Protein Kinase PKA pathways regulate autophagy in result to nutrient starvation in fission yeast

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Abstract

Autophagy plays a crucial role in differentiation and is an evolutionarily conserved process that degrades cellular organelles and antigens. All *Saccharomyces* mutants missing Atg proteins reduce survivability at nitrogen destitution, with eighty percent losing their viability after five days of deprivation, and consequently are incapable of grow. Both of the PKA and TOR pathways have been associated in regulation of autophagy. *S. pombe* has been engaged as an innovative classical organism to research autophagy in recent years. It reproduces asexually via the mitotic cell phase in the existence of nutrients. Nitrogen deficiency causes cell cycle capture in G1, and cells suffer sexual variation and meiosis, resulting in four resistant haploid spores that continue inactive up to they meet fortunate development situations. In *S. pombe,* cyclic AMP likewise acting an imperative character in the parameter of cellular development and sexual improvement. The ste11 gene in fission yeast encodes an HMG transcription factor, which is accountable for the manifestation of several genes mandatory for sexual growth to begin. Several nutrient-sensing pathways regulate autophagy, particularly after it has been established that

certain types of nutritional deficiencies can activate autophagy in *S. pombe*. The pathways of Pka has been discussed in the article. Different paralogs of PKA and TORC1 for *S. cerevisiae* was found but not in *S. pombe*. Three paralogs for ssu1 gene was found in S. pombe. It is concluded that, different genes are included in the regulation of Pka pathways as well as cgs1, cgs2, pka1, Rst2, Ste11 and Atf1. These results in the process of autophagy in *S. pombe*.

Keywords: Protein kinase pathways, *Schizosaccharomyces pombe*, Cell cycle, Yeast, Genes

Introduction

Macro autophagy as also known as autophagy, plays a key role in differentiation and is an evolutionarily conserved process that degrades cellular organelles and antigens. It must be done to alter membrane for the purpose to form compartments that encapsulate the cytoplasmic lumens maintaining the organelles/proteins to be diminished: The auto phagosome is a type of phagosome. Its outermost membrane is going to combine with lysosomes (in yeast and plants) to generate autophagy bulks, which are going to be emitted and wiped out by these divisions' protein proteases (1). Considering the yeast *Saccharomyces cerevisiae (S. cerevisiae)* as an exemplary structure, an assortment of genes known as ATG that are involved in autophagy have been identified. All saccharomyces mutants missing ATG proteins reduce survivability at nitrogen destitution, with eighty percent losing their viability after five days of deprivation, and consequently are incapable of grow. Both of the PKA and the TOR pathways have been associated in regulating the activity of autophagy in *S. cerevisiae* through food deprivation (2, 3). In terms of autophagy's biological roles, errors in this method are visibly connected to ageing and illness (4). When environmental supplies are limited, this route induces organelle destruction, and autophagy degradation may break down proteins into amino acids for usage in future protein synthesis pathways.

Schizosaccharomyces pombe has been engaged as an innovative model organism to research autophagy in recent years. This mechanism was first investigated in fission yeast by characterizing vacuolar functions, especially recognizing and analysis of vacuolar proteases (5-7). (8) revealed that autophagy is essential during nitrogen deficiency for providing adequate nitrogen inside the cell, justifying the mutants' mating irregularities. Cells, in general, exit their normal developmental cycle during lack of nutrition to explore different routes, such as sexual variation in fission yeast. Nitrogen deficiency, in specific, origins a G1 arrest and starts sexual differentiating themselves, while breakdown of proteins linked to autophagy process also takes place. It had been critical for

demonstrating that, regardless of having demonstrated that the autophagy process supports sexual variation, thereby ATG the mutants are not uncontaminated inspite of the existence of the nitrogen (8). As a result, the primary function of autophagy is to deliver nitrogen in absence from outside resources. Moreover, Takanawa's group demonstrated that some ATG mutations' pairing up imperfections are unfinished indicating that the fission yeast has the capacity of storing a sufficient amount of either intracellular nutrients pool to permit limited the sporulation process under nitrogen-limiting conditions even in an lack of autophagy, thereby offering almost all of the supply of nitrogen for the manufacture of proteins during sporulation (4).

