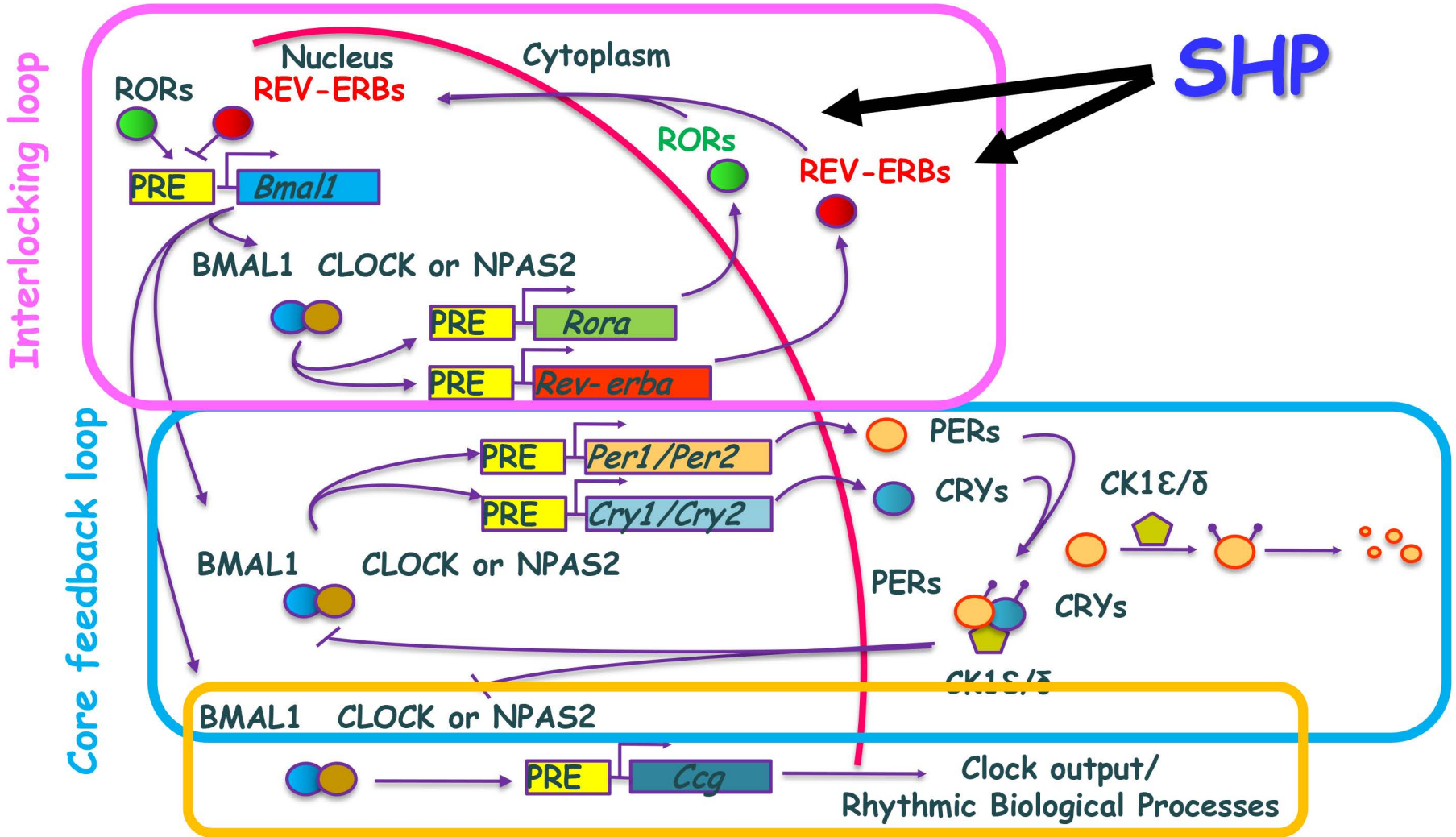
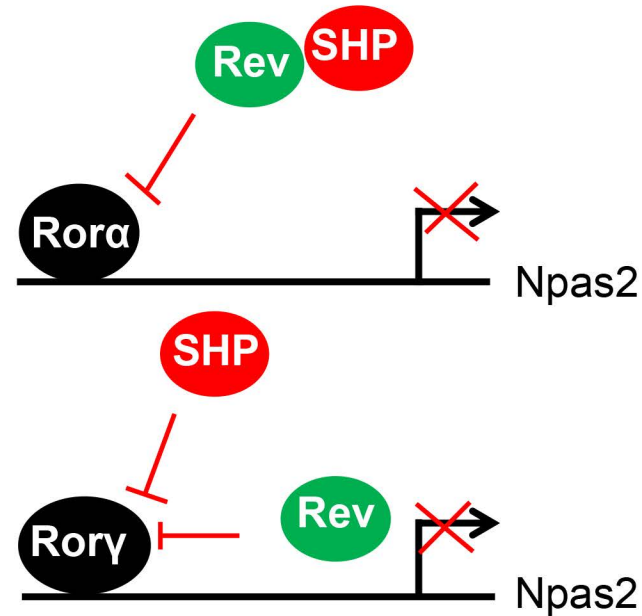


