



# 生命的發展與創意

## 科技產業與創意

# 上市生技-醫療類股

- [中化\(1701\)](#)[葡萄王\(1707\)](#)[五鼎\(1733\)](#)[永信\(1716\)](#)[生達\(1720\)](#)[必翔\(1729\)](#)[美吾華\(1731\)](#)[杏輝\(1734\)](#)[喬山\(1736\)](#)[佳醫\(4104\)](#)[雅博\(4106\)](#)[懷特\(4108\)](#)[旭富\(4119\)](#)[台硝\(1724\)](#)[元禎\(1725\)](#)[永記\(1726\)](#)[中華化\(1727\)](#)[花仙子\(1730\)](#)[毛寶\(1732\)](#)[日勝化\(1735\)](#)[臺鹽\(1737\)](#)[勝一\(1773\)](#)[信昌化\(4725\)](#)[中宇\(1535\)](#)[和大\(1536\)](#)[廣隆\(1537\)](#)[正峰新\(1538\)](#)[巨庭\(1539\)](#)[喬福\(1540\)](#)[鋁泰\(1541\)](#)[中砂\(1560\)](#)[程泰\(1583\)](#)[上銀\(2049\)](#)[東台\(4526\)](#)[瑞智\(4532\)](#)[帝寶\(6605\)](#)[羅昇\(8374\)](#)[理隆\(1469\)](#)[大統染\(1470\)](#)[三洋纖\(1472\)](#)[台南\(1473\)](#)[弘裕\(1474\)](#)[本盟\(1475\)](#)[儒鴻\(1476\)](#)[聚陽\(1477\)](#)[如興\(4414\)](#)
- <http://www.cpc.com.tw>
- [http://www.youtube.com/watch?v=BEPXjGP68Og&feature=player\\_embedded](http://www.youtube.com/watch?v=BEPXjGP68Og&feature=player_embedded) (德英生技)
- [https://www.youtube.com/watch?v=1f9NOLqgvvE&feature=player\\_detailpage](https://www.youtube.com/watch?v=1f9NOLqgvvE&feature=player_detailpage) (味全癌細胞)
- [http://www.youtube.com/watch?v=-Nf\\_rwXy6pk&feature=player\\_embedded](http://www.youtube.com/watch?v=-Nf_rwXy6pk&feature=player_embedded) (中心法則)
- [http://www.youtube.com/watch?feature=player\\_detailpage&v=J4wAHsOqbd8](http://www.youtube.com/watch?feature=player_detailpage&v=J4wAHsOqbd8) (生命起源)
- [http://www.youtube.com/watch?feature=player\\_embedded&v=X86UAnFGO9c](http://www.youtube.com/watch?feature=player_embedded&v=X86UAnFGO9c) (進化論與創造論)
- [http://www.youtube.com/watch?v=MgGITuAh3PE&feature=player\\_embedded#t=12](http://www.youtube.com/watch?v=MgGITuAh3PE&feature=player_embedded#t=12) (癌症知識)
- **Ernst & Young LLP, Biotechnology Industry Report**
- [https://www.youtube.com/watch?v=KSit35LaTIQ&feature=player\\_detailpage](https://www.youtube.com/watch?v=KSit35LaTIQ&feature=player_detailpage) (尼克Singer)
- <http://video.sina.com.cn/v/b/93233000-1354068193.html> (尼克語錄)
- [https://www.youtube.com/watch?v=qbiveMUveEM&feature=player\\_detailpage](https://www.youtube.com/watch?v=qbiveMUveEM&feature=player_detailpage) (創意字word-world)

# 創意：流暢性 (Creativity Flow)

- 創意是與現代人日常生活相關聯的**感想**
- 創意與個人的**生命**和價值觀有密切的關係，乃是**自己**對生活周遭環境與潮流的變化相關聯的想法與**做法**
- 創意和科學相輔相成，兩者並不相矛盾