TOR and PKA are two conspicuous, evolutionarily preserved signal transduction pathways that link the availability of nitrogen and carbon sources to control various cell responses that eventually start cell growth and propagation while inhibiting sexual differentiation (5). In *S. pombe*, cyclic AMP also play role in sexual development. The level of cAMP in several organisms varies according to environmental conditions. PKA is a serine protein kinase that reacts to glucose and is involved in biological procedures, as well as cells growth, and physiological stress responses (6). During cell growth and division, the intracellular level of cAMP is retained in elevation in fission yeast. Unfavorable growth conditions result in PKA down-regulation, cell phase exit. The *pombe* cells lacking cgs1, the gene encoding the regulatory subunit of cAMP-dependent protein kinase, generate dynamic PKA and mate and sporulate infrequently (7). In comparison, cells lacking the cyr1 gene, which codes for adenyl cyclase, or pka1 gene, which codes for the catalytic subunit of PKA, eagerly pledge sexual development in rich medium (13). This reaction is monitored by significant change in genes expression, showing that PKA is likely to regulate several transcription factors directly or indirectly. It regulates various cells regulatory paths in eukaryotes, such as signal transduction webs that govern cells growth and variation, cell phase regulation, cytoskeletal dynamics, metabolism, and physiological stress reactions (8). The PKA holoenzyme is a collection of two controlling subunits that are highly bound to 2 catalytic subunits when it is in its inactive state (11). At what time cyclic AMP binds to the PKA controlling subunits, the catalytic subunits separate from the regulatory subunits and become catalytically active monomers. PKA purpose has been demonstrated to be regulated by connections with multiple additional controlling factors in addition to its cAMP-binding regulatory subunits (9). PKA subcellular localization has been demonstrated to be regulated in mammalian cells through relations between PKA regulatory subunits and A-kinase fixing proteins (11, 17). *S. cerevisiae,* a budding yeast without AKAP or

AKIP homologs, regulates the localization of the PKA controlling subunit in part through interactions with the protein Zds1. Additionally, it has been demonstrated that, at least in certain organisms, phosphorylation and other post-translational alterations control PKA (18). For instance, it has been demonstrated that constitutive phosphorylation of a preserved threonine residue in the activation circle of the PKA catalytic subunit occurs in mammals and in *S. pombe* by phosphoinositide-dependent protein kinases (10). In *S. pombe,* the genes cgs1 and pka1 encode the PKA controlling and catalytic subunits, respectively (20). Moreover, this organism harbor's a single gene that codes for adenylate cyclase, cyr1 (also known as git2) (21). Like other eukaryotes, *S. pombe's* PKA regulates a variety of functions, such as osmoadaptation, sexual differentiation, cell cycle regulation, and nutrient sensing (11).

Moreover, it has been demonstrated that a variety of physiological stresses, such as oxidative, hyperosmotic, and dense metal pressures, can transcriptionally activate the pka1 gene. As a result, it has been categorized in *S. pombe* as a core environmental pressure reaction gene (23). They recently demonstrated that the nuclear-cytoplasmic scattering of the PKA catalytic and regulatory subunits, correspondingly, was achieved by means of analysis of functional Pka1-GFP and Cgs1-GFP fusion proteins, is controlled in *S. pombe* in response to a number of physiological stressors, such as nutrient and hyperosmotic stresses (24). In contrast to the condition in the evolutionarily detached yeast *S. cerevisiae*, neither PKA nor cAMP are necessary on behalf of the feasibility of *S. pombe* in standard culturing conditions, despite their involvement in the ruling of numerous cellular processes (12). Because of this feature, *S. pombe* is a desirable model organism for studying PKA regulation mechanisms.