# SHP clock Supp Fig. 1

Fig. S1: Nuclear Receptor in Circadian Clock Network

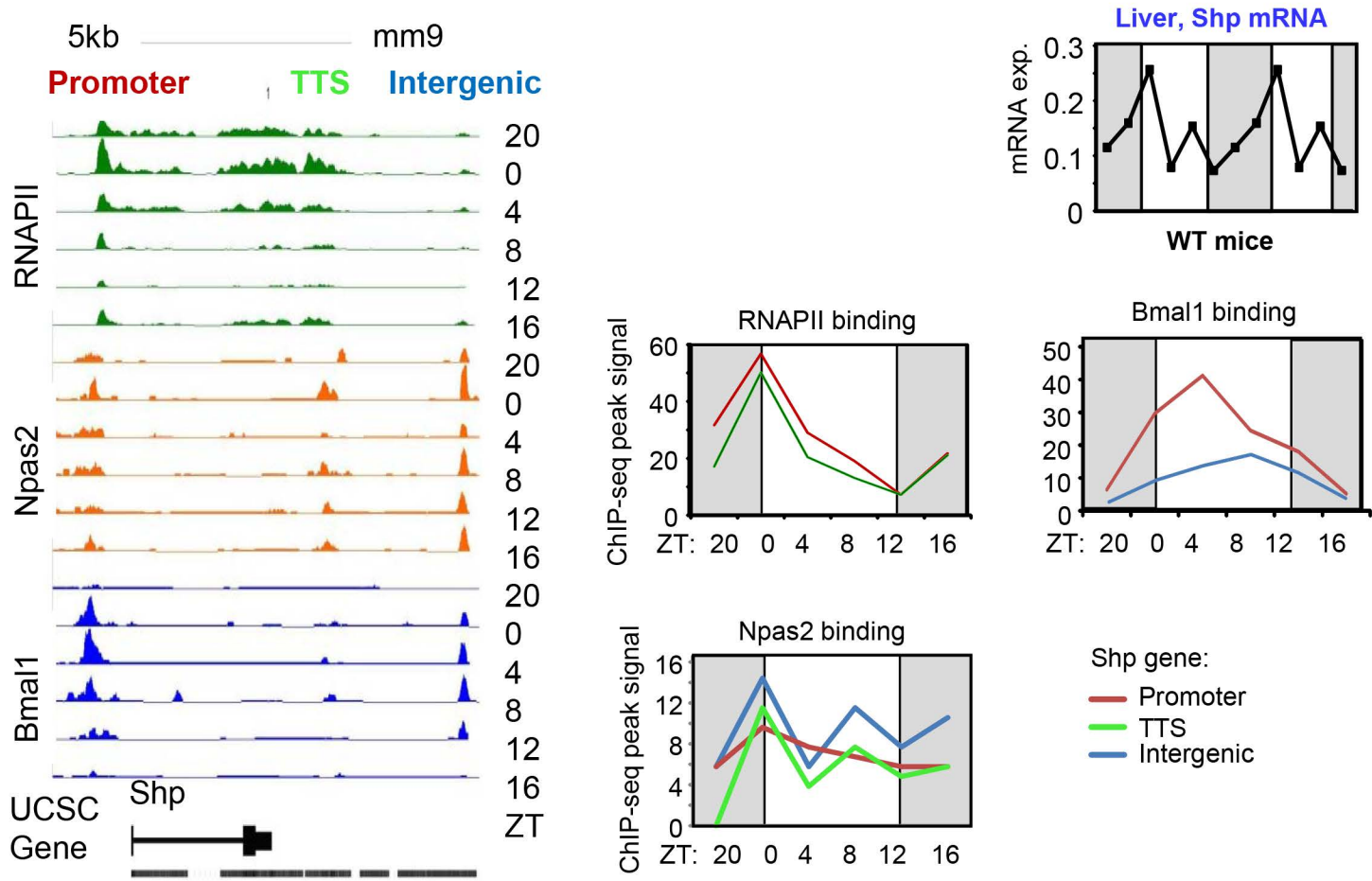


## SHP clock Supp Fig. 2



**Fig. S2: Schematic of SHP inhibition on *Npas2* expression via crosstalk with ROR $\alpha$ ,  $\gamma$ /REV-ERB $\alpha$ . Shp inhibits *Npas2* promoter activity through 1) interacts with Rev-erba to enhance Rev-erba repressive activity of Rora; and 2) interacts with Rory to directly repress Rory activity.