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Predictive value of plasma β2-microglobulin on human body function and senescence

X.-M. DONG[1,3], R. CAI[1], F. YANG[1], Y.-Y. ZHANG[2], X.-G. WANG[2], S.-L. FU[2], J.-R. ZHANG[1,2]

[1]Zhujiang Hospital of Southern Medical University, Guangzhou, Guangdong, China
[2]Guangdong Institute of Tumor Target Intervention and Prevention, Qingyuan, Guangdong, China
[3]The Affiliated People's Hospital of Inner Mogolia Medical University, Huhhot, China

Abstract. – OBJECTIVE: To explore the correlation between plasma β2-microglobulin (β2-MG) as senescence factor with age, heart, liver and kidney function as well as the predictive value of β2-MG in human metabolism function and senescence.

PATIENTS AND METHODS: 387 cases of healthy people of different ages were selected and the automatic biochemical analyzer was used to test β2-MG in plasma based on immunoturbidimetry and also all biochemical indexes. The correlation between β2-MG and age, gender and all biochemical indexes was analyzed.

RESULTS: β2-MG was positively correlated to age, r = 0.373; and the difference was of statistical significance ($p < 0.010$). It was significantly negative correlated to HDL-C but positively correlated to LP (a), BUN, CREA, UA, CYS-C, LDH, CK-MB, HBDH, AST, GLB and HCY.

CONCLUSIONS: β2-MG was closely correlated to age, heart, kidney and liver biochemical indexes, which can be taken as an important biomarker for human body function and anti-senescence and have significant basic research and clinical guidance values.

Key Words:
β2-microglobulin, Biochemical indexes, Predictive value.

Abbreviations

β2-MG = β2-microglobulin; BUN = blood urea nitrogen; CREA = creatinine; UA = uric acid; CYS-C = cystatin C; LDH = lactate dehydrogenase; CK-MB = creatine kinase-MB; HBDH, α-hydroxybutyrate dehydrogenase; AST, aspartate aminotransferase; GLB = globulin; HCY = homocysteine

Introduction

With the age increase, there will be multiple organ failures of the human body and the susceptibility for many chronic diseases is increasing. β2-microglobulin (β2-MG) is positively related to age, which is called the senescence factor in human body[1,2]. It is indicated in many studies that β2-MG level testing in blood is able to increase diagnostic rate of early damage of renal function[3-5]; if the level increases, then it will significantly increase the occurrence of cardiovascular disease[6-8]; for dementia patients, their cerebrospinal fluid and β2-MG in blood are in high expression, which is closely correlated to the cognitive function[9]. It is also pointed out in tumor study that endogenous β2-MG expression during the tumor development is higher than that of healthy people[10]. β2-MG may be a senescence factor that is closely related to heart, brain and kidney; however, it is still not the routine biochemical testing item and receives less attention. This report analyzes the influences of biochemical indexes changes on β2-MG for healthy people and explores the correlation of β2-MG with age, heart, liver and kidney function and also routine testing value and significance of β2-MG.

Patients and Methods

Patients

387 healthy people were selected from April 2014 to November 2015, among which, there were 246 male cases and 141 female cases with the age ranging from 20 to 80 years old and the average age of (49.93 ± 10.13); the inclusion criteria: blood routine examination, biochemical test and imaging examination were within normal range and not reaching the clinical disease diagnosis standard. Exclusion criteria: reaching the clinical disease diagnosis standard with communicable disease and psychological illness; patients or their families were not cooperative.

Corresponding Author: Jiren Zhang, MD; e-mail: j75258249diq@163.com

Method of β2-MG Testing

The immunoturbidimetry was used for β2-MG testing; Hitachi 7100 fully automatic biochemical analyzer was used to test β2-MG and all biochemical indexes; the reagent was provided by Mindray Medical International Limited and tested based on methodological requirements. Normal reference range for β2-MG is 1.0-3.0 mg/L. The correlation between β2-MG level and age and all biochemical indexes were analyzed.