# 創意：流暢性 (Creativity Flow)

- 創意是與日常生活相關聯的**感想**
- 與時代與潮流的變化相關聯的想法與做法

# 創意：流暢性

- **明確**的目標與意圖

- 要有趣

- 要有訴求重點

- 要新

- 要簡單

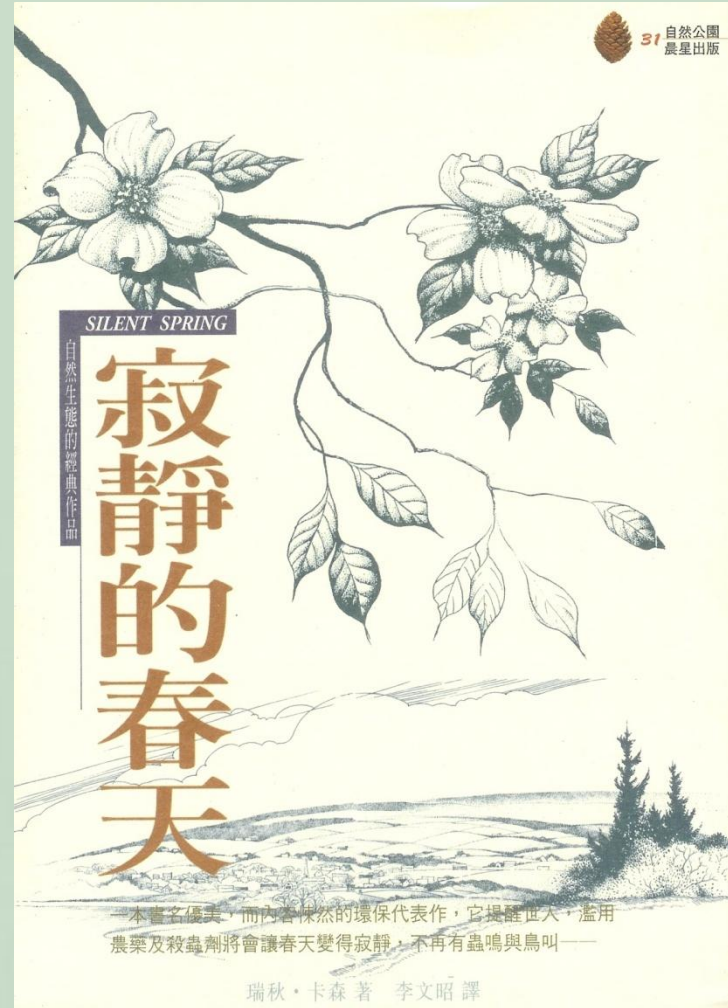
- 與現代**科技**與現代人知識相契合

- 與**市場**與現代社會的現況有直接的關係

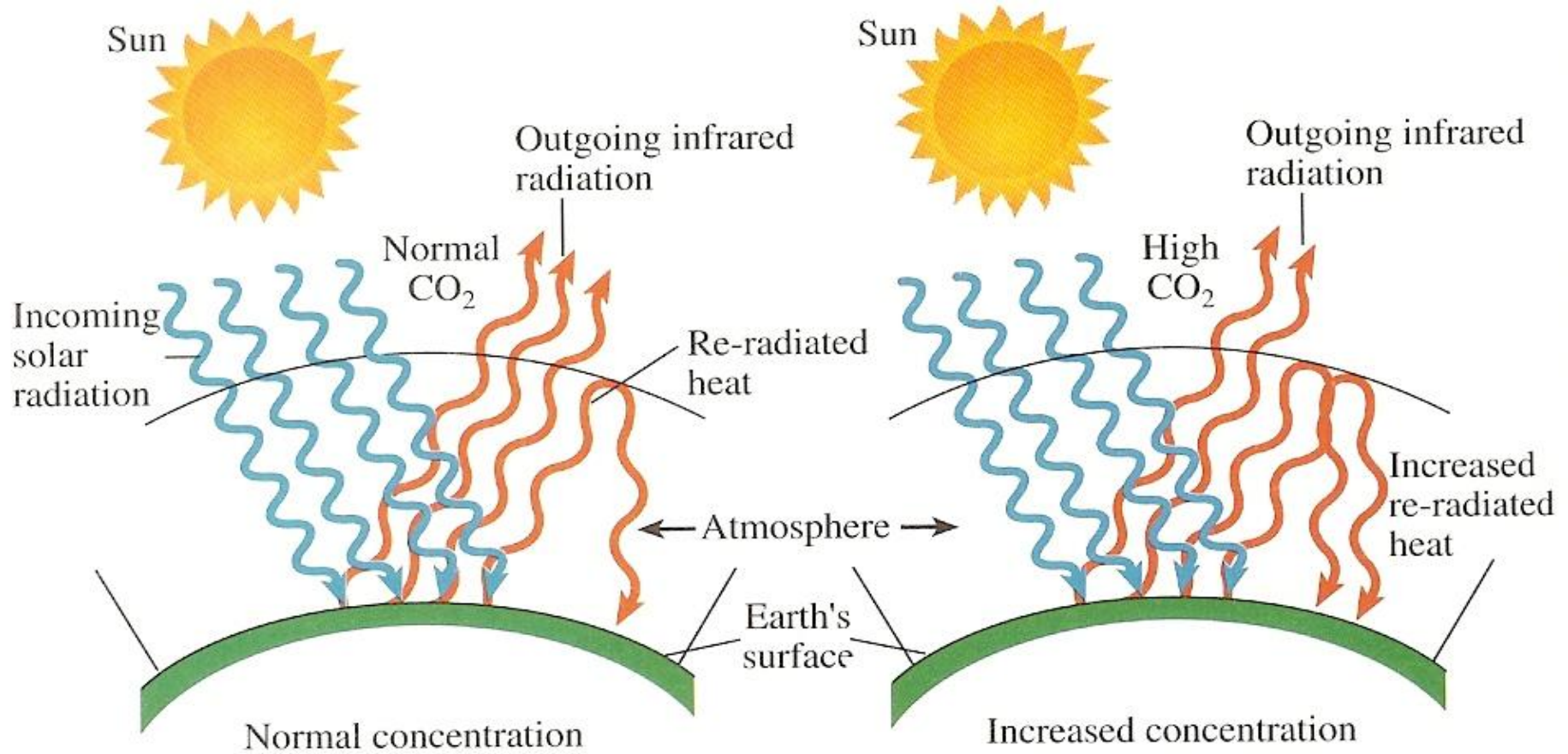
# 綠色科技產業的緣起



Rachel Carson

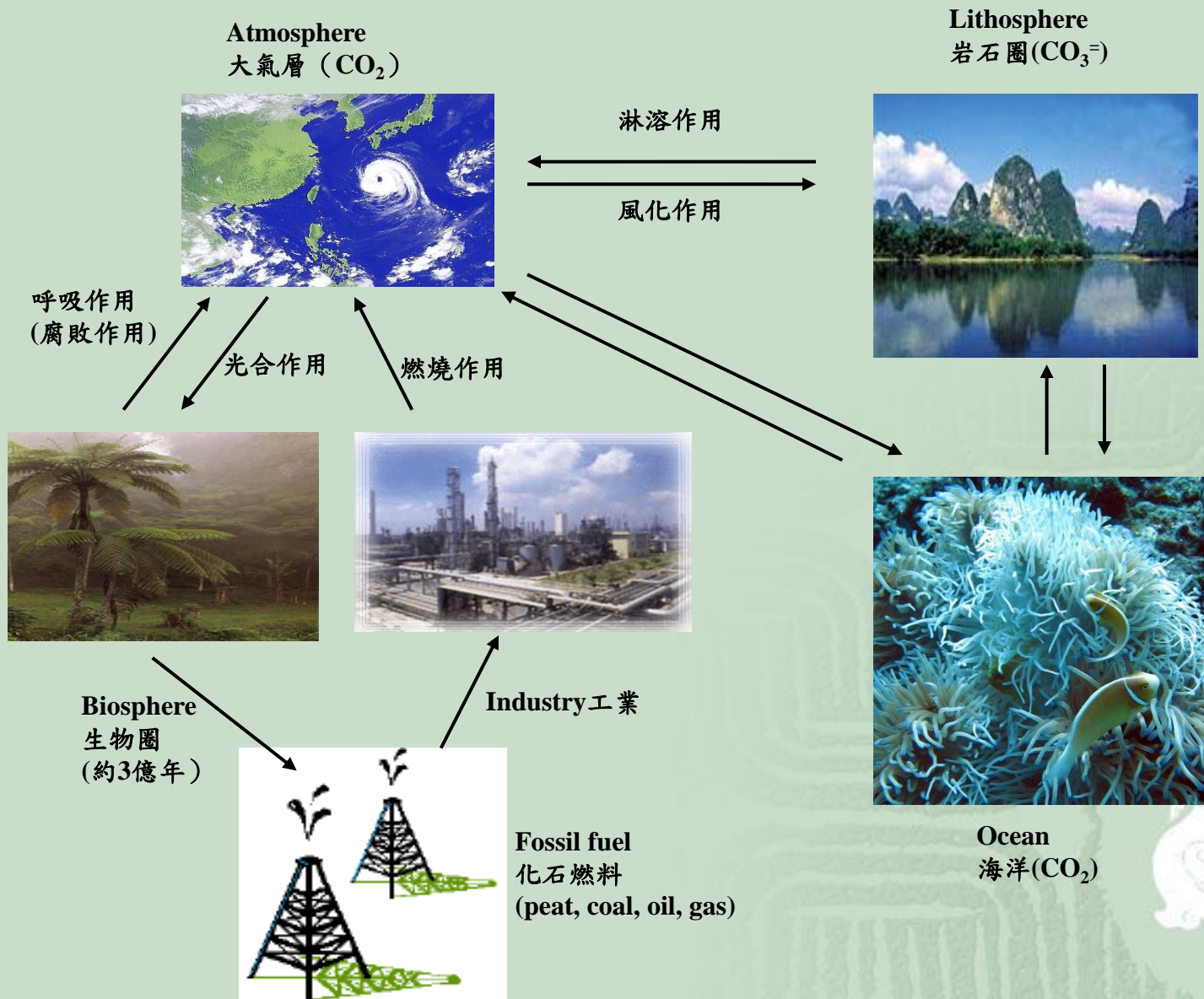


# 溫室效應(Greenhouse Effect)



太陽輻射以短波入射，經吸收後以長波反射。反射長波被大氣中溫室效應氣體吸收而保留在大氣層中，使地球溫度升高。

# 碳循環(Carbon cycle)







基因科技的  
興起與發展

Watson and Crick  
1953年DNA雙螺旋

# Transgenic “Animals”



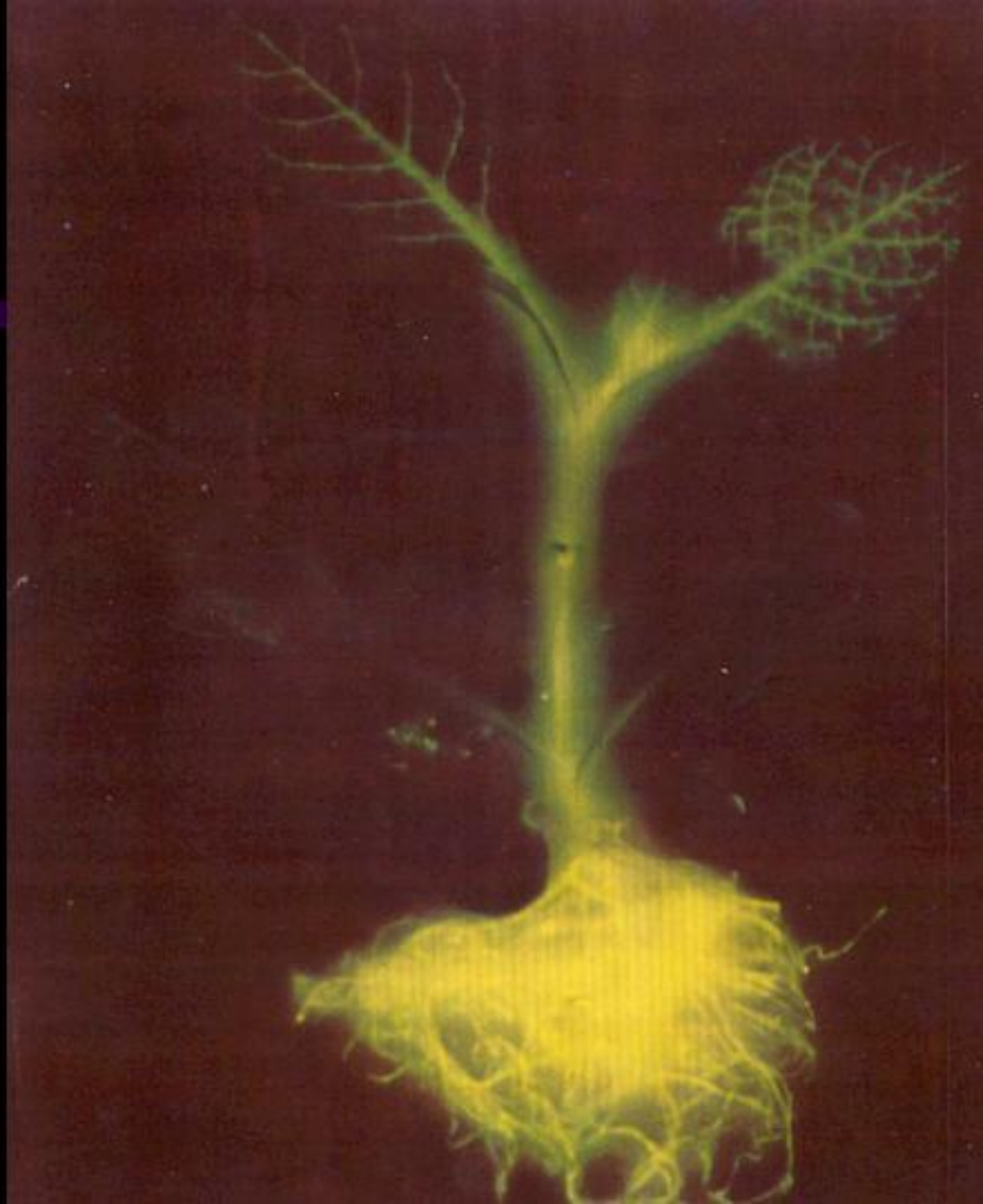
桃莉綿羊，使用細胞核轉移複製方法而產生的第一種  
