Journal of Energy Bioscience 2025, Vol.16, No.1, 42-52
http://bioscipublisher.com/index.php/jeb

Review Article Open Access

The Role of the Creatine Phosphate System in Energy Storage and Release: From Molecular Mechanisms to Physiological Functions

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Journal of Energy Bioscience, 2025, Vol.16, No.1 doi: 10.5376/jeb.2025.16.0005
Received: 03 Jan., 2024
Accepted: 12 Feb., 2025
Published: 21 Feb., 2025

Preferred citation for this article:
Hong W.Y., Huang W.Z., 2025, The role of the creatine phosphate system in energy storage and release: from molecular mechanisms to physiological functions, Journal of Energy Bioscience, 16(1): 42-52 (doi: 10.5376/jeb.2025.16.0005)

Abstract The creatine phosphate system helps process energy in cells, especially in tissues that require a lot of energy and change quickly, such as muscles and brains. This study mainly talks about how the creatine phosphate system works, its basic principles, the pathways involved, and its role in the body. We focused on creatine kinase, which helps cells regenerate ATP, and also plays a role in "storing" energy, and is even responsible for transmitting energy to where it is needed. This process is very critical during muscle contraction and brain function, especially in those organs that use a lot of energy, it can help cells maintain a stable energy state. The article also mentioned that supplementing creatine phosphate may help some diseases, such as muscle diseases and neurodegenerative diseases. Now, because of the increasing advancement of technologies such as molecular imaging and bioinformatics, people have a deeper understanding of how creatine is metabolized and how it cooperates with other cellular processes. In the future, researchers may try to develop some new therapies related to creatine. We will continue to explore how it is regulated at the molecular level and see how it is related to other metabolic pathways. These studies are expected to bring new ideas and treatments for treating some energy-related diseases.
Keywords Creatine phosphate system; Energy metabolism; Creatine kinase; ATP buffering; Therapeutic potential; Metabolic integration

1 Introduction

For cells to work properly, they must constantly obtain energy. This is inseparable from the energy storage and release systems. They help cells maintain internal balance, support various metabolic processes, and cope with energy changes in different situations. Among these systems, the creatine phosphate system is particularly important. It is like an energy "buffer" that can quickly provide energy, especially for tissues such as muscles and brains that have high energy requirements and fast changes (Saks et al., 1978; Jacobus, 1985; Kazak and Cohen, 2020).

The core of this system is creatine kinase (CK) and phosphocreatine (PCr). When cells need a lot of energy, creatine kinase (CK) and phosphocreatine (PCr) can quickly convert ADP and PCr into ATP to keep the ATP level stable. They are like an "energy transfer station" that quickly replenishes energy at critical moments (Saks et al., 1978; Jacobus, 1985; Greenhaff, 2001). There is also a "phosphocreatine shuttle" mechanism in the CK/PCr system, which transports energy from mitochondria to where energy is really needed, such as myofibrils in muscle cells (Saks et al., 1978; Tachikawa et al., 2004; Hettling et al., 2010). This mechanism is particularly suitable for tissues that use energy quickly, ensuring a continuous supply of ATP and avoiding energy deficiency during intense exercise (Saks et al., 1978; Greenhaff, 2001; Bonilla et al., 2021a).

The focus of this research is to understand how the phosphocreatine system stores and releases energy in cells. We want to look at the roles of creatine, PCr, and CK in different tissues to gain a more complete understanding of how they help cells maintain energy balance. This article will also analyze the performance of the CK/PCr system in energy buffering, transportation, and rapid supply, and explore its role in health and disease. We hope that these studies will show that adjusting creatine metabolism may be a potential treatment for energy metabolism disorders.

2 Biochemical Basis of the Creatine Phosphate System

2.1 Structure and function of creatine and phosphocreatine

Creatine (Cr) is a small molecule that the body can synthesize by itself, mainly in the liver, kidneys and pancreas. It relies on a special transporter protein to enter the cell, which requires sodium and chloride to work, called creatine transporter (CRT) (Bonilla et al., 2021a). Once creatine enters the cell, it will be converted into creatine phosphate (Phosphocreatine, PCr) under the action of creatine kinase (CK). This process is reversible, that is, it can be converted back and forth. This conversion is very useful for cells to maintain energy stability, especially those tissues with high energy consumption and rapid changes, such as skeletal muscle, heart, neurons and photoreceptor cells of the eye (Wallimann et al., 1998; Wallimann et al., 2011). PCr is like a "small energy warehouse". When the cell suddenly needs a lot of energy, it can immediately help ADP regenerate ATP. This is particularly important for muscle cells, because PCr helps keep ATP from dropping when muscle contraction begins (Greenhaff, 2001). In addition, the CK/PCr system can also transfer energy from mitochondria (where ATP is produced) to places such as myofibrils where ATP is actually consumed, a process called "phosphocreatine shuttling" (Greenhaff, 2001; Wallimann et al., 2011).

