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Functional diversity of cAMP response element-binding protein in insects: Implications for vector control

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A B S T R A C T

cAMP response element-binding protein (CREB), a member of the leucine zipper family of transcription factors, functions as a central hub in the networks of cellular signal transduction and gene expression regulation, responding to diverse intracellular and extracellular stimuli. This review mainly focuses on CREB's functions in key physiological processes in insects, particularly in development and metamorphosis, diapause and lifespan plasticity, neuroplasticity and behavior, as well as metabolism and insecticide resistance, providing valuable insights into potential targets for vector control, thereby providing innovative solutions for combating vector-borne infectious diseases.

1. Introduction

The cAMP response element-binding protein (CREB) is a stimulus-induced transcription factor that links extracellular stimuli to long-term adaptive intracellular responses.[1,2] Numerous studies have demonstrated that CREB plays a pivotal role in regulating specific gene expression programs governing cell survival, differentiation, plasticity, and the maintenance of physiological homeostasis.[3–6].

Structurally, CREB is a member of the leucine zipper family of transcription factors.[7,8] Its molecular architecture is characterized by four key functional domains: a basic leucine zipper (bZIP) domain, a kinase-inducible domain (KID), and glutamine rich 1 (Q1) and 2 (Q2) domains,[9,10] although interspecies variation exhibits in CREB isoform domain composition (Fig. 1).[11] In general, the C-terminal bZIP domain enables dimerization with partner proteins like CREB-binding protein (CBP),[12,13] which is essential for DNA binding.[14] The KID contains the critical Ser133 residue, serves as the central regulatory switch for CREB transcriptional activity upon its phosphorylation.[15,16] Flanking this is the basic region, Q1 and Q2 domains, are considered to be constitutive active domains directly recognizes and binds to a specific DNA sequence known as the cyclic adenosine monophosphate (cAMP) response element (CRE) in the promoter regions of target genes.[17–19].

CREB activation is a highly controlled process that integrates multiple signaling pathways. The canonical pathway is mediated by cAMP: extracellular signals like hormones activate adenylyl cyclase via G protein-coupled receptors, raising intracellular cAMP levels and subsequently triggering protein kinase A (PKA) activation.[20] Then PKA translocates to the nucleus to phosphorylate CREB at phosphorylation site like the critical Ser133 residue (pCREB).[21] Moreover, other pathways, such as the Ras/MAPK (mitogen-activated protein kinase) pathway and Ca^{2+}/calmodulin-dependent protein kinase pathways, also activate CREB by phosphorylating Ser133 or neighboring sites.[6,22] This property enables CREB to function as one of multiple interconnected mediators in the networks of cellular signal transduction and gene expression regulation, responding to diverse intracellular and extracellular stimuli.

Although CREB's structure, regulation, and functions have been extensively studied, our understanding of its role in the insect world continues to deepen and expand. As the most abundant and adaptable animal group in nature, insects, with their complex behavioral plasticity, unique developmental cycles, and remarkable environmental adaptability, offer an exceptional model for exploring both the universal and species-specific functions of CREB. This paper intends to review the current research progress on CREB in several insects, examining how this transcription factor governs key physiological processes including development and metamorphosis, diapause and lifespan plasticity,

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neuroplasticity and behavior, as well as metabolism and insecticide resistance.