哺乳動物。



# 植物可以帶有動物基因

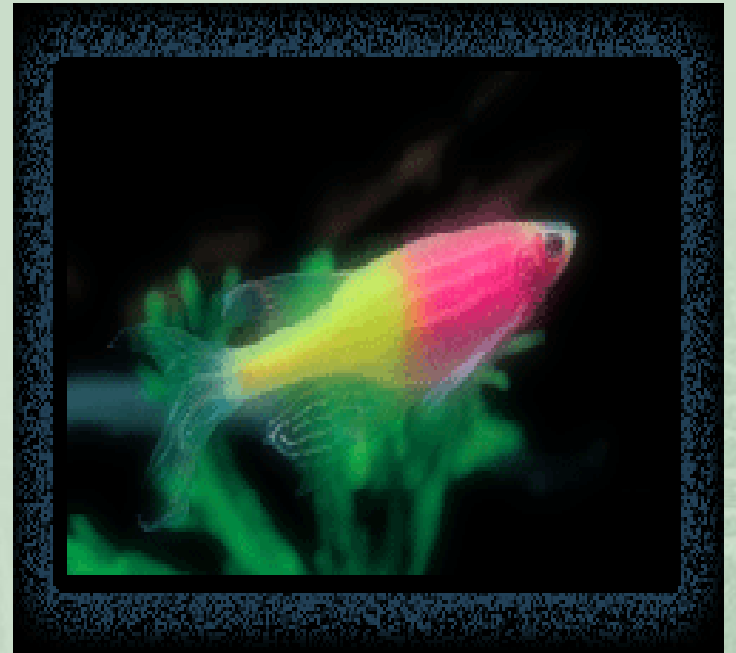
標幟：

螢火蟲的螢  
光酵素基因





原產型



變身後的金班馬



# 因基母水有帶 猴造改因基

評批及議爭發引也但 步一進又究研療醫類人 功成工加卵精類長靈度首

第一

一隻基因改造猴

安迪



術技程工因基用運「心中類長靈區地岡立奧」國美  
出產功成，中子卵的猴河恆入注酸核醣核氧去的母水將  
(透路)。「迪安」猴河恆的因基母水有帶隻一了

潘勛／綜合奧立岡波特蘭市十二日外電報導

美國奧立岡州波特蘭市的科學家今天表示，他們在一枚恆河猴卵子中，注入水母的去氧核醣核酸，而成功地產出一隻帶有該外加基因的幼恆河猴。此項發展讓科學家更接近改變人類。但此舉也引發科學界的爭議及批評。

以夏騰博士為首的「奧立岡地區靈長類中心」研究團隊表示，他們運用基因工程技術，把水母能在暗處發出綠色螢光的去氧核醣核酸注入兩百多枚恆河猴卵子，造出四十個胚胎，而讓五隻母猴懷孕，除兩胎死產外，共有三隻恆河猴出生。但其中只有一隻命為「安迪」(ANDY)的小猴細胞中，證實有該水母的基因。安迪出生於去年十月。夏騰博士等科學家表示，他們相信這是第一次運用基因工程技術，來改造靈