**

# SHP clock Supp Fig. 3



**Fig. S3: ChIP-seq signal showing rhythmic binding of RNAPII, Npas2 and Bmal1 to the Shp gene (Koike et al., Science, 338:349-354, 2012). Shp mRNA is shown (top, right)**

### Cloning information for PRSET vector (His vector)

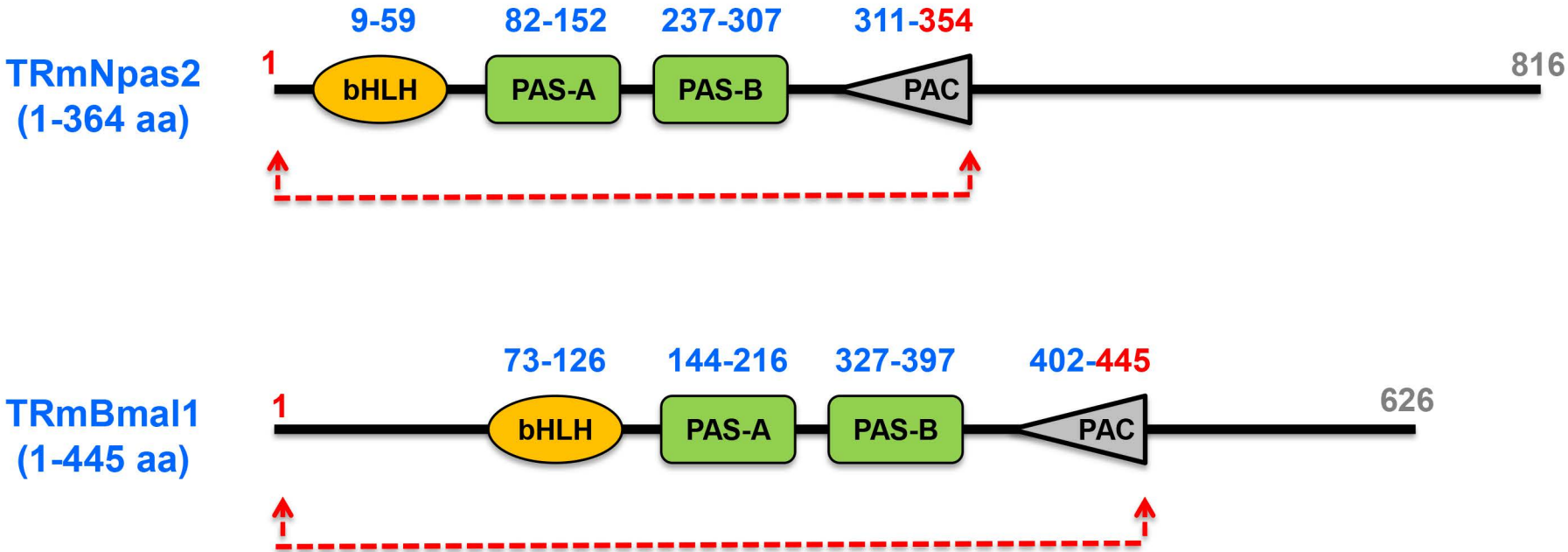
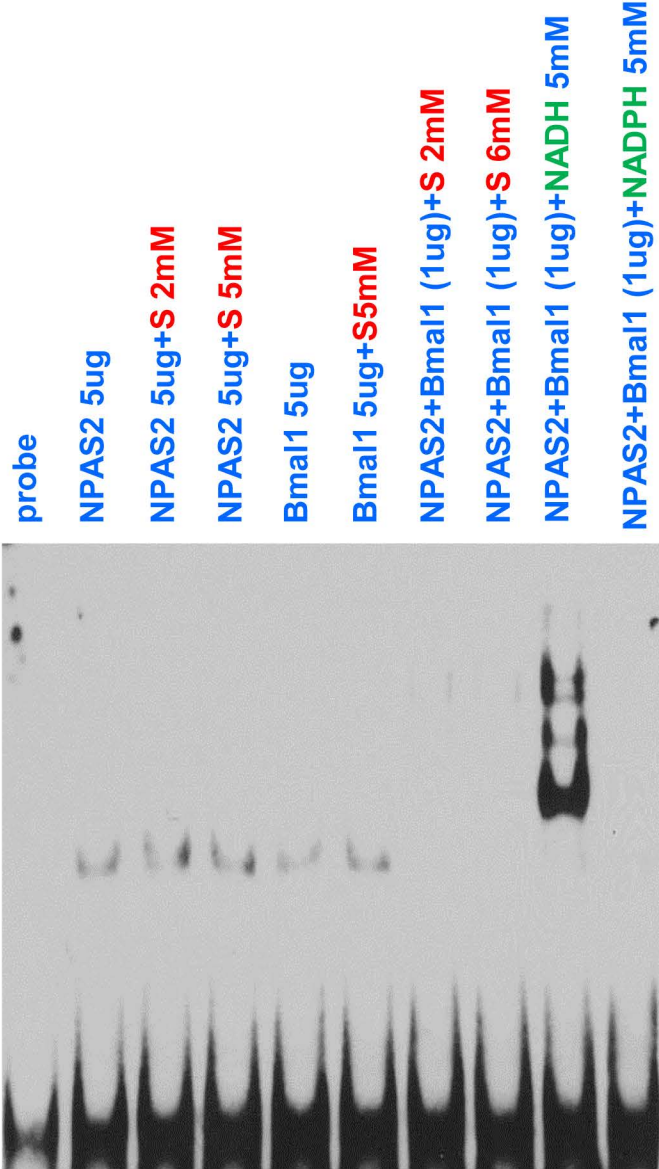