Statistical Analysis

SPSS23.0 statistical analysis software (SPSS Inc., Chicago, IL, USA) was used for data processing and statistical analysis; the measurement data was presented as ± the correlation analysis and the linear regression analysis were applied for different factors correlation; taking = 0.05 as the testing standard, $p < 0.05$ referred to difference of statistical significance.

Results

Difference Analysis between β2-MG and Gender

For 387 cases, there were 246 male cases and 141 female cases. Comparison between their age and β2-MG levels was of no difference (Table I, $p > 0.05$).

Influence of Age on β2-MG Level

For 387 cases, their average age was (49.83 ± 10.13) years old and average β2-MG level in blood was (1.13 ± 0.3) mg/L; Groups were divided according to the age: 20-29 years old, 30-39 years old, 40-49 years old, 50-59 years old, 60-69 years old, 70-80 years old, β2-MG levels were different for different age groups; the correlation coefficient of β2-MG levels of 387 cases with ages: r = 0.373, $p < 0.001$, it was positively correlated, as shown in Figure 1.

β2-MG level increased gradually, for 20-50 years old, it was in slow increase while for the age over 50 years old, it increased rapidly. Comparison between groups: there was no statistical significance ($p > 0.05$) regarding the differences of β2-MG levels (F = 0.712, $p = 0.900$) between 20-29 years old and 30-39 years old; comparing β2-MG level between 30-39 years old and 40-49 years old, p-value was reduced (F = 0.086, $p = 0.199$) without statistical significance ($p > 0.05$); comparing 40-49 years old with 50-59 years old in terms of their β2-MG levels, F = 1.812, $p < 0.001$, the difference was of statistical significance; comparing β2-MG levels between 50-59 years old and 60-69 years old, (F = 0.667, $p = 0.010$), taking $p < 0.05$ as standard, there were differences between two groups; comparing β2-MG levels between 60-69 years old and 70-80 years old, (F = 4.634, $p = 0.106$), $p > 0.05$, there were no differences regarding β2-MG level in two groups (Table II).

That is, for age less than 50 years old, β2-MG level increase gradually and the difference is of no obvious difference; for age over 50 years old, β2-MG level increase significantly and the difference between age group is 10-15%; for age over 70 years old, their β2-MG levels increase slowly and within normal reference range.

Correlation Analysis on β2-MG and All Biochemical Values

387 β2-MG cases: 1.125 ± 0.341 mg/L, linear regression analysis and correlation analysis are performed on different biochemical indexes; β2-MG is negatively correlated to HDL-C and positively correlated to LP (a), BUN, CREA, UA, CYS-C, LDH, CK-MB, HBDH, AST, GLB and HCY (Table III, Figure 2).

Discussion

β2-MG was generated by several karyocytes such as lymphocyte, monocyte and blood platelet and locates at cytomembrane. During metabolism, it was gradually separated from HLA and released into blood, and then widely spreaded in saliva, plasma, cerebrospinal fluid, urine and colostrum. β2-MG was able to pass through the

Table I. Correlation between β2-MG and gender.

Gender	Cases	Ge	β2-MG level (mg/L)
Male	246	49.77 ± 9.85	1.133 ± 0.334
Female	141	50.21 ± 10.63	1.110 ± 0.354

