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ARNTL Antibody

Purified Mouse Monoclonal Antibody
Catalog # AO1386a

Product Information

Application	WB, IHC, E
Primary Accession	O00327
Reactivity	Human
Host	Mouse
Clonality	Monoclonal
Clone Names	1C5
Isotype	IgG1
Calculated MW	68762
Description	The protein encoded by this gene is a basic helix-loop-helix protein that forms a heterodimer with CLOCK. This complex binds an E-box upstream of the PER1 gene, activating this gene and possibly other circadian rhythym-associated genes. Three transcript variants encoding two different isoforms have been found for this gene.
Immunogen	Purified recombinant fragment of human ARNTL expressed in E. Coli.
Formulation	Ascitic fluid containing 0.03% sodium azide.

Additional Information

Gene ID	406
Other Names	Aryl hydrocarbon receptor nuclear translocator-like protein 1, Basic-helix-loop-helix-PAS protein MOP3, Brain and muscle ARNT-like 1, Class E basic helix-loop-helix protein 5, bHLHe5, Member of PAS protein 3, PAS domain-containing protein 3, bHLH-PAS protein JAP3, ARNTL, BHLHE5, BMAL1, MOP3, PASD3
Dilution	WB~~1/500 - 1/2000 IHC~~1/200 - 1/1000 E~~N/A
Storage	Maintain refrigerated at 2-8°C for up to 6 months. For long term storage store at -20°C in small aliquots to prevent freeze-thaw cycles.
Precautions	ARNTL Antibody is for research use only and not for use in diagnostic or therapeutic procedures.

Protein Information

Name	BMAL1 (HGNC:701)

Function

Transcriptional activator which forms a core component of the circadian clock. The circadian clock, an internal time-keeping system, regulates various physiological processes through the generation of approximately 24 hour circadian rhythms in gene expression, which are translated into rhythms in metabolism and behavior. It is derived from the Latin roots 'circa' (about) and 'diem' (day) and acts as an important regulator of a wide array of physiological functions including metabolism, sleep, body temperature, blood pressure, endocrine, immune, cardiovascular, and renal function. Consists of two major components: the central clock, residing in the suprachiasmatic nucleus (SCN) of the brain, and the peripheral clocks that are present in nearly every tissue and organ system. Both the central and peripheral clocks can be reset by environmental cues, also known as Zeitgebers (German for 'timegivers'). The predominant Zeitgeber for the central clock is light, which is sensed by retina and signals directly to the SCN. The central clock entrains the peripheral clocks through neuronal and hormonal signals, body temperature and feeding-related cues, aligning all clocks with the external light/dark cycle. Circadian rhythms allow an organism to achieve temporal homeostasis with its environment at the molecular level by regulating gene expression to create a peak of protein expression once every 24 hours to control when a particular physiological process is most active with respect to the solar day. Transcription and translation of core clock components (CLOCK, NPAS2, BMAL1, BMAL2, PER1, PER2, PER3, CRY1 and CRY2) plays a critical role in rhythm generation, whereas delays imposed by post- translational modifications (PTMs) are important for determining the period (tau) of the rhythms (tau refers to the period of a rhythm and is the length, in time, of one complete cycle). A diurnal rhythm is synchronized with the day/night cycle, while the ultradian and infradian rhythms have a period shorter and longer than 24 hours, respectively. Disruptions in the circadian rhythms contribute to the pathology of cardiovascular diseases, cancer, metabolic syndromes and aging. A transcription/translation feedback loop (TTFL) forms the core of the molecular circadian clock mechanism. Transcription factors, CLOCK or NPAS2 and BMAL1 or BMAL2, form the positive limb of the feedback loop, act in the form of a heterodimer and activate the transcription of core clock genes and clock-controlled genes (involved in key metabolic processes), harboring E-box elements (5'-CACGTG-3') within their promoters. The core clock genes: PER1/2/3 and CRY1/2 which are transcriptional repressors form the negative limb of the feedback loop and interact with the CLOCK|NPAS2-BMAL1|BMAL2 heterodimer inhibiting its activity and thereby negatively regulating their own expression. This heterodimer also activates nuclear receptors NR1D1/2 and RORA/B/G, which form a second feedback loop and which activate and repress BMAL1 transcription, respectively. BMAL1 positively regulates myogenesis and negatively regulates adipogenesis via the transcriptional control of the genes of the canonical Wnt signaling pathway. Plays a role in normal pancreatic beta-cell function; regulates glucose-stimulated insulin secretion via the regulation of antioxidant genes NFE2L2/NRF2 and its targets SESN2, PRDX3, CCLC and CCLM. Negatively regulates the mTORC1 signaling pathway; regulates the expression of MTOR and DEPTOR. Controls diurnal oscillations of Ly6C inflammatory monocytes; rhythmic recruitment of the PRC2 complex imparts diurnal variation to chemokine expression that is necessary to sustain Ly6C monocyte rhythms. Regulates the expression of HSD3B2, STAR, PTGS2, CYP11A1, CYP19A1 and LHCGR in the ovary and also the genes involved in hair growth. Plays an important role in adult hippocampal neurogenesis by regulating the timely entry of neural stem/progenitor cells (NSPCs) into the cell cycle and the number of cell divisions that take place prior to cell-cycle exit. Regulates the circadian expression of CIART and KLF11. The CLOCK-BMAL1 heterodimer regulates the circadian expression of SERPINE1/PAI1, VWF, B3, CCRN4L/NOC, NAMPT, DBP, MYOD1, PPARGC1A, PPARGC1B, SIRT1, GYS2, F7, NGFR, GNRHR, BHLHE40/DEC1, ATF4, MTA1, KLF10 and also genes implicated in glucose and lipid metabolism. Promotes rhythmic chromatin opening, regulating the DNA

