Research Progress and Prospects of the Brown Adipocyte-Specific Gene PRDM16 (Postprint)

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Abstract

PR domain-containing 16 (PRDM16) is an important transcription factor in the differentiation of brown adipocytes, playing a crucial role in maintaining the unique morphological characteristics and cellular functions of brown adipocytes. PRDM16 not only regulates the differentiation of brown adipocytes, but may also serve as a 'switch'for the mutual transdifferentiation between adipocytes and myocytes, and is involved in the beigeing process of white adipocytes. Studies have revealed that the PRDM16 gene in humans and livestock harbors abundant SNP loci, which exhibit certain correlations with human diseases and livestock production traits. Given the importance of PRDM16 in adipose differentiation and human health, this review summarizes the research achievements of investigators worldwide over the past decade regarding the structure and function of the PRDM16 gene and protein, the correlation between this gene and diseases and livestock economic traits, and provides prospects for future research directions of PRDM16 and its application potential in human disease therapy and animal trait improvement.

Full Text

Advances and Prospects of Brown Adipocyte-Specific Gene PRDM16

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Abstract

PR domain-containing 16 (PRDM16) is a crucial transcription factor in brown adipocyte differentiation that plays an essential role in maintaining the unique morphological characteristics and cellular functions of brown adipocytes. PRDM16 not only regulates brown adipocyte differentiation but may also serve as a "switch" for interconversion between adipocytes and myocytes, and is additionally involved in the browning process of white adipocytes. Studies have revealed that the PRDM16 gene in humans and livestock is rich in SNP loci, which show correlations with human diseases and livestock production traits. Given the importance of PRDM16 in adipose differentiation and human health, this review summarizes research findings from the past decade on the structure and function of the PRDM16 gene and protein, its correlation with diseases and livestock economic traits, and prospects for future research directions and applications in human disease treatment and animal trait improvement.

Keywords: PRDM16; protein structure; biological function; regulation mechanism; polymorphism

Mammalian organisms contain three types of adipocytes: white, brown, and beige. White adipocytes serve as energy storage sites, while brown adipocytes, rich in mitochondria, function as energy-dissipating sites. Beige adipocytes likely arise from the transformation of white adipocytes under specific conditions (cold exposure, 3-adrenergic receptor agonists) and also contain mitochondria with energy-releasing capabilities. The thermogenic mechanism in both brown and beige adipocytes involves uncoupling protein 1 (UCP1) enriched in the inner mitochondrial membrane, which transports protons across the membrane to disrupt oxidative phosphorylation, dissipating energy that would otherwise be used for ATP synthesis as heat. Consequently, brown and beige adipocytes play crucial roles in maintaining energy balance and homeostasis. Brown adipocyte differentiation is regulated by numerous genes (MYF5, PPAR- / , CEBP- , PGC1- / , and UCP1), among which PRDM16 has been identified as an important transcriptional regulator.

PRDM16 is the 16th member of the PR domain family. The human PRDM16 gene was first discovered in a leukemia patient with a reciprocal translocation between chromosomes 1 and 3, t(1;3)(p36;q21). The gene is located on chromosome 1, and due to high amino acid sequence similarity with ecotropic viral integration site 1 or PR domain protein 3 (EVI1/PRDM3), PRDM16 is also known as myelodysplastic syndrome 1/ecotropic viral integration site 1-like gene 1 [MEL1 (MDS1/EVI1-LIKE GENE 1)] [1, 2].

Recent studies have confirmed that PRDM16 acts as a transcriptional regulator during brown adipocyte differentiation, playing a vital role in maintaining the specialized morphology of brown adipocytes (including lipid droplet and mitochondrial formation), promoting expression of related genes, and ultimately enabling thermogenic function [3, 4]. Consequently, structural alterations in PRDM16 are associated with various diseases. Deletion of the PR domain

may be linked to myelodysplastic syndrome (MDS) and leukemia [5-8], while PRDM16 variants also correlate with cancer [9, 10], cardiomyopathy [11], and obesity [12]. In livestock (sheep, cattle) and poultry (chickens), PRDM16 has also been found to correlate with production traits. Given the importance of PRDM16, this review summarizes its protein structure, biological functions, and regulatory mechanisms, and discusses future research directions and application prospects.

