「始皇」長生不老藥？
端粒酶(Telomerase)

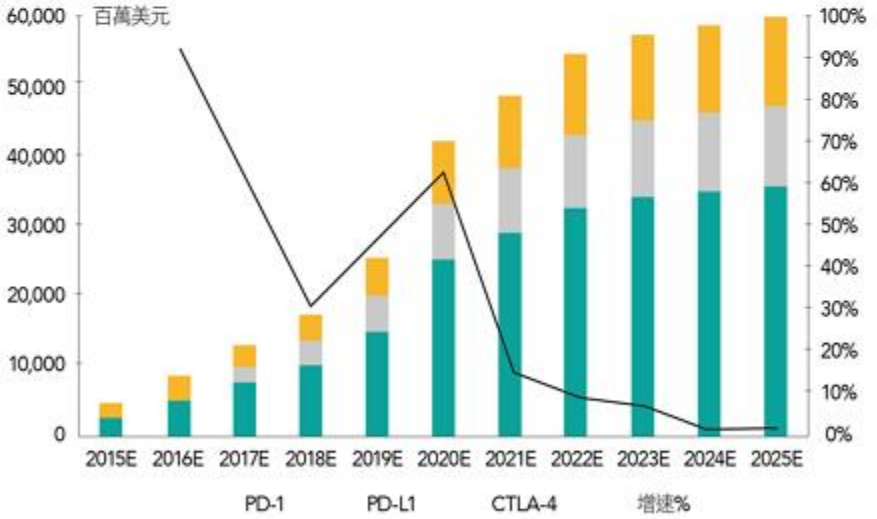
游伯齡 醫師(MD, PhD, EMBA)

聯醫再生股份有限公司 董事長

幹細胞市場規模最大
2030年將達5.4兆台幣，產能不足是隱憂！

細胞療法主要成長機會來自：

2025年，腫瘤免疫療法市場將達600億美元



聯醫再生

再生醫學的演進

20世紀
藥物時代

2000年

21世紀
細胞治療時代

*“ 如果說 20 世紀是**藥物治療**時代，*
*而 21 世紀就是**細胞治療**時代！ ”*

喬治·昆汀·戴利 George Quentin Daley
哈佛醫學院院長

聯醫再生

老化與癌症的最後一線生機：
細胞療法與端粒

您的親友罹患高血壓嗎？
藥物對他幫助多少？

您的親友罹患糖尿病嗎？
藥物對他幫助多少？

癌症、退化性疾病，
藥物對他幫助多少？

聯醫再生

為什麼老鼠壽命這麼短?

1960年代，李奧納多·海佛列克(Leonard Hayflick)，
他認為分裂能力的次數和細胞的衰老有關，
而**細胞衰老可能導致了身體的老化**。

老鼠壽命3年
海佛列克極限細胞
分裂15次

加拉巴戈象龜
壽命200年
海佛列克極限細胞
分裂110次

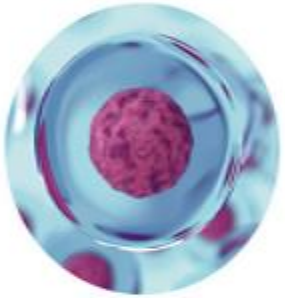
人類壽命約80年
海佛烈克極限細胞
分裂約為50次

聯醫再生

老化的問題在細胞

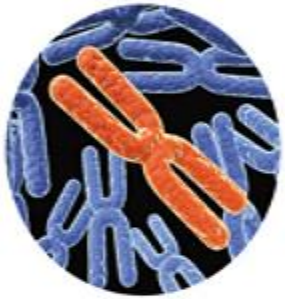
老化的問題在
細胞

細胞的問題在
基因

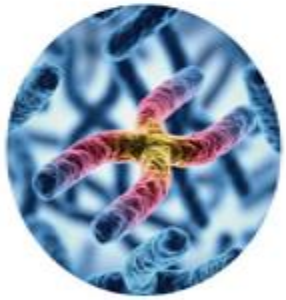


基因的問題在
DNA

DNA的問題在
染色體



染色體的問題在
端粒



端粒的問題在
端粒酶缺少

> “補充**端粒酶**會讓**細胞恢復健康**”