2.2 Enzymatic mechanisms of creatine kinase in ATP regeneration

Creatine kinase (CK) catalyzes an important reaction: it transfers a phosphorus group from ATP to creatine, thus generating ADP and PCr. This reaction is reversible, and for cells with particularly active energy metabolism, this process helps maintain ATP levels. There are several different types of CK. Some of them are found in the cytoplasm (such as MM-CK, MB-CK, BB-CK), while others are found in the mitochondria (Mi-CK). These different forms are cleverly distributed throughout the cell, helping to transfer energy from where it is generated to where it is used (Wallimann et al., 1998; McLeish and Kenyon, 2005). CK works in a linear manner, that is, it transfers the phosphorus group from ATP to creatine step by step. Its active site helps this reaction proceed smoothly. Researchers have seen the intermediate state of this reaction through methods such as X-ray crystallography, which also verifies some of the speculations from previous kinetic and mutation experiments (McLeish and Kenyon, 2005). In mitochondria, CK is often close to a transporter protein called ANT. This position is very critical because it allows the generation of ATP and the synthesis of PCr to be directly connected, thereby helping the cell buffer energy changes and maintain ATP levels in the cytoplasm (Jacobus, 1985; Guzun et al., 2011).

2.3 Comparison of creatine phosphate with other energy storage systems

The creatine phosphate system has a great advantage that it can regenerate ATP very quickly. This feature is particularly important for tissues that often require a large amount of energy suddenly, such as muscles during exercise. In contrast, energy storage methods such as glycogen or fat can provide more energy, but the release rate is not as fast (Greenhaff, 2001; Wallimann et al., 2011). Glycogen can provide energy continuously, but it is relatively slow to mobilize. To generate ATP from glycogen, many steps are required. Glycogen must first be converted into glucose-6-phosphate and then further produce ATP, which is not timely enough for the sudden increase in energy demand in a short period of time (Greenhaff, 2001). Similarly, triglycerides in adipose tissue can provide energy for a long time, but they also need to be lipolyzed and β-oxidized, which is a relatively slow process. This makes it not respond quickly enough when high-intensity and rapid energy use is required (Wallimann et al., 2011).

3 Molecular Mechanisms of Creatine Phosphate in Energy Storage and Release

3.1 Steps involved in phosphocreatine synthesis and breakdown

The generation and decomposition of creatine phosphate (PCr) is an important step in cellular energy management. First, creatine (Cr) is transported into the cell through a sodium/chloride-dependent transporter (CRT) (Bonilla et al., 2021a) (Figure 1). After creatine enters the cell, creatine kinase (CK) helps it get a phosphate group from ATP, thus turning it into PCr and generating ADP at the same time. This reaction is reversible, in other words, PCr can also turn back into creatine and release ATP. This process is particularly critical in tissues such as muscles and

brain because these places have a particularly high demand for energy (Kazak and Cohen, 2020; Bonilla et al., 2021a). When the body needs energy, CK will react in the opposite direction, breaking down PCr and releasing ATP at the same time. This ATP is then used for various cellular activities.