1. Human PRDM16 Protein Structure

Human PRDM16 protein comprises 1,276 amino acids [13]. As shown in Figure 1 [Figure 1: see original paper], several important functional domains have been identified: one PR domain, two zinc-finger domains (zinc-finger domain-1/2), one conserved repression domain (RD), one proximal regulatory region (PRR), and one acidic activation domain (AD). In the figure, (A) indicates that the PR domain is involved in histone H3 lysine 4 methylation; (B) shows that PRDM16 can bind via its zinc-finger domains to peroxisome proliferator-activated receptor- / (PPAR- /) [14], CCAAT-enhancer binding proteins- (C/EBP-) [15], peroxisome proliferator-activated receptor- coactivator 1- / (PGC1- /) [16, 17], mediator complex subunit 1 (MED1) [16, 18], or euchromatic histone-lysine N-methyltransferase 1 (EHMT1) [19]; (C) indicates the presence of small ubiquitin-like modifier (SUMO) binding sites in the RD domain; (D) shows phosphorylation sites in the RD domain; and (E) illustrates PRDM16 binding to C-terminal binding protein-1/2 (CtBP-1/2) through its repression domain [20].

Figure 1 Human PRDM16 protein structure (referred from Ishibashi, et al., 2015; Chi, et al., 2015)

1.1 PR Domain

The PR domain is located at the N-terminus of PRDM16 and is a characteristic feature of PRDM family proteins, possessing histone lysine methyltransferase activity that promotes monomethylation of histone H3-lysine 9 (H3K9) to generate H3K9me1, which can subsequently be di- and trimethylated by other methyltransferases [10, 21, 22]. Deletion of the PR domain is associated with diseases such as leukemia and MDS [1, 2].

In human cancer research, PRDM family members PRDM1, PRDM2, PRDM3, and PRDM4 have been found to express two different isoforms in patients: a full-length protein and a PR domain-deleted protein (ΔPR) [23, 24]. In cancer cells, the ΔPR protein is overexpressed. Based on differences in expression levels and mechanisms between full-length and ΔPR PRDM16 proteins, Huang et al. (1999) characterized this cancer regulation pattern as a "Yin-Yang" mechanism [24].

Human PRDM16 has also been found to exist as two similar mRNA transcripts and corresponding proteins. Nishikata et al. [2] identified two distinct

PRDM16 products using Western blotting (Figure 2 [Figure 2: see original paper]), where MEL1 represents the full-length PRDM16 protein (with PR domain) and MEL1S represents the PR domain-deleted PRDM16 protein. Additionally, Nishikata et al. found that overexpression of ΔPR could block granulocyte colony-stimulating factor (G-CSF)-induced granulocytic differentiation in interleukin-3 (IL-3)-dependent mouse myeloid L-G3 cells, whereas normal PRDM16 overexpression could not, suggesting that ΔPR overexpression might be a factor in inducing t(1;3)-positive myeloid leukemia [2]. However, in a patient with myelodysplastic syndrome type 2 (MDS-RAEB-2) caused by chromosomal translocation, Lahortiga et al. [25] found that the deleted ΔPR isoform was also expressed in normal tissues, with expression levels not significantly different from those of full-length PRDM16 protein.

Figure 2 Two different isoforms of human PRDM16 (referred from Nishikata, et al., 2003; Lahortiga, et al., 2003)

1.2 Zinc-Finger Domains

PRDM16 possesses two zinc-finger domains: the N-terminal zinc-finger domain ZF1 and the C-terminal zinc-finger domain ZF2, both composed of C2H2-type zinc-finger motifs. These domains serve as both sequence-specific DNA binding sites and protein-protein interaction sites [13, 20]. The zinc-finger domains can bind specific proteins (PGC-1 , MED1, PPAR- / , and C/EBP- /) to activate PRDM16 biological functions [15]. Kajimura et al. found that deletion or mutation of ZF1 significantly blocked brown adipocyte formation during PRDM16-regulated brown adipocyte differentiation, whereas ZF2 mutation had less significant effects. Similarly, Iida et al. [16] found that ZF1-deleted mutants (ΔZF1, ΔZF1/2) significantly affected the interaction between PRDM16 and PGC-1 .

1.3 Repression Domain

The PRDM16 repression domain is involved in regulating white adipocyte-specific genes (resistin, endothelin receptor A Ednra, and annexin Anxa1, etc.) [20]. Kajimura et al. [20] discovered that PRDM16 could bind to CtBP-1/2 via the PLDLS motif within its repression domain, thereby suppressing expression of these white adipocyte-specific genes.