Fig. S4: Diagram showing cloning of His-Npas2 or His-Bmal1 protein for gel-shift assay.

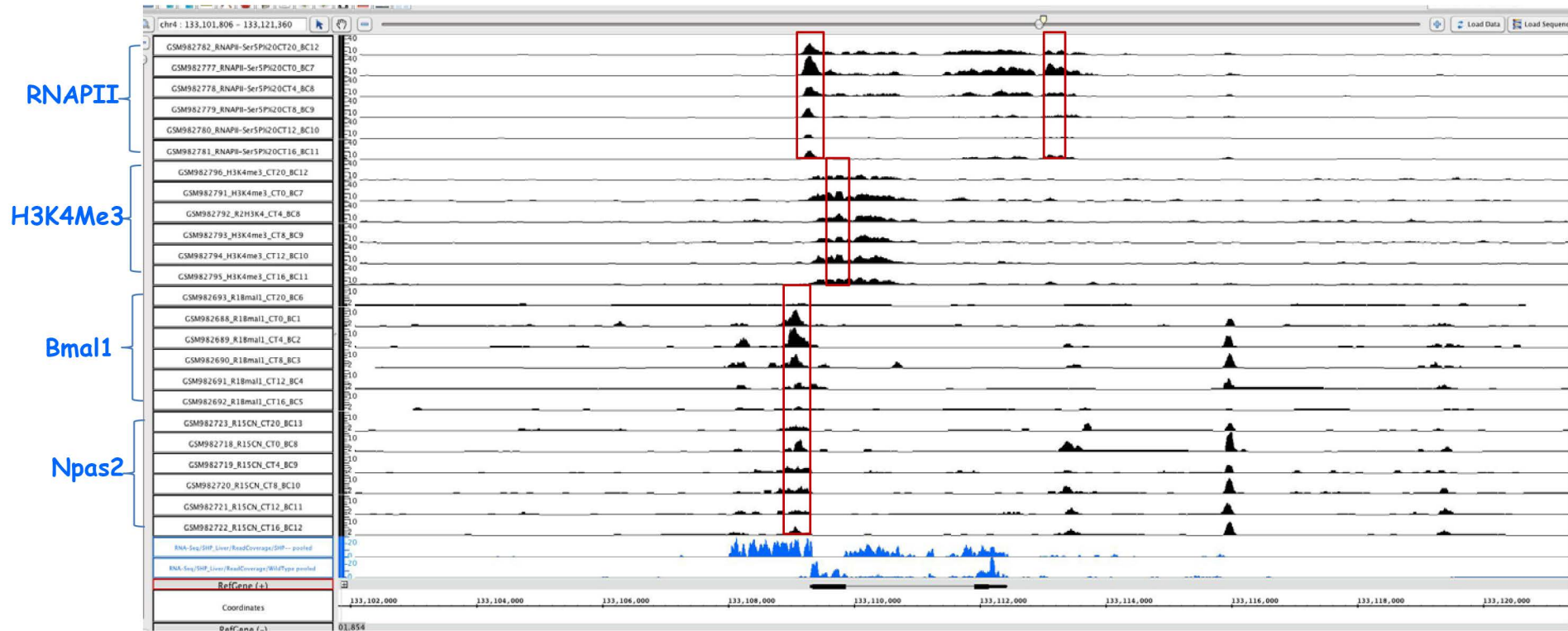
**SHP clock Supp Fig. 5**



**Fig. S5:** Gel-shift assay showing binding of His-Naps2 or His-Bmal1 protein to a Shp promoter probe.

**S: Serine**

ChIP-assay primer location and sequence in the SHP gene



133109056-9244, ChIP1

Npas2-shp chip1-188+: *CCTGCAATGGCCACTTCAT*  
 Npas2-shp chip1-188-: *GGGACTGGCCAAACAACCT*

133109224-9353, ChIP1

