Ultra-high sensitivity chromosomal instability monitoring in UCMSC anti-kids monkey aging

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Keyword: Ultra-high sensitivity chromoso; Instability; Monitor; UCMSC; Macaque; Anti-Aging;

Abstract: Objectives, Through experiment; The application of ultra-high sensitivity chromosome instability monitoring in UCMSC anti-cynomolgus aging is analyzed, which provides some reference and help for the clinical cancer treatment. The Methods: Rhesus macaques were divided into an experimental group and control group, respectively, and the data of the two groups were compared. RESULTS: Plasma cfDNA telomere length and 171 genes (to be re-validated) may also be used as an indicators for judging aging and evaluation of stem cell treatment efficacy; and certain characteristics of plasma cfDNA may be used as indicators for predicting the stem cell efficacy.

1. Introduction

Application Chromosome instability (CIN) is one of the hallmarks of cancer and a major driver of tumor progression, which has received an extensive attention and research in academia. UCAD (Ultrasensitive Chromosomal Aneuploidy Detection) which refers to the ultra-high sensitivity chromosomal instability detection. Through genome-wide sequencing of cfDNA (circulating DNA), one-time examination of tumor-related chromosomal variation can comprehensively and accurately analyze the chromosomal instability, which can help the Researchers provide good reference .Therefore, this paper focuses on the application of ultra-high sensitivity chromosome instability monitoring in UCMSC anti-cynomolgus aging, and puts forward the hypothesis that the CIN related index in cfDNA may be used as an indicator to judge the degree of aging, and also according to the design, the set of procedures, are series of experiments in order to draw the corresponding conclusions, and help the clinical treatment of cancer.

2. The experimental design

In this experiment, a control group and an experimental group were designed for monkeys of different ages. The control group mainly consist of young group, middle-aged group and old group (treatment group), mainly in parallel control; the experimental group is included in the elderly group (after treatment), and the old group is in the control group (before treatment) which was compared with and among the changes produced, the corresponding experimental data was obtained.

Table 1 control monkey number setting table

Young group	Serial No	Age	Middle age group	Serial No	Age	Elderly untreated group	Serial No	Age
16382	A1	3	12390	B1	7	96306	C1	23
16384	A2	3	12372	B2	7	96084	C2	23
16086	A3	3	12304	B3	7	95364	C3	24
16068	A4	3	12092	B4	7	95342	C4	24
16002	A5	3	11062	B5	7	94072	C5	25
						92330	C6	27

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Table 2 Number setting of the experimental group of the monkey

Elderly treatment group	Serial No	Age
96306	D1	23
96084	D2	23
95364	D3	24
95342	D4	24
94072	D5	25
92330	D6	27

3. The result analysis of experiment

3.1 Experimental results 1

Group A (young)		Group B (middle age)		Group C (elderly)	
A1-181214_rep1	21.58	B1-181214_rep1	19.92	C1-181214_rep1	16.18
A1-181214_rep2	21.77	B1-181214_rep2	19.93	C1-181214_rep2	15.89
A2-181214_rep1	20.64	B2-181214_rep1	15.67	C2-181214_rep1	16.58
A2-181214_rep2	21.41	B2-181214_rep2	15.53	C2-181214_rep2	16.98
A3-181214_rep1	20.82	B3-181214_rep1	15.71	C3-181214_rep1	17.48
A3-181214_rep2	20.55	B3-181214_rep2	14.44	C3-181214_rep2	16.83
A4-181214_rep1	24.69	B4-181214_rep1	16.90	C4-181214_rep1	13.42
A4-181214_rep2	23.63	B4-181214_rep2	16.58	C4-181214_rep2	13.50
A5-181214_rep1	17.37	B5-181214_rep1	18.05	C5-181214_rep1	13.25
A5-181214_rep2	18.62	B5-181214_rep2	17.09	C5-181214_rep2	12.77
				C6-181214_rep1	13.46
				C6-181214_rep2	13.08
Avg	21.11		16.98		14.95
3rd-1st quantile	1.15		2.13		3.26

