INTRODUCTION

The aging of cells and tissues refers to the phenomenon of degenerative changes in structure and function, during which the nervous system gradually deteriorates, resulting in behavior disorders and reduced learning and memory ability (Feng et al., 2016; Liu et al., 2016). Increased oxidative stress is an important cause of aging, and the degree of oxidative stress depends on the balance between oxidation and the endogenous antioxidant system (Ding et al., 2011; Tian et al., 2004; Xu et al., 2017); therefore, improving...
the anti-oxidative ability of the body can slow down the aging process. The use of natural products, which contain a large amount of antioxidative substances, to prevent aging and related diseases has attracted increasing attention in modern biological research.

Research regarding fungi as an important source of natural products containing anti-oxidative substances has shown broad developmental prospects. *Agaricus blazei* (*Agaricus blazei* Murill, *Agaricus*) is a large fungus with a strong almond-like flavor that belongs to the *Agaricus campestris* (*Stropharia*) genus, *Agaricaeaceae* (*umbelliferae*), *Agaricales*, *Hymenomycetes*, *Basidiomycotina* (Chang et al., 2011). *Agaricus blazei* is not only a popular food but also a valuable alternative treatment for cancer, infection, and other diseases (Jiang et al., 2018). The fruiting body of *Agaricus blazei* is rich in various substances such as proteins, saccharides, triacylcholins, and flavones possessing a wide range of bioactivities such as anti-tumor, hypoglycemic, anti-inflammatory, and immune-enhancing (Souza et al., 2017; Ren et al., 2018). *Agaricus blazei* protein has a marked anti-oxidative effect and increases the activity of acetylcholinesterase (Venkatesh et al., 2017). *Agaricus blazei* polypeptide (ABp) with biological activity can be obtained by partial hydrolysis of the protein by protease, which has the advantages of being safe and stable, easily water-soluble, and easily absorbed as a small biological polypeptide in comparison with macromolecular proteins. Its anti-oxidative capacity is correlated with its molecular weight, that is, the lower the molecular weight, the better the anti-oxidative ability (Uraga and Salvador, 2018). Our previous work confirmed the scavenging effect of ABp on both DPPH and hydroxyl radicals, displaying a significant in vitro anti-aging effect; however, the underlying mechanism of action requires further investigation (Feng et al., 2020).

In the present study, the extraction of ABp was optimized, a D-galactose (D-gal)-induced mouse model of aging was established, and the anti-aging effect of ABp was investigated in vivo. The differences in gene expression between aging mice prior to and following ABp intervention were analyzed by transcriptomic techniques, and the mechanism underlying the anti-aging effect of ABp was investigated with a view to finding an effective way to delay aging and providing a theoretical basis for the development and utilization of *Agaricus blazei*.

## 2 | MATERIALS AND METHODS

### 2.1 | Materials and instruments

The fruiting body of *Agaricus blazei* (Jiangsu Suwei Microbiology Research Co., Ltd., China) was identified by Associate Professor Handong, College of Pharmacy, Beihua University. Sephadex G-50 (Changzheng Pharmaceutical Factory, China); D-galactose (Sigma-Aldrich, USA); SPF male ICR mice 4–5 weeks old, weighing 20.0 ± 2.0g, license number: SCX (Ji)-20160003 (Changchun Yis Experimental Animal Technology Co., Ltd., China); Active oxygen species (ROS) kit, malondialdehyde (MDA) kit, total antioxidant (T-AOC) kit and catalase (CAT) kit (Nanjing Jiancheng Bioengineering Institute, China); rat monoclonal BrdU antibody, goat anti-rat IgG-Alexa Fluor 594 and goat anti-rabbit IgG-Alexa Fluor 488 (Abcam Company, USA); monoclonal antibody NeuN and HEOCHST 33258 (ABclonal Company, USA); Reverse transcription TUREscript 1st Stand cDNA SYNTHESIS Kit (Adelai, USA). The other reagents were analytically pure.

UV-2550 UV-vis spectrophotometer (Shimadzu International Trade Co., Ltd., Japan); MT-200 Morris water labyrinth analyzer (Chengdu Taimeng Technology Co., Ltd., China); BA-200 mouse darkness avoidance instrument (Chengdu Taimeng Technology Co., Ltd., China); Analytikjena-qTOWER2.2 fluorescence quantitative PCR (ANALYTIKJENA, Germany); Ultra-micro nucleic acid protein tester (ScanDrop, China).