RNAPII-shp chip1-129+: *CAAGGTTGTTTGGCCAGTCC*  
 RNAPII-shp chip1-129-: *GGCCGGAGCTCATGGTTAGT*

133113034-3184, ChIP2

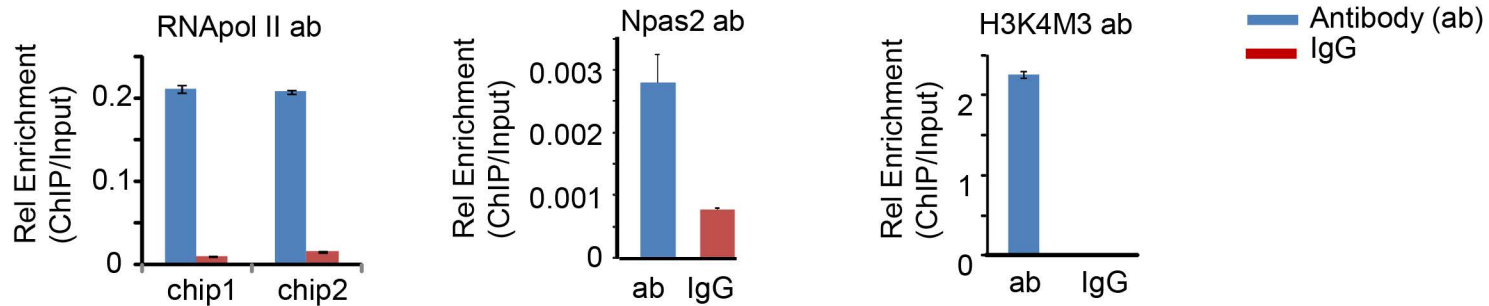
RNAPII-shp chip2-150+: *TGATCCTCCGACTCCTCCTG*  
 RNAPII-shp chip2-150-: *TCAGGCTTTAGCAACGAGGG*

133109521-9672, ChIP

K3H4me3-SHP CHIP 151+: *AGGCCTTGGATGTCCTAGCC*  
 K3H4me3-SHP CHIP 151-: *TCGAAGGTCACAGCATCCTG*

Fig. S6: The primers for ChIP-assay were designed based on the ChIP-seq signal in WT mouse liver (Koike et al., Science, 338:349-354, 2012).