長類的未受精卵。然而，雌性幼猴安迪細胞中雖有水母基因，卻未生產出能發光的蛋白質。同時目前要判定安迪的精細胞裡會不會含有該外加基因也過早。夏騰博士說，他的終極目標在造出成群的改造猴，體內含有會引發人類疾病的基因，如老年痴呆症、糖尿病、乳癌及愛滋病等，以便用來研究新的治療方，在基因的層面上就阻絕疾病。但是，全球科學界也傳出批評聲浪。造出複製羊「桃莉」的英國皇家學會基因改造動物委員會主席貝特森便表示，雖然產出基因改造猴可以帶來醫學進步，但這項工作必須受到嚴格的監督。而「醫學責任醫師委員會」發言人葛立克也質疑說，科學家已運用基因改造鼠廿年到卅年，試圖治療人類癌症及心臟病，但迄未成功，而運用猴子的成功機率也極為渺茫。

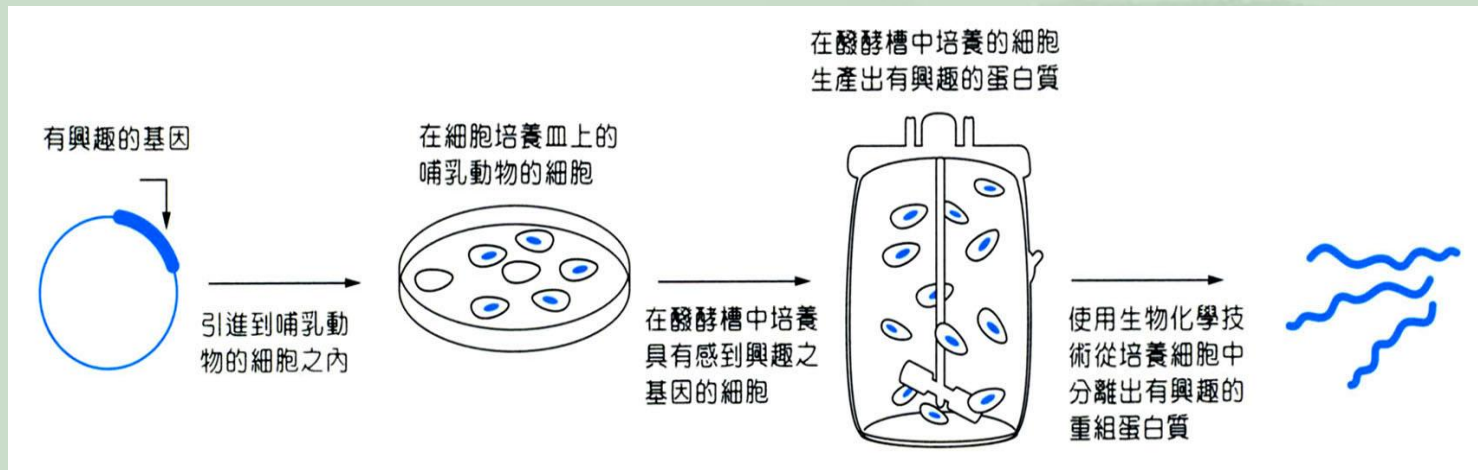


生命世界的多樣性正在迅速消失

二十年內已有  
1,000,000種  
生物絕種

# 現代生物技術的產品

- 重組蛋白質(recombinant protein)
- 基因治療(gene therapy)
- 人類糧食的需求(gene modified organism)
- 民生生化產品(biologicals product)
- 生技醫藥用品(biomedicine)
- 生質能源的開發(biofuel)
- 機能性保健產業(functional health)



使用遺傳基因改造的培養細胞來製造出有興起的蛋白質。

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- <http://www.ccpcc.com.tw>
- [http://www.youtube.com/watch?v=BEPXjGP68Og&feature=player\\_embedded](http://www.youtube.com/watch?v=BEPXjGP68Og&feature=player_embedded) (德英生技)
- [https://www.youtube.com/watch?v=1f9NOLqgvvE&feature=player\\_detailpage](https://www.youtube.com/watch?v=1f9NOLqgvvE&feature=player_detailpage) (味全癌細胞)
- [http://www.youtube.com/watch?v=-Nf\\_rwXy6pk&feature=player\\_embedded](http://www.youtube.com/watch?v=-Nf_rwXy6pk&feature=player_embedded) (中心法則)
- [http://www.youtube.com/watch?feature=player\\_detailpage&v=J4wAHsOqbd8](http://www.youtube.com/watch?feature=player_detailpage&v=J4wAHsOqbd8) (生命起源)
- [http://www.youtube.com/watch?feature=player\\_embedded&v=X86UAnFGO9c](http://www.youtube.com/watch?feature=player_embedded&v=X86UAnFGO9c) (進化論與創造論)
- [http://www.youtube.com/watch?v=MgGITuAh3PE&feature=player\\_embedded#t=12](http://www.youtube.com/watch?v=MgGITuAh3PE&feature=player_embedded#t=12) (癌症知識)
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- <http://video.sina.com.cn/v/b/93233000-1354068193.html> (尼克語錄)
- [https://www.youtube.com/watch?v=qbiveMUveEM&feature=player\\_detailpage](https://www.youtube.com/watch?v=qbiveMUveEM&feature=player_detailpage) (創意字word-world)



- [https://www.youtube.com/watch?feature=player\\_detailpage&v=sdyXxB76gBc](https://www.youtube.com/watch?feature=player_detailpage&v=sdyXxB76gBc) (企鵝家族-Never giveup)
- [https://www.youtube.com/watch?feature=player\\_detailpage&v=qHbVKFoe1hE](https://www.youtube.com/watch?feature=player_detailpage&v=qHbVKFoe1hE) (110米欄-激勵微電影)
- [https://www.youtube.com/watch?v=qbiveMUveEM&feature=player\\_detailpage](https://www.youtube.com/watch?v=qbiveMUveEM&feature=player_detailpage) (創意字word-world)
- [https://www.youtube.com/watch?v=c7x3qaXeC18&feature=player\\_detailpage](https://www.youtube.com/watch?v=c7x3qaXeC18&feature=player_detailpage) (Hall一生的關鍵-11字)
- [https://www.youtube.com/watch?v=CXodwVqkyJ0&list=PL716DABA4BBBD6306D&feature=player\\_detailpage](https://www.youtube.com/watch?v=CXodwVqkyJ0&list=PL716DABA4BBBD6306D&feature=player_detailpage) (激勵歌曲)
- [https://www.youtube.com/watch?feature=player\\_detailpage&v=d-DWZZ\\_4iiA](https://www.youtube.com/watch?feature=player_detailpage&v=d-DWZZ_4iiA) (一生的關鍵-字)



