

## Supplementary Information for

### **A High-throughput Liver-Kidney Metabolic Interaction Chip for Insights into the Nephrotoxicity Mechanisms of Triptolide**

Siyu Liu<sup>#</sup>, Yun Yang<sup>#</sup>, Yifei Yang, Guangfei Wei, Liu Zhou, Jiawei Lin, Zheng Yuan, Yingfei Li, Zhe Wu, Ting Liu<sup>\*\*</sup>, Guozhuang Zhang<sup>\*</sup>

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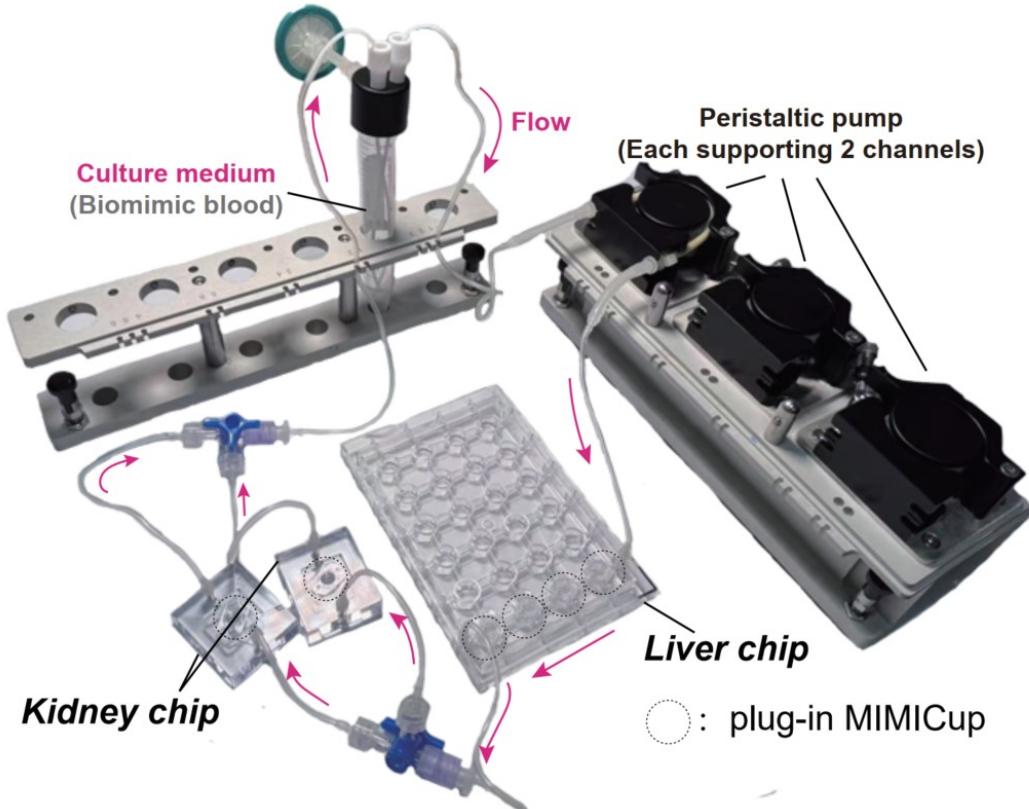
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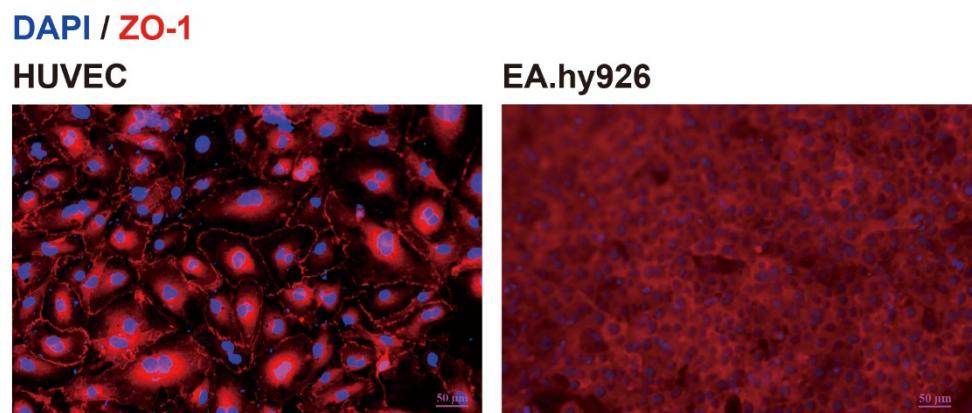
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**Figure S1** Photograph of the assembled HLKOC device. To facilitate clearer visualization of the structure, the system shown in the image was connected with only one channel. Each channel comprises four liver MIMICups connected in series and two kidney MIMICups connected in parallel.

