

ORIGINAL ARTICLE

The Expression and Clinical Significance of Serum Long Noncoding RNA TTTY15 in Patients With Multiple Myeloma

Yuan Zhang, Jun Chen, Xiaoye Sun, Qunyong Gu, Yi Chen, Jinyu Xie

Department of Blood Transfusion, Affiliated Hospital of Nantong University, Nantong Jiangsu, P.R. China

SUMMARY

Background: Multiple myeloma (MM) is a hematologic malignancy caused by the malignant proliferation of plasma cells, which lacks diagnostic markers. This study further explores the clinical significance and applicability of serum lncRNA TTTY15 in MM diagnosis and treatment.

Methods: Using quantitative real-time polymerase chain reaction (qRT-PCR), we measured its relative expression in male MM patients vs. healthy controls, analyzing correlations with MM clinicopathological features and traditional markers ALB, β_2 -MG to assess its potential in MM auxiliary diagnosis.

Results: Serum TTTY15 expression in male multiple myeloma (MM) patients was significantly higher than in healthy controls ($p < 0.001$). In 30 followed-up male MM patients, serum TTTY15 levels decreased after three months of chemotherapy compared to pre-treatment values. Furthermore, TTTY15 expression correlated with albumin levels and renal injury (both $p < 0.05$). Combining TTTY15 with ALB and β_2 -MG improved diagnostic performance for MM.

Conclusions: Serum TTTY15 was variably expressed in MM patients, indicating that serum TTTY15 may be a novel biomarker for MM diagnosis and dynamic monitoring.

(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250727)

Correspondence:

Professor Yuan Zhang
Department of Blood Transfusion
Affiliated Hospital of Nantong University
Nantong Jiangsu
P.R. China
Email: tdfyuan@163.com

KEYWORDS

multiple myeloma, long noncoding RNAs TTTY15, diagnostic efficiency, biomarker, serum

LIST OF ABBREVIATIONS

MM - multiple myeloma
lncRNA - long noncoding RNA
cDNA - complementary DNA
ALB - albumin
 β_2 -MG - β_2 -microglobulin
ROC - receiver operating characteristic
AUC - area under the curve
PPV - positive predictive value
NPV - negative predictive value

INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by abnormal clonal proliferation of plasma cells in the bone marrow, predominantly affecting middle-aged and elderly populations, with a significantly higher incidence in males than in females [1]. MM often involves multiple systems throughout the body, commonly presenting with symptoms such as anemia, hypercalcemia, bone pain, renal impairment, and immune dysfunction [2]. The disease has an insidious onset and lacks specific clinical manifestations, the probability of misdiagnosis or missing diagnosis is significantly elevated. Laboratory tests such as bone marrow cytology and serum protein electrophoresis hold certain diagnostic significance and value for MM, yet they suffer from limitations including high false-positive and false-negative rates, poor specificity, and low sensitivity. Consequently, in recent years, researchers worldwide have focused on exploring minimally invasive biomarkers with high sensitivity and good specificity to enhance the efficiency of early auxiliary diagnosis for MM.

Long noncoding RNAs (lncRNAs) are RNA molecules exceeding 200 nucleotides in length. They have diverse biological origins, lack protein-coding functions, and possess highly conserved secondary and tertiary structures [3]. lncRNAs are involved in various biological processes such as chromatin remodeling, cell differentiation regulation, DNA methylation, and histone modification, playing crucial roles in physiological and/or pathological processes within organisms [4]. Abnormal expression of lncRNAs can lead to abnormal tissue growth and differentiation, promoting tumor development. Many scholars both domestically and internationally have identified numerous dysregulated lncRNAs in tumor plasma cells through microarray analysis and RNA sequencing techniques, revealing their prognostic features [5-9]. These results indicate that lncRNAs have independent predictive roles in the disease outcome of MM. They also highlight the importance of elucidating the molecular pathways by which specific dysregulated lncRNAs affect myeloma cell growth, disease progression, and treatment response.

Y-chromosome-localized factors may be potential gene therapy targets, since the Y chromosome is haploid and has a smaller genome, making gene editing more efficient compared to other chromosomes. The fact that women can survive healthily without a Y chromosome suggests that targeting factors on the Y chromosome for drug therapy may cause fewer side effects, offering significant advantages in treatment. MM occurs at a significantly higher rate in men than in women, which may be related to genetic susceptibility. lncRNA TTTY15 located on the Y chromosome has been confirmed to be an oncogenic factor in various tumors [10,11], but its clinical significance in MM remains unproven. This study uses reverse transcription quantitative polymerase chain reaction (qRT-PCR) to detect differences in

TTY15 expression between male MM patients and healthy controls, analyzing its correlation with clinical pathological features and traditional auxiliary diagnostic indicators of MM, to explore the clinical significance of TTTY15 in the early auxiliary diagnosis of MM.