2. CREB functions in insects

2.1. Development and metamorphosis

CREB family proteins in insect development and metamorphosis has revealed evolutionarily conserved yet functionally diverse roles across multiple species. *Drosophila melanogaster* serves as the primary model organism, two major CREB family transcription factors with distinct properties have been characterized: dCREB-A (analogous to human CREB3) and dCREB-B (analogous to human CREB1, also known as dCREB2).[23–27] It produces multiple alternatively spliced transcripts and changes dramatically during development, at least two major classes of the activator isoform (dCREB2-A) and the repressor isoform (dCREB2-B) were identified, which has also been reported in some *Anopheles* CREB-A (CREBA-a and CREBA-b),[11] though the precise catalog of isoforms remains incomplete for most non-drosophilid species. dCREB-A is a structurally distinct CREB family member characterized by a unique leucine zipper with six hydrophobic repeats (vs. typical 4-5 in mammalian CREBs) and a tyrosine substitution, and the DNA-binding domain shares 48% identity with mammalian CREB (compared to 23% with *Drosophila* c-Jun). It lacks classical PKA phosphorylation sites but contains potential Ca^{2+}/calmodulin-dependent kinase II (CaMKII) sites, indicating regulation via calcium signaling rather than cAMP.[23] Gel shift assays confirmed its specific binding to the CRE sequence (TGACGTCA) rather than the related TRE (AP-1) site, but the binding specificity was partial: a 100-fold excess of unlabeled CRE did not fully compete for binding, and unlike mammalian CREB, dCREB-A could bind CRE in the absence of Mg^{2+}. Meanwhile, dCREB-B shows remarkable conservation in its DNA-binding basic region and leucine zipper domain (92% and 78% identity with mammalian CREB, respectively) but possesses a divergent amino-terminal activation domain.[26] *In situ* hybridization shows ubiquitous expression in embryos, with enrichment in the developing central nervous system.

dCREB-A expression is highly tissue-specific.[23,24] In embryos, dCREB-A is expressed in the developing salivary gland. Particularly, it is expressed in the nuclei of the embryonic salivary gland, proventriculus and stomadeum. Late in embryogenesis, tracheal cell nuclei and specific nuclei within the segments show staining with anti-dCREB-A antibodies. A more complex pattern of expression is detected in the adult, transcripts are found in the brain and optic lobe cell bodies, salivary gland, and midgut epithelial cells of the cardia. In females, dCREB-A is expressed in the ovarian columnar follicle cells, and in males, dCREB-A RNA is seen in the seminal vesicle, ejaculatory duct, and ejaculatory bulb. Null mutations of the dCREB-A gene give rise to animals that no longer express dCREB-A protein and die late in embryogenesis before or at hatching. These results suggest that dCREB-A is not only essential for terminal differentiation and secretory functions such as salivary gland differentiation, though not for organ specification,but may also be involved in fertility and neurological functions. Furthermore, dCREB-A also acts downstream of decapentaplegic (Dpp) and SPI-signaling as a terminal effector that interprets these signals to specify epidermal cell fates.[25] Null mutations cause complete lateralization of the cuticle, converting both dorsal and ventral surfaces to lateral identities. Concurrently, dCREB-B is absolutely required for heart development via two CRE consensus sites in the tinman myocardial enhancer.[28] It was proposed that these CRE sites may function as Dpp response elements, analogous to their role in the Ubx visceral mesoderm enhancer, potentially linking Dpp signaling to tinman activation via CREB-family transcription factors.

In addition, the CREB-CBP axis is functionally conserved across holometabolous and hemimetabolous insects, and functions as a core regulatory hub integrating several major signaling pathways. On one hand, CREB proteins are activated through phosphorylation by multiple kinases such as PKA via the cAMP pathway triggered by hormones like 20-hydroxyecdysone in *Helicoverpa armigera*,[29] CaMKII in response to ER calcium signals for juvenile hormone biosynthesis in the American cockroach *Periplaneta americana*,[30] and PKCα which phosphorylates Krüppel-homolog 1 (Kr-h1) at Ser154 - enabling them to recruit histone acetyltransferase CBP in *Locusta migratoria* and acetylate specific residues such as H3K18, H3K27 and H4K12 for chromatin remodeling and transcriptional activation in *Tribolium castaneum*.[31,32] On the other hand, CBP acts as a universal epigenetic regulator of insect development and metamorphosis. For instance, in the hemimetabolan cockroach *Blattella germanica*, CBP shows ubiquitous, low-level expression across multiple tissues, and plays as a vital hub integrating multiple endocrine and developmental pathways such as ecdysone, Juvenile hormone, MEKRE93, TGF-β, and feeding regulation, during insect metamorphosis.[33] Depleting CBP during the last nymphal instar of *B. germanica* causes high mortality during nymphal development or adult ecdysis, feeding impairment followed by metabolic starvation responses, delayed molting due to disrupted ecdysone signaling, defective ecdysis and wing expansion, and disrupted metamorphic switch.[33] In the red flour beetle *T. castaneum*, CBP is ubiquitously expressed throughout larval and pupal stages, RNAi-mediated CBP depletion disrupts Juvenile hormone-induced Kr-h1 expression while simultaneously impairing ecdysone response genes such as E74, E75 and Broad-Complex, creating a dual signaling blockade, and caused 100% mortality in larvae, pupae, and adults.[34] In mosquito *Aedes aegypti*, a specific CREB repressor isoform terminated yolk protein precursor expression mediated by the steroid 20-hydroxyecdysone via the cAMP signal-transduction pathway during late vitellogenesis through competitive binding to CRE sites, providing a post-translational off-switch for egg development.[35] Moreover, CBP not only suppresses expression of these mosquito adult