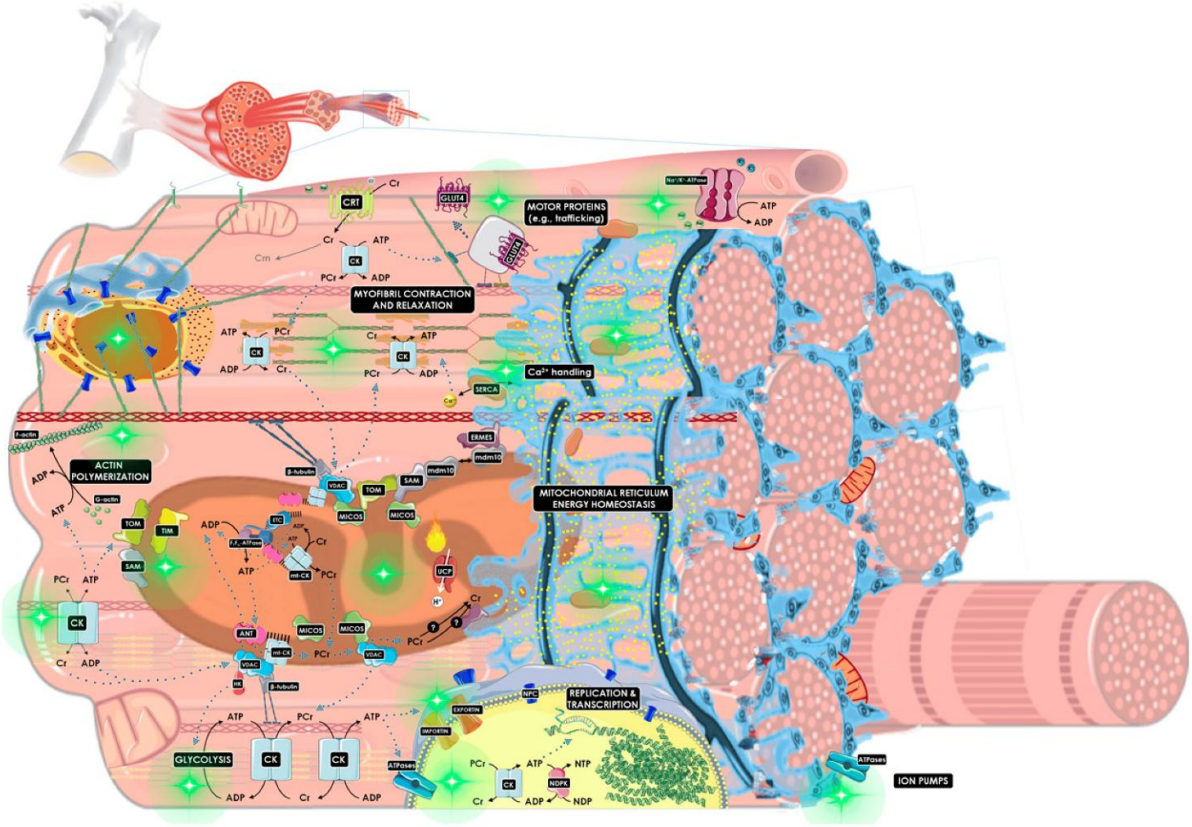

Figure 1 General overview of the CK/PCr system (Adopted from Bonilla et al., 2021a)

Image caption: This diagram illustrates the integrated subcellular network of energy production and mechanical processes in creatine (Cr) metabolism, highlighting the chemo-mechanical energy transduction system. Key components include the mitochondrial reticulum (involving oxidative metabolism and the mitochondrial interactosome), the phosphagen and glycolytic systems for ATP production, the linker of nucleoskeleton and cytoskeleton (LINC) complex interacting with nesprins, microtubules, actin polymerization, and β-tubulin, as well as motor proteins and ion pumps like SERCA and Na^+/K^+-ATPase for Ca^{2+} regulation. Green sparkles mark areas where the creatine kinase/phosphocreatine (CK/PCr) system is essential for functionality. To simplify visualization, detailed structures such as ER-mitochondria networks, TIM/TOM complexes, and cytoskeletal architecture are omitted. This representation underscores the interdependence of these systems in maintaining cellular energy and mechanical functions. CK: Creatine kinase; PCr: Phosphocreatine; SERCA: Sarco/Endoplasmic Reticulum Ca^{2+} ATPase; TIM/TOM: Translocases of the inner/outer mitochondrial membranes; VDAC: Voltage-dependent anion channel Source: designed by the authors (D.A.B.) using figure templates developed by Servier Medical Art (Les Laboratoires Servier, Suresnes, France), licensed under a Creative Common Attribution 3.0 Generic License. http://smart.servier.com/ (accessed on 14 January 2021) (Adapted from Bonilla et al., 2021a)

3.2 Role of mitochondria and cytosolic enzymes in creatine phosphate pathways

The enzymes in mitochondria and cytoplasm also play a key role in the phosphocreatine system. Creatine kinase (MtCK) in mitochondria is located in the gap of the mitochondrial membrane. It uses ATP produced by mitochondria to synthesize PCr. The synthesized PCr can diffuse into the cytoplasm, and then CK in the cytoplasm uses it to synthesize ATP from ADP. This method is like an energy transfer station, which can quickly provide ATP buffer (Kazak and Spiegelman, 2020; Wallimann et al., 2020). This "shuttle system" ensures that the ATP produced by mitochondria can be effectively delivered to where the cell needs energy (Franco et al., 2021; Sun et al., 2021). In addition, mitochondria can form a network, so that energy can be transmitted farther without too much diffusion of metabolites, making the entire PCr system work more efficiently (Kazak and Cohen, 2020; Franco et al., 2021).

3.3 Regulatory mechanisms at the molecular level

The operation of the creatine phosphate system is also regulated by some molecular mechanisms. The activity of CK is affected by several factors, such as the amount of ATP and creatine, as well as the current energy state of the cell (Bonilla et al., 2021a; 2021b). In thermogenic adipocytes, there is a special regulation method, which is the decomposition of PCr by an enzyme called TNAP. This reaction will start a repeated "dephosphorylation and rephosphorylation" process, thereby activating thermogenic respiratory activity (Sun et al., 2021). Different types of CK enzymes appear in different locations in the cell. This distribution helps energy to be effectively used and transmitted locally (Puurand et al., 2018; Branovets et al., 2020). This "spatial arrangement" allows cells to distribute energy more reasonably according to the needs of different regions.