MATERIALS AND METHODS

From January 2019 to August 2020, serum samples of 102 male patients clinically diagnosed with MM were collected at the Affiliated Hospital of Nantong University. All patients met the diagnostic criteria for MM, with ages ranging from 43 to 81 years and an average age of 63 years. All enrolled patients were newly diagnosed and had not received any treatment. During the same period, serum samples from 96 healthy controls who underwent physical examinations at the same hospital were collected as the control group. In the healthy control group, the ages ranged from 40 to 83 years, with an average age of 56 years. This study was approved by the Ethics Committee of the Affiliated Hospital of Nantong University.

Instruments

Total RNA was extracted from 300 μ L serum by using a serum extract Kit (Life Technologies, USA). The extracted total RNA was reverse-transcribed into single-stranded cDNA using a reverse transcription kit (Thermo Fisher Science, USA). Reverse transcription amplification instrument (BIO-RAD, USA). The expression of TTTY15 in serum samples was detected by LightCycler cobas Z480 PCR (Roche Diagnostics, Germany). The TTTY15 and 18S primers (Ribaud Corporation, Guangzhou, China). Biochemical index determination was carried out with the AU5800 fully automatic biochemical analyzer (Beckman Coulter, USA).

Methods sections

Collect 5 mL of blood specimens from subjects using red vacuum collection tubes containing separation gel. After centrifugation at 4,000 r/minute for 8 minutes at room temperature, transfer the upper-layer serum into 1.5 mL RNase-free EP tubes and store them at -80°C for later use. Extract total RNA from 400 μ L of serum according to the manufacturer's protocol. Detect the absorbance values of the final liquid at 260 nm and 280 nm by ultraviolet spectrophotometry. An A260/280 nm ratio between 1.8 and 2.0 indicates that the measured RNA has good purity and can be used for subsequent experiments. Synthesize cDNA by reverse transcription. Take 10 μ L of total RNA for the reverse transcription reaction. Transfer 3 μ L of the synthesized cDNA for qRT-PCR. Using 18S as the internal reference, the relative expression level of TTTY15 is calculated by the $2^{-\Delta\Delta\text{Ct}}$ method. The reaction system is shown in Table 1. After accurately adding samples in the dark, perform a short centrifugation. The reaction conditions are as follows: pre-denaturation at 95°C for 15 minutes; amplifi-

cation at 95°C for 15 seconds, 60°C for 30 seconds, 72°C for 30 seconds (with fluorescence signal collection), for 40 cycles. Each sample is set with 3 replicate wells, and the results are averaged. The TTTY15 primer sequence:

5'-GGTGGTATGATTGGCCTTAGAG-3' (forward);
5'-GGATTCCCTATGACTTATCAGTTCC-3 (reverse).

The 18S rRNA primer sequences are:

5'-GTAACCCGTTGAACCCATT-3' (forward);
5'-CCATCCAATCGGTAGTAGCG-3' (reverse).

The relative expression level of TTTY15 in serum was expressed using the $RQ = 2^{-\Delta\Delta C_t}$ method.

ALB and β_2 -MG were detected using the Siemens ADVIA 2400 fully automated biochemistry analyzer, while λ light chains and κ light chains were analyzed by the Sebia HYDRASYS 2 fully automated agarose gel electrophoresis system. Quality control for all experiments was within the acceptable.

Statistical analysis

Statistical analysis was performed using SPSS software (version 20.0), and graphical representations were generated using GraphPad Prism software (version 9.0). The Mann-Whitney test was used to compare the relative expression levels of TTTY15 between the MM group and the healthy control group. The Kruskal-Wallis H-test was employed for diversity analysis among multiple groups. Spearman's correlation analysis was used to evaluate the relationships between the relative expression levels of TTTY15 and the serum levels of ALB, β_2 M, λ light chain, and κ light chain in the MM group. The diagnostic efficacy of TTTY15 for MM was assessed using the receiver operating characteristic (ROC) curve and the area under the curve (AUC) with a 95% confidence interval (95% CI). Statistical significance was set at $p < 0.05$.