PKa pathway regulation

PKA is a serine or threonine kinase that is conserved in a wide diversity of organisms, including mammals and yeasts. Two catalytic (C) and two regulatory (R) subunits combine to form PKA. C-subunits are released at time cAMP binds to the R-subunit. Both the C- and R-subunits are found in the nucleus of fission yeast and are solitary sporadically found in the cytoplasm when high glucose situations cause the cAMP level to rise. Both subunits are mostly found in cytoplasm of cell grown in non-fermentable carbon source with low levels of cAMP (25). Pka1 is distributed throughout the cytoplasm in the stationary phase of cells lacking in cgs1, but irrespective of culture circumstances, Pka1 is focused in the nucleus in these cells (12).

In mammals, phosphorylation at amino acid residues on an initiation circle activates the inactive form of PKA that is synthesized (27). Mammalian PKA's C-subunit is phosphorylated at 2 preserved AA residues, Ser-338 and Thr-197. Like the Thr-356 residue in fission yeast, the Thr-197 residue is conserved in all recognized mammalian C-subunits. Nevertheless, none of the yeast isozymes have the conserved Ser-338 residue found in the mammalian C-subunits. The Thr-356 residues of fission yeast C-subunit was predicted to be phosphorylated based on its similarity to the mammalian protein, and it is most likely phosphorylated by Ksg1. An unregulated Pka1 phenotype was produced when alanine was substituted for Thr-356 (19), however the ensuing substrate narrowness or catalytic actions were not assessed. When cells are whichever worn-out of cAMP or grown under glucose-limited situations, Pka1 is hyperphosphorylated, likely at residue(s) other than Thr356. Though Cgs1 was exposed to be necessary for this hyperphosphorylation (28), the significance of Pka1 hyperphosphorylation was unclear. They confirmed the involvement of numerous nutrient-sensing cascades in the regulation of autophagy after establishing that any kind of nutritional undernourishment can cause autophagy in *S. pombe*: the PKA pathway. When TORC1 is activated in the presence of nutrients, it phosphorylates members of AGC kinase family: Psk1, Sck1, and Sck2. Psk1 is an RPS6KB1/S6K1 homolog with Rps6 (ribosomal protein S6) as a substrate (13). After a few minutes, the TORC1 complex, Psk1, and Rps6 are dephosphorylated or rendered inactive by Tsc1-Tsc2, which among other things results in translation inhibition (14). The regulatory pathways have been fetched from KEGG pathways (https://www.genome.jp/kegg/) and shown in figure 1.

