Transcriptional and biochemical analyses of *Planomicrobium* strain AX6 from Qinghai-Tibetan Plateau, China, reveal hydrogen peroxide scavenging potential

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**Abstract**

**Background:** The bacterial mechanisms responsible for hydrogen peroxide (H₂O₂) scavenging have been well-reported, yet little is known about how bacteria isolated from cold-environments respond to H₂O₂ stress. Therefore, we investigated the transcriptional profiling of the *Planomicrobium* strain AX6 strain isolated from the cold-desert ecosystem in the Qaidam Basin, Qinghai-Tibet Plateau, China, in response to H₂O₂ stress aiming to uncover the molecular mechanisms associated with H₂O₂ scavenging potential.

**Methods:** We investigated the H₂O₂-scavenging potential of the bacterial *Planomicrobium* strain AX6 isolated from the cold-desert ecosystem in the Qaidam Basin, Qinghai-Tibet Plateau, China. Furthermore, we used high-throughput RNA-sequencing to unravel the molecular aspects associated with the H₂O₂ scavenging potential of the *Planomicrobium* strain AX6 isolate.

**Results:** In total, 3,427 differentially expressed genes (DEGs) were identified in *Planomicrobium* strain AX6 isolate in response to 4 h of H₂O₂ (1.5 mM) exposure. Besides, Kyoto Encyclopedia of Genes and Genomes pathway and Gene Ontology analyses revealed the down- and/or up-regulated pathways following H₂O₂ treatment. Our study not only identified the H₂O₂ scavenging capability of the strain nevertheless also a range of mechanisms to cope with the toxic effect of H₂O₂ through genes involved in oxidative stress response. Compared to control, several genes coding for antioxidant proteins, including glutathione peroxidase (GSH-Px), Coproporphyrinogen III oxidase, and superoxide dismutase (SOD), were relatively up-regulated in *Planomicrobium* strain AX6, when exposed to H₂O₂.

**Conclusions:** Overall, the results suggest that the up-regulated genes responsible for antioxidant defense pathways serve as essential regulatory mechanisms for removing H₂O₂ in *Planomicrobium* strain AX6. The DEGs identified here could provide a competitive advantage for the existence of *Planomicrobium* strain AX6 in H₂O₂-polluted environments.

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Background
One of the critical challenges for living organisms is to overcome the oxidative stress caused by reactive oxygen species (ROS), including hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}), hydroxyl radicals (OH), and superoxide anions (O\textsubscript{2}\textsuperscript{-}), that cause damage to virtually all macromolecules of the cell [1, 2]. For instance, the higher concentration of ROS could damage cellular proteins [3], lipids [4], and DNA [5], leading to several growth and metabolic defects, thereby causing cell death. To counteract these lethal effects, living organisms have developed different mechanisms at the genetic, molecular, and biochemical levels [1, 6]. For instance, when bacteria were exposed to the mM levels of H\textsubscript{2}O\textsubscript{2}, they produced catalase (CAT) to scavenge H\textsubscript{2}O\textsubscript{2}, while mutants with impaired CAT activity lost their H\textsubscript{2}O\textsubscript{2} scavenging capability [7]. Furthermore, bacteria are equipped with enzymatic antioxidant defense systems to cope with higher or lower concentrations of H\textsubscript{2}O\textsubscript{2} [8, 9]. To avoid the lethal effects of H\textsubscript{2}O\textsubscript{2}, effective natural antioxidants seem a vital target to be discovered. Therefore, identifying new bacterial taxa that could produce potent antioxidants for removing H\textsubscript{2}O\textsubscript{2} remained the main aim of this study.

Since specific bacteria have preferred several vital ecological processes and sustaining life for decades [10]; therefore, understanding the bacterial ecosystem is gaining special attention. However, a major portion of these microbes and their ecological functions in desert ecosystems are yet to be explored. Coping with oxidative stress by activating antioxidant defense systems is among the vital functions of microbes [1, 11, 12]. The Qaidam Basin of the Qinghai-Tibet Plateau is a cold hyper-arid desert at an altitude of more than 4,500 m [13]. Diverse bacterial communities dominate these high-elevation cold-desert ecosystems, frequently subjected to stressful conditions like low atmospheric oxygen content, excessive ultraviolet (UV) radiation, low air temperatures, and low nutrient availability [13–15]. These extreme environmental conditions serve as a potential source of the genomic pool and are considered suitable regions for antioxidant-producing bacteria.