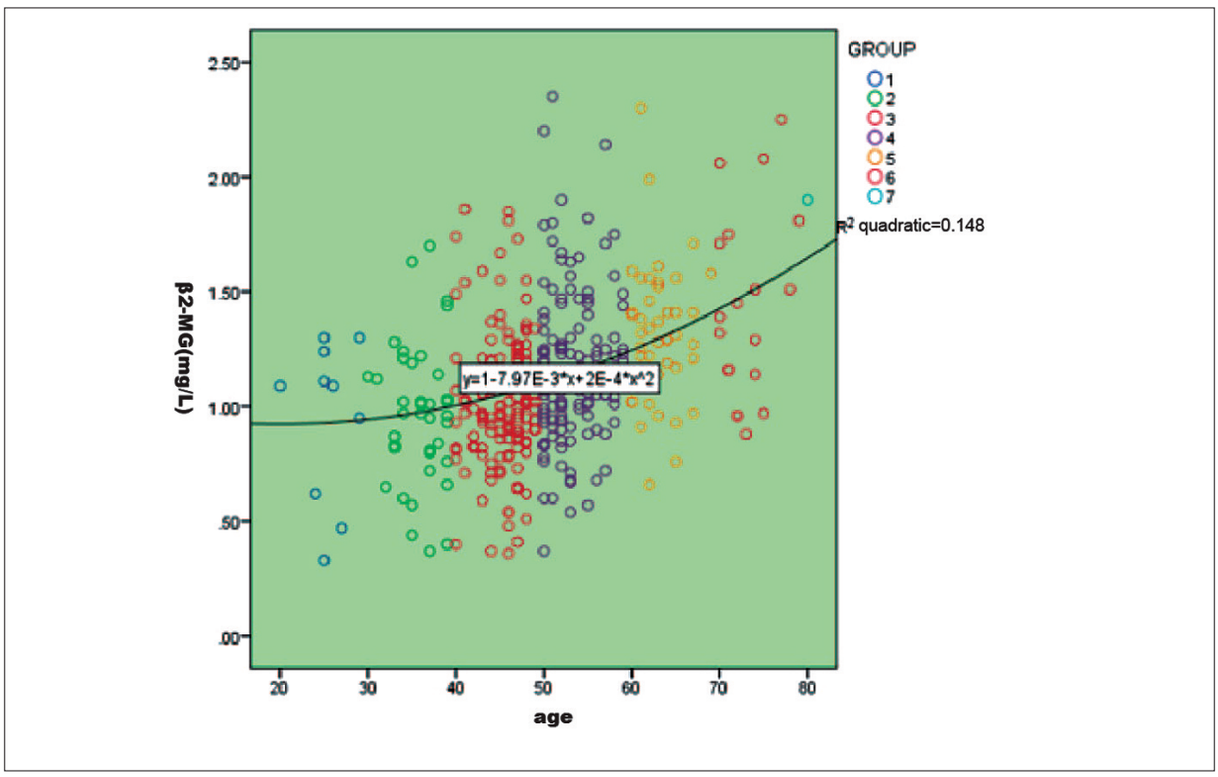


Figure 1. Correlation analysis between β2-MG and age for healthy people.

glomerular filtration membrane freely. When 95% of them passed through the glomerulus, about 99.9% of them would be reabsorbed and degraded by lysosome near kidney tubules in pinocytosis method and cannot get back into the blood. Therefore, β2-MG level in blood was constant and β2-MG in urine usually cannot be tested, however, when kidney tubules had reabsorption dysfunction, β2-MG in urine would increase obviously. When the filtration function of glomerulus was damaged, β2-MG in blood would increase greatly. β2-MG had become early diagnosis index[11] for renal function damage because its dependence on metabolism was closely related to the renal function. It was also pointed out in the control study on hypertension and coronary artery stenosis patients[6,7,12,13] that β2-MG was closely related to the systolic pressure and the score of coronary stenosis, which may be the independent risk factor of coronary heart disease[14,15].

Table II. Comparison of β2-MG levels of different Age groups.