RESULTS

Methodological validation of detecting the relative expression level of TTTY15 by qRT-PCR

The cDNA from serum samples of multiple myeloma patients was subjected to 10-fold serial dilution (1:10, 1:100, 1:1,000, 1:10,000, 1:100,000), and the CT values of TTTY15 and 18S rRNA were detected. The standard curve for TTTY15 was $y = -1.701x + 18.92$, $R^2 = 0.9998$; while the standard curve for 18S rRNA was $y = -3.018x + 10.85$, $R^2 = 0.9998$. Both standard curves met the experimental requirements.

Thirty serum samples (15 from multiple myeloma patients and 15 from healthy controls) were randomly pooled in equal volumes and aliquoted into 20 equal portions. RNA was extracted from 10 aliquots of the pooled serum samples in the same batch, and the Ct values of TTTY15 and 18S rRNA were measured in the same batch. The intra-batch CV was calculated based on the Ct values. Additionally, RNA was extracted from one aliquot of the pooled serum samples in each of 10

different batches, and the CT values of TTTY15 and 18S rRNA were measured in each of the 10 batches for each RNA aliquot. The inter-batch CV was calculated based on the Ct values. The results showed that the intra-batch CVs for both TTTY15 and 18S rRNA were $< 2\%$, and the inter-batch CVs were $< 5\%$, indicating that the repeatability met the experimental requirements, as showed in Table 2.

Twenty serum samples (10 from multiple myeloma patients and 10 from healthy controls) were randomly mixed in equal volumes and evenly divided into 10 aliquots. Five of these aliquots were incubated at room temperature for 0, 6, 12, 18, and 24 hours, respectively, while the other five underwent 0, 1, 3, 5, and 10 freeze-thaw cycles, respectively. RNA was extracted after the aforementioned treatments, and the CT values of TTTY15 and 18S rRNA were measured. The results showed that the CT values of both TTTY15 and 18S rRNA remained relatively stable, meeting the experimental requirements, as shown in Figure 1.

Expression differences of TTTY15 in serum between MM patients and healthy controls

The relative expression levels of TTTY15 in the serum of 102 male MM patients and 96 healthy male controls were detected by qRT-PCR. The results showed that the relative expression level of TTTY15 in the serum of MM patients was 1.450 ± 0.854244 , while that in the healthy control group was 0.714 ± 0.343028 . The expression level in the MM group was significantly higher than that in the healthy control group ($p < 0.001$). The results are shown in Figure 2.

Relationship between TTTY15 and clinical indicators

MM patients were grouped according to clinical and pathological parameters including age, total protein, albumin, globulin, M protein, hemoglobin, light chain, urine protein, renal damage, and bone damage. The results showed that the relative expression level of serum TTTY15 in 102 MM patients was correlated with albumin levels and renal damage ($p < 0.05$); however, there was no significant association with age, total protein, globulin, M protein, hemoglobin, light chain, urine protein, or bone damage ($p > 0.05$), as shown in Table 3.

Dynamic monitoring of MM patients with TTTY15 as an auxiliary marker

To assess the dynamic changes of serum TTTY15 expression levels in MM patients, the changes in TTTY15 levels were measured in 30 newly diagnosed MM patients who had not received treatment before and after 3 months of chemotherapy. Compared with pre-treatment levels, TTTY15 levels significantly decreased after treatment, with a statistically significant difference ($p < 0.001$). Additionally, TTTY15 levels were detected in a healthy control group ($n = 30$) and a relapsed MM patient group ($n = 30$). The results showed that TTTY15 levels in the relapsed MM patient group were signifi-

Table 1. qRT-PCR reaction system.

Component	Volume (μ L)
SYBR GreenImix	10
Forward primer	1
Reverse primer	1
RNase-freeH ₂ O	5
cDNA	3

Table 2. Intra-batch and inter-batch repeatability (CV, %) of TTTY15 and 18S rRNA.

	TTY15	18S
Intra-assay Mean \pm SD	27.766 \pm 0.84325	20.800 \pm 0.3793
Intra-assay CV, %	1.56%	1.82%
Inter-assay Mean \pm SD	27.368 \pm 0.8964	21.148 \pm 0.4119
Inter-assay CV, %	3.16%	1.82%

cantly higher than those in the healthy control group ($p < 0.001$). These findings indicate that the expression level of serum TTTY15 can assist in monitoring the therapeutic efficacy of MM patients to a certain extent, as shown in Figure 3.