# 未上市生技-醫療類股

- **太景生技**  
以研究為主、產品導向的醫藥公司，致力於開發與傳染病、癌症及糖尿病的併發症有關的新療法
- **天明製藥**  
符合GMP規範並為第一家領證之中藥廠，全力投入台灣生技製藥產業的發展
- **生寶生技**  
即將到海外掛牌「2008國家生技醫療品質獎」生寶臍帶血銀行勇奪生物科技類銀獎
- **紅景天**  
傳遞天然養生的健康概念。2010年8月建立第一家門市，推出以活力漢飲為主題的系列飲品，堅持不含化學添加劑及香料，並且以珍貴的天然棗蜜取代廉價的人工糖份，一上市即獲得大眾好評
- **展旺生命**  
展旺為西藥原料和精密化學品專業研發製造廠，展旺是台灣第一家、唯一有能力生產無菌抗生素原料藥的製藥廠
- **國璽幹細胞**  
研發將豬胚胎幹細胞應用於生醫級醫學美容、保健食品、新藥及商品的開發
- **善德生技**  
善德公司創始之初以透析用洗腎迴路導管為主力產品，但近幾年在研究開發部門的計劃性開展下，產品面朝多科別性發展: 全系列的透析用耗材、各式管類、袋類、筒類耗材，腹腔鏡器械耗材
- **賽亞基因**  
賽亞基因科技公司以人類基因組為研發重點，致力疾病與單一核苷酸多型性，賽亞基因科技獲Bio-Spectrum評選台灣最具爆發力生技公司
- **藥華醫藥**  
降血脂藥物、抗癌藥物、治療B型肝炎帶原者藥物
- **鑫品生技**  
現階段開發之細胞製劑相關產品涵蓋：(一) 感染性疾病、(二) 癌症腫瘤、(三) 幹細胞與基因治療三大領域
- **台灣浩鼎**  
發展乳癌新藥、全球乳癌用藥市場規模約200億美元
- **台灣尖端**  
臍帶血儲存與基因檢測、濫用藥物（毒品）與殘留藥物檢驗試劑、蛋白質新藥研發



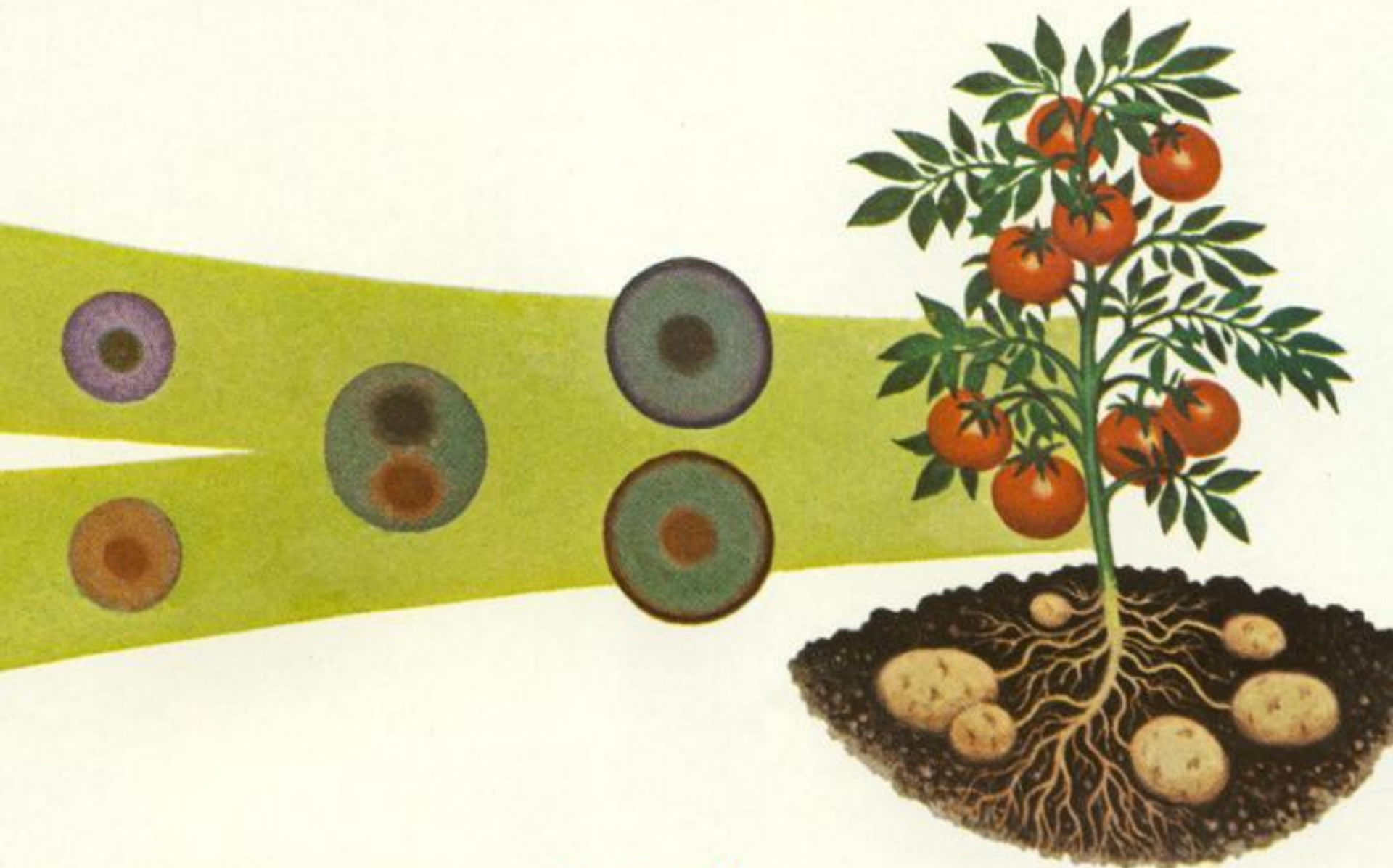
# 創意：流變性 (Flexibility)

- 創意與**知識體系**有密切的關係
- 創意與個人的**生命**與價值觀有密切的關係  
人生「三要」



# 轉基因木瓜（右）與對照組（左）單位產量之比較





Fusing a "pomato" 馬鈴茄

# 鈴馬就造

# 合融胞細

薯鈴馬茄番讓程工改基  
可科花字十、科茄前目



以人工方法，將番茄與馬鈴薯加以「細胞融合」培育出根部為馬鈴薯、植株是番茄的新品種「馬鈴薯番茄」。(記者李清貴攝)

記者李清貴／宜蘭報導

在二〇〇二宜蘭綠色博覽會「生物館」內，展出一株利用「細胞融合」技術所培育出的合新品種的合成果物，在這種新種植物上，不但上面長番茄，根部則長馬鈴薯，亦

一九七五年科學

家已經知道利用之烯甘油可以進行細胞融合，此後，這方面的研究不斷突飛猛進，一九七八年德國科學家融合馬鈴薯及番茄的細胞，成功

培育出新種的「馬鈴薯番茄」，也就是地下根部長出馬鈴薯，而地上植株卻長出番茄。

類似這種「基因改造」工程被廣泛的使用於動物身上，然而若要使植物及微生物細胞融合，則必須先行利用酵素將植物的細胞壁分解，再將植物細胞與細菌細胞融合，經過特殊方式培養，例如番茄 (tomato) 與馬鈴薯 (potato) 細胞融合而成的馬鈴薯茄 (potatoto)，具有番茄與馬鈴薯的雙重特性。目前已在茄科、十字花科等的種屬別合成成功，確實為未來的農業技術立下新的指標。

## 新新聞辭典

### 細胞融合

種新獲得種交細胞以改變細胞性能的技术，細胞融合可以在分類學上親緣關係較遠的生物之間進行，而能克服自然生理學上、生殖上或重組上的障礙。細胞融合技術只是生物技術的其中一種，其他生物技術尚包括遺傳工程、體反應利用技術、組織培養技術、細胞培養技術、胚及細胞核移植技術。