### 2.2 | ABp extraction and purification

The powdered fruiting body (approximately 2,500 g) of *Agaricus blazei* was homogenized in a mixture of 5,000 ml of ice and water. The homogenate was centrifuged at 4,000 rpm for 3 min to obtain the supernatant, from which the soluble protein was precipitated at 4°C overnight using 95% sulfuric acid ([NH₄]₂SO₄). The precipitate was collected by centrifugation, dissolved in deionized water, and dialyzed through a 30-kDa molecular weight cut-off dialysis membrane in deionized water at 4°C for 24 hr. The freeze-dried *Agaricus blazei* powder obtained by dialysis was dissolved 1:20 (g/ml) in distilled water, and the pH of the solution was adjusted to 2.5 using 0.1 mol/L of hydrochloric acid (HCl). Subsequently, 3,000 u/mg pepsin was added, and the solution was mixed and hydrolyzed at 37°C in a thermostatic water bath for 4 hr. The pepsin was considered inactivated after enzymolysis at 100°C for 10 min. The crude polypeptide fraction was extracted following the lyophilization of the solution.

ABp was separated by AKTAPurifier™ 10 protein chromatography. A pretreated DEAE-32 column was installed into a 5-ml Bio-Rad, and 1.5 mM trimethylaminomethane/hydrochloric acid (Tris–HCl) buffer was used to balance the volume (CV) of the three columns at a flow rate of 0.5 ml/min. The crude protein dissolved in Tris–HCl buffer was filtered through a 0.45-µm membrane, loaded onto the column, and continuously eluted with a linear gradient of 0–0.5 M sodium chloride (NaCl). The column effluents at the 220-nm absorption peak were collected using a fraction collector, mixed, and freeze-dried. The same method was used to install and balance the cellulose CM-52 column. The active fraction (DE2) was further loaded onto the CM-52 column, and a linear gradient of 0–0.5 M NaCl was used to elute the three CVs at a flow rate of 0.5 ml/min; the detection wavelength was 220 nm. The CM1 component was lyophilized into powder, dissolved in deionized water, and purified and desalted on a HiTrap™ desalting column (Sephadex G-25). Deionized water was used to elute the 1.5 CV at a flow rate of 1.0 ml/min. The detection wavelength was 220 nm, and finally, a single peak component was obtained and named ABp.
2.3 | Animal grouping and administration

Following acclimation to the laboratory environment, 52 6-week-old male ICR mice were randomly divided into four groups: blank control (Con), model (Mod), piracetam (Pir), and ABp groups, with 13 mice in each group. With the exception of those in the Con group, mice were subcutaneously injected with 300 mg·kg$^{-1}$ D-gal at a fixed time each day. Mice in the Con group were injected with an equal volume of normal saline in the same manner. Subsequently, mice in the Pir group were given 800 mg·kg$^{-1}$ piracetam; those in the ABp group were given 400 mg·kg$^{-1}$ ABp; those in the Con and Mod groups were given an equal volume of distilled water intragastrically once a day for 42 days. The Animal Ethics Committee of Beihua University approved all experiments.

2.4 | Behavioral experiments

The step-through passive avoidance test, known to require hippocampus-dependent learning and dependence on transcription, was carried out 42 days after the administration of the different agents. Mice were placed into the light chamber to acclimate to the environment, following which a continuous current was applied for 5 min. The mice were subjected to the electric shock and were returned to the light chamber when they entered the dark chamber. The training cycle was set as 2 days, that is, the training was performed again 24 hr later, in which the total number of errors within 5 min and the latency to the first electric shock were recorded.

The Morris water maze test was carried out 42 days after the administration of the different agents. Acquired memory training: mice were placed into the pool at a fixed point and the time it took for each mouse to find the invisible platform was recorded; success within 120 s was recorded as latency. The mice were trained in this way for 6 consecutive days. On day 7, the platform was removed, and the times passing through the central area, the central ring, and the target quadrant were recorded to evaluate the spatial learning and the times passing through the central area, the central ring, and memory ability of the mice (Planche et al., 2017).

2.5 | Detection of biochemical indicators

Twenty-four hours after the last administration, blood samples were taken by removing the eyeballs, and the serum was isolated by centrifugation at 4°C (10,000 rpm). The total antioxidant capacity (T-AOC), catalase activity (CAT), malondialdehyde content (MDA), and reactive oxygen species (ROS) in mouse serum were measured according to the kit’s instructions.