Analysis of the diagnostic efficacy of serum TTTY15

Diagnostic efficacy analysis of serum TTTY15 ROC curves were plotted based on the expression levels of serum TTTY15, β_2 -MG, and ALB in 102 newly diagnosed male MM patients and 86 healthy control subjects. The results showed that TTTY15 exhibited the highest diagnostic efficacy, with AUC of 0.823 (95% CI: 0.765 - 0.881, $p < 0.001$), which was higher than that of ALB (AUC = 0.779) and β_2 -MG (AUC = 0.662). Taken together, these findings indicate that serum TTTY15 could serve as a potential biomarker with favorable clinical auxiliary diagnostic value for MM, as shown in Figure 4.

Combined detection of serum TTTY15, ALB, and β_2 -MG

In this study, serum TTTY15, ALB, and β_2 -MG were jointly detected in newly diagnosed MM patients, and sensitivity (SEN), specificity (SPE), accuracy (ACCU), positive predictive value (PPV), and negative predictive value (NPV) were calculated. The combined detection of the three indices showed the highest specificity of 94.8%, which was significantly higher than the detection using a single index or the combination of two indices, as shown in Table 4.

Correlation analysis of relative expression of serum TTTY15 with ALB and β_2 -MG

Correlation analysis was conducted between the relative expression of serum TTTY15 and the levels of serum ALB and β_2 -MG in 85 MM patients. A statistically significant positive correlation was found between serum TTTY15 and ALB ($r = 0.2187$, $p = 0.0443$). In contrast, although a negative correlation was observed between serum TTTY15 and β_2 -MG, it did not reach statistical significance ($r = -0.8354$, $p = 0.4472$), as shown in Figure 5.

DISCUSSION

The etiology of MM is not yet fully understood, and it is currently believed to be associated with various factors such as gene mutations, cytokines and growth factors, chromosomal abnormalities, immune system disorders, environmental factors, and genetic predisposition. Early diagnosis and comprehensive treatment are key to improving survival rates and quality of life [12,13]. lncRNAs, once regarded as "transcriptional noise", have now become "star molecules" in the academic field. Despite lacking protein-coding capacity, they can regulate gene expression through epigenetic mechanisms and influence cellular functions. Numerous studies have reported their roles in the development and progression of MM. For instance, MALAT1 is upregulated during MM progression, and its high expression levels are significantly associated with poorer overall survival and progression-free survival [14]. FEZF1-AS1, which is aberrantly expressed in various cancers, promotes MM cell

Table 3. Correlation between TTY15 expression and clinicopathologic features of MM patients.

Clinical characteristics	n	Low expression	High expression	Pearson's χ^2	p
Age					
≤ 65	55	14	51	3.062	0.080
> 65	37	3	34		
M protein					
IgG	43	13	30	0.565	0.754
IgA	28	10	18		
Unclassified	31	9	22		
Light chain					
λ	55	12	45	1.048	0.306
κ	47	14	33		
Hb (g/L)					
≥ 120	29	4	25	0.241	0.624
< 120	73	13	60		
Total protein					
Abnormal	48	13	35	0.081	0.776
Normal	54	16	38		
Albumin					
Abnormal	39	4	35	5.463	0.019 *
Normal	63	19	44		
Globulin					
Abnormal	75	11	64	0.816	0.366
Normal	27	6	21		
Urine protein					
Positive	31	5	26	0.009	0.923
Negative	71	12	59		
Renal damage					
Yes	56	5	51	5.353	0.021 *
No	46	12	34		
Bone damage					
Yes	80	11	69	2.272	0.132
No	22	6	16		

* p < 0.05

Table 4. Comparison of diagnostic efficacy for MM by single or combined detection of TTY15 and other indices.

	Sensitivity	Specificity	Accuracy	PPV	NPV
ALB	76.5% (78/102)	70.8% (68/96)	73.7% (146/198)	73.6% (78/106)	73.9% (68/92)
β ₂ -MG	73.5% (75/102)	37.5% (36/96)	56.1% (111/198)	55.6% (75/135)	57.1% (36/63)
TTY15	83.3% (85/102)	68.8% (66/96)	76.3% (151/198)	73.9% (85/115)	79.5% (66/83)
ALB + TTY15	65.7% (67/102)	90.6% (87/96)	77.8% (154/198)	88.2% (67/76)	71.3% (87/122)
β ₂ -MG + TTY15	62.7% (64/102)	82.2% (79/96)	72.2% (143/198)	79.0% (64/81)	67.5% (79/117)
ALB + β ₂ -MG + TTY15	47.1% (48/102)	94.8% (91/96)	70.2% (139/198)	90.6% (48/53)	62.8% (91/145)