4 Physiological Functions of the Creatine Phosphate System

4.1 Role in muscle contraction and athletic performance

The phosphocreatine system is important for muscle movement, especially when fast and large amounts of energy are needed. For example, in high-intensity, short-duration exercises such as sprinting or weightlifting, the body's demand for ATP exceeds the rate at which the aerobic system can provide it. At this time, phosphocreatine (PCr) in the muscle will immediately give a phosphate group to ADP to quickly generate ATP. This can help the muscle continue to contract and delay fatigue (Stockebrand et al., 2018; Hao et al., 2021; Vulturar et al., 2021). Vulturar et al. (2021) found through research that creatine supplementation can increase the reserves of PCr in the muscle. This not only helps increase lean body mass, but also improves anaerobic and aerobic exercise performance.

4.2 Functions in the brain, heart, and other high-energy-demand organs

Not only muscles, but also organs such as the brain and heart cannot do without the creatine phosphate system. Creatine in the brain is important for maintaining normal thinking and nerve cell development. If the brain lacks creatine, intellectual problems and behavioral abnormalities may occur (Stockebrand et al., 2018; Balestrino and Adriano, 2019; Bonilla et al., 2021a). In the heart, the PCr system mainly maintains ATP stability and can also play a protective role when the heart is ischemic (Hao et al., 2021; Farr et al., 2022) (Figure 2). Creatine also plays a role in adipose tissue, regulating thermogenesis and energy consumption (Kazak and Cohen, 2020).

4.3 Adaptations in different types of muscle fibers and tissues

Because different types of muscles use different amounts of energy, the PCr system will adjust accordingly. Fast-twitch muscle fibers (those with strong explosive power) contain more creatine phosphate than slow-twitch muscle fibers (responsible for endurance activities) (Stockebrand et al., 2018; Vulturar et al., 2021). This shows that creatine is very important for muscle health. If muscles lack creatine transporter (CT1), their PCr levels will decrease, and muscles may become weak or even atrophy (Stockebrand et al., 2018). The creatine system will also adjust with changes in physiological state. For example, with age, changes in creatine kinase activity and PCr levels will affect muscle function and energy metabolism (Mosher et al., 2022).

4.4 Therapeutic potential and clinical applications

Creatine is not just a sports supplement, it also shows potential in the treatment of some diseases. Studies have found that creatine supplementation may be helpful for muscular dystrophy, muscle problems caused by statins, and even refractory depression. For vegetarians and vegans, because they do not consume creatine in their diet, their muscle creatine levels will be low. Creatine supplementation can improve their muscle state and psychological performance (Balestrino and Adriano, 2019). The role of creatine in cancer is also being studied. It may affect the survival of cancer cells and may also regulate the immune system (Kazak and Cohen, 2020).

5 Pathophysiological Implications

5.1 Alterations in creatine metabolism in muscle disorders

People with muscle diseases, such as muscular dystrophy and myopathy, often experience significant changes in creatine metabolism. Normally, creatine helps muscle cells store and regulate energy and maintain ATP levels. But when people develop muscle diseases, problems arise in the energy system of muscle cells. A study by Balestrino

and Adriano (2019) found that creatine supplementation can increase muscle strength and improve overall health. If the body lacks creatine transporters, creatine cannot enter muscle cells, causing muscles to become weaker, lose strength, and even atrophy (Stockebrand et al., 2018; Duran-Trio et al., 2021) (Figure 3).

