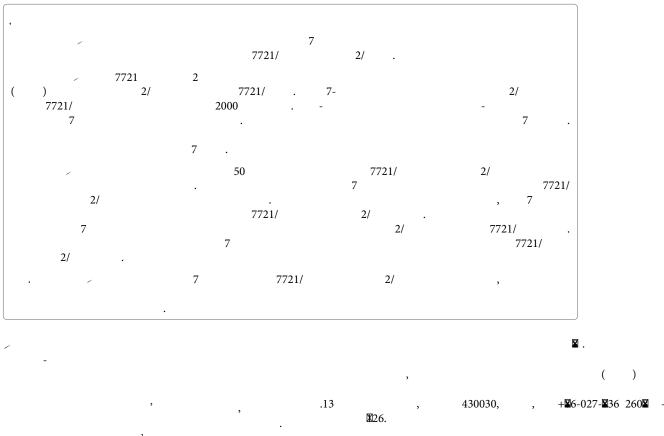


Silencing MRP7 Gene by siRNA Reversed Multidrug Resistance in HepatocellularCarcinomaResistantCellLineHepG2/ADMandSMMC7721/ADM

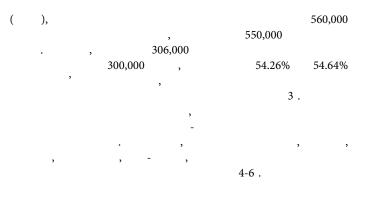
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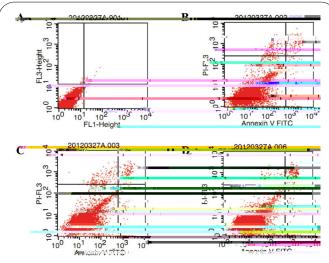


Figure 3: Results of HepG2ADM cell apoptosis. The apoptosis of HepG2ADM cells was analyzed by fow cytometry. (A) HepG2ADM-Control, (B) HepG2 ADM, (C) HepG2 ADM NCsiRNA and (D) HepG2 ADM MRP7 siRNA.

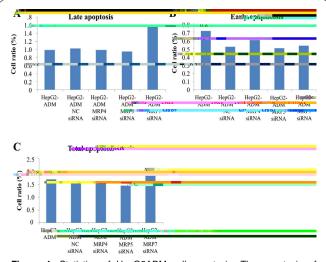


Figure 4: Statistics of HepG2ADM cell apoptosis. The apoptosis of HepG2ADM cells was analyzed by fow cytometry. **(A)** After silencing MRP7 gene, the proportion of late apoptotic cells was signifcantly increased, **(B)** After silencing MRP7 gene, the proportion of early apoptotic cells decreased slightly and **(C)** After silencing MRP7 gene, the total apoptosis of cells increased signifcantly.

Table 2: Data analysis of cell apoptosis.

Sample (%)	UL	UR	LL	LR	UR+LR
HepG2-ADM	1.14	0.98	97.17	0.71	1.69
HepG2-ADM NC siRNA	1.44	1.02	97.02	0.52	1.54
HepG2-ADM MRP7siRNA	0.53	1.60	97.34	0.53	2.13

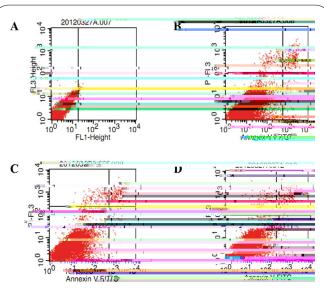


Figure 5: Results of SMMC7721/ADM cell apoptosis. The apoptosis of SMMC7721/ADM cells was analyzed by fow cytometry. (A) SMMC7721/ ADM-Control, (B) SMMC7721/ADM, (C) SMMC7721/ ADM NC siRNA and (D) SMMC7721/ADM MRP7 siRNA.

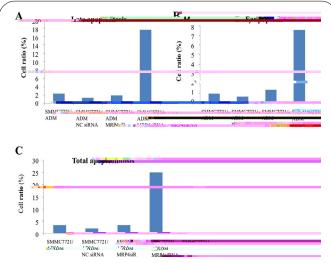


Figure 6: Statistics of SMMC7721/ADM cell late apoptosis. The apoptosis of SMMC7721/ADM cells was analyzed by fow cytometry. (A) After silencing MRP7 gene, the proportion of late apoptotic cells was signif cantly increased, (B) After silencing MRP7 gene, the proportion of early apoptotic cells decreased slightly and (C) After silencing MRP7 gene, the total apoptosis of cells increased signif cantly.

Table 3: Data analysis of cell apoptosis.

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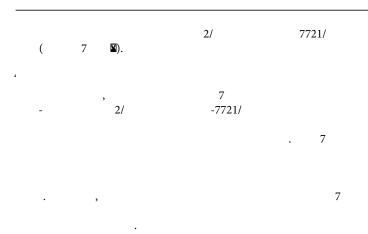
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Ethics Approval and Consent to Participate

The ethic approval was obtained from the Ethic Committee of Tongji Medical College, Huazhong University of Science and Technology.