2.1 PRDM16 Maintains Brown Adipocyte Morphological Characteristics and Thermogenic Function

Brown adipocytes are rich in mitochondria, and UCP1 in the inner mitochondrial membrane can transport protons across the membrane, disrupting oxidative phosphorylation and dissipating energy that would be used for ATP synthesis as heat [27]. Consequently, brown adipose tissue is considered a site for fat oxidation and heat release. PRDM16 deletion causes morphological changes in brown adipocytes, particularly reduced mitochondrial numbers, and

alters gene expression, including significant downregulation of brown adipocyte-specific genes (Cidea, Otop1, and PPAR-), thermogenic genes (Dio2, PGC1- , and UCP1), and mitochondrial electron transport genes (Cox3, Cox5b, and Cox8b) at both mRNA and protein levels. This leads to decreased oxygen consumption, weakened cellular oxidative respiration, and impaired thermogenic function due to reduced mitochondrial numbers and thermogenic gene expression [3, 4, 17, 28].

Altered cellular function can cause phenotypic changes at the organismal level. Harms et al. [4] found that under acute cold exposure (4°C, 3h), PRDM16-deficient mice showed significant decreases in core body temperature and scapular region temperature. They also observed that PRDM16 deficiency led to reduced oxygen consumption, decreased lean mass ratio, and reduced body weight and length in mice during norepinephrine (NE)-activated brown adipocyte thermogenesis.

2.2 The "Switch" Role of PRDM16 in Brown Adipocyte and Skeletal Muscle Cell Differentiation

Studies have shown that brown adipocytes and skeletal muscle cells share a common origin in Myogenic factor 5 (Myf5)-expressing progenitor cells. PRDM16 overexpression can induce Myf5-positive progenitor cells to differentiate into brown adipocytes, whereas absence of PRDM16 expression causes these precursor cells to differentiate into skeletal muscle cells [14, 15, 29].

Seale et al. [14] found that ectopic PRDM16 expression in mouse myoblast C2H2 cells and skeletal muscle precursor cells induced morphological and gene expression characteristics similar to brown adipocytes. These cells accumulated large amounts of lipids, with significantly elevated expression levels of adipocyte-related genes (PPAR- , AP2), brown adipocyte-specific genes, and thermogenic genes. In contrast, PRDM16-nonexpressing myoblasts and skeletal muscle precursor cells formed multinucleated skeletal muscle cells [14]. Kajimura et al. [15] observed similar results in mouse fibroblasts and skin fibroblasts, finding that the PRDM16-C/EBP- transcriptional complex could promote the conversion of muscle cells to brown adipocytes. Conversely, PRDM16-deficient brown adipocyte precursor cells exhibited muscle cell characteristics, displaying elongated tubular morphology with significantly increased expression of muscle differentiation-related genes including myosin heavy chain (MyHC), myosin light chain (Mlc), myogenic gene (Myod), and creatine kinase gene (Mck) [14].

2.3 PRDM16 Promotes "Browning" of White Adipocytes

Cousin et al. [30] found that cold exposure or -adrenergic receptor agonist stimulation increased UCP1 gene expression in mouse ovarian adipose tissue, acquiring thermogenic functions similar to typical brown fat. Seale et al. [28] observed that prolonged cold stimulation or adrenergic receptor agonist treatment induced "browning" in mouse subcutaneous white adipose tissue, which might

be associated with significantly increased PRDM16 gene expression. Ohno et al. [31] also found that PRDM16 overexpression could promote conversion of MYF5-negative (MYF5-) progenitor cells into beige adipocytes. These findings demonstrate the important role of PRDM16 in the browning process of white adipocytes [32-34].

White adipose tissue comprises white adipocytes and the stromal-vascular fraction (SVF), which contains differentiation-capable adipose precursor cells, fibroblasts, immune cells, and vasculature-related cells [28]. Seale et al. [28] found through adenovirus-mediated PRDM16 overexpression experiments that white adipose tissue browning only occurred in these differentiation-capable SVF cells. Therefore, PRDM16-induced browning of white adipose tissue is believed to occur exclusively in differentiation-competent cells.

