CIRCADIAN RHYTHM MAPK signaling pathway Circadian entrainment +p CREB CREB/MAPK signaling pathway Extracellular signals -O cAMP DNA ROR ► NFIL3 DNA ► BMAL1 REV-ERB REV-ERB → NFIL3 NFIL3 DNA REV-ERB **▶** DBP DBP **√** DBP **≠** DEC DEC CRY CKla/8 CKla/8 BMAL1 PER CRY PER CRY CLOCK DNA PER CKlε/δ +pAMPK PER CRY CRY SCF SCF β-TrCP FBXL21 FBXL3 +u Ubiquitin mediated proteolysis Proteasomal degradation Proteasomal degradation Clock outputs / rhythmic biological processes Ccg genes