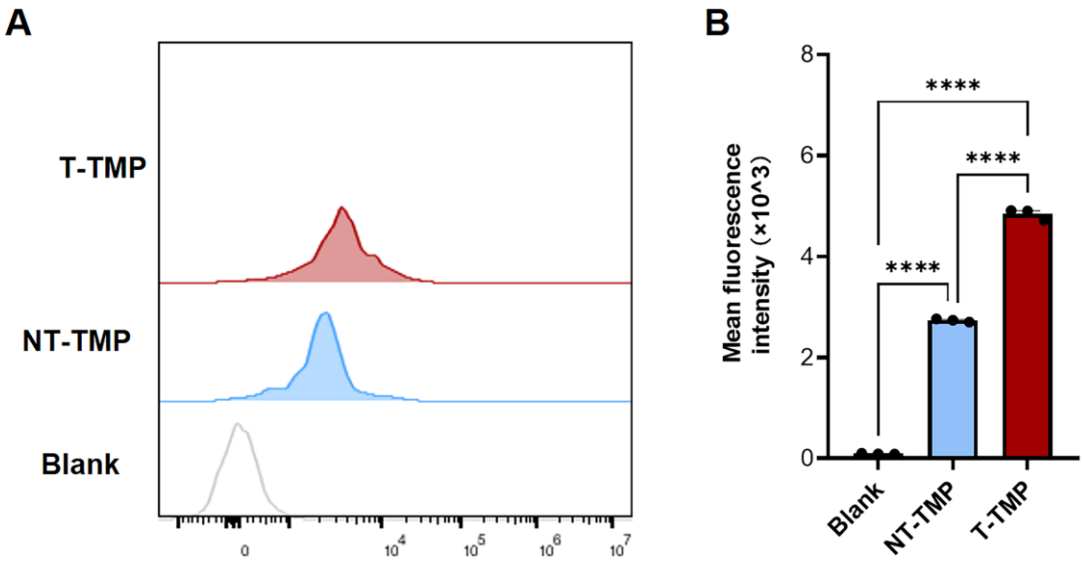


**Figure S4**. Activated neutrophils uptake Cy5-labeled NT-TMP and T-TMP NPs. (A) The neutrophils uptake Cy5-labeled NPs were performed by flow cytometry analysis.

(B) The quantitative analysis of flow cytometry. ****P <0.0001 (n = 3/group).

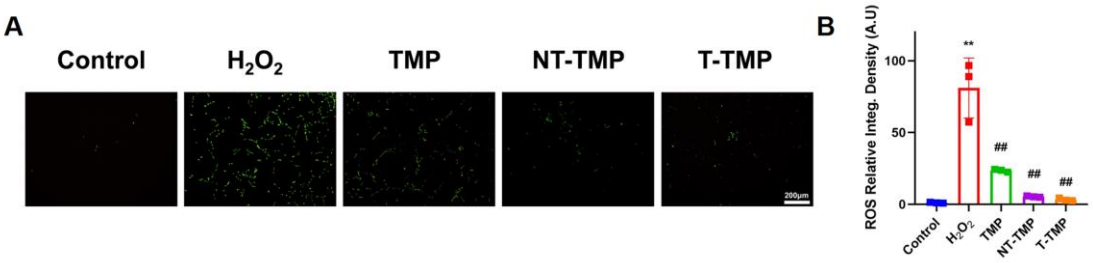


**Figure S5.** The expression of ROS in C6 cells of different groups was detected by DCFH-DA experiment. (A) Immunofluorescence results showed that T-TMP significantly reduced ROS production in C6 cells induced by hydrogen peroxide. (B) Quantitative analysis of the inhibition of ROS expression in C6 cells by different drugs. **P < 0.01 versus Sham; ##P < 0.01 versus $H_2O_2$.