聯醫再生

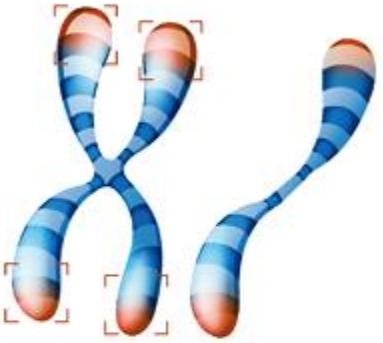
什麼是端粒？什麼是端粒酶？

端粒功能的發現，被認為是開拓了一條抗衰老與癌症新療法之路

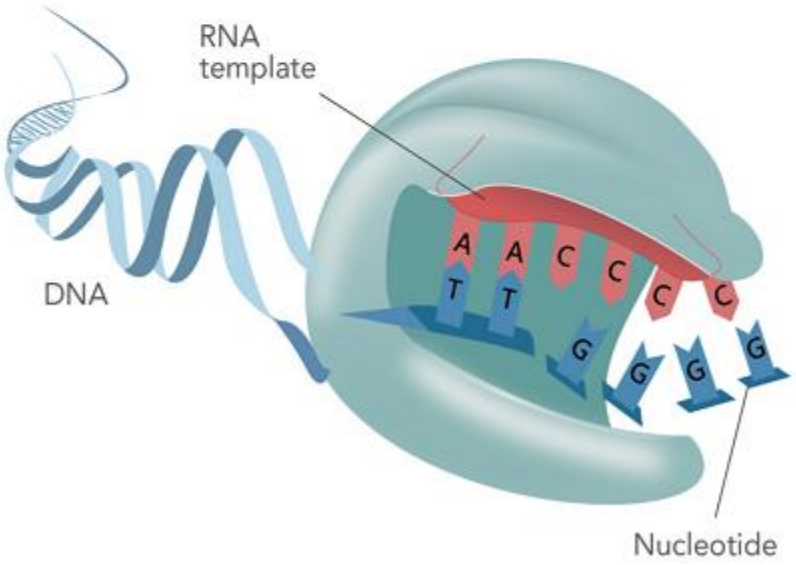
端粒是染色體末端的“帽子”結構，類似於鞋帶上的塑料尖頭，起著保護作用，可以防止染色體“磨損”。

每一次細胞分裂，端粒都會變短，直至細胞停止分裂並死亡。而端粒酶可以通過向染色體末端添加保護而減少遺失。

學界認為，如果能合理運用提取生物端粒酶技術，將揭開人類衰老和罹患癌症等嚴重疾病的奧秘。



1930年 赫爾曼·約瑟夫·馬勒
Hermann J. Muller 發現端粒，
1946年 諾貝爾獎得主



Telomerase

端粒酶：一種保護端粒的酵素

Telomerase來自希臘術語«telos»（結束）和«meros»（部分）

來自美國科學家團隊使用冷凍電鏡技術，
以迄今最高的解析度確定了端粒酶的結構。

聯醫再生

科學家解開端粒酶運作機制
2009年榮獲諾貝爾醫學獎

2006年	美國生技公司生產端粒酶活化劑
2009年	發現端粒和端粒酶保護了染色體
2016年	美國生技公司推出全新純端粒酶產品案例很少
2018年	案例、實驗證實純端粒酶對人體逆齡的功效十分顯著

聯醫再生

nature cell biology

REVIEW ARTICLE

https://doi.org/10.1038/s41556-022-00842-x

Telomere dysfunction in ageing and age-related diseases

Francesca Rossiello[1], Diana Jurk[2,3], João F. Passos[2,3] ✉ and Fabrizio d'Adda di Fagagna[1,4] ✉

Ageing organisms accumulate senescent cells that are thought to contribute to body dysfunction. Telomere shortening and damage are recognized causes of cellular senescence and ageing. Several human conditions associated with normal ageing are precipitated by accelerated telomere dysfunction. Here, we systematize a large body of evidence and propose a coherent perspective to recognize the broad contribution of telomeric dysfunction to human pathologies.