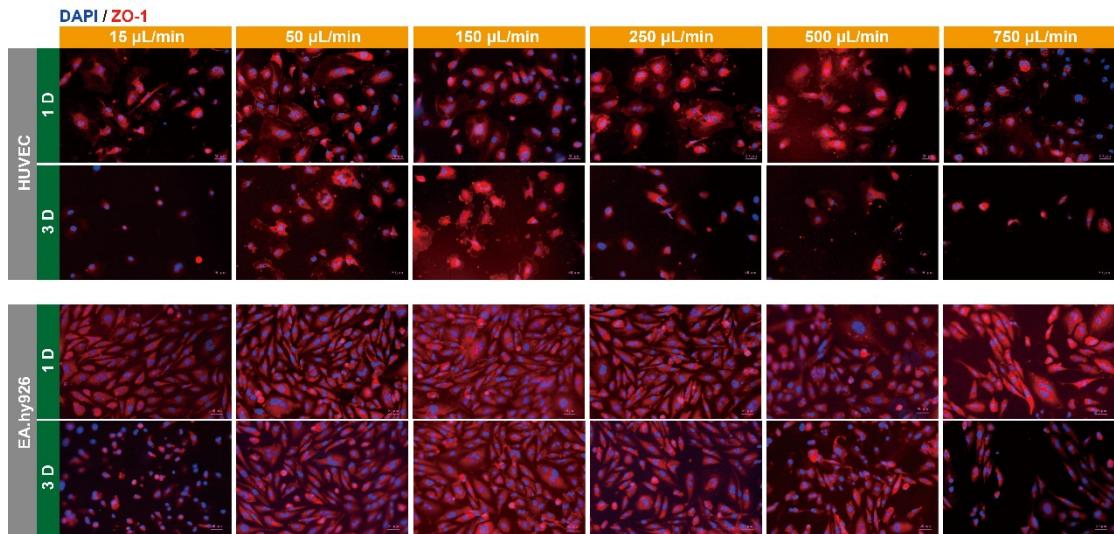
## HLKOC



**Figure S2** Immunofluorescence images show the expression of ZO-1 protein in HUVEC and EA.hy926 cells cultured in well plates (without perfusion). Blue: DAPI; Red: ZO-1.

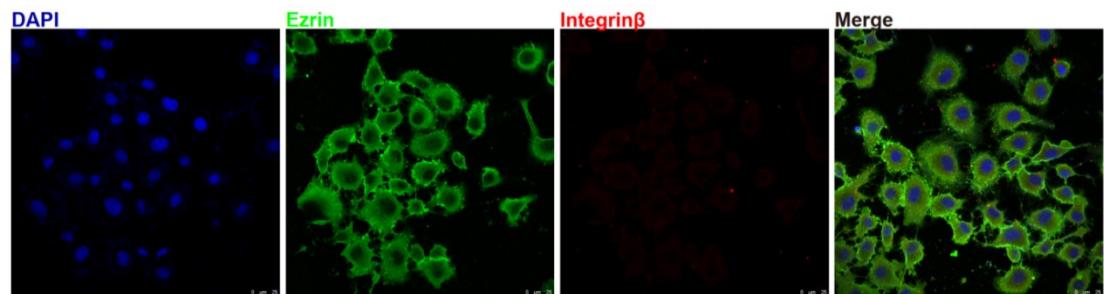


**Figure S3** Immunofluorescence images show the expression of ZO-1 protein in HUVEC and EA.hy926 cells adhering to the bottom of the PET membrane, under

