CLAIMS

1. An *in vitro* method of preparing rejuvenated and regenerative fibroblasts, comprising:

treating fibroblasts with a first combination consisting of 0.05-10 mM of VPA, 1-15 μM of CHIR99021, 0.5-10 μM of Repsox and 3-50 μM of Forskolin for 2-10 days which is replaced every two days and then with a second combination consisting of 0.05-10 mM of VPA, 1-15 μM of CHIR99021, 0.5-10 μM of Repsox, 3-50 μM of Forskolin, 1-50 μM of SP600125, 1-20 μM of Go 6983, 1-25 μM of Y-27632, 0.02-1 μM of AM580, 0.5-15 μM of EPZ004777, 0.2 mM of Vc and 0.2-20 μM of TTNPB for 4-20 days which is replaced every two days; or

treating the fibroblasts with a first combination consisting of 1-25 μM of Y-27632, 0.2 mM of Vc, 0.5-15 μM of EPZ004777, 3-50 μM of Forskolin and 0.5-10 μM of Repsox for 2-10 days and then with a second combination consisting of 0.05-10 mM of VPA, 1-15 μM of CHIR99021, 0.5-10 μM of Repsox, 3-50 μM of Forskolin, 1-20 μM of Go 6983, 1-25 μM of Y-27632, 0.02-1 μM of AM580, 0.5-15 μM of EPZ004777, 0.2 mM of Vc and 0.2-20 μM of TTNPB for 4-20 days.

2. The method according to claim 1, wherein the fibroblasts are derived from a connective tissue of a mammal;

wherein the connective tissue is blood, skin, bone marrow or heart; and

the mammal is human, monkey, mouse or pig.

3. The method according to claims 1 or 2, wherein compared to the fibroblasts, a telomere of the rejuvenated and regenerative fibroblasts is extended by 1.5-12 times.

4. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of the preceding claims, or secretions, lysates or differentiated cells thereof in the construction of tissue engineering materials.

5. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or secretions, lysates or differentiated cells thereof in the repairing of injured mammalian tissues and organs.

6. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or secretions, lysates or differentiated cells thereof in the repairing of aged and degenerated tissues and organs.

7. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or secretions, lysates or differentiated cells thereof in the delaying and reversing of the aging process of tissues, organs and bodies.

8. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or derivatives thereof in the manufacture of a kit, a drug, a health-care product, food, cosmetics or a medical device.

9. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or derivatives thereof in the preparation of tissue engineering materials as seed cells or scaffold sources, the repairing of injured mammalian tissues and organs and the repairing of aged and degenerated tissues and organs.

10. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or derivatives thereof in the medical research or the preparation of an immunomodulator.

11. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or derivatives thereof in the *in vitro*/*in*

vivo prevention, delaying and reversing of the aging process of mammalian tissues, organs and bodies.

12. An application of the rejuvenated and regenerative fibroblasts prepared by the method according to any one of claims 1-3, or derivatives thereof in the reprogramming or rejuvenation of cells, tissues, organs and organisms.