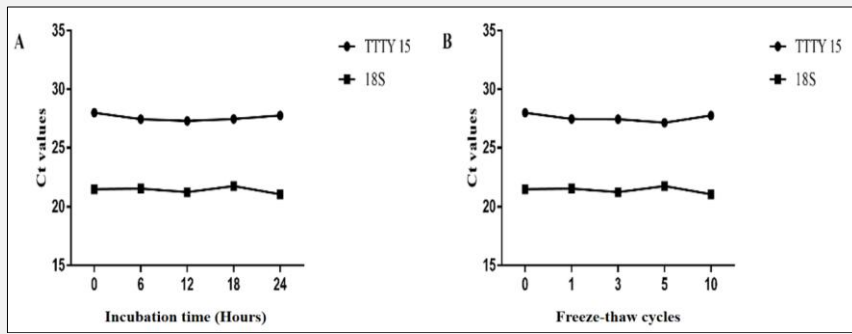


Figure 1. Stability of TTTY15 and 18S rRNA.

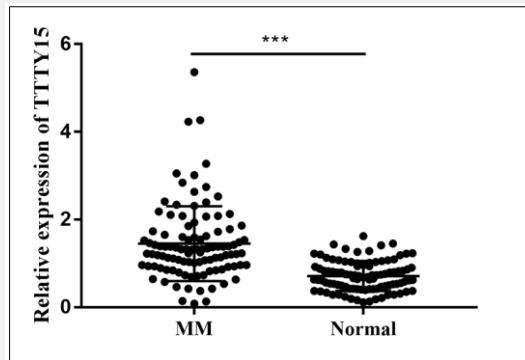


Figure 2. Relative expression levels of TTTY15 in serum of male MM patients and healthy controls (***p* < 0.001).

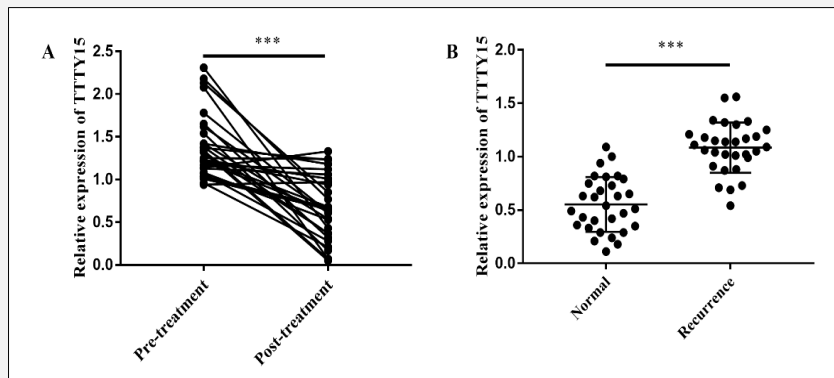


Figure 3. Dynamic changes of serum TTTY15 expression levels for auxiliary detection in MM patients.

A. There were differences in TTTY15 expression levels in serum before and after treatment; B. There were differences in TTTY15 expression levels in serum between the healthy control group and the relapsed MM patient group (***p* < 0.001).

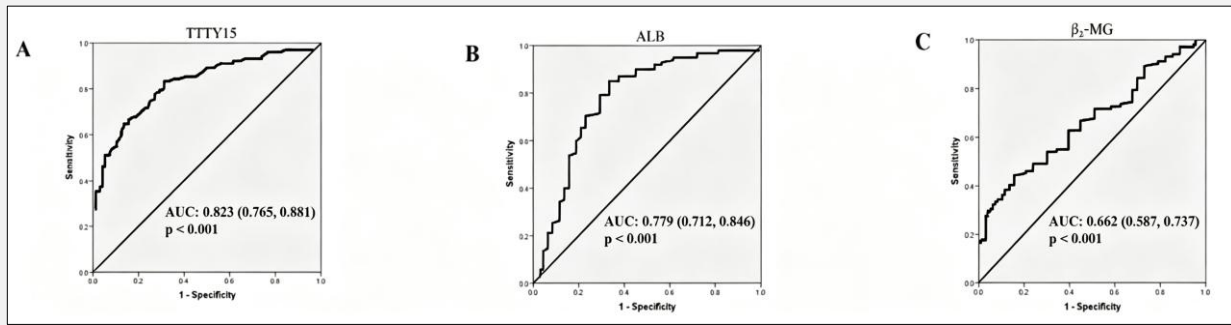


Figure 4. Roc curves of TTTY15, ALB, β_2 -MG.