To cope with H\textsubscript{2}O\textsubscript{2} stress, bacteria use multifaceted defense mechanisms by producing antioxidant enzymes, including superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and CAT [7, 16–18]. Among bacteria, Escherichia coli was the first identified model of enzyme regulator, and various defense-related genes have been activated for H\textsubscript{2}O\textsubscript{2} scavenging, thereby providing the best protective system against oxidative stress [2, 19, 20]. On the other hand, the Gram-positive bacterial strain Deinococcus radiodurans utilizes enzymatic antioxidants to sense oxidative stress and scavenge ROS [21, 22]. The H\textsubscript{2}O\textsubscript{2} stress could cause significant damage and inactive the functions of DNA, lipids, and proteins, leading to several metabolic deficiencies and mutations [2, 8, 23]. Previously, it was reported that the process of H\textsubscript{2}O\textsubscript{2}-mediated degradation of cellular machinery was more complex. Over the last decade, researchers have recognized enzymatic defense mechanisms in bacteria that can scavenge H\textsubscript{2}O\textsubscript{2} in vitro, while in vivo research displays a weaker response to H\textsubscript{2}O\textsubscript{2} [2, 8, 24]. The lack of knowledge about cellular resistance against H\textsubscript{2}O\textsubscript{2} and the resultant products of cellular metabolism hinders to development advance cellular approaches for combating toxic effects. Hence, a better understanding of the molecular events that respond to H\textsubscript{2}O\textsubscript{2} toxicity might improve bacterial adaptation and optimization [7, 16].

In the last decade, rapid advancements in next-generation sequencing techniques and bioinformatics have made the cost of sequencing reasonable. For instance, high-throughput RNA-sequencing (RNA-Seq) has been broadly used to analyze transcriptional changes across the whole genome [25, 26]. In various bacterial species for which genomic information is absent, transcriptional profiling seems a powerful technique for studying the H\textsubscript{2}O\textsubscript{2} adaptation mechanism and other biological characteristics [7, 8, 27]. In different species of bacteria, several H\textsubscript{2}O\textsubscript{2}-induced genes have been recognized, and the expression patterns and the function of specific H\textsubscript{2}O\textsubscript{2}-induced genes have been studied [28–30]. This suggests that the biochemical and physiological responses are governed by a network of DEGs that controls complex molecular mechanisms in bacteria to adapt against H\textsubscript{2}O\textsubscript{2} stress.

The genus Planomicrobium was originally described by Yoon et al. [31]. There were six valid species in the genus Planomicrobium until recently: Planomicrobium psychrophilum, P. chinense [32], P. koreense, P. mcmeekinii, P. okeanokoites [31], and P. alkanoclasticum [32, 33]. The known characteristics of the genus Planomicrobium are that the species are Gram-positive to Gram-variable, aerobic, yellow-to orange-pigmented, and non-spore-forming, respectively. Planomicrobium species contained DNA G and C in the range 35–47 mol% [34]. In this study, the Planomicrobium-AX6 strain was isolated from the cold-desert soil in the Qaidam Basin, Qinghai-Tibetan...
Plateau, China which elucidated a strong antioxidant activity. The H$_2$O$_2$ scavenging mechanisms of *Planomicrobium* are rarely explored. Therefore, in this study, we carried out the transcriptional profiling of the *Planomicrobium* strain AX6 intending to unravel the molecular aspects associated with H$_2$O$_2$ scavenging potential in cold-desert ecosystems. As per our knowledge, this is the first study that presents the transcriptional analyses of any strain belonging to *Planomicrobium* in response to H$_2$O$_2$ stress.

**Materials and Methods**

**Preparation and molecular identification of bacterial strain**

The bacterial *Planomicrobium* strain AX6 was isolated from the desert sand soils (0–10 cm) in the Qaidam Basin, Qinghai-Tibet Plateau, China (37.088°N, 95.427421°E). The medium used for isolation was composed of (g/L): yeast extract, 5; peptone, 10; sodium acetate, 1; ammonium nitrate, 0.2; sodium citrate, 0.5 and agar, 15; having a pH of 7.5, and incubated for 96 h at 20 °C, and further preserved in glycerol (20%, v/v) at -80 °C [35] for further processing. The bacterial isolate thrives in desert ecosystems due to ultra-high radiation resistance and antioxidant capabilities [37, 38]. The details pertaining to the respective bacterial isolates are shown in supplementary material Table S1. All these bacterial isolates were exposed to two different H$_2$O$_2$ concentrations (1.5 and 3 mM) for 4 h.

The effect of H$_2$O$_2$ on *Planomicrobium* strain AX6 growth was studied as follows: 100 μL inoculum of *Planomicrobium* strain AX6 in their exponential growth stage (OD$_{600}$=0.6) was inoculated in 50 mL Luria Broth (LB) medium containing 0, 0.5, 1.0, 1.5, 2.0, and 2.5 mM H$_2$O$_2$ and incubated at 28 °C for 103 h at the speed of 200 rpm/min. The bacterial cell concentration was estimated using the absorbance of a spectrophotometer (600 nm). All these experiments were done in triplicates.

