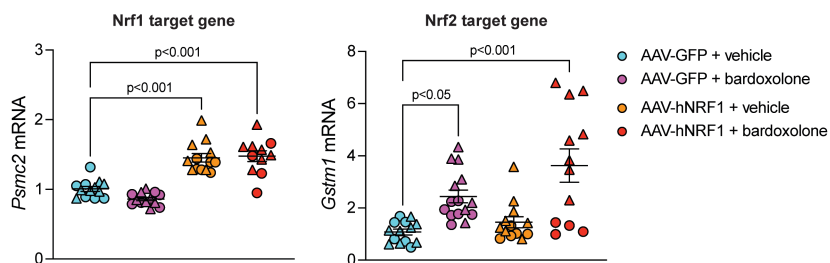


Supplemental Figure 1. Effect of hepatocyte deficiency for Nrf1, Nrf2, or both in mice chronically fed control diet. Mice were fed control diet for 24 weeks. In A-C), mice were infected with indicated virus on week 22. In D), mice were infected on week 16. A) Liver sections stained with hematoxylin and eosin, with scale indicated in panel, and steatosis and inflammation in liver ($n = 7-13$). B) Levels of triglyceride and cholesterol in liver ($n = 6-16$). C) Liver qPCR analysis for indicated gene expression, normalized by ribosomal protein 36b4 ($n = 5-16$). D) Representative liver sections that underwent immunohistochemistry (IHC) with antibody detecting ki67 or p62, with scale indicated in panel, and % of ki67 positive cells and % area of p62 ($n = 5-20$). Data are mean \pm standard error of the mean, with individual data points shown (males = circles; females = triangle). In A-C), the p-value was determined by two-way analysis of variance, with Sidak post-test. In D), the p-value was determined by one-way analysis of variance, with Dunnett post-test.

A. experimental validation that Nrf2-activating drug bardoxolone induces expression of Nrf2 target, *Gstm1*, and hepacyte hNRF1 over-expression induces expression of Nrf1 target, *Psmc2*, in the liver



Supplemental Figure 2. Validating liver induction of Nrf1 via hNRF1 and of Nrf2 induction via bardoxolone. Corresponding with figure 4 in which C57bl/6J mice were fed HFFC diet with 2% cholesterol for 24 weeks. Mice were injected with carbon tetrachloride once per week from week 0-15 to induce liver fibrosis. On week 16-24, mice were treated as indicated with modulators of Nrf1 and Nrf2 activity. Liver analysis was done at the endpoint. (A) Liver qPCR analysis for expression of Nrf1 target gene, *Psmc2*, and Nrf2 target gene, *Gstm1*. Expression was normalized by ribosomal protein 36b4 (n = 11-15). Data are mean \pm standard error of the mean, with individual data points shown (males = circles; females = triangle). The p-value was determined by one-way analysis of variance, with Dunnett post-test.

Supplemental Table 1

gene name	primer direction	primer sequence
<i>36b4</i>	forward	AGGGCGACCTGGAAGTCC
	reverse	CCCACAATGAAGCATTTTGGGA
<i>Ccl2</i>	forward	TTAAAAACCTGGATCGGAACCAA
	reverse	GCATTAGCTTCAGATTTACGGGT
<i>Ccnb1</i>	forward	AAGGTGCCTGTGTGTGAACC
	reverse	GTCAGCCCCATCATCTGCG
<i>Cnd1</i>	forward	GCGTACCCTGACACCAATCTC
	reverse	CTCCTCTTCGCACTTCTGCTC
<i>Colla1</i>	forward	TGCTAACGTGGTTCGTGACCGT
	reverse	ACATCTTGAGGTCGCGGCATGT
<i>Coll3a1</i>	forward	ACGTAAGCACTGGTGGACAG
	reverse	CCGGCTGAAAGAAGTCTGA
<i>Emr1</i> (F4/80)	forward	TGACTCACCTTGTGGTCTTAA
	reverse	CTTCCCAGAATCCAGTCTTTCC
<i>Gstm1</i>	forward	ATACTGGGATACTGGAACGTCC
	reverse	AGTCAGGGTTGTAACAGAGCAT
<i>Ihh</i>	forward	CTCTTGCCTACAAGCAGTTCA
	reverse	CCGTGTTCTCCTCGTCCTT
<i>Il1β</i>	forward	GCAACTGTTCTGAACTCAACT
	reverse	ATCTTTTGGGGTCCGTCAACT
<i>Krt19</i>	forward	AGCGTGATCAGCGGTTTTG
	reverse	CCTGGTTCTGGCGCTCTATG
<i>Psmc2</i>	forward	AGGTGCTGTGTAATCACCGAG
	reverse	GGATGGGCTTGTCTGCCTT
<i>Tnfrsf12a</i>	forward	GTGTTGGGATTCCGGCTTGGT
	reverse	GTCCATGCACTTGTCTGAGGTC