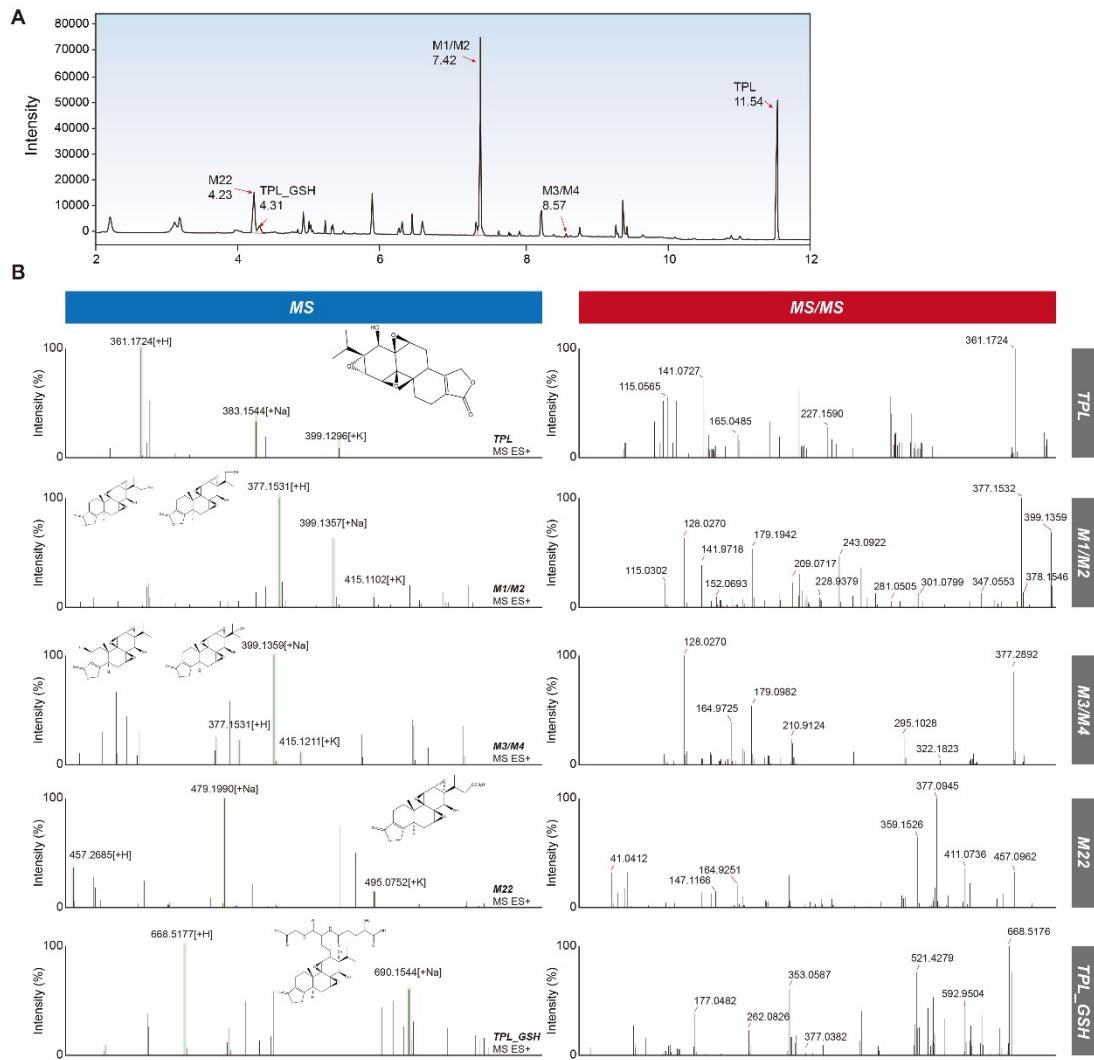


different flow rates and culture times. Blue: DAPI; Red: ZO-1.