細胞融合可以創造新種植物，要使植物及微生物細胞融合，必須利用酵素將植物的細胞壁分解，再將植物細胞與細菌細胞融合，經過特殊方式培養，目前已在茄科、十字花科等的種屬別合成成功，例如番茄 (tomato) 與馬鈴薯 (potato) 細胞融合而成的馬鈴薯茄 (potatoto)。

細胞融合技術，先取出成熟細胞的細胞核，再將之與卵細胞融合，此卵細胞不需經過精子授精，即可在母羊體內成長，最後順利生產。

如果將乳房細胞與除去細胞核的非細胞放在一起，經過電擊，兩個細胞便會融合成一個細胞。融合後好比是受精卵，由於動物細胞如果拿出來培養，通常幾次分裂後就不再分裂，所以需要藉助較複雜的細胞融合。

# 外美 太今



# 生活經驗學習

生長因子  
色澤因子  
香味因子  
甜味因子



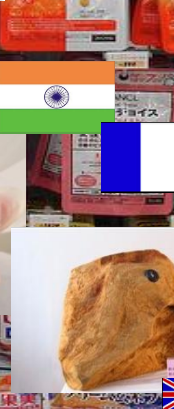
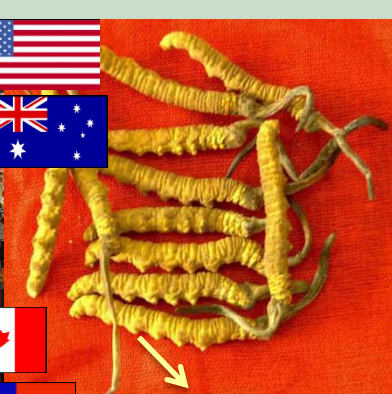
學術爭論  
農業政策  
商業利益  
媒體效應

# 民生生化產品

- 未來可能會有許多民生特化產品的生產製造，將以現代生物科技的方法取代傳統之化學合成方法。
- 例如澱粉酵素、工業用酵素、環保用酵素、可分解性特用塑膠品、精緻化學品、維他命、特用食品及食品原料或添加物等等。
- 利用生物技術於民生生化產品與特用酵素的生產，不但可以增加其製程效力，更有減低生產成本等好處。







# 創意：流變性

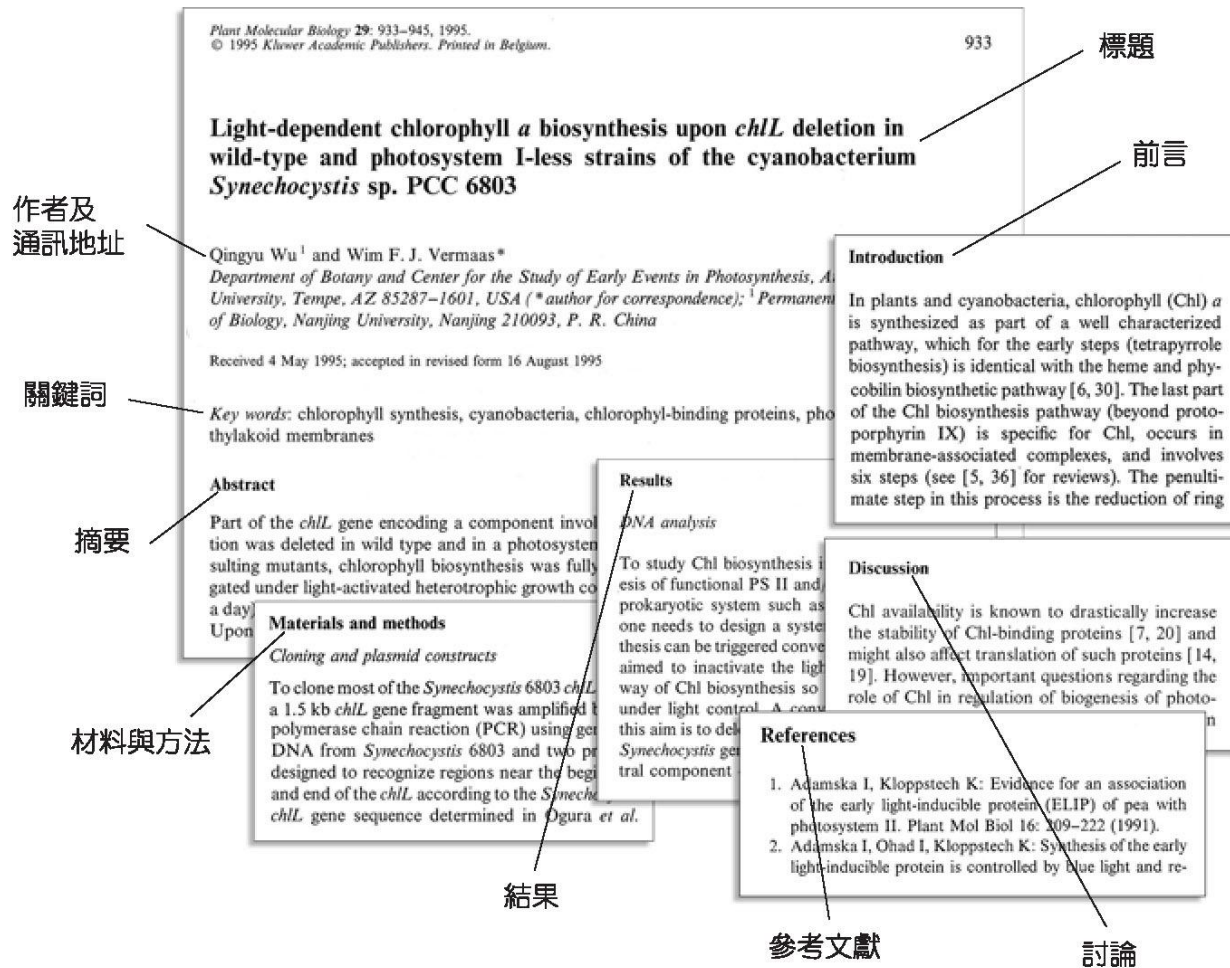
- 創意與個人的**生命**與價值觀有密切的關係
- 資訊與知識沒有直接關係
- 分析歸納過的情報才有用處  
知識就是力量？  
千萬家財不如一技在身？
- 學問與素養乃是一整體系統(**Integrated**)的知識組合
- 生命與價值觀與個人認同的**知識體系**有絕對的關聯性



# 科技論文與學術交流

科學家取得的新成果大部分都以科技論文（又稱學術論文）的形式發表在學術期刊上，撰寫科技論文是科學研究活動的一個組成部分，在論文通過評審接受發表以後，該項研究工作才能算告一段落。

1. 一篇完整的科技論文，通常包括題目、作者署名與通訊地址、摘要、關鍵詞、前言、研究方法和材料、結果、討論及結論、參考文獻等幾部分內容。
2. 一篇好的論文要求所報導的成果內容真實、創新性強、論點明確、數據可靠、條列清晰、文字精練、圖表簡潔、書寫形式合於規範。



**圖 1-24 科技論文的格式與組成** 不同的學術期刊（雜誌）對來稿的學科領域範圍及內容、質量、格式等都有各自的要求，作者可以查閱這些刊物的徵稿簡則獲取有關投稿的須知。一篇完整的科技論文通常包括題目、作者署名與通訊地址、摘要、關鍵詞、前言、研究方法和材料、結果、討論及結論、參考文獻等幾部分內容。

# 美國科學情報研究所 (Institute for Scientific Information, ISI)

<http://scientific.thomson.com/>

## 國際期刊分類

**SCI (Science Citation Index)**

科學引用索引

**SSCI (Social Science Citation Index)**

社會科學引用索引

**EI (Engineering Index)**

工程索引.