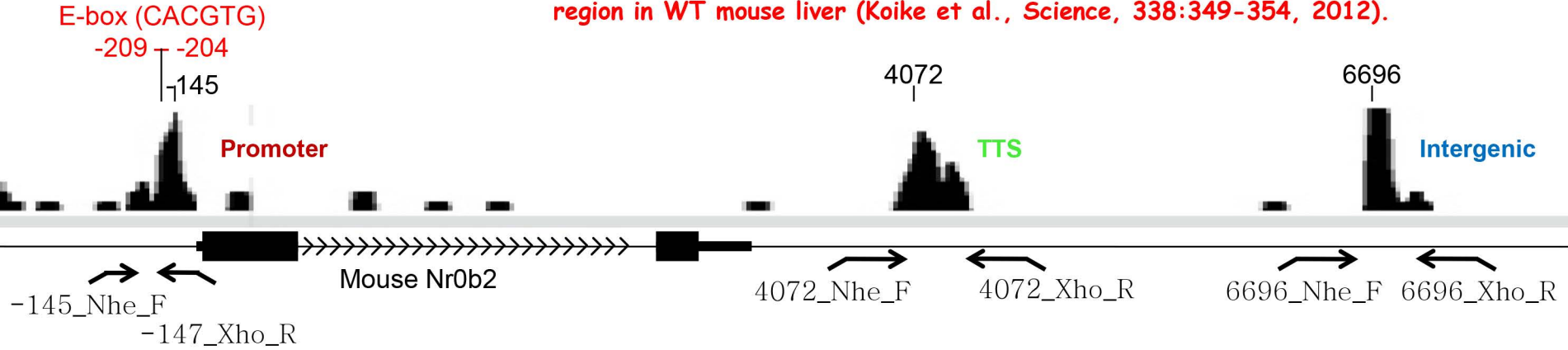
## SHP clock Supp Fig. 7



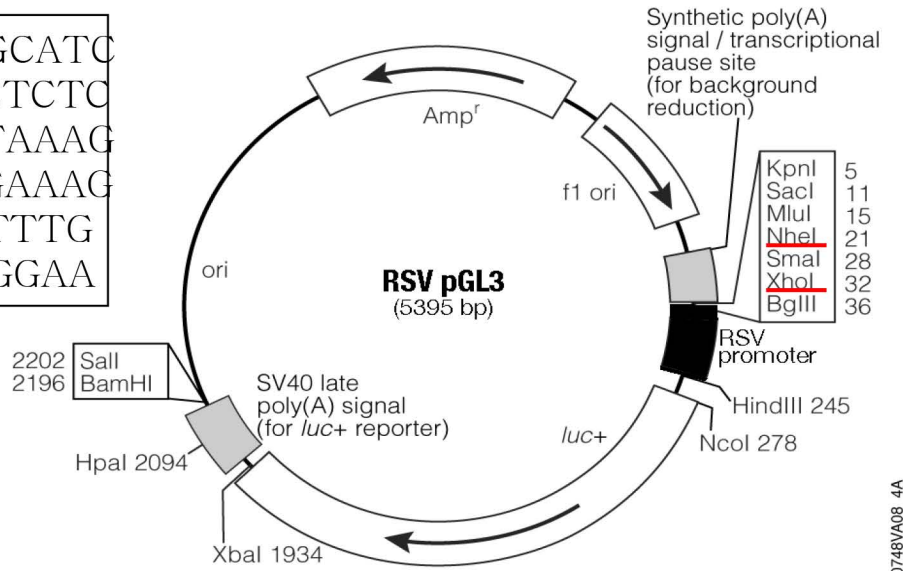
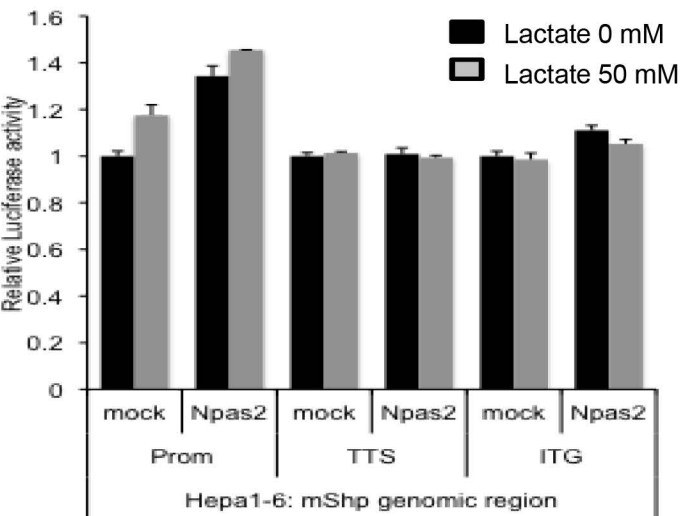
**Fig. S7: Validating antibodies against RNAPII, Npas2 and H3K4M3 in ChIP-assay.**

**SHP clock Supp Fig. 8**

ChIP-seq signal showing Npas2 binding to Shp promoter, TTS and intergenic region in WT mouse liver (Koike et al., Science, 338:349-354, 2012).