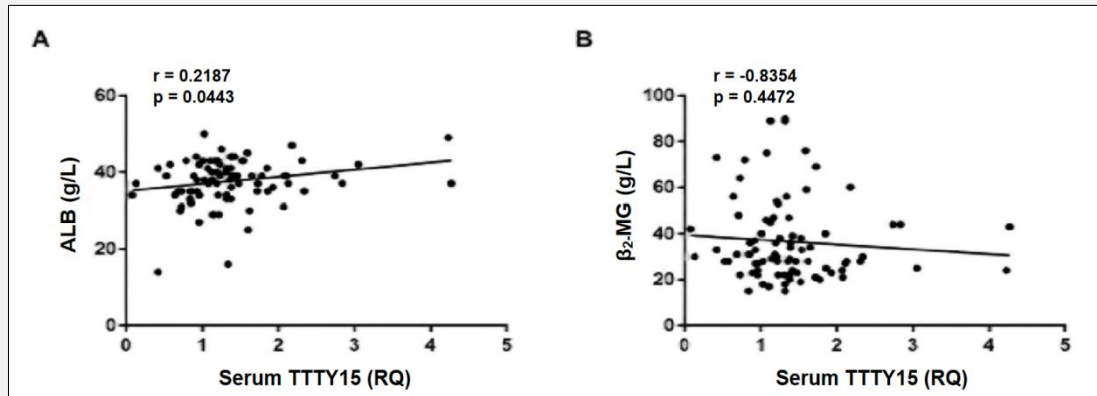


Figure 5. Correlation between serum TTTY15 levels and ALB/ β_2 -MG.

A. Correlation between serum TTTY15 levels and ALB; B. Correlation between serum TTTY15 levels and β_2 -MG.

proliferation and survival via the miR-610/Akt3 axis [15-18]. The lncRNA LUCAT1 inhibits TGF- β signaling, thereby impeding MM growth and bone lesions [19-23]. Maternally expressed gene 3 (MEG3), a 1.6 kb imprinted gene located on chromosome 14q32, exhibits tumor-suppressive functions. Recent research indicates that MEG3 deletion/methylation enhances angiogenesis-a critical step in MM pathogenesis-by disrupting miR-9 interactions and endothelial cell suppression [24]. lncRNAs, including MEG3, hold promise as important biomarkers for early diagnosis and prognosis in MM.

Long-chain noncoding RNA TTTY15 is a single gene located on the Y chromosome and has unique advan-

tages in gene editing therapy. TTTY15 may exhibit differential localization across various types of cancer and could play dual roles within both the cytoplasm and nucleus [25-28]. However, current research has yet to elucidate the application value of TTTY15 in the progression of multiple myeloma (MM).

In this study, the relative expression levels of TTTY15 in serum were measured in 102 male MM patients and 96 healthy male controls. Statistical analysis showed that MM patients had significantly higher serum TTTY15 expression than healthy controls, with a statistically significant difference ($p < 0.001$). Correlation analysis between TTTY15 expression and clinicopathological characteristics revealed that TTTY15 levels

were significantly associated with albumin levels and renal impairment (both $p < 0.05$). These findings indicate that TTTY15 is correlated with MM development and has potential diagnostic value for the disease. ROC curve analysis for differentiating MM patients from healthy controls across various indicators showed that at a TTTY15 cutoff value of 0.835, the sensitivity and accuracy for auxiliary diagnosis of MM were 83.3% and 68.8%, respectively. TTTY15 had an AUC of 0.823, higher than traditional markers ALB and β_2 -MG. As a standalone diagnostic indicator for MM, TTTY15 exhibited the highest accuracy and sensitivity, though its specificity was slightly lower than ALB. Combined detection of TTTY15 with these two auxiliary markers significantly increased specificity to 94.8%. Serum TTTY15 may serve as a potential biomarker with clinical value for auxiliary diagnosis of MM. Additionally, the combined use of TTTY15, ALB, and β_2 -MG enhances the efficiency of MM auxiliary diagnosis.