[1]IFOM Foundation–FIRC Institute of Molecular Oncology Foundation, Milan, Italy. [2]Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN, USA. [3]Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA. [4]Istituto di Genetica Molecolare, Consiglio Nazionale delle Ricerche (IGM–CNR), Pavia, Italy. ✉e-mail: passos.joao@mayo.edu; fabrizio.dadda@ifom.eu

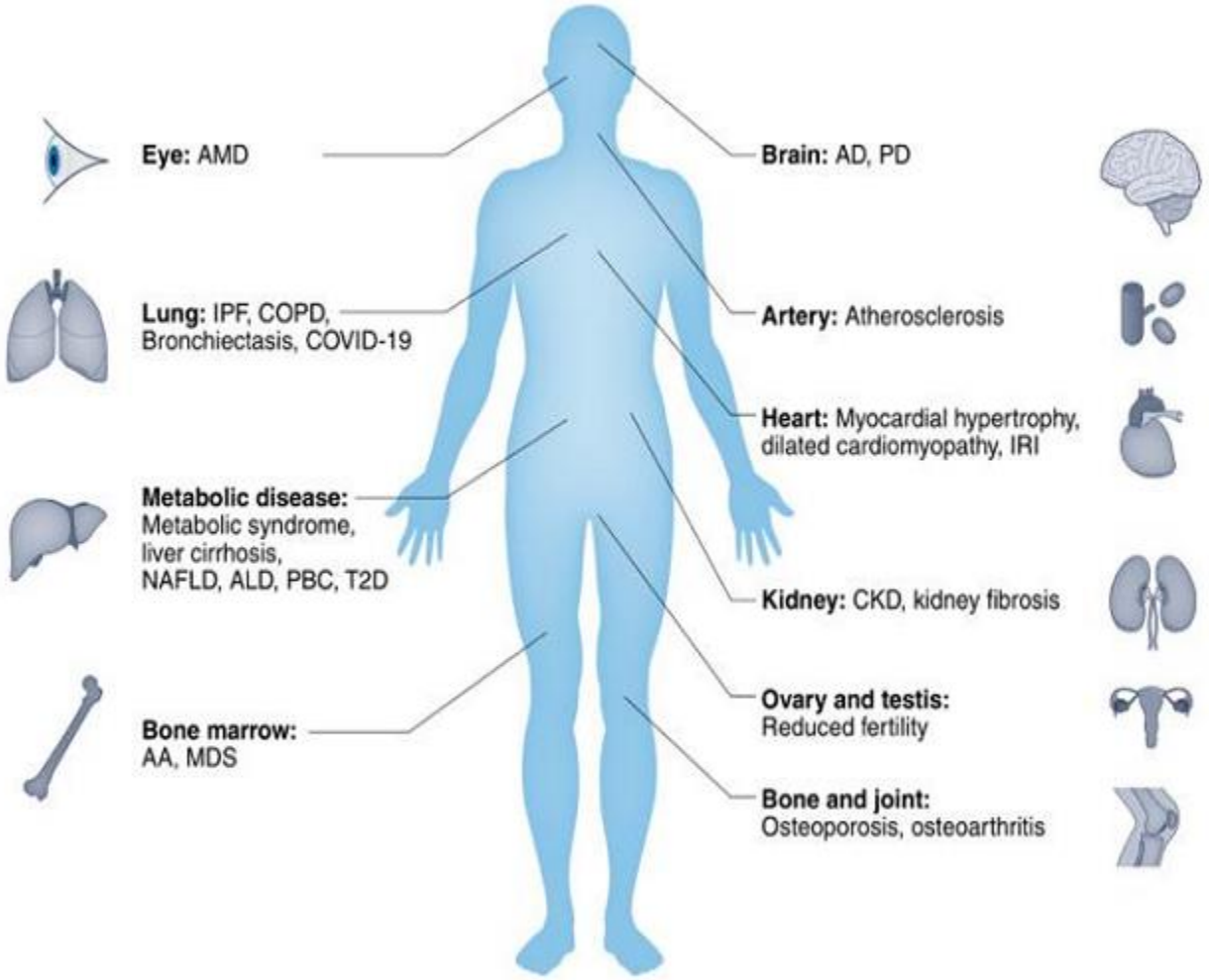


Fig. 2 | Evidence for a role of cellular senescence and telomere dysfunction in age-related diseases. Schematic representation of the age-related diseases described in this Review grouped by organs or systems. AA, aplastic anaemia; AD, Alzheimer's disease; ALD, alcholic liver disease; AMD, age-related macular degeneration; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; IPF, idiopathic pulmonary fibrosis; IRI, ischaemia-reperfusion injury; MDS, myelodysplastic syndrome; NAFLD, non-alcoholic fatty liver disease; PBC, primary biliary cirrhosis; PD, Parkinson's disease; T2D, type 2 diabetes.