**H$_2$O$_2$ scavenging potential**

*Escherichia coli* JM109 (strain number C1310) purchased from Solarbio Company has a low tolerance to oxidizing substances [37] and thus was used as a negative control. While *Deinococcus radiodurans* (strain number 1.3828) purchased from China Micro Ordinary Microbiology Center (CGMCC) was used as a positive control. This bacterial isolate thrives in desert ecosystems due to ultra-high radiation resistance and antioxidant capabilities [37, 38]. The details pertaining to the respective bacterial strains are shown in supplementary material Table S1. All these bacterial isolates were exposed to two different H$_2$O$_2$ concentrations (1.5 and 3 mM) for 4 h.

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**ROS scavenging potential assay**

The scavenging ability of three different ROS agents by *Planomicrobium* strain AX6 was evaluated. For this purpose, the bacterial inoculums were mixed with phosphate buffer solution (PBS) and further suspended with 2,2-diphenyl-1-picrylhydrazyl (DPPH)•ethanol according to the method used by Lee et al. [39], and DPPH scavenging was estimated. Moreover, the bacterial inoculum was mixed with Tris–HCl buffer, and the method used by Wang et al. [40] was adopted for studying the O$_2$ scavenging potential of the strain. For determining the hydroxyl radical (·OH) scavenging potential, the bacterial inoculum was mixed with sodium phosphate buffer according to the method and estimation used by Das and Goyal. [41]. The experiments mentioned above were repeated three times, and mean results were reported in this study.

**Estimation of SOD, CAT, and GSH-Px**

For enzymatic analyses, the SOD was extracted using the pyrogallol auto-oxidation method [42]. Furthermore, CAT content assay was determined by spectrophotometry, hydrogen oxide absorbance change value to characterize, the procedure was modified from Nakayama et al. [43]. The activity of GSH-Px was studied by using the colorimetric method with the help of Leagene kit (Beijing Leagene Biotech Co., Ltd., China).

**RNA-sequencing**

The extraction of total RNA from 0 and 1.5 mM H$_2$O$_2$ concentrations was performed using the TRizol® Reagent RNA Purification Kit for bacteria (Invitrogen) according to the manufacturer’s instructions. A Nanodrop 2000 spectrophotometer evaluated the integrity and the quality of the extracted total RNA. All RNA samples were DNase treated using the Ribo-Zero Magnetic kit to eliminate every contaminating genomic rRNA. The experiments were performed in triplicate for each stress treatment. RNA sequencing was done on the Illumina HiSeq4000 according to the manufacturer’s protocol (Illumina Inc., Majorbio, China). Briefly, the quality and the integrity of the total RNA were evaluated using the Agilent 2100 Bioanalyzer. RNA with an RNA Integrity Number (RIN) of 7.0 or higher was used for sequencing library preparation and processing. Sequencing libraries were adjusted using the TruSeq Stranded Specific mRNA Library sample Prep Kit as per the manufacturer’s guidelines (Illumina). Cluster generation was done according to the manufacturer’s references for onboard clustering (HiSeq 4000 PE Cluster Kit, Illumina). Next, sequencing (2 × 150 bp) was performed using Illumina Hiseq 300 platform.

**Bioinformatics analysis**

The quality of FASTQ files was evaluated using FASTQC v. 0.11.8 [44]. Generally, the default parameters were used to align the reads to the *Planomicrobium* strain AX6 genomes to assess contamination and further aligned to
the bacterial genomes assembly using Bowtie2 (http://www.bowtie-bio.sourceforge.net/bowtie2/manual). The transcript abundances were processed using RSeQC-2.6.3 (http://rseqc.sourceforge.net/), having strand-specific read counting. Data were normalized, and the DEGs were quantified using the edgeR (http://www.bioconductor.org/packages/2.12/bioc/html/edgeR.html) by applying criteria of having corrected P-value or FDR < 0.05 and fold change log2FC ≤−1 or ≥1 [45–47]. Differential gene enrichment analyses for Gene Ontology (GO) (https://github.com/tanghaibao/GOatools) and Kyoto Encyclopedia of Genes and Genomes (KEGG) metabolic pathways (http://www.genome.jp/kegg/) were performed using Goatools and KOBASE function [48, 49], respectively, and the statistical method used was Fisher’s exact test. The dominant metabolic pathways were analyzed through KEGG enrichment analysis having FDR < 0.05 [50]. The fitting growth curves of Planomicrobium strain AX6 were drawn with R-package (plyr, ggplot2) v 3.6. The Principal Component Analysis (PCA) was analyzed to find outliers and discriminate sample clusters with high similarities. The scatter plot represents genes’ expression level (FPKM value) in the control and treatment samples [47]. The heatmap was generated to find genes with significant differences by clustering their expression patterns using hcluster (complete algorithm). All analyses were carried out via R-Vagan v. 6.3.

