Table 2. Mouse circadian mutants and observed circadian and physiological phenotypes.

Gene	Circadian phenotype	Ref.	Associated physiological abnormality	Ref.
Bmal1/Mop3 (*Arntl*) Null mutant	Loss-of-circadian activity rhythm in DD	[1]	Infertility Decreased adult body weight Increased tendon calcification Abnormal gluconeogenesis and lipogenesis Hypersensitive to chemotherapeutic agent Premature aging syndrome Increased sleep fragmentation	[1-8]
Bmal2/Mop9/CLIF (*Arntl2*)	[Paralog of *Bmal1*; dimerizes with CLOCK, NAPS2, and HIF1α]	[9, 10]	ND	—
ClockΔ19 Antimorph	Semidominant, 4 hr longer period followed by loss-of-circadian activity rhythm in DD	[11]	Hyperphagic & Obese Abnormal gluconeogenesis Hypersensitive to chemotherapeutic agent Enhanced response to cocaine Mania phenotype Decreased duration of sleep time	[3, 7, 12-14]
Clock Null mutant	0.5 hr shorter period	[15]	ND	—

Npas2/Mop4 Null mutant	0.2 hr shorter period	[16]	Impaired memory Reduced sleep amount during night time	[16, 17]
Clock & Npas2 Double null mutant	Complete loss of circadian activity rhythm in DD	[18]	ND	—
Per1 Null mutant	0-0.5 hr shorter period/ some animals lose circadian activity rhythm in DD	[19-21]	Lack of sensitization to cocaine	[22]
Per2 *Per2*^{tm1Brd} Null mutant	1.5 hr shorter period and tendency for loss of circadian rhythm	[20, 23]	Increased tumor development following genotoxic stress Hyper-sensitization to cocaine Improper alcohol intake Early onset of sleep	[22, 24-26]
Per1 & Per2 Double null mutant	Complete loss of circadian activity rhythm in DD	[19, 20]	ND	—
Per3 Null mutant	0-0.5 hr shorter period	[27]	ND	—

Cry1 Null mutant	1 hr shorter period	[28, 29]	ND	—
Cry2 Null mutant	1 hr longer period	[30]	ND	—
Cry1 & Cry2 Double null mutant	Complete loss of circadian activity rhythm in DD	[28, 29]	Delayed hepatocyte re-generation Resistant to chemotherapeutic agent's toxicity Increased NREM sleep drive	[3, 24, 31]
CK1ε (*Csnk1e*) *tau** mutant	Semidominant, 4 hr shorter period	[32]	Reduced growth rate Enhanced metabolic rate	[33, 34]
CK1δ (*Csnk1d*) Null mutant	ND	—	Postnatal (within days) lethal	[35]
CK1δ (*Csnk1d*) *T44A* mutant	0.5 hr shorter period	[35]	ND	—

Rev-erbα (*Nr1d1*) Null mutant	0.5 hr shorter period/ Altered photic entrainment	[36]	ND	—
Rev-erbβ (*Nr1d2*)	ND	—	ND	—
Rora *Staggerer* mutant	0.5 hr shorter period	[37]	Cerebellar ataxia Abnormal bone metabolism	[38, 39]
Rorb Null mutant	0.5-hr longer period	[40]	Locomotor difficulties Retinal degeneration/blind Male reproductive abnormality during first 6-mo of age	[40]
Rorc Null mutant	ND	—	Disrupted lymphoid organ development	[41, 42]
Timeless Null mutant	ND	—	Embryonic lethal	[43]

Dec1/Stra13/ Sharp2/Clast5 (*Bhlhb2*) Null mutant	No circadian deficit in clock gene expression	[44]	Impaired T lymphocyte activation Age-related autoimmune disease Defect in skeletal muscle regeneration following injury	[45, 46]
Dec2/Sharp1 (*Bhlhb3*)	ND	—	ND	—
E4bp4 (*Nfil3*)	Upstream regulator of *Per2*, no behavioral analysis	[47]	ND	—
Melanopsin (*Opn4*) Null mutant	Reduced phase-shift response to light	[48, 49]	Diminished pupilary light reflex	[50]
Vip Null mutant	Abnormal entrainment to light cycles Dissociated circadian wheel-running rhythms in DD Reduced amplitude in behavioral rhythms in DD	[51, 52]	Impaired temporal regulation of metabolism and feeding	[53]

Vipr2 Null mutant	Abnormal entrainment to light cycles Dissociated circadian wheel-running rhythms in DD Reduced amplitude in behavioral rhythms in DD Impaired responses to light	[51, 54]	Impaired temporal regulation of metabolism and feeding	[53]
Nocturnin (*Ccrn41*) Null mutant	No circadian behavioral deficits	[55]	Resistance to diet-induced obesity	[55]

*Hamster mutation.
ND = None determined

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