accessibility of other transcription factors. The NPAS2-BMAL1 heterodimer positively regulates the expression of MAOA, F7 and LDHA and modulates the circadian rhythm of daytime contrast sensitivity by regulating the rhythmic expression of adenylate cyclase type 1 (ADCY1) in the retina. The preferred binding motif for the CLOCK-BMAL1 heterodimer is 5'- CACGTGA-3', which contains a flanking adenine nucleotide at the 3-prime end of the canonical 6-nucleotide E-box sequence (PubMed:23229515). CLOCK specifically binds to the half-site 5'-CAC-3', while BMAL1 binds to the half-site 5'-GTGA-3' (PubMed:23229515). The CLOCK-BMAL1 heterodimer also recognizes the non-canonical E-box motifs 5'-AACGTGA- 3' and 5'-CATGTGA-3' (PubMed:23229515). Essential for the rhythmic interaction of CLOCK with ASS1 and plays a critical role in positively regulating CLOCK-mediated acetylation of ASS1 (PubMed:28985504). Plays a role in protecting against lethal sepsis by limiting the expression of immune checkpoint protein CD274 in macrophages in a PKM2-dependent manner (By similarity). Regulates the diurnal rhythms of skeletal muscle metabolism via transcriptional activation of genes promoting triglyceride synthesis (DGAT2) and metabolic efficiency (COQ10B) (By similarity).

Cellular Location

Nucleus {ECO:0000255|PROSITE-ProRule:PRU00981, ECO:0000269|PubMed:24005054}. Cytoplasm {ECO:0000250|UniProtKB:Q9WTL8} Nucleus, PML body {ECO:0000250|UniProtKB:Q9WTL8}. Note=Shuttles between the nucleus and the cytoplasm and this nucleocytoplasmic shuttling is essential for the nuclear accumulation of CLOCK, target gene transcription and the degradation of the CLOCK-BMAL1 heterodimer. The sumoylated form localizes in the PML body. Sequestered to the cytoplasm in the presence of ID2. {ECO:0000250|UniProtKB:Q9WTL8}

Tissue Location

Hair follicles (at protein level). Highly expressed in the adult brain, skeletal muscle and heart

References

1. Chronobiol Int. 2007;24(5):783-92. 2. Mol Cell Biol. 2008 Oct;28(19):6056-65. 3. J Affect Disord. 2009 Sep;117(1-2):87-97.

Images

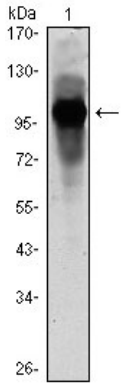
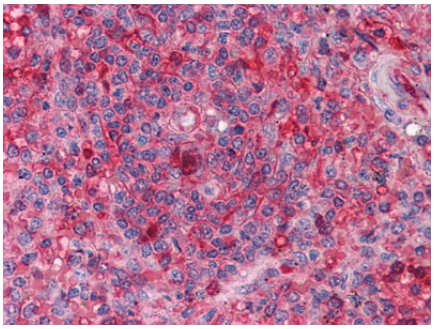


Figure 1: Western blot analysis using ARNTL mouse mAb against ARBTL(AA: 1-310)-hIgGFc transfected HEK293 cell lysate.

Figure 2: Immunohistochemical analysis of paraffin-embedded human Spleen tissues using anti-ARNTL mouse mAb



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