Results
Identification and growth adaptation attributes of Planomicrobium strain AX6 against H2O2 stress
Planomicrobium strain AX6 was identified at the molecular level by Ting et al. [36] using 16 s rRNA sequencing. More than 80% of the Planomicrobium strain AX6 showed resistance to 0.02—1.0 mM H2O2, and there was no significant variation in the survival rate. Though, after 1.5 mM H2O2 it reduced to 56% and showed a substantial change in survival rate, then to 45% and 27% on 2.0 mM and 3.0 mM, respectively (Fig. S1A). Planomicrobium strain AX6 growth was decreased (cultural density at OD600) after 103 h in 2.0 and 2.5 mM H2O2 treatment (Fig. S1B). We selected a concentration of 1.5 mM H2O2 for further study. As shown in Figure S1B, the growth rate was significantly inhibited by 1.5 mM of H2O2 between 10 and 49 h of treatment, demonstrating that Planomicrobium strain AX6 is directly involved in H2O2 scavenging.

Bacterial comparison for H2O2 scavenging ability
The DPPH free radical scavenging rate is usually used to determine the antioxidant capacity. Therefore, the scavenging rates of DPPH, OH, and O2− were measured to characterize the antioxidant characteristics of Planomicrobium strain AX6 (Table S1). In addition, Planomicrobium strain AX6 to remove H2O2 with different concentrations (0, 1.5, and 3 mM) was verified. The DPPH, O2•−, and OH scavenging potentials of Planomicrobium strain AX6 were significantly higher (16.6, 18.3, and 36.4%) than the negative control (5.0, 9.5, and 6.1%) (P < 0.05) while lower than the positive control (20.7, 21.8, 53.0%) when treated with 1.5 mM of H2O2 (Table S1). These results confirmed the antioxidant potential of Planomicrobium strain AX6.

Estimation of SOD, CAT, and GSH-Px
As illustrated in Fig. 1A, upon 1.5 and 3 mM of H2O2 treatment, GSH-Px activity was significantly higher than the control (0 mM H2O2) (P < 0.05). With the increase in H2O2 levels, the SOD and CAT activity of Planomicrobium strain AX6 decreased significantly (Fig. 1B and C). This suggests that SOD is likely to be responsible for the conversion of O2− into H2O2, where the oxidation environment dominated by H2O2 inhibits the process of SOD [51], which as a result, might decrease the SOD activity.

Transcriptional profiling of the Planomicrobium strain AX6 in response to H2O2 stress
To gain insights into genes and key metabolic pathways responsible for H2O2 regulation by Planomicrobium strain AX6, their transcriptional profiling was conducted in response to H2O2 stress. The Illumina/Truseq™ RNA platform generated two libraries of bacterial included (AX6) and control (CK) groups comprising 22,260,393 and 23,723,531 raw reads, respectively (Table S2). The length of a single read was 200 bp. After removing the short reads, contaminated reads, and adaptor sequences from Planomicrobium strain AX6 and CK group libraries, a total of clean reads comprising 21,936,575 and 23,271,179, having Q20 values 98.89 and 98.75%, respectively, and Q30 values were 96.59 and 96.17%, respectively. Moreover, the GC content values were 44.03 and 45.66%, while 98.90 and 98.62% of transcripts have been mapped, respectively (Table S2). Furthermore, 770,388 transcripts were composed of high-quality reads using Glimmer 3.02 software. The average length was 832 bp. Scaffold N50 and N90 values were 55, 2, and 59,610.

Gene expression pattern and correlation between control and H2O2 stress
According to RSEM software, the log2FPKM distribution between the control and H2O2 suggested the highly expressed genes under stress conditions compared to the control (Fig. 2A, B), which exhibited a pattern consistent with the main biological replicates that meet the expectations of the experimental design. The statistical results of each sample’s correlation are shown in Fig. 2B. The columns correspond to the FPKM ≥ 0.01 of each gene, and...
Fig. 1  Antioxidant enzyme activity of Planomicrobium-AX6 exposed to H$_2$O$_2$ treatments. A glutathione peroxidase (GSH-Px), B superoxide dismutase (SOD), and (C) catalase (CAT) production rate when exposed to H$_2$O$_2$ (0, 1.5, and 3 mM) for 4 h. Where asterisks indicate significant differences. ***$P$ < 0.001; **$P$ < 0.01; *$P$ < 0.05