However, due to the small sample size and limited scope of disease data collection, the research findings are inevitably influenced by regional and disease-specific characteristics of *Parazacco spilurus* subsp. *Spilurus*. In subsequent studies, it is necessary to further validate the above conclusions by expanding the sample size, thereby enhancing their universality and reliability. Unresolved questions include its unclear pathogenic mechanism and influences of specimen collection timing or disease progression stage. Further research with larger cohorts and mechanistic/functional studies is warranted to address these gaps and solidify TTTY15's clinical utility. Subsequent long-term follow-up will be conducted on the prognosis and survival time of MM patients, with further in-depth exploration of the mechanistic role of TTTY15 in disease prognosis.

This study systematically analyzed serum samples from male MM patients and healthy male controls, employing qRT-PCR to quantify relative TTTY15 expression and evaluate its clinical significance and potential as an auxiliary diagnostic biomarker for MM. Key findings reveal that serum TTTY15 levels were significantly elevated in MM patients compared to healthy controls, providing mechanistic insights into the gender disparity in MM incidence. Additionally, TTTY15 expression showed utility in monitoring treatment response in MM patients. Correlational analyses demonstrated that TTTY15 levels were associated with albumin levels and renal impairment but not with age, total protein, globulin, M protein, hemoglobin, light chains, urinary protein, or bone lesions. Diagnostic efficacy analysis showed that TTTY15 alone exhibited favorable performance, and its combination with ALB and β_2 -MG further enhanced diagnostic specificity. Collectively, these results highlight TTTY15 as a promising novel auxiliary diagnostic marker for MM with clinical translation potential.

Acknowledgment:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interest:

None.

References:

1. Rajkumar SV. Multiple myeloma: 2024 update on diagnosis, risk-stratification, and management. *Am J Hematol* 2024;99(9):1802-24. (PMID: 38943315)
2. Chen Q, Zhang M, Zheng S, Tong Y, Tan Y. Therapeutic progress in relapsed/refractory multiple myeloma. *Ann Hematol* 2024; 103(6):1833-41. (PMID: 38609727)
3. Wu R, Su Y, Wu H, Dai Y, Zhao M, Lu Q. Characters, functions and clinical perspectives of long non-coding RNAs. *Mol Genet Genomics* 2016;291(3):1013-33. (PMID: 26885843)
4. Bailey C, Pich O, Thol K, et al. Origins and impact of extrachromosomal DNA. *Nature* 2024;635(8037):193-200. (PMID: 39506150)
5. Ronchetti D, Agnelli L, Pietrelli A, et al. A compendium of long non-coding RNAs transcriptional fingerprint in multiple myeloma. *Sci Rep* 2018;8(1):6557. (PMID: 29700321)
6. Samur MK, Minvielle S, Gulla A, et al. Long intergenic non-coding RNAs have an independent impact on survival in multiple myeloma. *Leukemia* 2018;32(12):2626-35. (PMID: 29749396)
7. Hu AX, Huang ZY, Zhang L, Shen J. Potential prognostic long non-coding RNA identification and their validation in predicting survival of patients with multiple myeloma. *Tumour Biol* 2017; 39(4):1010428317694563. (PMID: 28378636)
8. Ronchetti D, Agnelli L, Taiana E, et al. Distinct lncRNA transcriptional fingerprints characterize progressive stages of multiple myeloma. *Oncotarget* 2016;7(12):14814-30. (PMID: 26895470)
9. Zhou M, Zhao H, Wang Z, et al. Identification and validation of potential prognostic lncRNA biomarkers for predicting survival in patients with multiple myeloma. *J Exp Clin Cancer Res* 2015; 34(1):102. (PMID: 26362431)
10. Wang W, Yang J. Long noncoding RNA TTTY15 promotes growth and metastasis of esophageal squamous cell carcinoma by sponging microRNA-337-3p to upregulate the expression of JAK2. *Anticancer Drugs* 2020;31(10):1038-45. (PMID: 32868648)
11. Xiao G, Yao J, Kong D, et al. The long noncoding RNA TTTY15, which is located on the Y chromosome, promotes prostate cancer progression by sponging let-7. *Eur Urol* 2019;76(3): 315-26. (PMID: 30527798)
12. Perrot A, Corre J, Avet-Loiseau H. Risk Stratification and Targets in Multiple Myeloma: From Genomics to the Bedside. *Am Soc Clin Oncol Educ Book* 2018;38:675-80. (PMID: 30231368)
13. Bong IPN, Esa E. Molecular genetic aberrations in the pathogenesis of multiple myeloma. *Asian Biomed (Res Rev News)* 2023; 17(4):152-62. (PMID: 37860676)