2.6 | Immunofluorescence dual staining of brain tissue

A solution of 20% bromodeoxyuridine (BrdU) was intraperitoneally injected to label the last 5 days of modeling. The brain tissue was removed after ventricular perfusion and dehydrated serially with 4% paraformaldehyde, 20% sucrose solution, and 30% sucrose solution. Frozen slices were created by embedding. The slices were boiled in 0.01 M citric acid buffer (pH = 6.0) for 5 min and cooled to room temperature, following which they were soaked in PBS and rinsed with water. Subsequently, 0.3% Triton X-100 was added and the slices were incubated at room temperature for 5 min, then 10% BSA/PBS-T (+ 0.05% NaN$_3$) solution was dropped onto the slices, which were incubated for 1.5 hr. The slices were incubated with rabbit anti-NeuN (1:500) and mouse anti-BrdU (1:200) primary antibodies at 4°C overnight, washed, and then incubated with the mixed secondary antibody composed of 1:1,000 anti-mouse IgG-Alexa Fluor 488 and 1:1,500 anti-rat IgG-Alexa Fluor 594 at 4°C in the dark overnight. The next day, the slices were washed three times with PBS and incubated with Hoechst 33258 solution at room temperature for 30 min, following which they were washed with PBS, mounted with neutral balsam, and observed under a laser confocal fluorescence microscope.

2.7 | Sequencing of the transcriptome and screening of differentially expressed genes

The study on the gene expression differences was conducted based on the data analysis program described above. The HISAT software was used to align the sequencing data with the reference genome, and the alignment results were used to assemble the transcripts. EdgeR was used to analyze differential expression, and the R language results were used for graphical display, including the differential gene expression thermal plot, scatter map, volcanic map, and analytical map of the main components (Kowalczyk et al., 2015; White et al., 2015).

The expression of genes in each group was examined. FPKM (Fragments Per Kilobase of exon model per Million mapped reads) was used in the examination to measure gene expression, that is, the expression level was equal to the FPKM value. Attention was also paid to the t test threshold (P value) and FDR correction Q threshold for the t test P value (q value). Therefore, the target genes in each sample group were screened out by the FPKM value, P value, and Q value. The differentially expressed genes were screened in accordance with the criteria: FPKM > 10, P < .05, and FC > 1.5 or FC < 0.6, simultaneously. Accordingly, of the significantly differentially expressed genes, those with the largest FPKM values were selected for further verification.

2.8 | Verification of differentially expressed genes by real-time fluorescence quantitative PCR (RT-qPCR)

A PC18 TUREscript 1st Stand cDNA synthesis kit (Aidlab, China) was used for reverse transcription to cDNA. The reaction was performed in 20 µl under the following cycling parameters: 94.0°C for
5 min, followed by 35 cycles (94.0°C 30 s, 60°C 30 s, 72°C 30 s), and 72°C for 7 min. The primers are shown in Table 1. The detection software was SDS v2.2; the calculation was based on the Ct method; the expression level of target genes was calculated using the formula $2^{-\Delta CT}$.

### 2.9 Determination of differential protein expression by western blotting

Proteins were extracted from mouse hippocampal tissue using RIPA lysis buffer, and the protein concentration was determined by the Bradford method. An equal amount of protein was separated by 12% SDS-PAGE and transferred to the membrane. Membranes were blocked with 5% skimmed milk in PBS for 1 hr, washed with PBS, and incubated overnight with primary antibodies against Nrf2, HO-1, Keap1, p53, Hsph1, ApoE, and Trim32 at 4°C. The specific dilution ratio for each antibody was 1:500. The next day, the membranes were washed three times in PBS and incubated with the secondary antibodies at 37°C for 1 hr, following which the membranes were washed three times in TBS-T and incubated with photoluminescence solution. A film processor was used to expose the target protein bands, and the films were scanned for storage.

### 2.10 Statistical analysis

The SPSS v16.0 statistical software was used to process the data in each group. The results are expressed as the mean ± standard deviation (mean ± SD). A t test was used to evaluate the significance of the results, and $p < 0.05$ was considered statistically significant.