Consent to Publish

All of the authors have consented to publish this research.

Availability of Data and Materials

The data are free access to available upon request.

Competing Interests

All authors declare no confict of interest.

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Authors' Contributions

Each author has made an important scientifc contribution to the study and has assisted with the drafting or revising of the manuscript.

References

- Bruix, J., Han, K. H., Gores, G., Llovet, J. M., & Mazzaferro, V. Liver cancer: Approaching a personalized care. J Hepatol., 2015;62(1 Suppl): S144-S156.
- Kudo, M. Chronic liver diseases and liver cancer: An update in 2015.
- Dig Dis., 2015;33(6): 705-707.
 Wei, K. R., Yu, X., Zheng, R. S., Peng, X. B., Zhang, S. W., Ji, M. F., et al. Incidence and mortality of liver cancer in China, 2010. Chin J Cancer., 2014;33(8): 388-394.
- Fan, J. H., Wang, J. B., Jiang, Y., Xiang, W., Liang, H., Wei, W. Q., et al. Attributable causes of liver cancer mortality and incidence in China. Asian Pac J Cancer Prev., 2013;14(12): 7251-7256.
- Marengo, A., Rosso, C., & Bugianesi, E. Liver cancer: connections with obesity, fatty liver, and cirrhosis.
- Annu Rev Med., 2016;**67**: 103-117. 6. Yang, Y., Gao, J., Li, H. L., Zheng, W., Yang, G., Zhang, W., et al.
- Dose-response association between hepatitis B surface antigen levels and

liver cancer risk in Chinese men and women. Int J Cancer., 2016;**139**(2): 355-362. Guglielmi, A., Ruzzenente, A., Conci, S., Valdegamberi, A., Vitali, M., Bertuzzo, F., et al. Hepatocellular carcinoma: surgical perspectives beyond the barcelona clinic liver cancer recommendations. World J Gastroenterol., 2014;**20**(24): 7525-7533. Sun, T. Y., Yan, W., Yang, C. M., Zhang, L. F., Tang, H. L., Chen, Y., et al. Clinical research on dendritic cell vaccines to prevent postoperative recurrence and metastasis of liver cancer. Genet Mol Res., 2015;**14**(4): 16222-16232. Li, S., & Zheng, L.

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- Efect of combined treatment using wilfortrine and paclitaxel in liver cancer and related mechanism. Med Sci Monit.. 2016:**22**: 1109-1114.
- Fortner, J. G., Mulcare, R. J., Solis, A., Watson, R. C., & Golbey, R. B. Treatment of primary and secondary liver cancer by hepatic artery ligation and infusion chemotherapy. Ann Surg., 1973;178(2): 162-172.
- Wang, C. F., Wang, Y. Q., Huang, F. Z., Nie, W. P., Liu, X. Y., & Jiang, X. Z. Association between reversal of multidrug resistance by methyl jasmonate and P-glycoprotein ATPase activity in hepatocellular carcinoma. J Int Med Res., 2013;41(4): 964-974.
- Slot, A. J., Molinski, S. V., Cole, & S. P. C. Mammalian multidrug resistance proteins (MRPs). Essays Biochem., 2011;50(1): 179-207.
- Korita, P. V., Wakai, T., Shirai, Y., Matsuda, Y., Sakata, J., Takamura, M., et al. Multidrug resistance-associated protein 2 determines the ef cacy of cisplatin in patients with hepatocellular carcinoma. Oncology Rep., 2010;23(4): 965-972.
- Folmer, Y., Schneider, M., Blum, H. E., & Hafkemeyer, P. Reversal of drug resistance of hepatocellular carcinoma cells by adenoviral delivery of anti-ABCC2 antisense constructs. Cancer Gene Ther., 2007;14(11): 875-884.
- Seo, S., Hatano, E., Higashi, T., Nakajima, A., Nakamoto, Y., Tada, M., et al. P-glycoprotein expression afects 18F-fuorodeoxyglucose accumulation in hepatocellular carcinoma *in vivo* and *in vitro*. Int J Oncol., 2009;**34**(5): 1303-1312.
- Zhao, J., Yu, B. Y., Wang, D. Y., & Yang, J. E. Promoter polymorphism of MRP1 associated with reduced survival in hepatocellular carcinoma. World J Gastroenterol., 2010;**16**(48): 6104-6110.
- Ye, L., Zhao, X., Lu, J., Qian, G., Zheng, J. C., & Ge, S. Knockdown of TIGAR by RNA interference induces apoptosis and autophagy in HepG2 hepatocellular carcinoma cells. Biochem Biophys Res Commun., 2013;437(2): 300-306.
- 18. (2): 300-306 .Biochem BiophyEMC 362-365