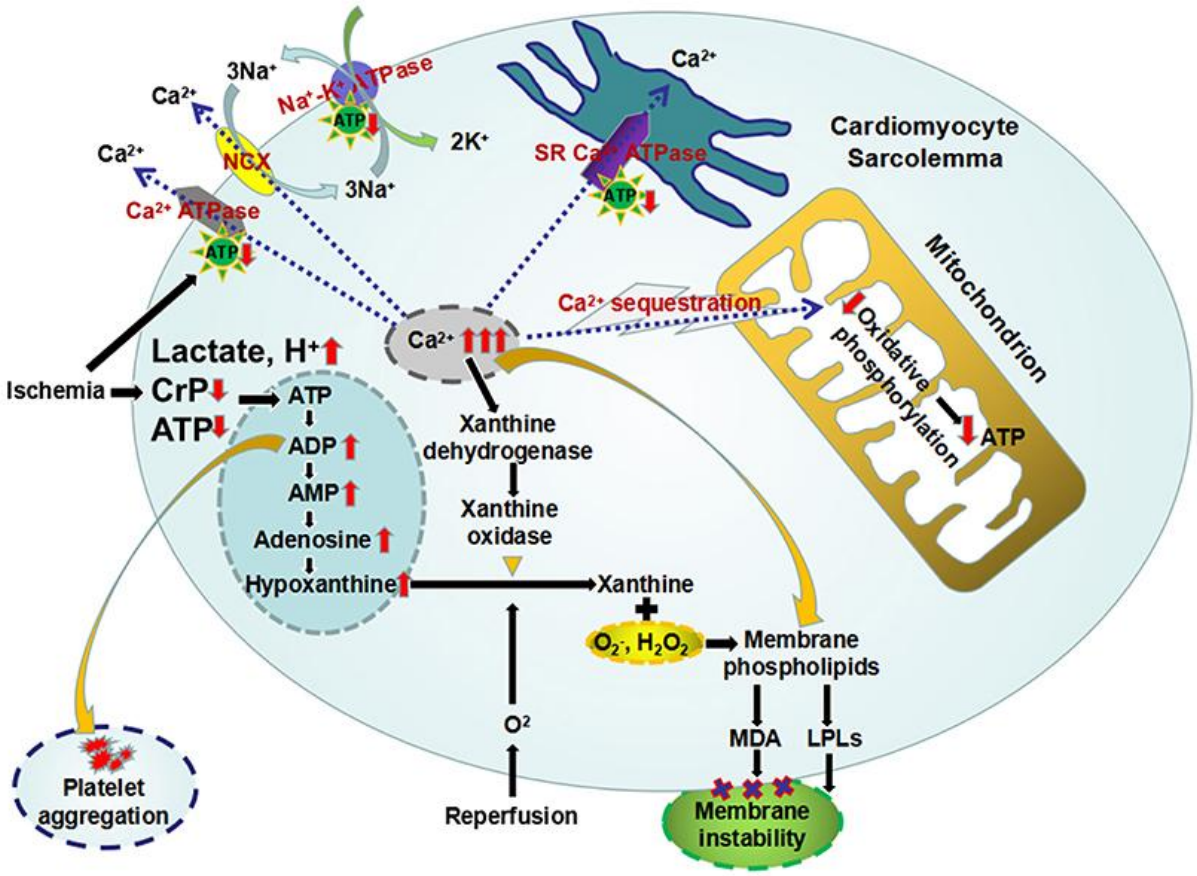

Figure 2 The primary metabolic changes and the secondary celluar injuries during myocardial ischemia/reperfusion (Adopted from Hao et al., 2021)

Image caption: The ischemic myocardium primarily utilizes creatine phosphate (CrP) as an energy source, followed by ATP, ADP, and AMP. The breakdown of AMP into adenosine and hypoxanthine reduces the adenine nucleotide pool, while glycolysis-induced lactate accumulation causes intracellular acidosis. Loss of high-energy phosphates (HEPs) disrupts calcium homeostasis, leading to intracellular Ca^{2+} overload. This overload impairs mitochondrial oxidative phosphorylation due to excessive Ca^{2+} sequestration. The activation of xanthine oxidase generates oxygen free radicals, oxidizing membrane phospholipids and producing malondialdehyde (MDA), contributing to membrane instability. Additionally, the accumulation of metabolic intermediates such as AMP, lactic acid, Ca^{2+}, and H^+ activates phospholipases, degrading membrane lipids into lysophospholipids (LPLs), further destabilizing the membrane. Increased ADP levels also promote platelet aggregation. ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; CrP, creatine phosphate; HEPs, high-energy phosphates; LPLs, lysophospholipids; MDA, malondialdehyde (Adapted from Hao et al., 2021)

5.2 Creatine phosphate deficiency syndromes and their impact on energy homeostasis

Some people suffer from creatine phosphodeficiency syndrome due to mutations in the creatine transporter (CT1). This disease causes the body's energy regulation system to be out of balance. In the muscles of these patients, PCr and ATP levels are significantly reduced, resulting in muscle weakness and even atrophy (Stockebrand et al., 2018; Duran-Trio et al., 2021). The body will try to compensate, such as increasing the expression of enzymes related to creatine synthesis. But these compensation methods are usually not enough to restore energy levels to normal. And the problem is not just in the muscles. The metabolism of the entire body is also affected, such as changes in glucose metabolism and activation of AMPK (an energy-sensing enzyme) (Stockebrand et al., 2018).