Fig. 2  Density curve, hierarchical cluster heatmap, and Principal component analysis (PCA) of Planomicrobium-AX6 transcriptome data, exposed to hydrogen peroxide for 4 h under H$_2$O$_2$ (1.5 mM). A Density curve. The probability density distribution of the expression of all genes was log$_2$FPKM, the peak of the density curve represents the region where the gene expression of the entire sample is most concentrated. Each color in the figure represents a sample, and the sum of all probabilities is 1. B Hierarchical cluster heatmap. The correlation analysis between samples, the closer the correlation coefficient is to 1, the higher the similarity between samples. According to the quantitative results of FPKM, I calculated the correlation between all the samples. C Principal component analysis (PCA). The PCA demonstrates of expressed genes (FPKM $\geq$ 0.01) a clear separation (Axis 1) of AX6 vs. CK treatment. CK designate RNA sample replicates obtained from Planomicrobium-AX6 without H$_2$O$_2$ (1.5 mM) for 4 h, whereas AX6 is RNA sample replicates obtained from Planomicrobium-AX6 with H$_2$O$_2$ (1.5 mM) for 4 h. CK1-3 control; AX1-3 treatments, $n$ = 3
the rows correspond to the six samples. Similarly, the scores matrix delivered sample scores for gene expression patterns, labeling the profiling of gene expression distribution between control and stress treatment. The biological triplicate samples of each group were clustered together. The control and stress treatment groups were plotted distinctly along the PC1 direction (Fig. 2C).

**Identification of DEGs in Planomicrobium strain AX6 exposed to H$_2$O$_2$**

To find the variation in transcriptional profiling of *Planomicrobium* strain AX6 exposed to H$_2$O$_2$, the gene expression changes of both control and stress treatments were compared. In this study, statistical comparisons employed ($P$-value) indicating significant differences between *Planomicrobium* strain AX6 and CK control. The DEGs were regarding the two criteria, the average fold change was ≤2 having $P$-value > 0.01 and FDR ≤0.001 (For instance of AX6 vs. CK, Fig. 3A and B). A total of 3,427 significant DEGs were identified. Among them, the number of up-regulated transcripts (2833) was higher compared to down-regulated (594) at the 4 h under H$_2$O$_2$ ($P$ > 0.05) (Table 1; Fig. 3A and B), there was rich variation in response to H$_2$O$_2$. We found that the expressions differed

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![Fig. 3](image-url)  
**Fig. 3** Heatmap, scatter, and volcano plot of DEGs of *Planomicrobium*-AX6 transcriptome data, exposed to hydrogen peroxide for 4 h under H$_2$O$_2$ (1.5 mM). **A** Scatter plot. The horizontal and vertical coordinates have logarithmic values, indicate the expression levels (FPKM value) of genes in the AX6 and CK. **B** Volcano plot. Each colored point in the volcano plot represents a single gene. Plotted along the x-axis is the log2 fold change of each gene. The y-axis represents the negative logarithm of the corresponding $P$-value of that gene. **C** Heatmap. The scale bar shows the z-score for a differentially expressed gene. The color represents the amount of gene expression in the group of samples (log$^{10}$/FPKM), referring to the color key at the upper left. **D** Line plot. The sub-cluster of the heatmap represents a gene, and the blue line represents the average expression of all genes in the sub-cluster. CK designate RNA sample replicates obtained from *Planomicrobium*-AX6 without H$_2$O$_2$ (1.5 mM) for 4 h, whereas AX6 is RNA sample replicates obtained from *Planomicrobium*-AX6 with H$_2$O$_2$ (1.5 mM) for 4 h. CK1-3 control; AX1-3 treatments, $n = 3$
Clusters of Orthologous Groups (COG) assignments were also used to estimate and classify possible functions of the DEGs. Based on sequence homology, DEGs could be characterized into 21 COG groups. Metabolism group and amino acid transport with 173 COG were the most prominent groups, followed by an unknown function (161), general function prediction only (143), ribosomal structure, translation, and biogenesis (136), and metabolism group and inorganic ion transport (123) (Fig. S2). The chromatin structure and dynamics groups were the smallest, with only one COG.

for analyzed genes, with significant differences between control and stress treatment. For transcriptional profiling of Planomicrobium strain AX6 in response to H$_2$O$_2$ stress, the transcription profiles of 6 samples were analyzed using a clustering algorithm and tree view (Fig. 3C). They exhibited different profiles at the time points of the pairing between the two groups and each group had a different sample-specific profile. Commonly, similar transcription patterns were identified across control (CK1, CK2, CK3), while the up-regulated genes were reported in stress treatment (AX6-1, AX6-2, AX6-3), respectively. The samples of CK3 and AX6-3 shared similar transcription patterns (Fig. 3C). In addition to this, 976 stress-responsive DEGs were found that were further divided into 10 sub-clusters. The average profile for each group in each sub-cluster and the existent profile variances between the Planomicrobium strain AX6 and the control group are shown in Fig. 3D. For instance, in sub-clusters 1, 2, and 4 to 7, the gene expression level under stress was up-regulated, while it was down-regulated in CK. In sub-cluster 8, the gene expression was down-regulated upon stress, whereas it was up-regulated in CK. Similarly, in sub-cluster 9, the gene expression was down-regulated in AX6-1 and up-regulated in AX6-2 and AX6-3, remaining stable from CK1 to CK3, respectively. Finally, in sub-cluster 10, the gene expression in AX6-2 was comparable with the control (Fig. 3D).