<table>
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<th>Forward primer</th>
<th>Reverse primer</th>
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<td>Trim32</td>
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<td>GGACTTCTCACCAGCAAAG</td>
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<td>Hsph1</td>
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### Table 1 Primer sequences

**Figure 1** Purification and identification of ABp by column chromatography. (a) DEAE-32 column chromatography elution diagram; (b) CM-52 column chromatography elution diagram; (c) HiTrap® desalting column chromatography elution diagram; (d) Tricine-SDS-PAGE. Lane 1: Trypsin inhibitor (20.1 kD), whey protein (14.4 kD), azurin (6.5 kD), acetylated cytochrome C (3.3 kD). Lane 2: Component ABp; (e) ABp secondary mass spectrum.
3 | RESULTS

3.1 | Preparation of ABp

Four main absorption peaks were obtained by DEAE-32 ion-exchange chromatography (Figure 1a), and two main peaks of the DE2 active fraction were obtained by CM-52 ion-exchange chromatography (Figure 1b). The highest activity was observed in CM1 by an in vitro DPPH scavenging experiment; the best clearance rate was 70% at a concentration of 1.0 mg/ml; the EC50 was 0.468 mg/ml. A homogeneous component (ABp) was obtained by Sephadex G-25 gel chromatography (Figure 1c). ABp showed a single band on Tricine-SDS-PAGE (Figure 1d) and M was equal to 3 kD. LC-MC/MS analysis of peptide sequences. The amino acid sequence is EHEHEHEHEHEPEDPNSSESYW.

3.2 | Behavioral experiments

The results of the step-through passive avoidance test are shown in Figure 2. In comparison with the Con group, the number of errors made by the mice in the Mod group was significantly increased and the latency was significantly prolonged ($p < .05$). Moreover, in comparison with the Mod group, the number of errors made by the mice in the ABp group was significantly reduced and the latency was significantly shortened ($p < .05$).
The results of the Morris water maze test are shown in Figure 3. In comparison with the Con group, the latency in finding the platform was significantly prolonged in mice in the Mod group from Days 4 to 5 \((p < .05)\). Moreover, the latency in finding the platform was significantly shorter in mice in the ABp group than that in mice in the Mod group \((p < .05)\). In the space exploration test on day 7, the time taken by the ABp group to enter the space where the platform had previously been placed was significantly prolonged \((p < .05)\), and the number of times passing through the central area, the central ring, and the target quadrant was significantly decreased as compared with that in the Con group. Moreover, in comparison with the Mod group, the time to enter the space where the platform had previously been placed was significantly shortened, and the number of times passing through the central area, the central ring, and the target quadrant was significantly increased in the ABp group \((p < .05)\).

### 3.3 Effects of ABp on oxidative stress markers in D-gal-induced aging mice

As shown in Figure 4, in comparison with the Con group, the MDA and ROS content was significantly increased and the CAT activity and T-AOC levels were significantly decreased in the serum of mice in the Mod group \((p < .05)\). Moreover, in comparison with the Mod group, the MDA and ROS content was significantly decreased \((p < .05)\) and the CAT activity and T-AOC levels were significantly increased in the serum of mice in the ABp group \((p < .01)\).

### 3.4 Immunofluorescence dual staining

The more BrdU/NeuN dual labeled positive cells, the more neonatal cells. As shown in Figure 5, the number of BrdU/NeuN dual labeled
positive cells in the Mod group was significantly lower than that in the Con group. Moreover, the number of BrdU/NeuN dual labeled positive cells in the ABp group was significantly higher than that in the Mod group.

3.5 Transcriptome sequencing

Transcriptome results showed that in comparison with the Mod group, 295 differentially expressed genes were screened out in the ABp
The differentially expressed genes were mainly involved in the regulation of transcription, distributed among the processes of cell membrane formation and protein binding, and their specific functions were neuroactive ligand-receptor interaction and GABA synaptic function (Figure 6). This experiment finally screened out nine significantly differentially expressed genes: ApoE, Hsp1, Trim32, ATP1A3, STXBP1, Mapk8ip1, HnRNPA1, HK1, and Grik5 (Table 2).

### 3.6 Expression of differentially expressed genes detected by RT-qPCR

The mRNA expression levels of ApoE, Hsp1, Trim32, ATP1A3, STXBP1, Mapk8ip1, HnRNPA1, HK1, and Grik5 were detected by RT-qPCR. In comparison with the Mod group, the mRNA expression levels of Hsp1, Trim32, HK1, HnRNPA1, and Grik5 were significantly increased \( (p < .05) \), and those of ATP1A3, STXBP1, ApoE, and Mapk8ip1 were significantly decreased \( (p < .05) \) in the hippocampal tissue of mice in the ABp group (Figure 7).