**Figure S4** HK-2 cell monolayer culture fails to establish polarity. Blue: DAPI; Green: Ezrin; Red: Integrin $\beta$ .

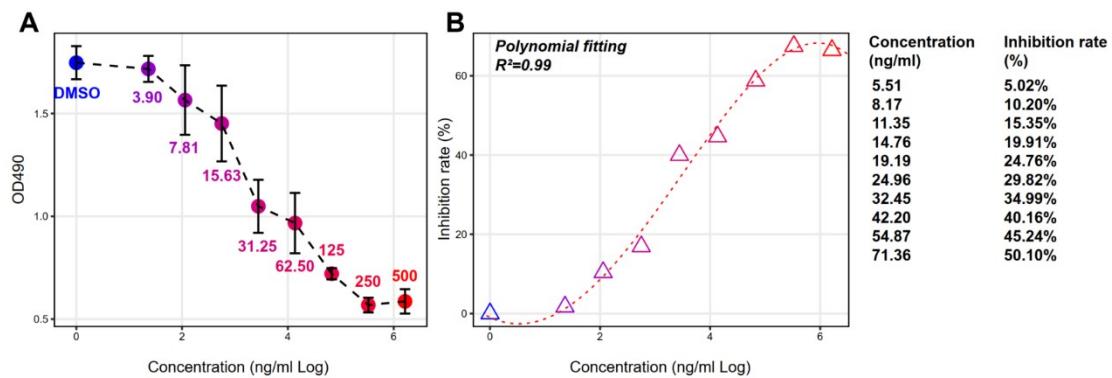


**Figure S5** Total ion chromatogram (TIC) from LC-MS/MS analysis (A) of the HLKOC biomimetic blood treated with TPL, and (B) the low-energy and high-energy mass spectra of the target metabolites.

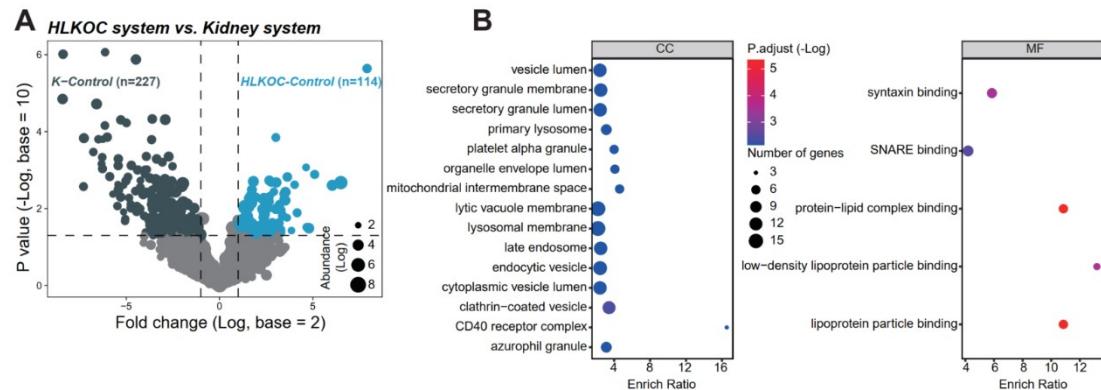


spectra of the target metabolites.

**Figure S6** Determination of the triptolide dosage based on the MTT assay. **A.** The OD<sub>490</sub>-triptolide concentration relationships. **B.** The inhibition rate-triptolide concentration relationships. The curve represents polynomial fitting.



**Figure S7** Differential expression genes between HLKOC and single-kidney OoC control groups and the enrichment analysis. **A.** The volcano plot illustrates the differential expression genes (DEGs) between HLKOC and single-kidney OoC (without triptolide treatment). **B.** GO enrichment analysis of DEGs.



**Figure S8** Interaction networks of proteins in docking analysis and RNA-Seq. Only highly confident links (score > 0.7) were retained.