frontiers in Molecular Neuroscience

REVIEW
published: 16 May 2018
doi: 10.3389/fnmol.2018.00160

The Emerging Roles for Telomerase in the Central Nervous System

Meng-Ying Liu[1,2], *Ashley Nemes*[3] *and Qi-Gang Zhou*[1,3]*

[1]*Department of Clinical Pharmacology, Pharmacy College, Nanjing Medical University, Nanjing, China,* [2]*The Affiliated Hospital of Nanjing University Medical School, Nanjing Drum Tower Hospital, Nanjing, China,* [3]*Department of Stem Cell Biology and Regenerative Medicine, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, United States*

Brain Tumors

More than 85% of the tumor cells show telomerase activation for preventing progressive shortening of the telomere as excessive divisions (Harley, 1991). Tumors that originate in the brain are known as primary brain tumors, including astrocytomas, oligodendrogliomas and ependymomas. High telomerase activity was observed in astrocytoma including glioblastoma (GBM, grade IV astrocytoma), the most common type of malignant

Aging Brain

Telomeres play a central role in aging. Shortening of telomeres has been linked to the mechanisms responsible for the aging of cells (López-Otín et al., 2013). Telomerase, preventing the telomere from being too short, thus acts as an anti-aging enzyme, proposing a "telomere theory of aging", a prominent concept in research (Jaskelioff et al., 2011). Since the secret of "the end replication problem" was uncovered owing to the finding of telomerase, its role in cellular aging was predicted and revealed (Greider and Blackburn, 2004). TERT gene knockout studies provide direct evidence that TERT loss provoked tissue degeneration including progressive atrophy of tissues, depletion of stem cells, failure of organ systems and impairment of tissue

Parkinson's Disease

Parkinson's disease (PD) is an aging-associated long-term degenerative disorder (Singleton and Hardy, 2016). Contrary to short telomeres observed in the aging brain, the relationship between telomere and PD remains unclear. An analysis of 131 PD patients and 115 healthy controls performed by Eerola et al. (2010) found no difference in telomere length between PD patients and healthy controls. Consistently, a case-control study from Wang et al. (2008) reported that shorter telomeres are not associated with a higher risk of PD. Moreover, a large nested case-control study also found that telomere shortening

Brain Ischemia

Normally, TERT expression and telomerase activity are at a very low level and undetectable in post-mitotic cells including neurons in the brain. After ischemic injury, ectopic expression of TERT was detected in neurons (Kang et al., 2004). Transgenic overexpression of TERT showed a significant resistance to injury. Induction of TERT in injured neurons protects against NMDA excitotoxicity, ameliorating ischemic neuronal cell death (Kang et al., 2004). Aside from neurons, astrocytes appear to have a role in TERT-related neuronal protection. Baek et al. (2004) show TERT co-localization with glial fibrillary acidic protein (GFAP), a marker of astrocyte, in the neonatal brain 3 days after stroke. Consistently, it was reported that TERT mRNA and protein were up-regulated in neurons 2 days after hypoxia-ischemia but shifted to astrocytes at day 3 (Qu et al., 2011). The distribution of temporary ectopic expression of TERT supports the concept that both promotion of neuronal survival and attenuation of astrocyte proliferation in the developing brain contribute to a

Mood Disorders

The World Health Organization ranks mood disorders as the leading causes of years (Murray and Lopez, 1996). Brain structural and functional abnormalities mediate the pathophysiology of mood disorders, including major depressive disorder (MDD), bipolar disorder (BD), and anxiety. Increasing studies suggest a strong causal link between impaired neurogenesis and etiology of mood illnesses. Considering the function of telomerase in stem cells, especially ANSCs/ANPCs, it is highly expected that

which may be related to dysregulation of
HPA axis, and autonomic system functi
Okereke et al., 2012; Wolkowitz et al
2014).