Functional annotation

The functions of all the DEGs recognized in this work were classified by GO assignments (http://www.geneontology.org/). A total of 3,427 DEGs were annotated into 2,345 functional groups in the two categories in the three basic ontologies as cellular component, molecular function, and biological process. The study covered 39 functional groups comprising 11 for cellular components and molecular function and 17 for biological processes. Metabolic process and catalytic activity were the two largest groups, and the smallest group were extracellular region part, nucleoid, and biological adhesion, with only one GO enrichment predicted for each group (Fig. 4).

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| Differently expressed genes | Number of DEGs |
|-----------------------------|---------------|
| DEGs Up-regulation          | 2,833         |
| DEGs Down-regulation        | 594           |
| No change                   | 81            |
| Total                       | 3,508         |

* Limma was used to identify DEGs (FDR < 0.05)
In addition, changes in gene expression levels analysis and DEGs between *Planomicrobium* strain AX6 and CK were primarily related to coenzyme transport and metabolism. Consequently, the DEGs involved in these functions were further described in detail (Table S3).

Most of the genes were involved in thiamine metabolism, including the iron cysteine desulfurase, thiamine biosynthesis protein *ThiL*, hypothetical protein, and alkaline phosphatase up-regulated by the addition of *H₂O₂*. The genes related to cysteine desulfurase (*iscS, NFS1*)

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**Table 2** Bacterial antioxidant genes differently expressed when exposed to hydrogen peroxide for 4 h under *H₂O₂* concentration (1.5 mM)

| Antioxidant defense proteins | Sequence ID | KEGG gene name | Samples  | CK   | AX6   | Differently expressed genes* |
|-----------------------------|-------------|----------------|----------|------|------|-----------------------------|
| Glutathione peroxidase      | orf03455    | E1.11.1.9       |          | 9.24 | 93.78 | Up-regulated                |
|                             | orf02189    | E1.11.1.9       |          | 462.43 | 383.68 | Down-regulated              |
| Coproporphyrinogen III oxidase | orf00260 | hemN, hemZ      |          | 16.00 | 85.00 | Up-regulated                |
|                             | orf03367    | hemL            |          | 85.32 | 199.63 | Up-regulated                |
|                             | orf00170    | hemL            |          | 1900.68 | 2279.58 | Up-regulated                |
| Superoxide dismutase        | orf00300    | SOD2            |          | 1455.85 | 1088.24 | Down-regulated              |
|                             | orf03456    | guaB            |          | 224.89 | 229.00 | Up-regulated                |
|                             | orf03437    | cysK            |          | 179.85 | 210.48 | Up-regulated                |
| Catalase                    | orf02500    | katE, CAT, catB, srpA | 1059.43 | 875.26 | 1154.82 | Down-regulated              |
|                             | orf03059    | K07217          |          | 1449.28 | 4254.75 | Up-regulated                |
|                             | orf01958    | katE, CAT, catB, srpA | 3430.97 | Down-regulated |

* The differentially expressed antioxidant genes were identified using limma (FDR < 0.05)
might be providing sulfur, which is later combined during in vivo Fe-S cluster synthesis, were observed to be up-regulated in \( \text{H}_2\text{O}_2 \) treatment (Table S3). Thiamine biosynthesis protein-encoding genes (such as \textit{thl} and \textit{thiE}) were also up-regulated by adding \( \text{H}_2\text{O}_2 \).

Besides, three genes encoding alkaline phosphatase (\textit{E3.1.3.1}, \textit{phoA}, \textit{phoB}) were up-regulated. In addition, the environmental bacterial regulatory genes were down-regulated in \( \text{H}_2\text{O}_2 \) treatment. Moreover, genes responsible for oxidative stress adaptation were detected in the amino acids biosynthesis, mismatch repair, bacterial chemotaxis, fatty acid, cysteine and methionine metabolism, pentose phosphate pathway, and two-component system substitutions that might have allowed for effective functionality (Table S3).

**Discussion**

The potential scavenging ability of \( \text{H}_2\text{O}_2 \) toxicity in the \textit{Planomicrobium} strain AX6 recovered from desert soil in the Qaidam Basin, Qinghai-Tibetan Plateau, China, was carried out here by studying its growth and transcriptional profiling in response to \( \text{H}_2\text{O}_2 \) stress. This area is characterized by low temperature, oxygen level, and high radiation [13, 52], which directly cause light-induced damage to organisms, and forms an environment with high oxidation intensity [53]. In the higher \( \text{H}_2\text{O}_2 \) concentration, \textit{Planomicrobium} strain AX6 showed a high survival rate coupled with a strong oxidative stress response. Previous studies have shown that different bacterial strains isolated from cold environments can adapt to the desert oxidative stress environment [12, 54–59]. In addition, \textit{Planomicrobium} strain AX6 showed potential DPPH, \( \text{O}_2^- \), and OH, scavenging ability (Table S1), where the bacteria generate basal levels of ROS-scavenging enzymes to avoid the accumulation of endogenous \( \text{H}_2\text{O}_2 \) and \( \text{O}_2^- \) [60]. The mechanism mainly comprises SOD that catalyzes the dismutation of \( \text{O}_2^- \) to \( \text{H}_2\text{O}_2 \) and CAT that convert \( \text{H}_2\text{O}_2 \) to \( \text{O}_2 \) and \( \text{H}_2\text{O} \) [61, 62].