**AHCI (Arts and Humanities Citation Index )**

藝術與人文索引

# Impact factor (期刊點數)

ISI每年對包括SCI收錄在內的4,700種期刊之間的引用和被引用數據進行統計、運算，並針對每種期刊定義了影響係數（impact factor）等指標加以報導。一種期刊的影響係數，指的是該刊前二年發表的文獻在當前年的平均被引用的次數。一種刊物的影響係數越高，也即其刊載的文獻被引用率越高，一方面說明這些文獻報導的研究成果影響力大，另一方面也反映該刊物的學術水準高。

JCR (Journal Citation Report)查詢 Impact factor (期刊點數)

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圖 1-25 許多科學家都希望能在有高影響力的學術期刊，發表高水準的科技論文 Nature, Science 屬於國際上影響最大的綜合性學術期刊，與其他各學科領域相比，近年來所刊登的生命科學領域重要成果的比例最大。Cell 屬於生命科學領域高影響力的專業期刊。一般情況下，科學家們以在這些學術期刊上發表研究成果為榮。



# Paper content

**Title**

**Author**

**Abstract**

**Keyword**

**Introduction**

**Material and method**

**Results(figures and tables)**

**Discussion (Conclusion)**

**Acknowledge**

**Reference**

Research

Open Access

## Comparison in a rat thigh abscess model of imipenem, meropenem and cefoperazone-sulbactam against *Acinetobacter baumannii* strains in terms of bactericidal efficacy and resistance selection

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### Abstract

**Background:** We compared imipenem, meropenem and cefoperazone-sulbactam against hospital originated *A. baumannii* strains in terms of bactericidal efficacy and selection of resistant mutants during treatment in a rat thigh abscess model.

**Methods:** A total of 18 strains were inoculated in 54 animals (one strain for three animals). Randomly selected 10 among these 18 strains were inoculated in another 10 rats as the control group. Imipenem, meropenem and cefoperazone-sulbactam were the antibiotics compared. After four days of treatment, Wistar albino rats (200 to 250 g) were sacrificed and the abscess materials were processed for mean colony counts and for the presence of resistant mutants.

**Results:** The mean CFUs per gram (mean  $\pm$  (std. deviation) [ $\times 10^4$ ]) of the abscess were: 9,14 (25,24), 2,11 (3,78), 1,20 (1,70) in the imipenem (n = 17), meropenem (n = 18) and cefoperazone-sulbactam (n = 17) groups, respectively. The differences were not significant. On the other hand, no resistant mutant was detected in abscess materials.

**Conclusion:** This study indicated; first, cefoperazone-sulbactam is comparable to carbapenems in bactericidal efficacy in this particular abscess model and second, emergence of resistance due to spontaneous mutations is not at least a frequent phenomenon among *A. baumannii*.





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## Two different propionicins produced by *Propionibacterium thoenii* P-127

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Received 25 June 2003; accepted 12 August 2003

### Abstract

The bacteriocin GBZ-1 was purified from the growth media of *Propionibacterium thoenii* P-127 and was found to have a molecular weight of 6000 Da. *P. thoenii* P-127 also known as the producer of the bacteriocin PLG-1 (MW 10 kDa). Under specific growth conditions, on semi-solid media, *P. thoenii* P-127 produced both PLG-1 and GBZ-1. The N-terminal of GBZ-1 was microsequenced, the gene was cloned and the DNA sequence was determined and identified. GBZ-1 is highly homologous to a protease-activated antimicrobial peptide (PAMP). In contrast to PAMP, it was purified in its active form and no protease digestion was required for its activation. The survival curve of indicator bacteria *Lactobacillus delbrueckii* subsp. *lactic* ATCC 4797 showed two phases. The fast phase of 20 min was followed by a slow phase. While bacterial survival was reduced by 2 logs during the fast phase, bacterial survival was reduced by additional 3 logs up to 200 min during the slow phase. GBZ-1 activity was affected by magnesium and its activity was completely abolished at 50 mM magnesium chloride. Other divalent cations had no effect on GBZ-1 activity of GBZ-1. To the best of our knowledge this is the first report of a bacterium producing two different bacteriocins under different growth conditions.

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**Keywords:** *Propionibacterium thoenii*; PAMP; Bacteriocins

# Comparison in a rat thigh abscess model of imipenem, meropenem and cefoperazone-sulbactam against *Acinetobacter baumannii* strains in terms of bactericidal efficacy and resistance selection

Kolayli Fetiye<sup>1</sup>, Aynur Karadenizli<sup>1</sup>, Erdem Okay<sup>2</sup>, Sarpkaya Oz<sup>3</sup>, Fatma Budak<sup>1</sup>, Sibel Gundes<sup>4</sup> and Haluk Vahaboglu\*<sup>4</sup>

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## Potential of the Polyvalent Anti-*Staphylococcus* Bacteriophage K for Control of Antibiotic-Resistant Staphylococci from Hospitals

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The increasing prevalence of antibiotic-resistant staphylococci has prompted the need for antibacterial controls other than antibiotics. In this study, a lytic bacteriophage (phage K) was assessed *in vitro* for its ability to inhibit emerging drug-resistant *Staphylococcus aureus* strains from hospitals and other species of *Staphylococcus* isolated from bovine infections. *In vitro* inhibitory assays, phage K lysed a range of clinically isolated methicillin-resistant *S. aureus* (MRSA) strains, *S. aureus* with heterogeneous vancomycin resistance and vancomycin resistance, and teicoplanin-resistant strains. In these assays, 14 of the MRSA strains were initially only weakly sensitive to this phage. However, propagation of phage K on these less-sensitive strains resulted in all 14 being sensitive to the modified phages. The results endorse the principle that, while certain target bacteria may be relatively insensitive to lytic phage, this can be overcome by obtaining modified phage variants from passage of the phage through the insensitive strains. Model *in situ* hand wash studies using a phage-enriched wash solution resulted in a 100-fold reduction in staphylococcal numbers on human skin by comparison with numbers remaining after washing in phage-free solution. Infusion of the phage into a nonimmunogenic bismuth-based cream resulted in strong anti-*Staphylococcus* activity from the cream on plates and in broth.