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<th>FPKM. ABp2</th>
<th>FPKM. ABp3</th>
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<th>FPKM. Mod2</th>
<th>FPKM. Mod3.</th>
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### 4 DISCUSSION

Aging is a process of degenerative changes in the function of various tissues and organs over a lifetime. Aging can reduce the ability of the body to maintain a dynamic balance in the face of environmental stress, thus increasing the possibility of illness and death. The occurrence of aging is closely related to the accumulation of ROS and oxidative stress (Da et al., 2017). The model induced by D-gal is a classic animal model of aging, in which the binding sites of receptors in the cerebral cortex, septum, and hippocampus can be blocked, and excessive free radicals cause aging, which resembles the law of natural aging (Kou et al., 2016; Li et al., 2018). The specific mechanism is the production of a large number of reactive oxygen species (ROS) that leads to damage to the mitochondrial system and the production of high levels of lipid peroxides. An increase in oxidative reactions, such as those via malondialdehyde, and a decrease in the activity of antioxidant enzymes, such as catalase (CAT), eventually cause a decrease in antioxidant levels or even injury of the antioxidant system. As a result, various senescence changes occur, such as the dispersion of neurons in the hippocampus, reduced

**FIGURE 7** Effects of ABp on the mRNA expression of ApoE, Hsp1, Trim32, ATP1a3, STXBP1, Mapk8ip1, HnRNPA1, HK1, and Grik5 in the hippocampal tissue of aging mice. Mod: model group; ABp: Agaricus blazei polypeptide group. \( p < .05 \), vs. Mod group; \( ^* p < .05 \), vs. Con group
nuclei, and loose arrangement of cells (Maltese et al., 2017; MaGorzata & Andrzej, 2016). In the present study, it was found that the mice in the Mod group had obvious symptoms of aging, including a decline in learning and memory, a decrease in behavioral ability, and slower reactions. After intervention with ABp, the exercise and stress tolerance of aging mice were improved and the activities of antioxidant enzymes in

**FIGURE 8** Effects of ABp on the protein expression of Keap1, PS3, ApoE, Nrf2, HO-1, HnRNA1, and Trim32 in the hippocampal tissue of aging mice. (a) STRING protein-protein network diagram; (b) Western blot. Con: blank control group; Mod: model group; Pir: piracetam group; ABp: *Agaricus blazei* polypeptide group. *p < .05, **p < .01 vs. Mod group; #p < .05, ##p < .01, vs. Con group
the serum, such as T-AOC and CAT, were increased, since the excessive ROS could be scavenged and the production of lipid peroxides was reduced. In addition, the structural integrity of nerve cells in hippocampal tissue was improved and the number of cells with degeneration and pyknosis was significantly decreased in the ABp group, suggesting that ABp had a marked anti-aging effect in mice.

Oxidative stress is an important cause of aging. Our results indicate that the increase in free radicals and peroxides in aging mice confers a stage of oxidative damage that was improved following intervention with ABp, suggesting that ABp could effectively counter the oxidative stress to slow the process of aging. Nrf2 is a key regulator of oxidative stress in cells, which has an extreme susceptibility in brain tissue. Improvement in Nrf2 activity can effectively antagonize the injury induced by oxidative stress, reducing symptoms of aging (Jeong et al., 2017). ApoE and Keap1 are negative regulators of Nrf2, and their ubiquitination, phosphorylation, and nuclear transport can affect the activity of Nrf2, playing an important role in the development, repair, and remodeling of neurons (Lallemand et al., 2018). Hsph1, a strong endogenous antioxidant and a regulatory factor of Nrf2, can prevent stress-induced injury and apoptosis of neurons (Khayyer et al., 2017). Moreover, HO-1 is also negatively regulated by some Nrf2 repressors, following which the expression of various basic and induced antioxidant genes decreases and oxidative damage significantly increases (Li et al., 2014). The present study shows that ABp could downregulate the protein expression of Keap1 and upregulate that of Nrf2, HO-1, and Hsph1 in the brain tissue of aging mice. P53, as a key protein in a variety of pathways, is involved in cell cycle progression and is also regulated by Nrf2, inducing cell growth arrest or apoptosis in response to oxidative damage. Trim32 is the regulatory gene and E3 ubiquitin ligase of p53; following damage, Trim32 forms a negative feedback loop, and the negative regulation of p53 mediates cell cycle arrest, apoptosis, and aging to cope with the stress. Thus, Trim32 and p53 form a novel self-regulating negative feedback loop for the regulation of p53 (Borlelawar et al., 2017; Zhao et al., 2018). Our results show that ABp downregulated the protein expression of p53 and upregulated that of Trim32 in the brain tissue of aging mice, suggesting that ABp may reduce oxidative stress by regulating the Keap1/Nrf2/ARE and P53/Trim32 signaling pathways to produce an anti-aging effect in mice.