Furthermore, we studied the mechanisms that might play an essential role in the resistance of \textit{Planomicrobium} strain AX6 against \( \text{H}_2\text{O}_2 \) stress using RNA sequencing. Based on RNA-seq profiling, a substantial number of genes (3,508) was reported to be distinctly expressed in the \textit{Planomicrobium} strain AX6, signifying an extreme variation in the transcriptional profile of bacterial strain (Table 1) upon exposure to \( \text{H}_2\text{O}_2 \) stress. The genes are expressed differentially to elaborate on the resistant mechanism and the metabolic pathways that provide the energy needed to cope with oxidative stress. Therefore, it is reasonable to assume that might cause the weak resistance response produced against the bacterial strain or basis nutrients to be easily accessible to the bacteria to accomplish their metabolic pathways.

Transcriptional dynamics were examined in the CK and \( \text{H}_2\text{O}_2 \) stress-treated \textit{Planomicrobium} strain AX6 strain (Fig. 2). The differences between the \( \text{H}_2\text{O}_2 \) stress treatment and CK responses were also revealed in the PCA of the transcriptional data (Fig. 2), which separated the \( \text{H}_2\text{O}_2 \) stress treatment and CK samples. Toxic levels of \( \text{H}_2\text{O}_2 \) can reach up to millimolar due to the oxidative stress caused in the host immune cells [7]. To prevent the toxicity of \( \text{H}_2\text{O}_2 \), the bacteria produce several scavenging enzymes to maintain intracellular \( \text{H}_2\text{O}_2 \) levels at the nanomolar [61]. The accumulation of high concentrations of \( \text{H}_2\text{O}_2 \) might cause serious damage to many cellular organelles by amending proteins and DNA. However, several genes encode antioxidant proteins/enzymes that detoxify \( \text{H}_2\text{O}_2 \) or repair the oxidative damage caused by oxidative stress. Furthermore, these antioxidant proteins/enzymes are vital in regulating the antioxidant defense system's expression, including the thioredoxin and catalase systems, against \( \text{H}_2\text{O}_2 \) and at extreme pressure with MgCl\(_2\) supplementation [63–65]. However, it is currently unclear what bacterial-specific genes respond to and which antioxidant enzymes regulated genes contribute to \( \text{H}_2\text{O}_2 \) toxicity. These are exciting concerns for future research exploring the relations between \( \text{H}_2\text{O}_2 \) stress and CAT defense mechanisms of cold-desert isolated bacteria.

In this study, the CAT enzymes coding genes such as \textit{(katE, CAT, catB, srpA, K07217, katE, CAT, catB, srpA)} were slightly down-regulated, signifying that CAT might not play a key role in the scavenging of \( \text{H}_2\text{O}_2 \). So we were also surprised to find that relatively down-regulation of these genes had no seeming effect on \( \text{H}_2\text{O}_2 \) resistance in \textit{Planomicrobium} strain AX6, despite the circumstance that CAT expression genes were invoked more strongly by CK treatment than by \( \text{H}_2\text{O}_2 \) [66, 67] (Fig. 1; Table 2). This might be due to the redundant nature of bacterial resistance mechanisms [7] or could be predictable since \( \text{O}_2 \) is produced in its reaction [65]. Another possibility is that increased production of SOD likely to combine with CAT, resulting in a decreased ability of cells to remove \( \text{H}_2\text{O}_2 \) [51, 68]. Glutathione is a vital antioxidant, and GSH-Px catalyzes the reaction of glutathione and an extensive range of oxides [69–71]. The genes \textit{Gpx}, orf03455\_E1.11.1.9 were up-regulated while orf02189\_E1.11.1.9 was down-regulated (Table 2). We investigated that \textit{Planomicrobium} strain AX6 has the complete KEGG pathway of glutathione metabolism and encodes as many as 2 copies of GSH-Px genes (Table 2), which shows that glutathione likely plays a key role in avoiding cellular substrates from \( \text{O}_2 \) inactivation. In addition, coproporphyrinogen III oxidase and SOD can also protect the bacterial cells against \( \text{H}_2\text{O}_2 \) stress [72, 73]. \textit{Planomicrobium} strain AX6 contains 4 genes (\textit{hemN}, \textit{hemZ},...
hemL1,2) which were slightly up-regulated and thought to be involved in the coproporphyrinogen III oxidase system and 3 SOD genes in which 2 were up-regulated (guaB and cysK) whose products may also assist Planomicrobium strain AX6 in relieving H2O2 stress, while SOD2 gene was relatively down-regulated.