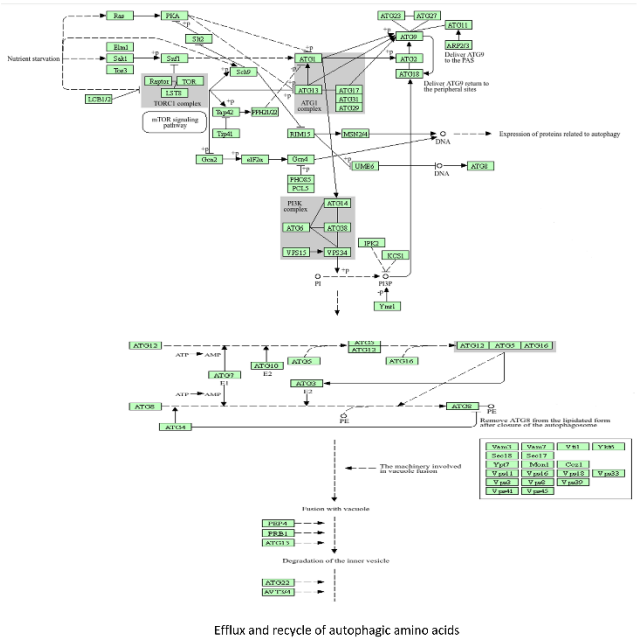

Figure 1: Shows the PKA and TOR pathways regulating autophagy in yeast

Literature study and background

In eukaryotes, macroautophagy/autophagy is a vital adaptive physiological reaction that is brought on by nutrient starvation, including glucose, which serves as the cells' instant carbon and energy source. While much research has been done on the molecular mechanisms in the budding yeast that trigger autophagy during glucose starvation, slight is recognized about the regulation of this managing response in evolutionary distant fission yeast. In contrast to *S. cerevisiae*, we demonstrate here that *S. pombe* autophagy in response to glucose restriction depends on mitochondrial respiration and electron transport chain. However, under these conditions, DNA damage response pathway components and AMP-activated protein kinase do not influence fission yeast autophagic flux. The transcription factor Rst2 is downregulated in the existence of glucose by the cAMP-protein kinase A signaling pathway, which in turn stimulates the expression of respiratory genes necessary for the initiation of autophagy beneath conditions of limited glucose obtainability. Additionally, autophagy is positively modulated by Sty1. This is in response to glucose restriction at the transcriptional level by straight in vivo phosphorylation of Rst2 at S292 and its downstream effector Atf1. Thus, our findings reveal the being of complex and diverse tools that regulate this self-preservation and persistence response and show that the gesturing pathways

that control autophagy during glucose deficiency or starvation have grew inversely in *S. pombe* (15).

In eukaryotes, overall autophagy is a natural process that recycles intracellular materials during times of starvation by moving those materials into and breaking them down inside lysosomes or vacuoles. *Saccharomyces cerevisiae* is the model system used to first characterize the exact roles of Atg proteins in the procedure of autophagy, whose molecular underpinnings have been extensively documented in this organism. Significant advancements have been complete in *S. pombe* that demonstrate the diversity and evolutionary resemblance of Atg components in autophagy. On the other hand, little is understood about the pathways, signals, and function of autophagy in this detached yeast.

They show that autophagy is activated not only via nitrogen but as well by a number of nutritional deprivations such as a shortage of carbon, sulphur, phosphorus, or leucine bases. Additionally, we show that the onset of autophagy is regulated by the TORC1, TORC2, and MAP kinase Sty1 paths. Additionally, they discover a surprising characteristic of autophagy-defective mutants: their incapacity to endure in the nonexistence of leucine after this amino acids biosynthesis is compromised (16). One of the most crucial mechanisms for preserving cell homeostasis is autophagy, which regulates both cell survival and death. It is currently accepted that, liable on the internal and external atmosphere as well as the type of cell, autophagy either stimulates or inhibits cell death. On the other hand, autophagy controls cell survival in a normal nutritional environment by detecting energy through the primary energy kinases. As it controls both cell survival and death, autophagy is one of the most imperative mechanisms for maintaining cell homeostasis. It is acknowledged that autophagy either stimulates or inhibits cell loss, dependent on the type of cell and the internal and exterior environments. Under standard nutritional situations, autophagy regulates cell survival by using the primary energy identifying cascade kinases to detect energy. Moreover, autophagy controls apoptosis by means of epigenetic modifications like histone modifications. There is still more research being done on the connection among autophagy and cell death. The investigation of the connection between autophagy and cell survival and death will face additional difficulties in the future. The connection between autophagy and known and unknown cell death types is expected to grow more intricate as cell death research becomes more prevalent. Further investigation is necessary to clarify the monitoring function of autophagy in cell

survival and death. Certain investigation findings may serve as popular subjects for additional studies on illnesses associated with disorders of cell death and as an investigational foundation for the precise control of autophagy in order to treat particular illnesses (17).