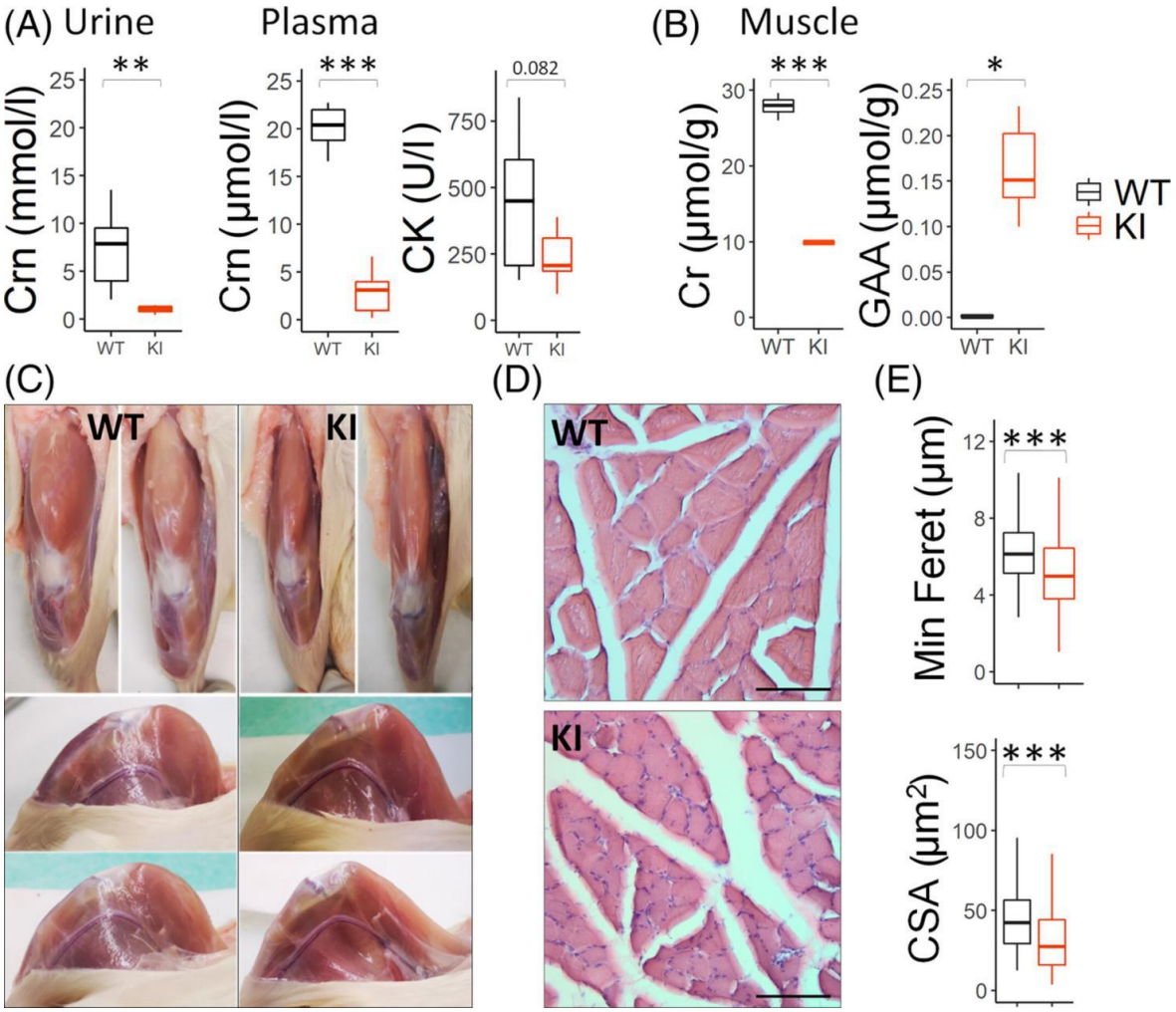

Figure 3 *Slc6a8x*$^{Y389C/y}$ KI males present reduced muscular mass and smaller myocytes (Adopted from Duran-Trio et al., 2021)

Image caption: A, Urinary Crn (left panel) as well as plasmatic Crn and total CK levels (middle and right panel, respectively) as indicative of the muscular mass. Six WT and six KI: two-tailed t test. B, Significant decrease of Cr ([µmol/g tissue], two-tailed t test) and significant increase of GAA levels in muscle ([µmol/g tissue], Mann-Whitney test) in KI male rats, five WT and five KI. C, Representative macroscopic pictures of WT and KI male hind limbs in frontal/longitudinal (upper panels) and medial/inner lateral views (lower panels) showing reduced volume of quadriceps in KI male rats. D, Representative microscopic pictures of hematoxylin/eosin staining in transversal sections of WT and KI male quadriceps showing significant smaller myocyte diameter in KI males. Scale bar = 15 µm. E, Quantifications of myocyte minimum Feret diameter and cross-sectional area per each genotype. Mann-Whitney test, three WT, and three KI (319-382 measurements per WT and 414-555 per KI male). Statistical analysis was conducted with R-3.5.1. (R Core Team, 2018) Graphs were done using ggplot2 package. (Wickham, 2016) Cr, Creatine; Crn, creatinine; GAA, guanidinoacetate; KI, knock-in; WT, wild type. *P < .05; **P < .01; ***P < 0.001 (Adopted from Duran-Trio et al., 2021)

5.3 Implications in neurodegenerative diseases

Creatine metabolism not only affects muscles, it is also important for the brain. Because the brain also requires a lot of energy, once the creatine system has problems, neurological function may also be impaired. If the creatine transporter is missing, it may cause intellectual problems, abnormal behavior, and even motor coordination disorders (Stockebrand et al., 2018; Duran-Trio et al., 2021). Some studies have also found that creatine may have a protective effect on nerves. It helps maintain cellular energy balance and reduces oxidative stress, potentially slowing the progression of neurodegenerative diseases (Balestrino and Adriano, 2019; Bonilla et al., 2021a). Currently, scientists are continuing to study the therapeutic effects of creatine supplementation on neuropathies. Research by Balestrino and Adriano (2019) showed that creatine supplementation may be helpful for diseases such as Huntington's disease and Parkinson's disease.