We next focused on the expression patterns of thiamine metabolism-related genes, which might regulate the enzymatic activity of bacteria [29, 63]. The genes that were up-regulated include iscS, NFSJ (Cysteine desulfurase), E2.7.6.2, THI80, thiM, thiD (hypothetical protein), and thiE (thiamin-phosphate pyrophosphorylase), and the down-regulated genes of the environmental bacterial metabolism were glk, E2.3.3.9, aceB, glcB, kdgK, glk, E5.1.3.3, galM, and hemL, under Planomicrobium strain AX6 compared to CK condition. In addition, numerous genes associated with cysteine were up-regulated (Table S3). Cysteine plays a key role in iron transport, as a high level of cysteine is a crucial component for the biosynthesis of siderophores in iron transport [63, 74]. Cysteine is mainly derived from the conversion of other amino acids to directly acquire extracellular cysteine in the bacterial cell [75]. The expression of genes in E. coli is mostly controlled by S-adenosylmethionine concentrations and intracellular cysteine [76–79], signifying that methionine synthesis, cysteine, and transport genes are up-regulated by H2O2 in Planomicrobium strain AX6. The up-regulated genes encode permease, SAM-dependent methyltransferase, 5'-methylthioadenosine/S-adenosylhomocysteine nucleosidase, and aspartate kinase. Furthermore, chemotaxis plays a crucial role and the genes that were up-regulated include fltN, fliM, fliN, fliE (Hypothetical protein), motB (Flagellar motor protein MotB), and motA (Flagellar motor protein MotA), under Planomicrobium strain AX6 compared to CK condition. However, it is not clear whether the up-regulation of these genes could protect cells against H2O2 stress. An overview of Planomicrobium strain AX6, when exposed to H2O2 concentration (1.5 mM) for 4 h, including antioxidant genes that avoid cell damage, was summarized in Table 2.

Overall, the findings of this study provide a clue to the biological roles and mechanism of the Planomicrobium strain AX6 in H2O2 scavenging. The above-mentioned antioxidant systems proposed that the bacterial strain could protect proteins from the toxicity produced during H2O2 stress. In addition to the above-annotated genes, numerous genes with unknown functions exist in the function of Planomicrobium strain AX6. In this study, several genes coding for antioxidant proteins, including glutathione peroxidase (GSH-Px), Coproporphyrinogen III oxidase, and superoxide dismutase (SOD), were induced in Planomicrobium strain AX6 in response to H2O2 when compared with the control. Taken as a whole, the findings propose that the induced transcripts responsible for antioxidant defense pathways serve as important regulatory mechanisms for scavenging H2O2 in Planomicrobium strain AX6. The DEGs presented in this study could provide a competitive advantage for the survival of Planomicrobium strain AX6 in H2O2-polluted environments.

Conclusion

In this study, Planomicrobium strain AX6 has been studied for its remarkable H2O2 scavenging potential. Based on RNA-seq data, it is evident that Planomicrobium strain AX6 could potentially lead to severe variations in the numerous metabolic pathways involved in generating an antioxidant defense system in response to H2O2 stress, consequently reducing the toxicity of the H2O2 stress. We found many slightly up-regulated DEGs encode proteins involved in antioxidant defense like GSH-Px, Coproporphyrinogen III oxidase, SOD, and other H2O2 scavenging-related metabolisms. To our surprise, in this study, CAT was relatively down-regulated, signifying that CAT might not play a key role in the scavenging of H2O2 in Planomicrobium strain AX6. Collectively, the data have provided several pathways and candidate genes for future functional genomics work. This study opens new research doors to explore bacterial H2O2 scavenging mechanisms and further expands our knowledge of the cold-desert bacteria coping mechanism under extreme environmental stresses.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12866-022-02677-w.

Additional file 1: Table S1. The ability of antioxidant strains to remove various oxidants: different concentrations of hydrogen peroxide (0, 1.5, and 3 mM of H2O2). Planomicrobium-AX6 is an antioxidant strain isolated from the Qaidam Basin; the model strain Escherichia coli was used as a negative control; Deinococcus radiodurans was used as a positive control. Table S2. Summary of the sequencing data of strain Planomicrobium-AX6. Table S3. Selected significantly differentially expressed genes (DEGs) for strain Planomicrobium-AX6 when exposed for 4 hr to H2O2 concentration (1.5 mM). Fig. S1. Response of Planomicrobium-AX6 to H2O2 treatments. A: Survival rate. On the survival response of exponentially growing Planomicrobium-AX6 exposed to H2O2 treatment. B: Challenge time. At specific time intervals, samples were diluted and plated on agar medium to monitor cell viability. The data are means of triplicate points. Fig. S2. Clusters of Orthologous Groups (COG) classification of the Planomicrobium-AX6 were annotated and grouped into 21 specific categories.

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