Fig. 1. Schematic representation of the key functional domains of CREB in *Drosophila melanogaster* and mosquitoes.[11] Q1: glutamine rich 1; KID: kinase-inducible domain; Q2: glutamine rich 2; bZIP: basic leucine zipper; TAD: transactivation domain.

specifier gene E93 and pupal specifier Broad-Complex through upregulation of Kr-h1, but also represses ecdysone receptors (EcR-A and USP-A) via the early ecdysone response gene E75A, creating a negative feedback loop that prevents premature activation of metamorphosis.[36] Additionally, CBP is required for compound eye development of this yellow fever mosquito by activating the retinal determination gene network and TGF-β/EGFR pathways.[36]

2.2. Diapause and lifespan plasticity

Diapause represents a complex physiological adaptation that results in low metabolic activity and enables insects to survive under adverse environmental conditions, with numerous signaling pathways contributing to its intricate regulation.[37] CREB acts as a master coordinator of insect diapause, uniquely positioned to translate oxidative stress signals into epigenetic modifications and transcriptional programs that maintain protein homeostasis, suppress metabolism, and extend healthspan. Its ability to integrate multiple inputs via alternative phosphorylation mechanisms reveals a sophisticated molecular architecture underlying developmental plasticity and lifespan regulation in insects.

In diapause-destined insects, CREB binds distinct promoters to coordinate the diapause phenotype. In the moth *H. armigera*, it was previously speculated that CREB's function was not related to insect diapause, because its overexpression did not affect the mRNA levels of Hexokinase (HK), which is considered critical for the developmental arrest of *H. armigera*, as well as its expression was similar in diapause and nondiapause pupal brains,[38] although previous studies have demonstrated that the CREB regulates mammalian HK expression.[39] Further research revealed that CREB-mediated pathways elucidate how elevated physiological ROS levels enhance longevity rather than inflicting damage by orchestrating a multifaceted cellular response. First, a TOR signaling-related protein, phosphorylated S6 kinase (p-S6K), was found to be elevated in the brains of diapause-destined pupae of *H. armigera* respond to upstream signals from reactive oxygen species (ROS) and Akt, and that activated S6K subsequently enhances CREB activity (Fig. 2).[40] Then activated CREB binds to the hypoxia-inducible factor-1α (HIF-1α) promoter to upregulate its expression, resulting in reduced mitochondrial activity to facilitate insect diapause. Moreover, high physiological levels of ROS in the brains of diapause-destined pupae of the moth *H. armigera* activate c-Jun N-terminal kinase (JNK) expression, which in turn activates the transcription factor CREB (Fig. 2).[41] Then, activated CREB directly binds to the protein arginine methyltransferase 1 (PRMT1) promoter to upregulate its expression, thereby preventing Akt-mediated FoxO phosphorylation and enabling FoxO nuclear localization, CREB-PRMT1-FoxO is a core molecular module for insect diapause programming (Fig. 2). Here, FoxO is also an evolutionarily conserved master transcriptional regulator dominating insect nutrient-dependent development, diapause and lifespan programming. In addition, ROS are also widely recognized as a major cause of aging and age-related diseases through the process of carbonylation, and the moth *H. armigera* brain can naturally regulate protein carbonyl levels through a distinct ROS-Akt-CREB-CBR1 (carbonyl reductase 1) pathway, thereby extending lifespan while preventing ROS-mediated aging damage (Fig. 2).[42] In detail, ROS can activate Akt, which subsequently phosphorylates CREB to facilitate its nuclear import, then nuclear CREB binds to CBR1 promoter to upregulate its expression. The resulting high CBR1 levels effectively reduce protein carbonyl levels, maintaining them within a physiological range. In the silkworm *Bombyx mori*, CREB expression is significantly higher in diapause-type embryos, with peaks during critical signal-reception windows, suggesting a molecular memory function for diapause determination.[43]