Age (years old)	Causes	β2-MG level (mg/L)
20-29	10	0.950 ± 0.352
30-39	40	0.966 ± 0.303
40-49	143	1.035 ± 0.289
50-59	130	1.170 ± 0.336
60-69	44	1.313 ± 0.301
70-80	20	1,463 ± 0.413

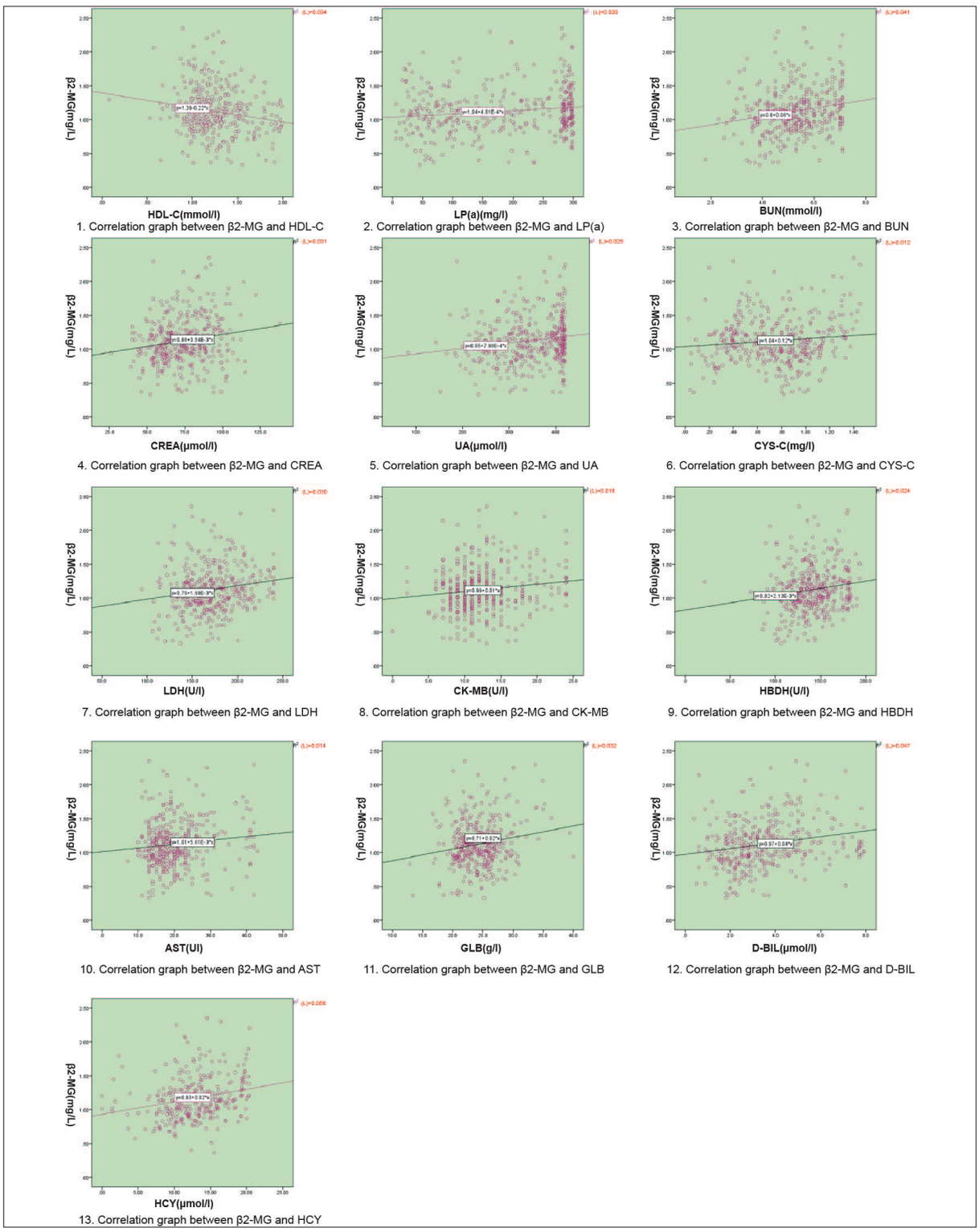
This study was different from the control analysis on β2-MG levels of patients. 387 healthy people were selected and divided into groups for 10 years as a period and β2-MG level analysis is performed. The results showed that β2-MG was positively correlated to age; for 20-50 years old, β2-MG level increased but slowly. The comparison between groups had no significant difference; for 50-69 years old, β2-MG level increased steadily and the comparison of β2-MG levels in two groups showed $p<0.05$; for over 70 years old, β2-MG increased slowly and compared with 60-69 years old, $p>0.05$. The β2-MG level was positively correlated to the senescence and can be taken as the evaluation index for senescence, which was higher in aged groups and an independent predictive factor for total death rate[16].