The results of transcriptome sequencing show that the distribution of differentially expressed genes involved in transcriptional regulation, the formation of cell membranes, and the binding of proteins was more extensive in the ABp group, including neuroactive ligand-receptor interaction and GABA synaptic function. Among them, ApoE encodes members of the apolipoprotein A1/A4/E family, and its different alleles are directly related to Alzheimer’s disease in the elderly. When cells are susceptible to stress or injury, ApoE promotes the synthesis and secretion of neurons (Krasemann et al., 2017). In the central nervous system, ApoE can regulate a variety of oxidative damage-related genes, including Atp1a3, Mapk8ip1, and Hnrnpa1, which play an important role in the development, repair, and remodeling of neurons (Schirinzi et al., 2018). Atp1a3, located on chromosome 19q13.2, encodes Na+/K+-ATPase, which plays a key role in maintaining the transmembrane electrochemical gradient of Na+ and K+ and can cause nervous system disease profiles with different phenotypes, including dystonia, ataxia, and cognitive impairment, affecting normal growth and development (Ikeda et al., 2017). The Stxbp1 complex forms to regulate presynaptic vesicle fusion in developing neurons, and may be involved in brain development and disorders of neurotransmission (Carvill et al., 2014). HK1, the outer mitochondrial membrane protein hexokinase gene and the first rate-limiting enzyme in the process of glycolysis, is involved in the metabolism of glucose and lipids (Sullivan et al., 2014). The signal transduction pathway of Mapk8ip1 (mitogen-activated protein kinase 8-interacting protein) is involved in the hyperphosphorylation of the tau protein, Alzheimer’s disease (AD), and learning and memory, concentrating on the improved hippocampus-dependent spatial memory and enhanced associative fear conditioned reflex. The mechanism is the binding of the amyloid precursor protein intracellular domain (AICD) to c-Jun N-terminal kinase (JNK). Mapk8ip1 associates with JNK and activates signal transduction, through which the hyperphosphorylation of tau induces the occurrence of AD (Fateme et al., 2018; Lu et al., 2017). HnRNPA1 (heterogeneous nuclear ribonucleoprotein A1), a new necessary factor, plays a role in the expression of multiple genes, participating in packaging pre-mRNA into hnRNP particles, transporting poly(A) mRNA from the nucleus to the cytosol, and regulating the selection of splicing sites (Howard et al., 2018). Grik5 (inotropic glutamate receptor, kainic acid 5, glutamic acid receptor) acts as an excitatory neurotransmitter in a variety of synapses (Korytina et al., 2017). Following intervention with ABp, the mRNA expression levels of Hsph1, Trim32, and HK1 in the brain tissue of aging mice were significantly increased, while those of Atp1a3 and Stxbp1 were significantly decreased. The RT-qPCR results were consistent with those of RNA-seq, suggesting that ABp may exert an anti-aging effect by improving lipoprotein metabolism, neurotransmission dysfunction, oxidative damage, and the growth and development of new neurons, and by regulating the mRNA expression of Atp1a3, Stxbp1, Mapk8ip1, Hnrnpa1, Hk1, and Grik5.

5 | CONCLUSION

The extraction of ABp was optimized and the in vitro DPPH scavenging activity was used as the screening condition. ABp improved the oxidative stress injury and exerted an anti-aging effect in a mouse model of aging. The specific underlying mechanism may be related to the regulation of the Keap1/Nrf2/ARE and P53/Trim32 signaling pathways and the expression levels of ApoE, Hsph1, Trim32, Atp1a3, Stxbp1, Mapk8ip1, HnRNPA1, Hk1, and Grik5. This study provides a theoretical and practical basis for Agaricus blazei Murrill as a health product or drug with anti-aging function.

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CONFLICT OF INTEREST
The authors confirm that there are no conflicts of interest associated with this publication.

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