Figure 1 Comparison of the test results

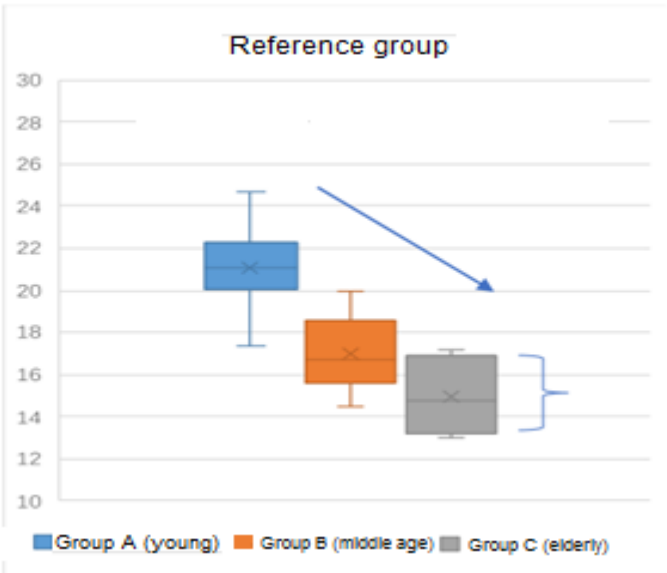

Figure 2 Technique reproducibility

Through the above analysis, Telomere grew significantly with age, and the two were inversely proportional compared to the other groups, group C (the older) telomere showed the greatest

difference (As shown in Figure 1 and Figure 2).

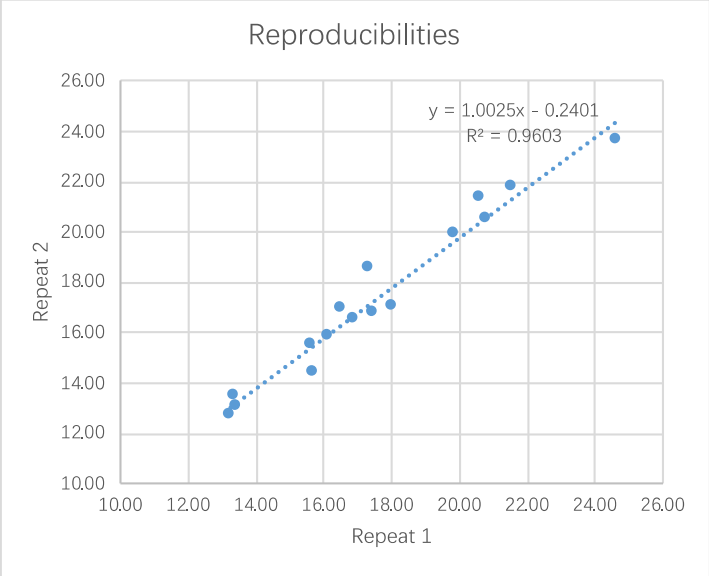

Figure3 Telomere dynamics after treatments

When combined with the specific experimental results, the cfDNA telomeres detected in the blood will be significantly shortened by age, which is consistent with the telomere and the shortening of chromosomes in tissues and cells by other scholars; The individual telomere length detected by cfDNA which are the biggest difference among the elderly group.

3.2 Experimental results 2

Table 3 Schematic diagram of the treatment group

Collection date /detection individual	C1	C2	C3	C4	C5	C6
Before treatment:						
2018/12/14	16.035	16.778	17.155	13.459	13.010	13.270
After treatment:						
2019/01/02	13.595	15.316	13.042	13.538	11.880	14.030
After treatment:						
2019/01/10	13.059	19.338	13.561	14.727	11.774	14.055