Table III. Correlation analysis between β2-MG and biochemical indexes.

Biochemical indexes	Comparison cases	Mean value ± standard deviation	r correlation coefficient with β2-MG	*p*-value correlated with β2-MG
HDL-C (mmol/L)	387	1.25 ± 0.29	-0.186	0.000*
LP(a) (mg/L)	387	183.17 ± 99.79	0.141	0.006*
BUN (mmol/L)	387	5.29 ± 1.13	0.204	0.000*
CREA (umol/L)	387	73.88 ± 16.91	0.176	0.001*
UA (umol/L)	387	343.59 ± 67.76	0.159	0.002*
CYS-C (mg/L)	387	0.743 ± 0.323	0.110	0.031*
LDH (U/L)	387	171.45 ± 29.83	0.174	0.001*
CK-MB (U/L)	387	12.57 ± 4.39	0.136	0.007*
HBDH (U/L)	387	141.59 ± 24.63	0.154	0.002*
AST (U/L)	387	20.43 ± 7.21	0.118	0.020*
GLB (g/L)	387	24.39 ± 3.59	0.179	0.000*
HCY (umol/L)	387	12.86 ± 4.13	0.237	0.000*

Through regression analysis, it has been known that β2-MG level in blood was correlated to seven cardiac function indexes (CHOL, TG, HDL-C, LDL-C, ApoA, ApoB and LP (a)), r = 0.280, $p < 0.01$. It was indicated that β2-MG level in blood was closely correlated to the cardiovascular function changes. Among which, it was known through bivariate correlation analysis between β2-MG and all indexes that β2-MG level was negatively correlated to HDL-C (r = -0.186, $p < 0.01$), positively correlated to the independent risk factor of coronary heart disease LP (a) (r = 0.141, $p < 0.01$) and not correlate to others. As a protective index in cardiovascular disease, HDL-C, called "good cholesterol", was effective in anti-atherosclerosis and reduction of the occurrence risks of cardiovascular disease; besides, it was negatively correlated to senescence factor β2-MG. Previous studies found that atherosclerosis can also be regarded as an inflammatory response of blood vessel endothelium on all kinds of physical and pathological damage factors[17,18] along with β2-MG level in plasma increase, which can be taken as an independent risk factor of coronary heart disease and had interactive influences.

It has been proved in this study that β2-MG level was positively correlated to four renal function indexes (CREA, UA, BUN and CYS-C) based on the regression analysis, r = 0.272, $p = 0.001$. It was indicated that β2-MG level in blood was closely correlated to the renal function changes. Among which, based on bivariate correlation analysis between β2-MG and all indexes, β2-MG level was positively correlated to all variables (r = 0.176, 0.159, 0.204, 0.110, $p < 0.05$): the serum creatinine was mainly filtered out thorough glomerulus and cannot be reabsorbed by kidney tubules. When the exogenous creatinine intake was stable, the serum creatinine depended on the filtering capacity of glomerulus; however, the sensibility of judging filtering capacity of glomerulus on serum creatinine was lower than that of β2-MG level and they were positively correlated. The uric acid was the end product of purine nucleotide metabolism, generally speaking, over 2/3 uric acid was filtered out through glomerulus to maintain the metabolism balance; and then it was reabsorbed, secreted and then absorbed again. This complex discharge process depended on perfect functions of glomerulus and kidney tubules and is easily influenced by foods. BUN was the end product of protein metabolism and mainly filtered out through the glomerulus. About 30-40% of them were reabsorbed at kidney tubules and, therefore, BUN was able to observe the function of the glomerulus roughly. Blood CYS-C was a cysteine protease inhibitor and it was only filtered out through glomerulus, and then it was reabsorbed at proximal tubule and fully resolved. It was not influenced by the factors inside or outside kidney because it was not back into the blood. It was closely related to the filtering rate of glomerulus; therefore, it was an objective index for evaluating the filtering capacity of the glomerulus. As a result, early evaluation function of β2MG on kidney was better than that of CREA, UA and BUN but the same as CYS-C. Both of them can be taken as the early diagnosis indexes for renal function damage. It can also be concluded that for healthy people,