Schizophrenia

Generally, schizophrenia is not regard
disorder. However, pathology of aging
of this disorder, since there are si
abnormalities (Buchsbaum and Hazlet
Surtees et al., 2011; Okereke et al., 2

genes

MDPI

Review

The Telomere/Telomerase System in Chronic Inflammatory Diseases. Cause or Effect?

Vasileios Kordinas [1,2,*], Anastasios Ioannidis [2,3] and Stylianos Chatzipanagiotou [2]

1 Third Department of Internal Medicine and Diabetes Centre, Saint Panteleimon General Hospital, Nikea-Pireaus 18454, Greece

2 Department of Clinical Microbiology and Medical Biopathology, Athens Medical School, Aeginition Hospital, Athens 11528, Greece; tasobi@uop.gr (A.I.); schatzi@med.uoa.gr (S.C.)

3 Department of Nursing, Faculty of Human Movement and Quality of Life Sciences, University of Peloponnese, Sparta 23100, Greece

* Correspondence: kordinasv@med.uoa.gr; Tel.: +30-210-7289-192

Academic Editor: Gabriele Saretzki

Received: 20 May 2016; Accepted: 29 August 2016; Published: 3 September 2016

2. The Telomere/Telomerase System in Chronic Disorders. Is Inflammation to Blame?

2.1. Chronic Lung Diseases

Chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF) are very serious chronic disorders and major public health issues [69,70]. COPD is a lung condition associated with irreversible airflow obstruction as a consequence of small airways disease, excessive mucous production and emphysema. Smoking and inflammation have been identified as the leading causes for COPD onset and progression [69–71]. TNF-a among other cytokines has been found to be

2.2. Diabetes

Diabetes mellitus is a major public health issue, which contains a spectrum of diseases with the most important ones being type 1 diabetes (T1D) and type 2 diabetes (T2D). T1D is an autoimmune disease while T2D which accounts for approximately 90%–95% of diabetic patients has a complex disease pathogenesis [92]. There have been many reports recognizing a low grade chronic inflammation in diabetes as pathogenesis and a disease progressing mechanism [92,93]. IL-1b, IL-6, TNF-a and

2.3. Autoimmune Diseases

There is a long list of autoimmune diseases like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis, etc. that are characterized by immune system dysfunction and thus inflammatory cascades seem to play a major part in disease onset and progression [104,105]. The mechanisms involving immune system impairment in autoimmunity are numerous and

2.4. Renal Failure

There is accumulating evidence the past few years that persistent low grade chronic inflammation plays a major part in disease progression, severity, mortality and morbidity in patients suffering from renal failure or chronic kidney disease (CKD) [126,127]. That is why chronic inflammation in CKD is extensively studied since it has been hypothesized to be a potential therapeutic target [128]. TNF-a, CRP, IL-6, IL-1, IL-23, reactive oxygen species (ROS) and others, have all been implicated in promoting

2.5. Cardiovascular Disease

Atherosclerosis is the dominant cause of cardiovascular disease (CVD) including myocardial infarction (MI), heart failure, stroke and claudication [138,139]. Activated endothelium with the expression of adhesion molecules seem to be early events in atherosclerosis, allowing monocytes, T-cells, dendritic cells, mast cells, neutrophils and B-cells to accumulate to the endothelium [140].

2.6. Psychiatric and Neurological Disorders

Psychiatric disorders such as depression, schizophrenia, anxiety disorder, bipolar disorder (BD) and post-traumatic stress disorder (PTSD) pose serious and emerging global health threats and have in recent years been associated with accelerated aging, chronic inflammation and immune

2.7. Chronic Infections

Since leucocytes are among the very few cell types of a mature organism to exhibit telomerase activity, the enzyme's proper regulation inside the host's defense system should be crucial in handling acute and chronic infections [168]. Telomeres and telomerase biology is being studied in HIV and other viral chronic infections since these patients exhibit signs of chronic inflammation, accelerated aging and premature immune system senescence [168–171]. HIV in particular is characterized by CD4 T