2.4 PRDM16 Deletion Leads to Subcutaneous Fat Exhibiting Visceral Fat Characteristics

PRDM16 deletion causes macrophage infiltration (CD11b F4/80) in mouse inguinal subcutaneous adipose tissue, while significantly increasing expression of visceral adipocyte-related proinflammatory factors including serum amyloid A3 (Saa3), angiotensinogen (Agt), lipoxygenase (Alox15), osteoprotegerin (Opgn), retinaldehyde dehydrogenase 2 (Raldh2), and transcription factors (Tcf21, Bnc1, and Wt1) [35, 36], all of which correlate with visceral fat characteristic formation.

3.1 Mechanism of PRDM16 in Promoting Brown Adipocyte-Related Gene Expression

PRDM16 can recruit related proteins (PPAR- / , C/EBP- , and MED1) to promoters or enhancer regions of brown fat-specific genes (PGC1-), thereby promoting brown fat-specific gene expression. Studies have identified PRDM16 binding sites in promoter regions of brown fat-specific genes (C/EBP- , PPAR- , and PGC1-) [15, 16, 18]. Recent research revealed numerous PRDM16 binding sites in enhancer regions of these genes, which are located near transcription start sites and bear the active histone mark H3K27ac (histone H3 lysine 27 acetylation) [18]. Harms et al. [18] found 507 super-enhancers (SEs) in the PPAR- gene sequence, with 78% of these super-enhancers containing at least one PRDM16 binding site. PRDM16 binding to super-enhancers was significantly stronger than to typical enhancers. PRDM16 can recruit the mediator complex MED1 to enhancer regions of target genes via its zinc-finger domains, thereby enhancing brown fat gene promoter activity and promoting gene transcription. These findings confirm that enhancer regions in brown fat-related genes may also serve as PRDM16 binding sites.

Kajimura et al. [15] proposed that the PRDM16-C/EBP- transcriptional complex induces expression of PPAR- and PGC-1 , after which PRDM16 subsequently binds to PPAR- and PGC-1 to promote UCP1 expression.

CCAAT-enhancer binding protein is an important adipogenic gene highly expressed in brown adipocytes. Two isoforms exist in brown adipocytes: an active form called LAP (liver-enriched transcriptional activator protein) and an inhibitory form called LIP (liver-enriched transcriptional inhibitory protein) [37, 38]. In vitro experiments revealed that the active form of C/EBP- could bind to PRDM16' s zinc-finger domains to form a transcriptional complex that not only promotes expression of adipogenic genes (PPAR- , PGC-1) but also induces conversion of muscle cells or fibroblasts (C2C12 cells, MEFs, and human skin fibroblasts) into adipocytes [15].

The PRDM16-PGC1- / transcriptional complex promotes UCP1 expression and regulates brown adipocyte thermogenic function. Iida et al. [16] proposed a multi-step model for PRDM16 regulation of UCP1 expression (Figure 3 [Figure 3: see original paper]). This regulatory process comprises two main parts: First, the retinoid X receptor- (TR) bound to ligand enhancers in the UCP1 chromatin template directly binds to PGC1- / through its nuclear hormone receptor binding motif (LXXLL binding motifs, where L represents leucine and X can be any amino acid). PRDM16 then binds to the TR-PGC1- / -enhancer complex through its zinc-finger domains. This complex promotes protein acetylation and chromatin remodeling by binding histone acetyltransferase p300. Subsequently, MED1 replaces PGC1- / , binding PRDM16 through its N-terminus and PGC1- / through its C-terminus, ultimately forming a complex preinitiation complex. This complex can act on RNA polymerase II through MED1 to promote UCP1 expression and thereby regulate brown adipocyte thermogenesis.

Figure 3 Multistep model for activation of UCP1 by PRDM16 (referred from Iida, et al., 2015) (1) PRDM16 and p300 are recruited to a TR-PGC-1 / -enhancer complex in UCP1 gene, leading to histone acetylation and chromatin remodeling. (2) The recruitment of MED1 by PRDM16 regulates the preinitiation complex formation and induces the expression of UCP1.

3.2 Mechanism of PRDM16 in Inhibiting White Adipocyte-Related Gene Expression

PRDM16 can recruit CtBP-1/2 to promoters of white adipocyte-specific genes (resistin and angiotensinogen), inhibiting their expression. Studies show that CtBP-1 is a protein dimer composed of two subunits (CtBP-1L and CtBP-1S) [39, 40].