1. Correlation graph between β2-MG and HDL-C
2. Correlation graph between β2-MG and LP(a)
3. Correlation graph between β2-MG and BUN
4. Correlation graph between β2-MG and CREA
5. Correlation graph between β2-MG and UA
6. Correlation graph between β2-MG and CYS-C
7. Correlation graph between β2-MG and LDH
8. Correlation graph between β2-MG and CK-MB
9. Correlation graph between β2-MG and HBDH
10. Correlation graph between β2-MG and AST
11. Correlation graph between β2-MG and GLB
12. Correlation graph between β2-MG and D-BIL
13. Correlation graph between β2-MG and HCY

Figure 2. ***1.*** Correlation graph between β2-MG and HDL-C. ***2.*** Correlation graph between β2-MG and LP(a). ***3.*** Correlation graph between β2-MG and BUN. ***4.*** Correlation graph between β2-MG and CREA. ***5.*** Correlation graph between β2-MG and UA. ***6.*** Correlation graph between β2-MG and CYS-C. ***7.*** Correlation graph between β2-MG and LDH. ***8.*** Correlation graph between β2-MG and CK-MB. ***9.*** Correlation graph between β2-MG and HBDH. ***10.*** Correlation graph between β2-MG and AST. ***11.*** Correlation graph between β2-MG and GLB. ***12.*** Correlation graph between β2-MG and D-BIL. ***13.*** Correlation graph between β2-MG and HCY.

β2-MG was positively correlated to BUN, CREA, UA and CYS-C; therefore, β2-MG was not only the early diagnosis index for renal function damage but also the predictive index for early damage.

Through regression analysis, it was discovered that β2-MG level in blood was correlated to four myocardial enzymes (LDH, CK, CK-MB and HBDH), r = 0.229, $p < 0.01$. It was indicated that β2-MG level in blood was closely correlated to the myocardial function changes, among which, based on bivariate correlation analysis between β2-MG and all indexes, it was concluded that β2-MG level was positively correlated to LDH, CK-MB and HBDH (r = 0.174, 0.136, 0.154, $p < 0.01$) and not related to CK. LDH was distributed all over the body and most of it was in kidney and then skeletal muscle and myocardium. For acute myocardial infarction, 80% LDH increased within 12-24h. HBDH was similar to LDH, both of them were positively related to β2-MG maybe because it had a high amount in kidney and β2-MG was closely related to renal function; CK-MB was a kind of enzyme generated by myocardium and therefore it reflected the myocardial function and was correlated to β2-MG. In combination of the fact, LDH and HBDH were related to it; therefore, it was considered that β2-MG may be closely correlated to the myocardial function.

Conclusions

In this study, it work discovered through regression analysis that β2-MG level in blood was positively correlated to the liver function indexes (AST, ALT, TBA, TBIL, IBIL ALB, GLB, ALP, GGT, etc.), r = 0.361, $p < 0.001$, which showed that β2-MG level in blood was closely correlated to the liver function changes. Through bivariate correlation analysis between β2-MG and all indexes, the β2-MG level was positively correlated to AST and GLB (r = 0.118, 0.179, $p < 0.05$) and not related to others.

Above all, this work innovatively studied and explored the correlation between β2-MG levels and all biochemical indexes for healthy people to prove that β2-MG should be correlated to senescence, renal function, myocardial function, liver function and immune function. It can be taken as an important estimation index for human metabolism function and senescence and may have super early predictive value for many diseases.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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