14. Eshraghi R, Sadati S, Bahrami A, et al. Unveiling the role of long non-coding RNA MALAT1: a comprehensive review on myocardial infarction. *Front Cardiovasc Med* 2024;11:1429858. (PMID: 39171328)
15. Wu X, Zhang P, Zhu H, Li S, Chen X, Shi L. Long noncoding RNA FEZF1-AS1 indicates a poor prognosis of gastric cancer and promotes tumorigenesis via activation of Wnt signaling pathway. *Biomed Pharmacother* 2017;96:1103-8. (PMID: 29239821)
16. Jin S, Chen S, Ma Y, Yang B, Liu Y. LincRNA FEZF1-AS1 contributes to the proliferation of LAD cells by silencing p57 expression. *Oncotarget* 2017;8(61):103004-13. (PMID: 29262540)
17. Liu J, Feng G, Li Z, Li R, Xia P. Long non-coding RNA FEZF1-AS1 modulates CXCR4 to promote cell proliferation, warburg effect and suppress cell apoptosis in osteosarcoma by sponging miR-144. *Onco Targets Ther* 2020;13:2899-910. (PMID: 32308422)
18. Li QY, Chen L, Hu N, Zhao H. Long non-coding RNA FEZF1-AS1 promotes cell growth in multiple myeloma via miR-610/Akt3 axis. *Biomed Pharmacother* 2018;103:1727-32. (PMID: 29864963)
19. Morelli E, Ribeiro CF, Rodrigues SD, et al. Targeting acetyl-CoA carboxylase suppresses de novo lipogenesis and tumor cell growth in multiple myeloma. *Clin Cancer Res* 2025;31(10):1975-87. (PMID: 40053701)
20. Passos RMA, Marcolino MAZ, Passos JA, et al. Cost-effectiveness of preemptive plerixafor versus rescue plerixafor for mobilization and collection of hematopoietic stem cells in patients with multiple myeloma and lymphoma. *J Clin Apher* 2025;40(3):e70026. (PMID: 40317777)
21. Liu J, Yao L, Yang Y, et al. A novel stemness-related lncRNA signature predicts prognosis, immune infiltration and drug sensitivity of clear cell renal cell carcinoma. *J Transl Med* 2025;23(1):238. (PMID: 40016772)
22. Yoon JH, You BH, Park CH, Kim YJ, Nam JW, Lee SK. The long noncoding RNA LUCAT1 promotes tumorigenesis by controlling ubiquitination and stability of DNA methyltransferase 1 in esophageal squamous cell carcinoma. *Cancer Lett* 2018;417:47-57. (PMID: 29247823)
23. Zheng Z, Zhao F, Zhu D, et al. Long non-coding RNA LUCAT1 promotes proliferation and invasion in clear cell renal cell carcinoma through AKT/GSK-3 β signaling pathway. *Cell Physiol Biochem* 2018;48(3):891-904. (PMID: 30032137)
24. He C, Yang W, Yang J, et al. Long noncoding RNA MEG3 negatively regulates proliferation and angiogenesis in vascular endothelial Cells. *DNA Cell Biol* 2017;36(6):475-81. (PMID: 28418724)
25. Jackstadt R, Röh S, Neumann J, et al. AP4 is a mediator of epithelial-mesenchymal transition and metastasis in colorectal cancer. *J Exp Med* 2013;210(7):1331-50. (PMID: 23752226)
26. Chapuy B, Wood T, Stewart C, et al. DLBclass: a probabilistic molecular classifier to guide clinical investigation and practice in diffuse large B-cell lymphoma. *Blood* 2025;145(18):2041-55. (PMID: 39680847)
27. Huang S, Tao W, Guo Z, Cao J, Huang X. Suppression of long noncoding RNA TTTY15 attenuates hypoxia-induced cardiomyocytes injury by targeting miR-455-5p. *Gene* 2019;701:1-8. (PMID: 30898696)
28. Zheng X, Peng B, Wu X, et al. Male-specific long non-coding RNA testis-specific transcript, Y-linked 15 promotes gastric cancer cell growth by regulating Wnt family member 1/ β -catenin signaling by sponging microRNA let-7a-5p. *Bioengineered* 2022;13(4):8605-16. (PMID: 35287556)