The TOR and PKA gesturing transduction paths control the manifestation of genes necessary for cell growth and sexual variation in the fission yeast in response to nutritional atmosphere. Even in conditions of optimal nutrition, inhibition of Tor2 signaling leads to the instruction of genes elaborate in sexual variation, which causes the cells to go through meiosis. Mutants with an inactive PKA pathway exhibit the same phenotype. In contrast, even in low-nutrition environments, sexual differentiation impaired by Tor2 overexpression that activate PKA signaling. Therefore, deciphering the molecular mechanism by which these two pathways cooperate to control gene manifestation in response to nutrients is a critical question. Here, they show that the nuclear accrual of the Ste11 transcription factor is inhibited by the coordinated action of the TOR and PKA pathways, which negatively adjust sexual differentiation. Under favorable nutritional conditions, however, the Tor2 pathway cannot prevent the nuclear localization of Ste11 when the PKA pathway is dormant. By preventing ste11-dependent gene expression, they were able to determine that both pathways impede sexual differentiation through microarray analyses. They concluded Ste11-dependent gene expression is repressed by both the TOR and PKA pathways, which both block Ste11 nuclear accumulation. Nonetheless, in this process, the PKA pathway is quantitatively additional significant than the TOR path (5). Because cyclic AMP-dependent protein kinase is not required for the fission yeast to survive under typical culturing conditions, this organism is a good choice for studying the mechanisms governing PKA parameter. Now, they demonstrate that *S. pombe* cells with a removal in the adenylate cyclase gene direct PKA1 at significantly higher levels than cells of the wild type. Fascinatingly, a significant amount of Pka1 protein is hyperphosphorylated in cyr1D cells but not in rough type cells. PKA1 hyperphosphorylation is induced by KCl stress, glucose starvation, stationary phase pressures (which are linked to decreased cAMP-dependent PKA activity), and to varying degrees in wild type cells. Interestingly, under all tested conditions, hyperphosphorylation of Pka1 was not observed in also the cyr1+ or cyr1D. *S. pombe* strains carrying a removal in the PKA regulatory subunit gene, cgs1. They showed PKA catalytic subunit phosphorylation has a cAMP-independent mechanism, and may be used to induce or sustain particular PKA functions when the protein's cAMP-dependent activity is downregulated (18).

In *Schizosaccharomyces pombe,* the primary glucose-sensing path that controls sexual distinction is cAMP–PKA. The pka1 locus of recessive sam mutants, whose cells have a strong tendency towards sexual differentiation, was sequenced. This allowed for the identification of mutations in sam5 (pka1-G441E) and sam7 (pka1-G441R). Even in conditions with high glucose, the proteins Rst2 and Ste11 were tempted and found their way to the nucleus of the sam5 and sam7 mutants. suggesting that mutations entirely eliminated Pka1's function. Even in glucose-rich environments, the cytoplasm is home to the Pka1-G441E and Pka1-G441R mutant proteins, whereas the nucleus is home to wild-type Pka1, suggesting that Pka1 functionality is crucial for its nuclear localization. The Pka1-T356A mutant, which is partly devoid of Pka1, was found to be localised in both the cytoplasm and the nucleus. Conversely, in the presence of glucose, the active phosphomimetic Pka1-T356D mutant protein was found to be localised in the nucleus. Pka1 was found to be hyperphosphorylated when it was glucose-starved, in addition to its basal phosphorylation at T356. Mutants carrying the pka1-G441E, pka1-G441R, pka1-T356A, or pka1-T356D all did not exhibit this hyperphosphorylation. The lack of interaction between these mutant proteins and the regulatory subunit Cgs1 led to the assumption that Cgs1 interaction was necessary for the hyperphosphorylation of Pka1 mutant proteins. They observed the construction of a Cgs1–Pka1 complex before Pka1 hyperphosphorylation, which is steady by a role for Cgs1 in Pka1 phosphorylation. This suggested location of Pka1 is nuclear and influenced by its activity and that Pka1 hyperphosphorylation is influenced by the interaction with Cgs1 (19).