Chinnadurai et al. [40] found that each CtBP-1 subunit contains two protein motif PLDLS binding sites, with the two subunits forming two hydrophobic PLDLS binding grooves through non-covalent binding. Kajimura et al. [20] identified a PLDLS motif within PRDM16' s repression domain, consisting of five consecutive amino acids (aa 804-808) that form an evolutionarily conserved sequence. They further revealed that PRDM16 could recruit CtBP-1/2 to proximal promoter regions of white adipocyte-specific genes via PLDLS, thereby suppressing promoter activity and ultimately inhibiting gene expression. Chromatin

immunoprecipitation (ChIP) results for white adipocyte-specific genes resistin and angiotensinogen confirmed this mechanism: the PRDM16 and CtBP-1/2 binding region in the resistin gene sequence is located between -179 bp and -26 bp upstream of the promoter, while in the angiotensinogen gene sequence, the binding region is located between -127 bp and +23 bp in the proximal promoter [20].

4.1 Application Prospects of PRDM16 Gene Research

Research on PRDM16 gene variants holds significant importance for clinical medicine and livestock production trait improvement. Current reports on correlations between PRDM16 gene variants and human diseases or animal traits are summarized in Table 1 .

Table 1 The SNPs reported in PRDM16 gene and their association with human diseases or animal traits

Gene Locus	Associated Disease or Trait
CM000663.2: g.3414616T>C	Dilated cardiomyopathy, left ventricular noncompaction [41]
CM000663.2: g.3412301A>T	Metabolic syndrome [42]
CM000663.2: g.3412644A>G	Migraine without aura [43-45], dyslipidemia (decreased HDL cholesterol) [46]
CM000663.2: g.3402986C>T	Increased HDL cholesterol [46]
CM000663.2: g.3411770_3411771insC	Dyslipidemia (hypertriglyceridemia, low HDL cholesterol) [47]
CM000663.2: g.3402940delG	Increased body weight and daily weight gain in Nanyang cattle [48]
CM000663.2: g.3178267C>G	Increased body weight, daily weight gain, body length, and chest circumference in Nanyang, Jiaxian Red, and Qinchuan cattle [49, 50]
CM000663.2: g.3167148T>A	Increased body length, body height, and hip width in Jiaxian Red cattle [49, 50]
CM000663.2: g.3167148T>C	Increased chest circumference, body weight, hip width, and rump length in Qinchuan cattle [49, 50]
CM000663.2: g.3426240G>A	Increased heart weight, liver weight, and four-day lower leg length [51]
CM000663.2: g.3426240G>T	Increased body weight and body length [52]
CM000663.2: g.3041036T>C	
CM000663.2: g.3385157C>T	

Gene Locus	Associated Disease or Trait
CM000677.2: g.61396368T>C	
XM_001788152: m.1641T>C(547aa)	
XM_001788152: m.1881G>A(627aa)	
NC_007314.3: g.577G>T	
NC_007314.3: g.614T>C	
NC_007314.3: g.212237T>C	
Chicken XM_417551: c.1161C>T(Ala/Ala, 387aa)	
XM_417551: c.1433G>A(Ser/Asn,478aa)	

4.1.1 PRDM16 and Human Disease Treatment

PRDM16-regulated thermogenesis in brown adipocytes is crucial for maintaining energy balance. At the individual level, PRDM16 variants are associated with obesity, dyslipidemia, migraine without aura, and other diseases (Table 1). Deletion of PRDM16 functional domains may also correlate with hematological disorders such as myelodysplastic syndrome and leukemia. Implantation of engineered fibroblasts ectopically expressing PRDM16/PPAR- or PRDM16/C/EBP- into mouse subcutaneous white adipose tissue successfully induced high expression of brown adipocyte-specific genes Cidea, PGC-1 , and UCP1 [3, 15]. These tissues strongly oxidized ingested glucose [15], which is significant for consuming excess energy and maintaining energy balance. Therefore, ectopic PRDM16 expression is considered a potential future therapeutic approach for human metabolic diseases such as obesity.