2.3. Neuroplasticity and behavior

CREB serves as a fundamental molecular machinery governing activity-dependent gene expression underlying neuroplasticity and behavior across various animal species.[44,45] In *D. melanogaster*, the dCREB2 gene generates multiple alternatively spliced isoforms with opposing transcriptional activities: activator isoforms (such as dCREB2-a) that promote transcription and repressor isoforms (such as dCREB2-b) that inhibit it.[46] This molecular architecture positions CREB as a "molecular switch" that gates the formation of protein synthesis-dependent long-term memory (LTM) while leaving short-term memory (STM) and learning unaffected.[47,48] In other words, induced expression of a dominant-negative CREB repressor specifically blocks LTM without impairing STM or learning,[48] but overexpression of activator isoforms can enhance memory formation and even enable "photographic memory" after single training sessions—an effect normally requiring spaced training.[46] The ratio of functional activator to repressor isoforms determines the threshold for LTM induction, with spaced training protocols gradually shifting this balance toward

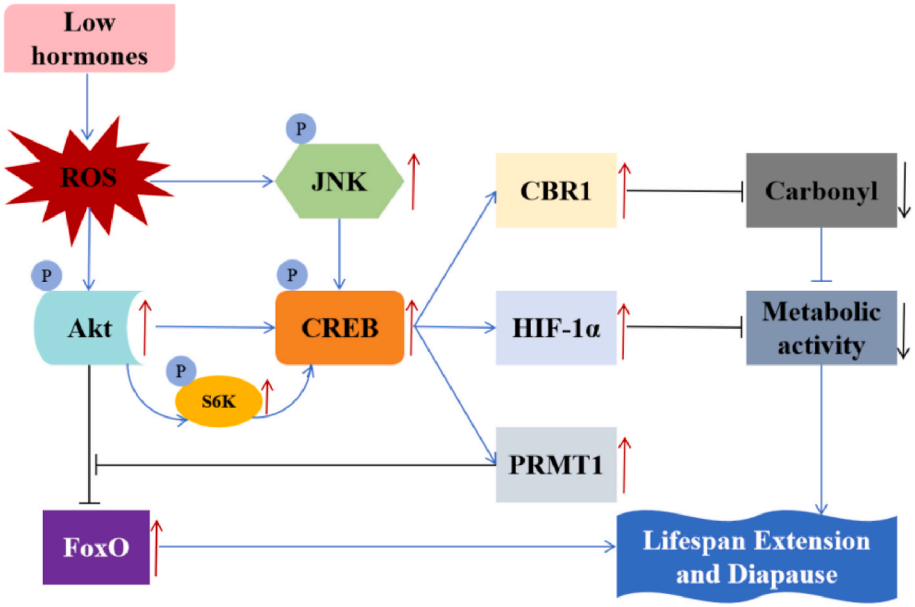


Fig. 2. Schematic representation of CREB-related signaling pathways in the regulation of insect diapause using *Helicoverpa armigera* as an example[40–42].