Stress on the body is something that every cell experiences. Cells need to adapt to the stressor in order to survive, even though these stresses frequently interfere with normal cellular function. This work employs the *Schizosaccharomyces pombe,* also referred fission yeast, to investigate an original stress responses path involving phospholipase B1 (Plb1) and elements of the cyclic AMP-PKA pathway for adaptation to nutrient scarcity and hyperosmotic stress. According to a prior study, deletion of plb1 results in sensitivity to potassium chloride (KCl), a hyperosmotic stressor. Over-expression of cAMP-PKA pathway components can rescue this phenotype; conversely, removal of these mechanisms causes KCl sensitivity phenotypes. This study demonstrates that increased mitochondrial fragmentation during hyperosmotic stress is correlated with the deletion of these genes. The plb1 mutant's phenotypes were made worse by the addition of rotenone or the loss of mitochondrial PE production, two circumstances that have previously been linked to improved mitochondrial disintegration. In plb1 cells treated with KCl, mitochondrial

disintegration was also attended by an increase in mitophagy. In KCl-treated cells with the deletion of the gene encoding the PKA catalytic subunit pka1, cell cycle arrest in G2/M and cytokinesis were seen. The failure to finish cytokinesis and fragmentation of the mitochondria could be the result of dysregulated PS and PE synthesis and cellular distribution. Apart from their involvement in the hyperosmotic stress response, Plb1 and the cAMPPKA path collaborate to react to a reduction in nutrients. It is well known that the cAMPPKA pathway in yeast is involved in glucose sensing. Phospholipases B (PLBs) have been implicated in nutrient scavenging in previous research; however, fewer studies have looked at the relationship between nutrient content and PLB secretion. According to their study, media with low nutrient levels cause an increase in Plb1 secretion. Plb1 excretion is particularly prejudiced by the amount of glucose present, as high secretion is obtained during incubation in low-glucose media, while low excretion is obtained upon addition of glucose. Given that the cAMP-PKA pathway is in charge of identifying glucose in the media, they anticipated that Plb1 secretion would rise as a result of pka1 deletion. In contrast, a pka1 mutant showed no discernible change in Plb1 secretion. Plb1 protein was found to be elevated in PKa1 cells, and Plb1's localization in these cells was alike to that of glucose-starved cells, indicating a potential collaboration in Plb1 and the cAMP-PKA path in relation to glucose sensing (20).

Paralogs of PKA in *S. cerevisiae* and *S. pombe*

In this study, we identified homologous proteins for PKA and TOR Complex 1 across different yeast strains, which provide insights into their conserved functional roles in cellular processes. The table 1 presents a collection of protein complexes from various yeast strains, including *Saccharomyces cerevisiae*. There was no any paralog for Pka1 in *S. pombe* was seen. This describes a protein from the PKA complex, the Guanine nucleotide-binding protein subunit beta 2 (GPB2), which is composed of 880 amino acids and is associated with multiple functions, such as histone binding, protein tagging, and ligase activity. This protein, encoded by the GPB2, KRH1, and YAL056W genes, plays a role in cellular processes involving gene regulation and protein modification. The functions of PKA includes histone binding, protein tag activity and ligase activity.

The remaining belong to the TORC1 complex, a crucial controller of cell growth in response to nutrient accessibility. These proteins, identified across different yeast strains, share a common

length of about 242-245 amino acids and are encoded by the LST7 gene or related variants. Despite minor differences in strain origin, their primary functions remain consistent, focusing on nutrient reservoir activity, where they help store or regulate cellular nutrients, and translation regulator activity, which involves controlling the synthesis of proteins from mRNA. Strains such as *Saccharomyces cerevisiae* (ATCC 204508, YJM789, RM11-1a) contribute different versions of the LST7 protein, reflecting the functional conservation of these proteins in nutrient management and protein synthesis across various strains. In summary, while the PKA protein GPB2 stands out for its distinct roles in histone binding and ligase activity, the TORC1 proteins exhibit remarkable similarity in their function across different yeast strains, emphasizing their central role in cellular nutrient regulation and protein synthesis. The TORC1 is to act as nutrient reservoir activity and translation regulator activity.