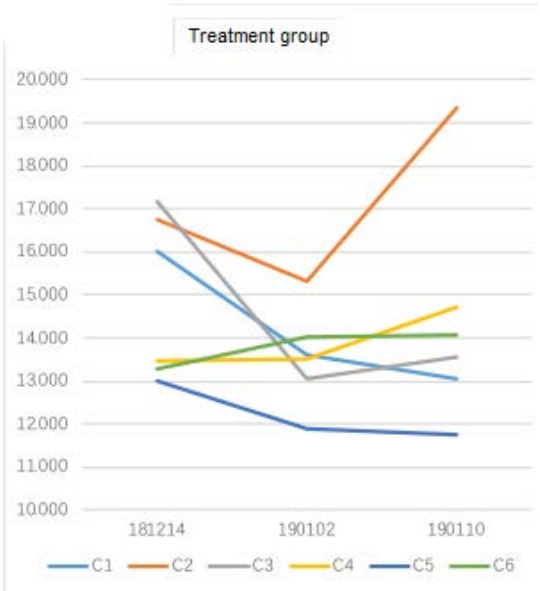

Figure 4 Schematic diagram of copy number change gene

Through actual observation and comparison, it can be seen from the above chart that after treatment, C2, C4, C6 showed a significant increase in the length of telomere, 16.778 before C2 treatment, 19.338 after treatment, and 13.459 before C4 treatment. After treatment, it was 14.727; before C6, it was 13.270, and after treatment, it was 14.055. After treatment, C1, C3, C3 showed a significant reduction in the length of telomere, 16.035 before C1 treatment, 13.059 after treatment, 17.155 before C3 treatment, 13.561 after treatment, 13.010 before treatment, 13.010 after treatment, 11.774 after treatment. .

Through this experiment, the following two conclusions are drawn: First, the condition of in vitro culture expansion needs to be considered. Second, after the cell treatment, it was observed that the cfDNA telomere changes detected by the subjects were inconsistent, and the individual differences were large.

3.3 Experimental results 3

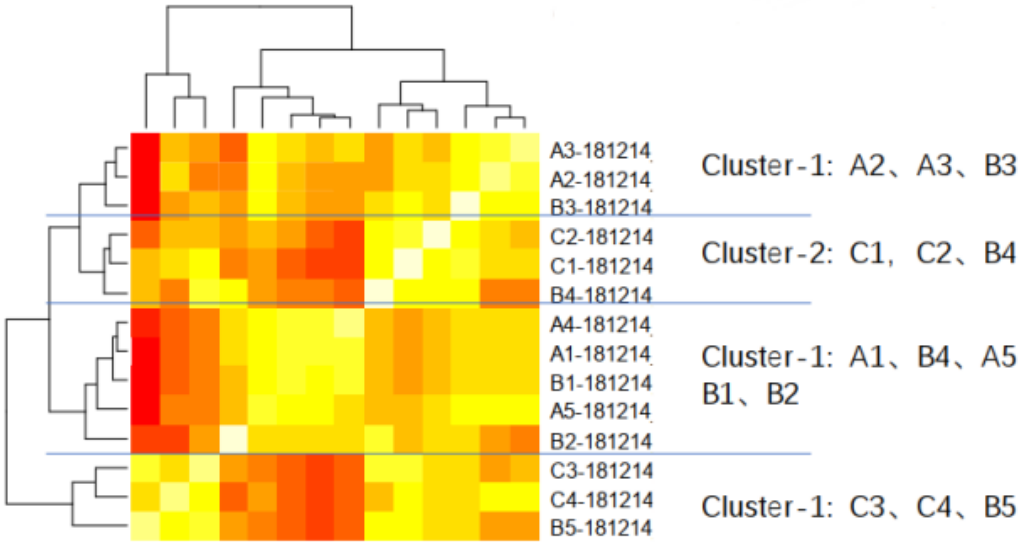

Figure 5 Schematic diagram of copy number change gene

According to the previous discussion, the age of the monkeys is as follows: C1, C2, C3, C4 > B4, B5 > B1, B2, B3> A1, A2, A3, A4, A5. From Figure 6, we can see that the blood free genome copy number will change with the age of the apes. Therefore, through experiments we can make a conjecture: under the premise that the age of the apes is increasing, and the risk of chromosomal instability inside the body will increase, and the corresponding diseases will then appear.