activation through PKA-mediated phosphorylation at conserved serine residues.[44,47] Notably, the dCREB2-b repressor isoform contains an additional C-terminal leucine zipper that enables homodimer formation, effectively sequestering activator isoforms and thereby raising the threshold for memory formation.[46] Recent studies have revealed that spaced training activates ERK phosphorylation during rest intervals, which is required for increased expression of CREB and c-Fos specifically in a subset of *Drosophila* mushroom body α/β Kenyon cells, creating a positive feedback loop essential for LTM formation and recall.[49] While the mushroom body has long been recognized as the primary center for olfactory learning and memory in insects, recent studies have revealed that CREB exerts circuit-specific effects on neuroplasticity through distinct neuronal populations, and CREB-dependent LTM formation involves a distributed network extending beyond traditional boundaries. In *Drosophila*, two dorsal-anterior-lateral (DAL) neurons have been identified as critical sites where CREB-mediated transcription is required specifically for LTM consolidation and retrieval, but not for acquisition.[50] Training induces CREB-dependent activation of downstream genes, including *CaMKII* and *period*, in these DAL neurons, both of which are necessary for normal LTM.[51] The circuit-specific requirement for CREB extends to appetitive memory as well. Multiple neurons encode CrebB-dependent appetitive long-term memory in the mushroom body circuit, with distinct populations contributing to different phases of memory processing.[52] Similarly, in crickets (*Gryllus bimaculatus*), CREB-A functions in adult mushroom body neuroblasts to regulate LTM formation through a positive feedback loop with the novel gene *oskar* and the conserved stem cell factor *piwi*.[53] Another example of the role of CREB in non-learning behaviors is that in the migratory locust (*Locusta migratoria*), CREB-B serves as a key mediator of phase-related locomotor plasticity.[54] During crowding-induced behavioral gregarization, neuropeptide F2 (NPF2) activates its receptor NPFR, triggering cAMP/PKA signaling that phosphorylates and activates CREB-B. Activated CREB-B then directly activates nitric oxide synthase (NOS) transcription in the pars intercerebralis, generating NO that promotes behavioral transitions between solitarious and gregarious phases.[54] This signaling cascade exemplifies how CREB integrates environmental stimuli with transcriptional responses to modulate behavioral plasticity beyond the memory domain. A recent study in the brown planthopper (*Nilaparvata lugens*) further extended CREB's role to gustatory-mediated feeding behavior.[55] The bitter taste receptor NlGr23a, upon binding to oxalic acid, activates the PI3K-AKT signaling pathway, which promotes CREB phosphorylation and induces feeding rejection responses, while RNAi-mediated knockdown of CREB significantly increases food intake, demonstrating that CREB negatively regulates feeding behavior in this agricultural pest.[55]

The functional versatility of CREB in insect neuroplasticity is further expanded through differential recruitment of transcriptional coactivators under varying physiological contexts. Previous research has revealed that *Drosophila* utilizes distinct LTM machinery depending on their hunger state, although both fasting-dependent LTM (fLTM) and spaced training-dependent LTM (spLTM) required protein synthesis and CREB activity, fLTM required CREB activity only in mushroom body neurons and depends on the coactivator CRTC (CREB-regulated transcription coactivator), and spLTM required CREB activity in mushroom body and DAL neurons and utilizes the coactivator CBP.[56] Furthermore, the CRTC-CREB axis extends beyond metabolic regulation to proteostatic stress responses, functioning as a transcriptional sensor that protects against proteotoxic stress by inducing cytoprotective genes in *Drosophila*.[57] Additionally, transcriptomic analyses have begun to map the downstream gene networks activated by CREB in memory-relevant neurons, identifying essential long-term memory transcription factors including Hr38 and stripe as components of the CREB-activated transcriptional program in mushroom body neurons.[58]

Upstream regulatory inputs further diversify CREB's functional repertoire. Beyond the canonical cAMP/PKA pathway, CREB activity is regulated by Notch signaling, which induces hyperphosphorylated CREB in conjunction with PKC activity, and triggers its ultradian oscillation patterns during memory formation in *Drosophila*.[59] Mg^{2+} block of NMDA receptors is required for normal LTM, potentially through regulation of calcium-dependent signaling to CREB.[60] In addition, environmental toxicants such as pesticides can modulate CREB phosphorylation levels through its associated upstream signaling pathways like BDNF/Trk, Pi3K/AKT, RAS/MEK/ERK, PLC/PKC, etc., potentially disrupting neuronal plasticity, learning, and memory formation.[61] Azadirachtin, as a broad-spectrum insecticide, can affect the cognitive behavior of *Spodoptera litura* through downregulating gene and protein expression of CREB and its pathway proteins such as PKA and extracellular signal-regulated kinase (ERK).[62]

Regarding circadian rhythms, CREB pathway is thought to play a crucial role in transmitting light signals to the transcription of clock genes in the mammalian suprachiasmatic nucleus, while cell-specific knockout of CrebA or CrebB in clock neurons did not affect free-running locomotor behavior, rhythmic *period* oscillations, or light-dependent synchronization, questioning the conserved circadian role of the CREB pathway in *Drosophila*.[63]