6 Creatine Supplementation: Applications and Mechanisms

6.1 Effects of creatine supplementation on muscle performance and recovery

There have been many studies looking at the effects of creatine supplementation on exercise performance and recovery. Creatine supplementation can significantly increase muscle strength, power, and lean body mass, especially during short, high-intensity training (Balestrino and Adriano, 2019; Kazak and Cohen, 2020). This is because creatine can quickly help cells regenerate ATP, which is the main energy source for cells. This ability to quickly replenish energy is critical during intense exercise (Kazak and Cohen, 2020). Creatine supplementation can also reduce muscle damage and inflammation and speed up recovery after exercise, a process related to the activity of satellite cells. Creatine can stimulate the activation and proliferation of these cells, which play an important role in repairing and growing muscles (Vulturar et al., 2021).

6.2 Mechanistic insights into how supplementation impacts cellular energy levels

From a cellular perspective, creatine supplementation can enhance the capacity of the PCr system, allowing cells to replenish ATP more quickly when they need a lot of energy (Bonilla et al., 2021a; 2021b). When creatine enters the cell through the Na^+/Cl−-dependent creatine transporter (CRT), it is converted into phosphocreatine (PCr) by creatine kinase (CK) (Bonilla et al., 2021a). PCr transfers a phosphate group to ADP and then regenerates ATP, a mechanism that helps cells maintain energy stability during exercise (Bonilla et al., 2021a; 2021b). Creatine also affects some intracellular pathways (such as those related to oxidative stress and inflammation), which can further improve the overall metabolic function and energy level of the cell (Clarke et al., 2020; Bonilla et al., 2021b).

6.3 Potential therapeutic roles in neurodegenerative and muscle diseases

Creatine not only helps with athletic performance, but can also help treat related diseases. In muscular dystrophy and inflammatory myopathy, creatine supplementation can improve patients' muscle strength and health (Balestrino and Adriano, 2019; Vulturar et al., 2021). Balestrino and Adriano (2019) also found that creatine is also very useful in preventing and treating statin-related myopathy, and it also has a certain effect on refractory depression in some female patients (Balestrino and Adriano, 2019). In neurodegenerative diseases, creatine works in two ways: one is to help cells increase energy, and the other is to reduce oxidative stress (Clarke et al., 2020; Kreider and Stout, 2021). Creatine can increase the creatine content in the brain and improve cognitive ability and memory in the elderly (Prokopidis et al., 2022). Creatine also affects the immune system and has anti-inflammatory effects (Clarke et al., 2020; Kazak and Cohen, 2020).

7 Advances in Research Techniques for Studying Creatine Phosphate Metabolism

7.1 Imaging and molecular methods for tracking creatine phosphate levels

In recent years, there have been many advances in imaging technology, especially magnetic resonance spectroscopy (MRS). This technology makes it easier for us to track phosphocreatine (PCr) levels in the body. The advantage of MRS is that it can detect creatine (Cr) and PCr in living tissue without surgery. This allows us to see how the creatine kinase (CK) system changes in the body. Specifically, 1H MRS can measure the concentration of Cr and PCr, while 31P MRS can also estimate the reaction rate of CK, so that we can see if there is any problem with the entire Cr/PCr/CK system (Račkayová et al., 2017). These technologies are very helpful in our understanding of the role of creatine in the brain, especially when studying creatine deficiency, they can provide important information.

7.2 Emerging genetic and biochemical tools in creatine-related research

Now, people who study creatine metabolism have more tools in their hands. For example, genetic engineering and new biochemical methods have made the research more detailed. These tools allow scientists to study how creatine works not only in muscle and brain, but also in other tissues, such as adipose tissue, the immune system, and cancer cells (Kazak and Cohen, 2020). Some genetic tools have found that creatine is also involved in regulating thermogenesis and even affects the survival of cancer cells. Researchers are also using bioinformatics methods to combine various data from public databases. These reviews can help everyone understand the overall situation of creatine metabolism, especially in the study of cellular energy metabolism and the distribution of the CK/PCr system (Bonilla et al., 2021a).

7.3 Recent breakthroughs in understanding the creatine phosphate system

Recent studies have brought many new discoveries. The creatine phosphate system not only has an energy storage function, but also helps cells maintain balance and protect cells. The CK/PCr system is like an "energy sensor" and plays an important role in the survival, growth and movement of cells (Bonilla et al., 2021a). Tachikawa et al. (2004) found in their research that the distribution of creatine synthase and CK in the brain is very special. They are expressed differently in different types of cells. There may be an energy cooperation relationship between glial cells and neurons. After glial cells synthesize creatine, they may transport it to neurons for use. Creatine is not only active in normal physiological processes, but also plays a certain therapeutic role in diseases such as ischemia or inflammation (Kitzenberg et al., 2016).