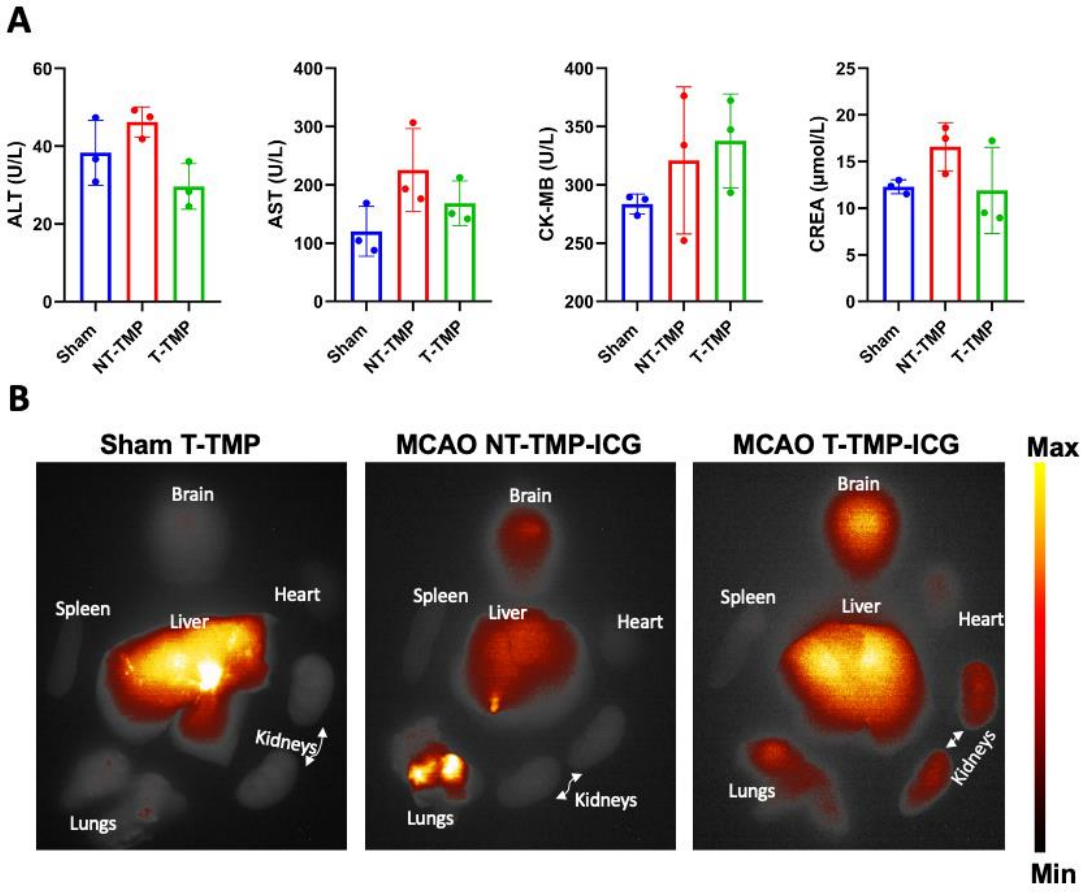


**Figure S6**. Measurement of **A)** blood toxicity and **B)** biodistribution of nanoparticles *in vivo*.

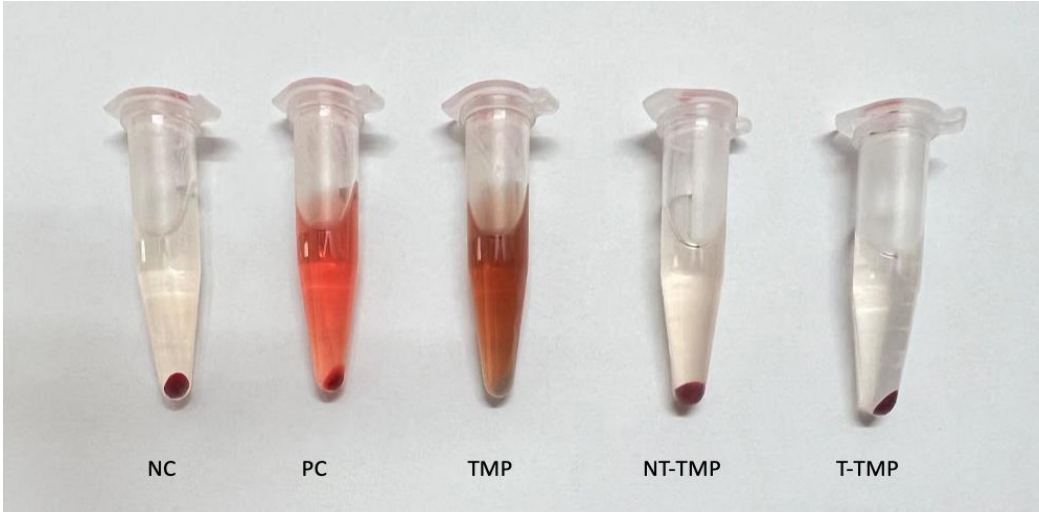


**Figure S7**. Blood sample was treated with TMP, NT-TMP and T-TMP for 3 hours at room temperature. PBS was used as negative control (NC), and ddH2O was used as positive control (PC).