2.4. Metabolism and insecticide resistance

CREB has emerged as a critical regulator of insecticide resistance through its control over detoxification enzymes (particularly, cytochrome P450 monooxygenases) expression across different insect species. In the whitefly *Bemisia tabaci*, CREB directly regulates the expression of CYP6CM1, a cytochrome P450 enzyme that confers high-level resistance to neonicotinoid insecticides such as imidacloprid.[64] CREB binds to a CRE-like site in the CYP6CM1 promoter, and both CREB overexpression and increased phosphorylation contribute to enhanced CYP6CM1 expression in resistant strains. It was also validated through RNAi knockdown of CREB or pharmacological inhibition of its upstream kinases, which significantly reduced CYP6CM1 expression and increased whitefly susceptibility to imidacloprid.[64] Similarly, in the cotton aphid *Aphis gossypii*, CREB/ATF (activating transcription factor) was constitutively upregulated and directly activates CYP6CY14 transcriptional activity by binding to its promoter region under cycloxaprid. Meanwhile, silencing CREB/ATF via RNAi reduced CYP6CY14 expression and increased *Aphis gossypii* mortality when exposed to cycloxaprid.[65] In the brown planthopper *Nilaparvata lugens*, CREB was significantly induced after chemical insecticides exposure, and RNAi-mediated knockdown of CREB reduced cytochrome P450 enzyme activity and increased sensitivity to imidacloprid, further supporting the conserved function of CREB in regulating detoxification metabolism.[66]

Further, CREB activation integrates stress signals through well-conserved signaling cascades, particularly the MAPK pathway, providing a dynamic response to insecticide pressure. In imidacloprid-resistant *B. tabaci*, insecticide exposure activates ERK and p38 MAP kinases, which subsequently phosphorylate CREB at Ser111, leading to its activation and nuclear translocation (Fig. 3).[64] This MAPK-directed CREB activation signaling axis represents a "trans-regulatory" mechanism of cytochrome P450 overexpression, distinct from cis-acting promoter mutations. The use of specific MAPK inhibitors (PD98059 for ERK and SB203580 for p38) significantly reduced CYP6CM1 expression and restored insecticide susceptibility, both in laboratory strains and field-collected resistant populations (Fig. 3).[64] In the silkworm *Bombyx mori*, exposure to dinotefuran activates multiple signaling pathways including MAPK/CREB, CncC/Keap1, PI3K/Akt, and Toll/IMD pathways, leading to coordinated upregulation of detoxification enzymes. The MAPK/CREB pathway specifically induces CREB and its upstream regulators (TRAF3, MAPKKK7, Mek, and Erk), demonstrating its central role in the transcriptional response to neonicotinoid insecticides.[67] Moreover, ROS also serve as important signaling molecules upstream of the MAPK-CREB pathway. It has been demonstrated that imidacloprid exposure decreases adipokinetic hormone (AKH) expression, leading to ROS accumulation and subsequent activation of the MAPK/CREB

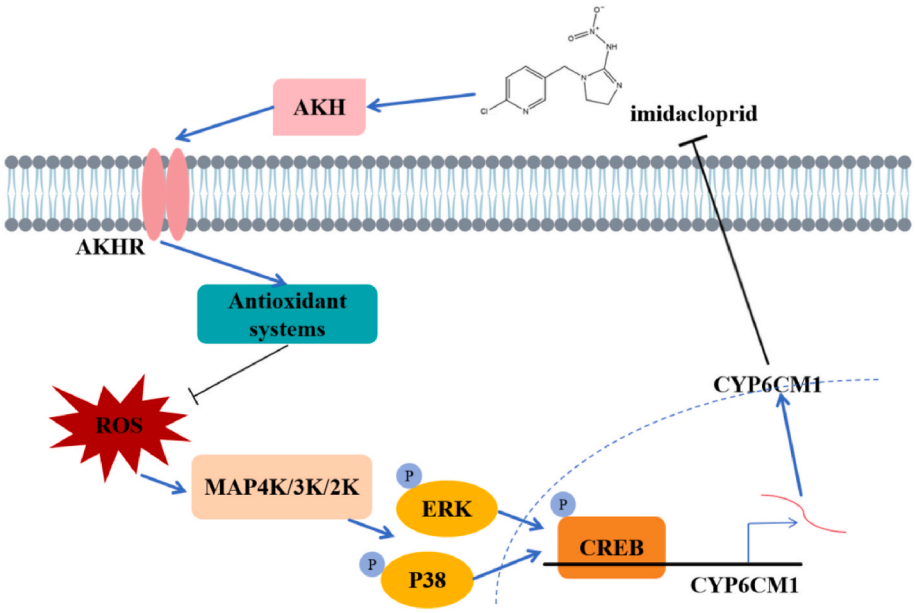


Fig. 3. Proposed regulation mechanism of CREB-mediated imidacloprid resistance in *B. tabaci*[64,68].