Table 1: Presents a collection of protein complexes from various yeast strains

Sr. no.	Protein complex	Entrance	Entrance name	Protein name	Gene name	Organism *S. cerevisiae* (Baker's yeast)	Length
1.	PKA's	P39717	GPB2_YEAST	Guanine nucleotide-binding protein subunit beta 2[...]	GPB2, KRH1, YAL056W	*Saccharomyces cerevisiae* (strain ATCC 204508 / S288c)	880 AA
2.	TORC1	P53237	LST7_YEAST	Protein LST7[...]	LST7, YGR057C	*Saccharomyces cerevisiae* (strain ATCC 204508 / S288c)	242 AA
3.	TORC1	N1P3V8	N1P3V8_YEASC	Lst7p	CENPK1137D_3024	*Saccharomyces cerevisiae* (strain CEN.PK113-7D)	242 AA
4.	TORC1	A6ZV42	A6ZV42_YEAS7	Lethal with sec13	LST7, SCY_2275	*Saccharomyces cerevisiae* (strain YJM789)	242 AA
5.	TORC1	B3LIG6	B3LIG6_YEAS1	UDENN FLCN/SMCR8-type domain-containing protein	SCRG_00957	*Saccharomyces cerevisiae* (strain RM11-1a)	242 AA
6.	TORC1	B5VJ07	B5VJ07_YEAS6	YGR057Cp-like protein	AWRI1631_72840	*Saccharomyces cerevisiae* (strain AWRI1631)	245 AA

Paralogs of ssu1 in *S. cerevisiae* and *S. Pombe*

There was no any paralog was found in *S. cerevisiae*. There are three paralogs of *S. pombe* ssu1 gene associated with plasma membrane sulfite transmembrane transporters including ssu1, ssu3, and ssu4. Each includes the gene's systematic name and its functional identity as a sulfite transporter located in plasma membrane. The genomic locations of genes are specified on chromosome II, with details on the coding sequence (CDS) range and the sequence including untranslated regions (UTRs). For each gene, the table notes the nucleotide length of the CDS

from the coding start to stop as well as the total nucleotide length, including UTRs. All three paralogs encode proteins consisting of 379 amino acids, with a molecular weight of approximately 43.12 kDa. It was found that *S. pombe* has some of the paralogs (https://www.pombase.org/gene/SPBPB10D8.04c). This can be seen in table 2.

Table 2: The paralogs of *S. pombe*

Sr. no	Species	Paralogs	Name/identity	Genomic location	Protein size (AA)
	S. cerevisiae	Not found			
	S. Pombe				
1		ssu1 (SPBPB10D8.04c)	plasma membrane sulfite transmembrane transporter Ssu1	II, 92863-91724 (1140nt) coding start to stop, 92863-91376 (1488nt) including UTRs	379 aa, 43.12 kDa
2		ssu3 (SPBPB10D8.06c)	plasma membrane sulphite transmembrane transporter Ssu3	II, 98381-97242 (1140nt) coding start to stop, 98381-97242 (1140nt) including UTRs	379 aa, 43.12 kDa
3		ssu4 (SPBPB10D8.07c)	plasma membrane sulphite transmembrane transporter Ssu4	II, 101140-100001 (1140nt) coding start to stop, 101140-99860 (1281nt) including UTRs	379 aa, 43.12 kDa

Conclusion

It is concluded that, PKA is a serine kinase that is conserved in wide diversity of organisms, including mammals and yeasts. Different genes are found in the regulation of Pka pathways comprising cgs1, cgs2, pka1, Rst2, Ste11 and Atf1. These results in autophagy in *S. pombe*. In mammals, phosphorylation at amino acid residues on an initiation coil activates the inactive form of PKA that is synthesized. No any paralog was found in *S. cerevisiae* while several paralogs of *S.*

pombe ssu1 gene were also found that are associated with plasma membrane sulfite transmembrane transporters

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Authors contribution

All authors participated equally for the work.

Conflict of interest

None

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