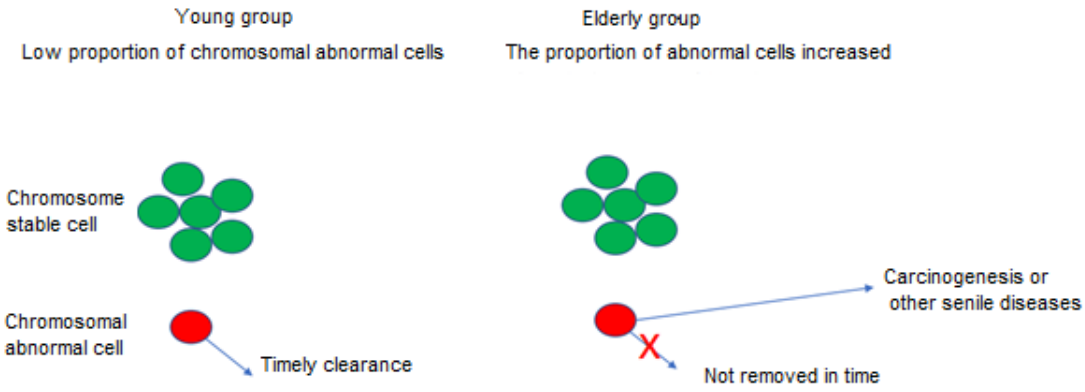

Figure 6 copy number change gene map

It can be seen from Fig. 7 that the young group has the advantage of age, the chromosome stabilizes the cell angle, the internal body machine can clear the chromosomal abnormal cells in time, the deformed cells are less, and the lesions are usually not induced; the proportion of chromosomal abnormal cells in the elderly group is rising, not Cleared in time to induce diseases

such as cancer.

3.4 Experimental results 4

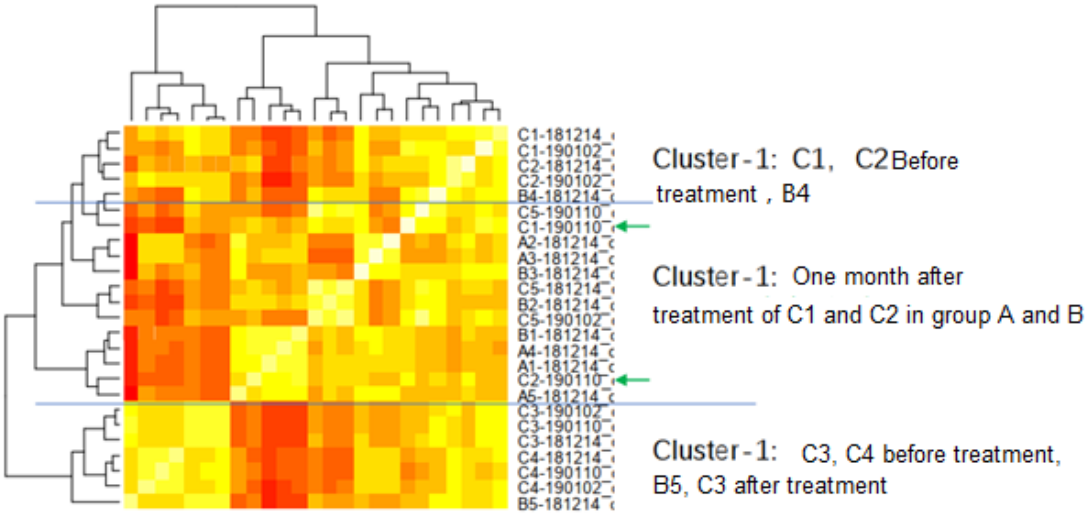

Figure 7 Schematic diagram of copy number change gene after treatment

After 1 month of treatment of C1 and C2, the genomic characteristics of the old cynomolgus monkeys will be close to that of young marmosets; however, there is no new change in C3.

3.5 Experimental results 5

By analyzing genes whose copy number changes 'slightly' with age, the main gene functions are reflected in the following aspects: first, loss and alteration of immune-related genes in MHC region; second, sex chromosome loss and alteration; third, other More functional analysis of genes and changes is needed.

4. The summary of experimental results

Through the above analysis and research, the following conclusions were drawn: First, plasma cfDNA telomere length and 171 genes (to be repeatedly verified) may be used as indicators for judging aging and evaluation indicators for stem cell therapy. Second, the differences in cell treatment are more important, and further reasons for differentiation may be needed (further observation: correlation between immune-related genes and sex chromosome-related genes in MHC regions and efficacy). Third, certain characteristics of plasma cfDNA may be used as an indicator to predict the efficacy of stem cells.

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