4.1.2 PRDM16 and Livestock Trait Improvement

As shown in Table 1, livestock PRDM16 exhibits rich polymorphism, with these SNP loci showing significant correlations with production traits. Wang et al. [53] found that loci XM_001788152:m.1641T>C (547aa) and 1881G>A (627aa) were significantly associated with body weight and daily weight gain in 12-month-old Nanyang cattle, with CC genotype showing significantly higher body weight and average daily gain than TT and TC genotypes, and AA genotype showing significantly higher average daily gain than AG and GG genotypes. Studies revealed that locus NC_007314.3:g.577G>T was significantly associated with body weight, daily weight gain, body

length, and chest circumference in Nanyang, Jiaxian Red, and Qinchuan cattle; locus NC_007314.3:g.614T>C was significantly associated with body length, body height, and hip width in Jiaxian Red cattle; and locus NC_007314.3:g.212237T>C was significantly associated with chest circumference, body weight, hip width, and rump length in Qinchuan cattle [49, 50]. Han et al. [51] found that locus XM_417551:c.1161C>T (Ala/Ala, 387aa) in chickens was significantly associated with heart weight, liver weight, and lower leg length, with TT genotype showing higher heart weight and four-day lower leg length; locus XM_417551:c.1433G>A (Ser/Asn,478aa) was significantly associated with body weight (hatch weight, four-day weight, eight-day weight, and carcass weight) and body length (lower leg length, lower leg circumference, sternum length, body length, and pelvic width), with AA genotype showing significantly higher body weight and length than other genotypes. PRDM16 is therefore considered a potential genetic marker for livestock trait detection, though extensive research is still needed to validate this possibility.

4.2.1 Elucidating the Role of the PR Domain in PRDM16-Mediated Regulation of Brown Adipocyte Differentiation

The PR domain is a characteristic feature of PRDM family proteins, and regulating brown adipocyte differentiation is an important biological function of PRDM16. However, studies have found that PR domain deletion does not prevent PRDM16-induced brown adipocyte differentiation [15]. Therefore, it is currently hypothesized that an undiscovered mechanism may regulate brown adipocyte differentiation.

4.2.2 PRDM16 Function May Be Regulated by Different Developmental Stages

Studies have shown that PRDM16 deletion does not significantly affect brown adipocyte function during embryonic and juvenile stages but significantly impacts brown adipocyte function in 6-month, 9-month, and 11-month-old mice. Harms et al. [4] found that in 6-month-old mice, PRDM16 deletion caused significant decreases in mRNA and protein levels of brown adipocyte-specific genes UCP1 and PPAR- ; in 9-month-old mice, PRDM16 deletion led to significant reduction in brown adipocyte mitochondrial numbers and functional degeneration; however, in 11-month-old PRDM16-deficient mice, entire brown adipocytes were replaced by white adipocytes. Since PRDM3 shares similar structure and function with PRDM16 [4, 54], it is hypothesized that PRDM3 may compensate for PRDM16 deficiency, preventing significant changes in embryonic and juvenile brown adipocytes.

4.2.3 Discovering Unknown Factors That Can Bind to PRDM16

Uldry et al. [17] discovered in 2006 that PGC1- / could form transcriptional complexes with PRDM16; in 2008, Seale et al. [14] reported that PPAR- /

could form transcriptional complexes with PRDM16; Kajimura et al. [20] reported that CtBPs could form transcriptional complexes with PRDM16; and in 2009, Kajimura et al. [15] identified 49 protein factors that could form transcriptional complexes with PRDM16, of which only 8 were known or predicted proteins, highlighting the C/EBP- -PRDM16 transcriptional complex and its role in initiating myocyte-to-adipocyte conversion. However, research on the remaining 7 protein factors—B-cell lymphoma-2-related transcription factor, zinc finger protein 655, tumor suppressor protein p53/Trp53, CCHC-type zinc finger protein 8 (Zcchc8), zinc finger protein with KRAB and SCAN domains 3 (Zkscan3), zinc finger protein 143, and vascular endothelial zinc finger protein 1 (Vezf1)—remains scarce. In recent years, additional factors including EHMT1, MED1 [16, 18], and GTF2IRD1 [55] have been found to bind PRDM16 and form transcriptional complexes. Therefore, many unknown protein factors may still bind PRDM16, requiring extensive future research to identify these potential proteins and elucidate their binding mechanisms and related functions.

This review primarily summarizes research progress on the brown adipocyte-specific gene PRDM16, including its protein structure, biological functions, and related regulatory mechanisms. Additionally, based on correlations between PRDM16 gene polymorphisms and human diseases and livestock traits, we discuss potential application prospects for PRDM16 gene research. Finally, we propose future research directions for PRDM16 based on current research gaps.

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