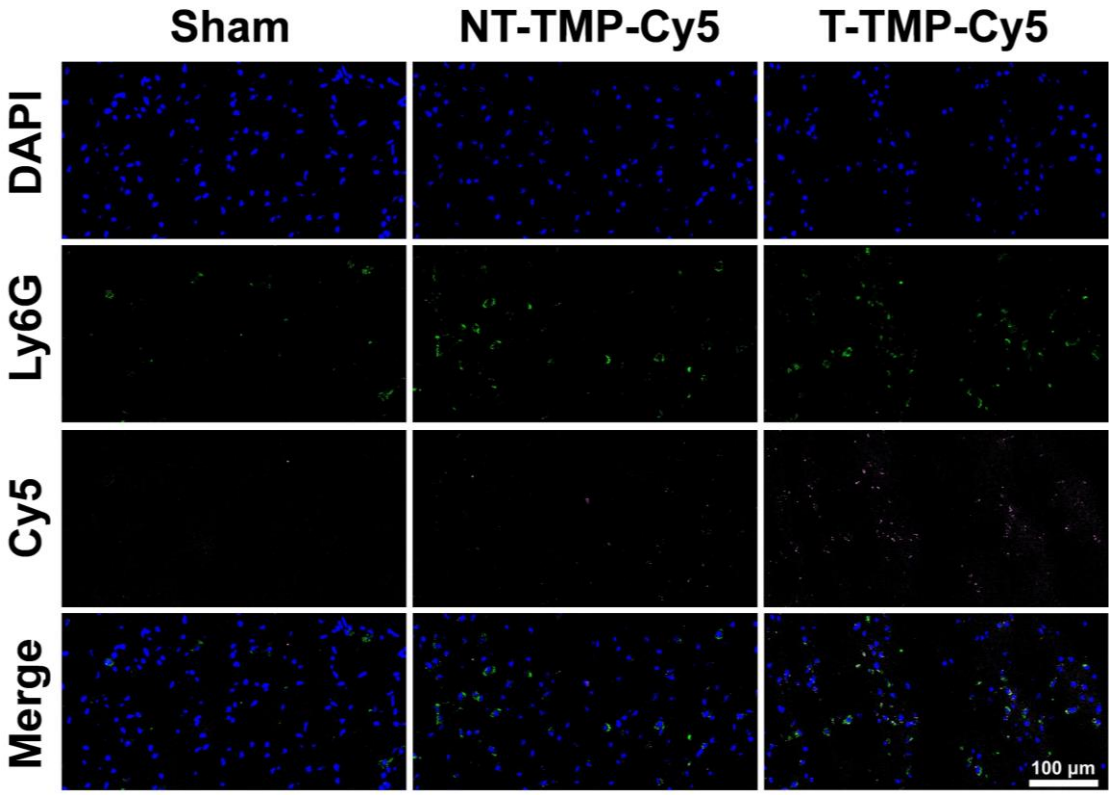


**Figure S8.** Immunofluorescent staining of brain sections in Sham, NT-TMP-Cy5 and T-TMP-Cy5.

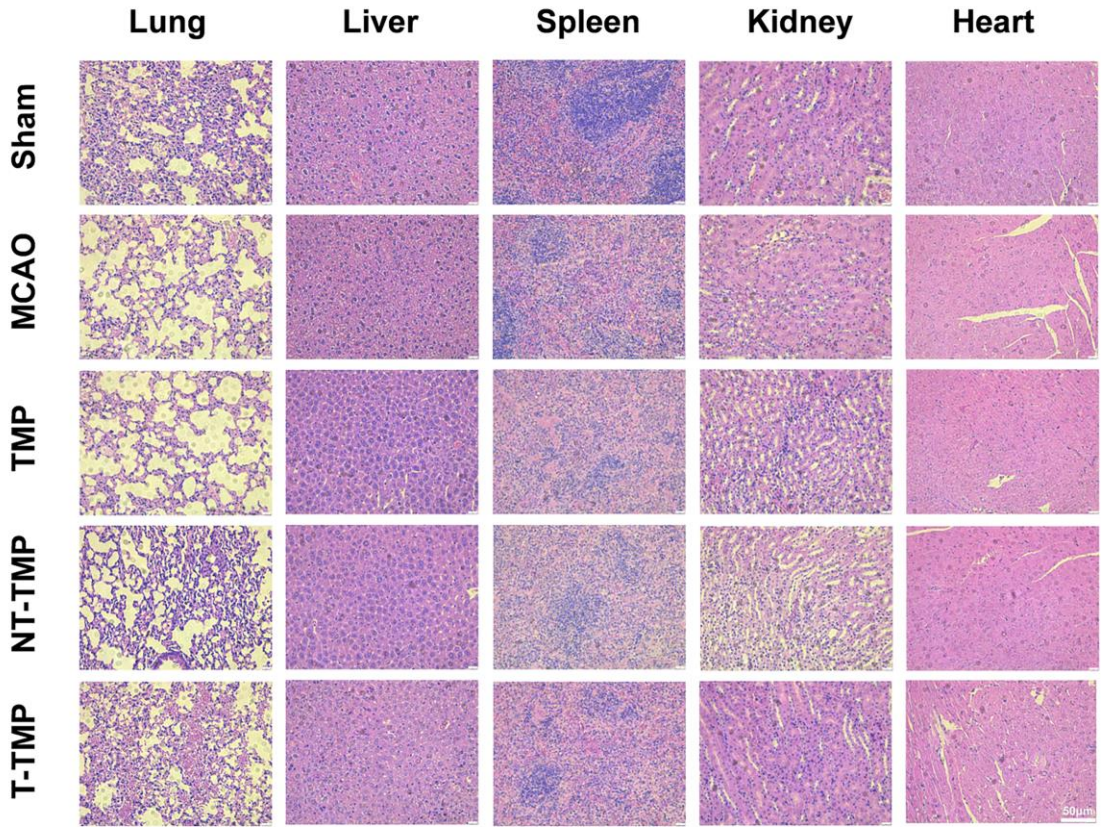


**Figure S9.** HE Staining of lung, liver, spleen, kidney, and heart showed no histology differences in Sham, MCAO, TMP, NT-TMP, and T-TMP groups.

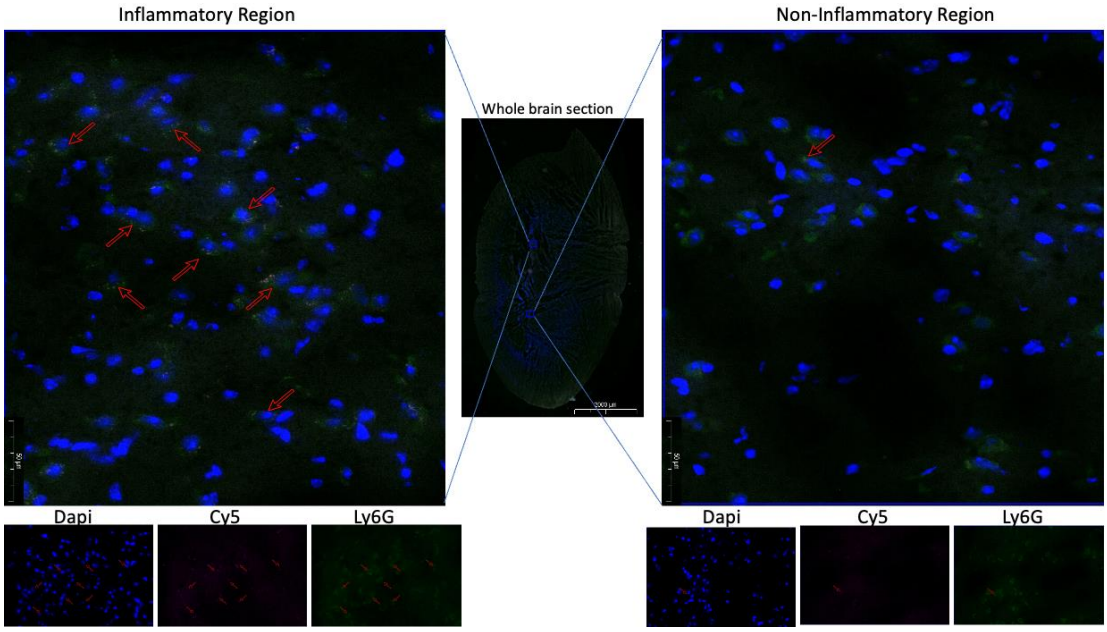

**Figure S10.** Representative image of whole brain sections from MCAO mice treated with T-TMP-Cy5 mouse. The zoomed windows in the image represent the inflammatory region and the normal region. Ly6G is stained with green fluorescence, while the pink fluorescence (dotted) of Cy5 represents the nanoparticles. Arrows are pointed at neutrophils with nanoparticle binding.