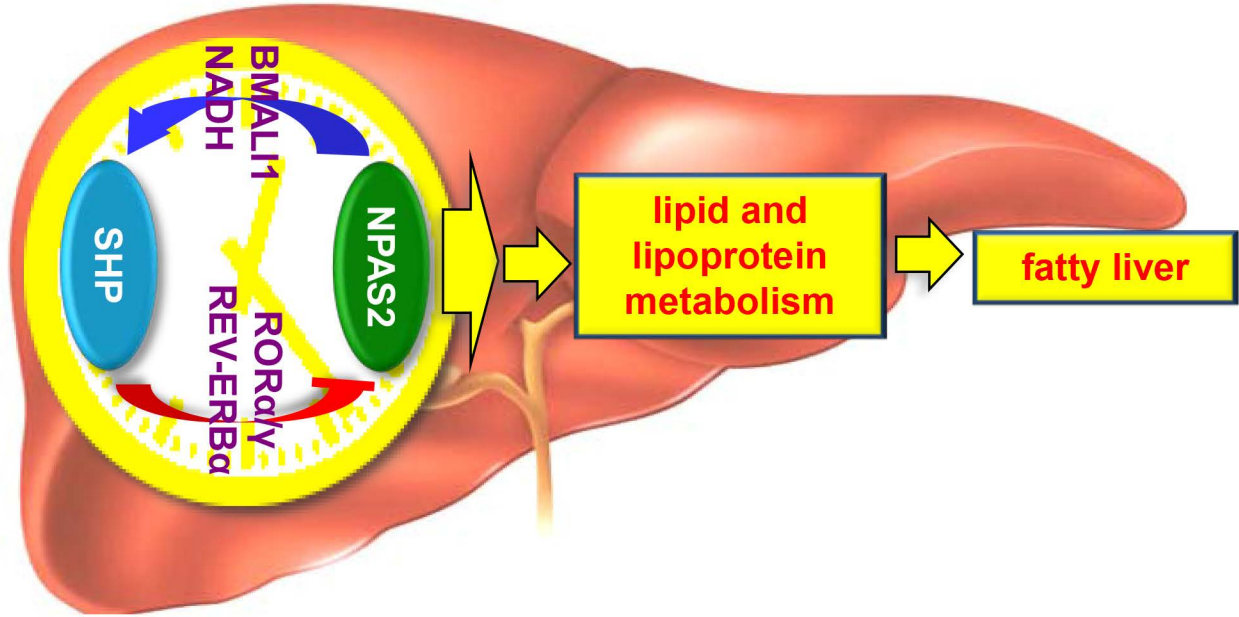
-145_Nhe_F	gctcgctagcGTCATCCGATAAAGGGCATC
-145_Xho_R	cgctctcgagCAGCTATCTGGCCCTCTCTC
4072_Nhe_F	gctcgctagcGGTCACCCTCGTTGCTAAAG
4072_Xho_R	cgctctcgagCTAGGCTGTTGCCCTGAAAG
6696_Nhe_F	gctcgctagCCCAAGAGAAGCAACCTTTG
6696_Xho_R	cgctctcgaGATACTTGGTGGCCTTGGAA



**Fig. S8: Top: Cloning strategy and primers to clone Shp promoter, TTS and intergenic luciferase reporter. Bottom left: Transient transfection assays in mouse Hepa-1 cells treated without or with lactate.**



**SHP clock Supp Fig. 9**



**Fig. S9: Schematic of liver circadian clock network integrated by the Shp/Npas2 regulatory axis. Shp inhibits Npas2 expression via crosstalk with Rorα,γ/Rev-erβα, and Npas2 activates Shp expression which is mediated by Bmal1/NADH. Shp/Npas2 crosstalk is critical to maintain hepatic lipid metabolism.**