2.8. Lifestyle Habits

Telomerase activity and telomeric length have been associated with many everyday life characteristics prevalent in modern societies. Several studies have linked reduced telomerase activity with several unhealthy lifestyles. For example, chronic everyday stress is associated with decreased telomere length and reduced telomerase activity [183,184]. In addition, higher levels of nocturnal cortisol expression, a hormone associated with chronic stress, is related to shorter telomeres while in vitro the addition of cortisol seems to diminish telomerase activity [183]. Apart from everyday psychology, dietary habits also seem to influence telomere/telomerase homeostasis. Short telomeres and a decrease in telomerase activity have been reported in patients with high body mass index (BMI), higher circulating glucose levels and abdominal fat while a healthy lifestyle with the intake of many

2.9. Other Disorders

Telomere shortening and reduced telomerase activity with or without an inflammation connection have also been studied in many more pathological contexts than those described in the present study. For example, patients with advanced primary biliary cirrhosis retain significantly less telomerase activity than patients with early stage disease while these subjects also exhibit signs of premature cellular senescence [191]. Ulcerative colitis is a well-known inflammatory disorder were premature

聯醫再生

聯醫再生公司專注於細胞療法，
希望爲專業醫療人員、專業客戶，於再生醫學領域裏
提供具科學性、可靠性、精準性的實證醫學平台。

期待這個平台，能對細胞療法有一份貢獻，
造福人群、嘉惠社會、厚實國家！

聯醫再生 基礎醫學專家陣容

王錫崗教授 (Dr. Paulus. Shyi-Gang Wang)
現職：陽明大學退休兼任教授
學歷：臺大理學士，碩士/美國伊利諾大學博士(1980)
經歷：陽明大學生理科所副教授，教授/醫學院副院長/實驗動物中心主任
專長: 生理學，內分泌學，生殖生理/已發表論文288篇(1973-2021)

卓文隆教授 (Dr. Wen-Long Cho /wenlong_mmc@mmc.edu.tw)
現職：馬偕醫學院生物醫學研究所教授
學歷：師範大學理學士，輔仁大學碩士，美國密西根州立大學博士(1991)
經歷：陽明大學熱醫科所教授，主任，所長/副研發長/馬偕醫學院教務長，主秘
專長：細胞分子生物學，熱帶醫學，登革熱病毒/已發表論文50篇(1991-2021)

王錫五教授 (Dr. Shyi-Wu Wang /swwang@mail.cgu.edu.tw)
現職：長庚大學醫學院生理科退休教授
學歷：臺大農學士，碩士/美國北卡洛來納州立大學博士(1994)
經歷：長庚大學醫學院生理學科助理教授，副教授，教授
專長：生理學，生殖生理，免疫生理學/已發表論文80篇(1986-2021)

張文瑋教授 (Dr. Wen-Wei Chang /changwenwei@gmail.com)
現職：中山醫學大學生物醫學科學系教授
學歷：成功大學生物系理學士/成大醫學院基礎醫學研究所博士(2006)
經歷：中山醫學大學生物醫學科學系助理教授，副教授，教授，主任
專長: 幹細胞，癌病乳癌，肺癌/已發表論文62篇(2002-2021)，專利4件

彭賢祐教授 (Dr. Hsien-Yu Peng /hsien.yu@gmail.com)
現職：馬偕醫學院醫學系教授兼研發長
學歷：中興大學博士(2009)
專長：中國醫藥大學生理科助理教授/馬偕醫學院醫學系助理教授，副教授，教授
專長：神經科學，泌尿神經生理學，行為神經生理學/已發表論文60篇(2006-2021)

蕭家仁博士 (Dr. Morris Shaw)，首席細胞治療專家

聯醫再生 臨床醫學專家陣容

李威傑醫師
台大醫院外科教授
專長：消化系外科腫瘤切除、減肥手術

吳濬哲醫師
前台北榮民總醫院運動醫學科主任、前台北市大安區中山醫院院長、吳濬哲骨科診所院長
專長：運動醫學，膝關節，肩關節，肌腱、韌帶及肌肉受損纖維化等

施俊雄醫師
長庚大學骨科教授，林口長庚醫院骨科主任，前台北市大安區中山醫院院長
專長：運動醫學，脊椎損傷，膝關節，肌肉、韌帶等軟組織受傷，神經修復等

游伯齡醫師
日本國立滋賀醫科大學醫學博士
日本再生醫療學會創始會員（2002）
台北市川柳紀念外科診所院長
專長：細胞療法，再生醫學，組織工程學


人的盡頭
神的起頭

現代醫學的盡頭

再生醫療的起頭