8 Future Perspectives and Potential Research Directions

8.1 Unresolved questions regarding molecular regulation and system integration

Although much progress has been made in the study and understanding of the phosphocreatine (PCr) system, there are still many questions that need to be answered. One of the important questions is how creatine transport is regulated and how it cooperates with the cell's energy system. Current research results have not yet involved the specific process of how creatine transporter (CRT-1) works with substrates and ions in different body states, and how creatine transporter maintains creatine concentration in cells (Farr et al., 2022). The specific distribution of creatine kinase (CK) and PCr in cells, as well as their respective roles in cellular energy regulation, also require researchers to conduct more research (Puurand et al., 2018; Bonilla et al., 2021a). Another question is: In addition to creatine kinase, are there other proteins involved in PCr metabolism? For this question, there are only some indirect clues (Kazak and Spiegelman, 2020). If we can understand these mechanisms, we can further understand why various diseases occur when creatine metabolism goes wrong (Kazak and Cohen, 2020; Bonilla et al., 2021a).

8.2 Prospects of creatine-based therapies and enhancement of energy systems

Current studies have shown that creatine supplementation may help many health problems, such as improving the energy system, alleviating neurodegenerative diseases, metabolic abnormalities, and even cardiovascular diseases (Clarke et al., 2020). The mechanism of how creatine exerts these effects is not fully understood. Future studies need to focus on the relationship between dose and effect, and further explore the molecular pathways through which it works, such as whether certain kinases or ubiquitin-related mechanisms are involved (Bonilla et al., 2021b). Whether creatine can improve vascular function and whether it has antioxidant or anti-inflammatory effects are also worth further study (Clarke et al., 2020). These issues need to be verified through high-quality clinical studies. In particular, more large-scale multicenter randomized controlled trials (RCTs) are needed to determine whether creatine treatment is really effective and safe in the long term (Hao et al., 2021).

8.3 Integration of creatine phosphate metabolism with other metabolic pathways

The relationship between creatine phosphate and other metabolic pathways is a promising research direction. It is not clear how the CK/PCr system interacts with oxidative phosphorylation (OXPHOS) in cells, and how they work together to help cells maintain energy balance in different tissues (Puurand et al., 2018). Whether creatine affects thermogenic respiration and overall energy expenditure in adipose tissue is also a topic that needs further study (Kazak and Cohen, 2020; Kazak and Spiegelman, 2020). Whether there is a connection between creatine metabolism and glucose metabolism is also a question worthy of attention. Some studies have found that in creatine transporter-deficient models, the expression of glucose transporters has changed, and even the efficiency of glucose clearance has increased (Stockebrand et al., 2018). Understanding these mechanisms will be of great help in finding new ways to treat metabolic diseases and energy-related diseases in the future.

9 Conclusion

The creatine phosphate system is an important mechanism for maintaining cellular energy balance, especially in high-energy-consuming tissues such as muscles and the brain. Creatine kinase (CK) can catalyze the reversible reaction between creatine and ATP to generate creatine phosphate (PCr) and ADP. PCr is like an "energy backup

battery" in the cell, which can quickly provide ATP in a short period of time. This mechanism allows muscles to quickly obtain energy during contraction, and can also support the continuous operation of tissues such as the brain. Different types of CK are distributed in different areas of the cell, making energy transfer more accurate and efficient. In addition, the creatine phosphate system can also participate in cell signaling and play a protective role during oxidative stress.

The creatine phosphate system plays an important role not only in muscles, but also in other tissues. In the brain, the special distribution of creatine synthase and CK supports energy cooperation between neurons and glial cells and maintains the stability of neural activity. In adipose tissue, creatine is involved in regulating thermogenic respiration and affects the body's overall energy consumption. These findings also suggest that creatine may play a positive role in regulating obesity. Current studies have shown that creatine supplementation can improve muscle diseases, ischemic injuries, and neurodegenerative diseases by not only improving ATP stability, but also speeding up recovery and reducing oxidative damage.

Future research will further expand our understanding of the creatine phosphate system, especially its role in non-muscle tissues, such as the brain and adipose tissue, which may have some new physiological functions. With the development of genetic engineering and bioinformatics technology, the molecular mechanism of creatine metabolism may be revealed more clearly. We are expected to gain a deeper understanding of its disorder process in various diseases and develop more targeted treatment strategies. In general, the creatine phosphate system is not only a basic component of cellular energy, but also may provide new solutions for a variety of energy-related diseases such as metabolic diseases and neurological diseases.

Acknowledgments

As we complete this thesis, the authors would like to express our deepest gratitude to Ms. Cherry Xuan.

Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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