signaling cascade in *B. tabaci*. The ROS scavenger N-acetylcysteine (NAC) effectively reduced the expression of CREB, ERK, p38, and their downstream target CYP6CM1, while increasing whitefly susceptibility to imidacloprid (Fig. 3).[68] This ROS-mediated regulation highlights the intricate connection between oxidative stress and detoxification gene expression. As mentioned above, the CRTC-CREB axis functions as a transcriptional sensor for proteotoxic and oxidative stress in *Drosophila*. Proteasome inhibition or ROS induction activated CREB through the JNK signaling pathway, leading to upregulation of molecular chaperones, proteasome subunits, and antioxidant genes.[57]

Beyond detoxification, CREB plays multifaceted roles in insect metabolic homeostasis such as energy metabolism. In *Drosophila*, CREB activity in neurons regulates glycogen and lipid storage, with neuronal disruption of CREB reducing both energy reserves and starvation resistance.[69] Interestingly, blocking CREB specifically in the fat body, the primary energy storage organ, produced distinct metabolic phenotypes. It also reduced glycogen levels but paradoxically increased lipid accumulation, resulting in an obese-like phenotype. This tissue-specific effect demonstrates that CREB can differentially regulate metabolic pathways depending on cellular context.[69]

3. Implications and perspectives

In summary, CREB is a pivotal transcription factor that functions as master integrators of multiple signaling cascades in different physiological processes rather than simple cAMP responders in insects. Understanding the CREB-mediated regulatory networks provides valuable insights into the insect development and metamorphosis, diapause and lifespan plasticity, neuroplasticity and behavior, as well as metabolism and insecticide resistance, and offers potential targets for developing novel vector control strategies, thereby providing innovative solutions for combating vector-borne infectious diseases.

Furthermore, it provides the potential for an innovative dual strategy for resistance control. The CREB-CBP axis and its upstream regulators serve as both direct intervention targets and core nodes for multi-pathway synergistic enhancement. First, the cross-species conservation highlights its significance as a broad-spectrum molecular target for next-generation insecticide resistance management strategies. For instance, CREB-mediated overexpression of *CYP6CM1* in *B. tabaci* confers imidacloprid resistance,[64] pharmacological or RNAi-mediated disruption of this axis restores susceptibility. This regulatory pattern exhibits similar characteristics in mosquito vectors. Second, the essential role of CBP in post-embryonic development of insects provides a species-specific intervention target. Rather than inducing outright lethality, a next-generation gene drive could spread a transgene encoding an inducible RNAi hairpin against CREB or a dominant-negative CBP variant that disrupts the KIX domain. Importantly, the KIX-KID interface in vector insects is structurally divergent enough from vertebrate homologs to enable the development of species-selective analogs (such as small-molecule disruptors of the CREB-CBP interface), thereby minimizing nonspecific effects on non-target organisms. Third, CREB-mediated transcriptional regulation, together with orthogonal pathways, has an additive protective effect, indicating that jointly targeting the CREB-CBP axis and parallel pathways could yield a synergistic effect in resistance management.[70] Therefore, this dual advantage of "target specificity plus strategic synergy" opens new avenues for designing precise enhancer combinations and RNAi cocktail formulations to overcome metabolic resistance in field vector populations.

CRediT authorship contribution statement

Zhenyu Yue: Writing – original draft. **Mei Zhang:** Writing – review & editing. **Qingqiu Zuo:** Writing – review & editing. **Xiaokai Jia:** Writing – review & editing. **Congshan Liu:** Writing – review & editing. **Hua Liu:** Writing – review & editing. **Jianhai Yin:** Writing – review & editing, Supervision, Conceptualization.

Data availability

The authors confirm that the sources of data supporting this study's findings are available within the article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Authors hereby provide the consent for the publication under open access and declare that there are no objections.

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Declaration of competing interest

The authors declare that the review was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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