The increasing prevalence of antibiotic resistance in clinical isolates of *Staphylococcus aureus* is a major problem, given that the bacterium causes a wide variety of human infections ranging from simple abscesses to fatal sepsis, as well as endocarditis, pneumonia, mastitis, phlebitis, meningitis, and toxicoses (for a review see reference 24). The rapid emergence of penicillin-resistant *S. aureus* in the 1950s led to the use of methicillin and related drugs for treatment of infections. In the 1960s, methicillin-resistant *S. aureus* (MRSA) strains emerged and have since become endemic in many hospital environments (14). In addition, these MRSA strains also frequently exhibit resistance to a variety of other common antibiotics (20). Indeed, over 95% of patients worldwide with *S. aureus* infections do not respond to first-line antibiotics, for example, ampicillin and penicillin (33). Recently, the SENTRY antimicrobial surveillance program reported that 36.8% of *S. aureus* isolates retyped belonged to multidrug-resistant, oxacillin-resistant *S. aureus* strains (7). In Ireland, Naylor et al. (23) found that MRSA was the commonest single organism cultured from patients with complex wound and graft infections after vascular surgery. In addition, the latest data from the European Antimicrobial Resistance Surveillance System showed an increase in MRSA from 39% in 1999 to 45% in 2002 in Ireland (37). Until recently, *S. aureus* has exhibited sensitivity to the glycopeptide antibiotics vancomycin and teicoplanin, and therefore these antibiotics represent one of the last lines of defense available against staphylococcal infection. However, the recent emergence of vancomycin-resistant

*S. aureus* and also teicoplanin-resistant strains in hospital infections poses a major threat to this approach (13). As a result, investigations for new and alternative antimicrobials effective against *S. aureus* have become increasingly relevant.

Bacteriophages (phages) were investigated as far back as 1921 to eliminate bacteria including staphylococci in human infections (35). The majority of human phage therapy studies have been performed in Poland (29) and the former Soviet Union and have included challenges against *Staphylococcus* (for a review see reference 36). Although research on phage therapy diminished outside of the former Soviet Union with the advent of antibiotics, it has been revisited primarily as a result of the antibiotic resistance problem. This renewed interest is evident from the number of reviews published recently (2, 3, 5, 8, 9, 19, 22, 36). For *S. aureus* the potential of phage as an antibacterial therapeutic was shown by Matsuzaki and coworkers (21), who significantly reduced the mortality of mice previously injected with *S. aureus* by intraperitoneal injections of phage MR11 (21). Moreover, since the early 1990s, a variety of new companies that have placed major emphasis on bacteriophage research, with the aim of treating multidrug-resistant bacteria causing infections, have been established worldwide.

Phage K is a polyvalent phage with a broad host range, inhibiting both coagulase-positive and -negative staphylococci (32). It is a member of the family *Myoviridae* (1) and has been the subject of previous studies (15–17, 28–30). The origin of phage K is unclear. Both Rountree in 1949 (32) and Rippon in 1956 (31) state that phage K of Krueger and Northrop (18) is identical to phage Au2 described by Burnet and Lush in 1935 (4). Burnet and Lush also state that the phage used by Krueger and Northrop in 1930 (18) is Au2 and suggest that phage Au2 could be derived from the H strain of *S. aureus* of Grant and

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## **Acknowledgements**

2.

We thank Josiane Ferreira for technical assistance during molecular assays.

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change. This was done by crossing the virus with a virus that had a deletion in genomic segment L and a segment M that carried the host attachment genes of bacteriophage  $\phi 13$  (17, 24). Products of the cross were plated on strain LM2509, which does not support the attachment of bacteriophage  $\phi 6$ . These

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enzyme that also contains iron (Zahn & DiSpirito, 1996). Genes designated *pmoA* and *pmoB* have been characterized, and the nucleotide sequence of a third gene, *pmoC*, is described in the sequence databases (Semrau *et al.*, 1995; Zahn & DiSpirito, 1996; accession numbers L40804 and U94337). The AMO is also believed

**Sayavedra-Soto, L. A., Hommes, N. G. & Arp, D. J. (1994).** Characterisation of the gene encoding hydroxylamine oxidoreductase in *Nitrosomonas europaea*. *J Bacteriol* **176**, 504–510.

**Semrau, J. D., Chistoserdov, A., Lebron, J., Castello, A., Davagnino, J., Kenna, E., Holmes, A. J., Finch, R., Murrell, J. C. & Lidstrom, M. E. (1995).** Particulate methane monooxygenase genes in methanotrophs. *J Bacteriol* **177**, 3071–3079.

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洪

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**Hung**

比爾

柯林頓

**Bill**

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陳總統.... 等

**Ex.**

**Shiroh Onodera, Xueying Qiao, Jian Qiao and Leonard Mindich**

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0021-9193/99/\$04.00+0

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## Isolation of Additional Bacteriophages with Genomes of Segmented Double-Stranded RNA

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Received 15 March 1999/Accepted 26 May 1999


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## Acquisition of a Fourth Genomic Segment in Bacteriophage $\phi 6$ , a Bacteriophage with a Genome of Three Segments of dsRNA

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enzyme that also contains iron (Zahn & DiSpirito, 1996). Genes designated *pmoA* and *pmoB* have been characterized, and the nucleotide sequence of a third gene, *pmoC*, is described in the sequence databases (Semrau *et al.*, 1995; Zahn & DiSpirito, 1996; accession numbers L40804 and U94337). The AMO is also believed

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JOURNAL OF BACTERIOLOGY, June 1995, p. 3071–3079  
0021-9193/95/\$04.00+0  
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Vol. 177, No. 11

## Particulate Methane Monooxygenase Genes in Methanotrophs

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Received 29 December 1994/Accepted 21 March 1995

By Chih-Hsin Hung, 2007

## 四、科學研究的驅動力

生命科學領域有兩方面是根本的：

**第一、在知識經濟時代，科學技術是先進的生產力，它直接為人類創造財富和利益，滿足人類日益增長的物質與文化需求。**

例如：社會越進步、物質生活越豐富，人類對健康和長壽的期望值就越高。從更高的視角來看，人類從事的一切生產活動（包括製造出最先進的電視機、汽車、電腦等，還包括其他學科的研究）都是服務於人類。

**第二、求知慾和好奇心是人的天性，而創新性研究才能夠滿足人類的求知慾和好奇心，生命科學研究更能滿足人類對自身瞭解的需求。**

為了探索未知世界，為了追求真理，在好奇心驅動下許多優秀的科學家，在不同的科學領域獲得了重大發現和突破。

# Effect of mucilage from yam on activation of lymphocytic immune cells

## 山藥黏液對淋巴免疫細胞活性的影響

學生：黃柏弦 4BT980034

方奕閔 4BT980070



# 摘要

- 利用1~25  $\mu\text{g}/\text{ml}$ 的山藥黏液刺激BSA培養基培養出的淋巴細胞可提高約4.1~10.9倍增殖率。
- 人蔘萃取物、雙歧桿菌M101-4、山藥黏液都是提升免疫能力的促進劑。



- Con A(刀豆蛋白 A)和LPS(脂多醣)能誘導淋巴細胞作有絲分裂。
- 利用1~25ug/ml的山藥黏液去培養脾臟細胞和淋巴細胞可增殖分別約5.0~14.1倍和2.4~6.4倍。



- 山藥黏液可增加巨噬細胞所產生的細胞因子TNF- $\alpha$ 和IL-6。
- 未被LPS(脂多醣)刺激的巨噬細胞，加入山藥黏液後，細胞因子TNF- $\alpha$ 和IL-6分別增殖至15.6~60.1倍和2.3~9.1倍；所以山藥是可維持宿主免疫和生理調節的功能性食品。



# 簡介



- 強化免疫活性，可防止老化並降低罹患疾病的機率。
- 山藥(Yam)是一種多年生草本植物，原產於中國，野生型的山藥則遍布全世界。
- 秋末採收，可食用部位為根，去皮後陰乾，可用於烹飪。







**DIOSCOREA BATATAS.** Beauv.  
Tubercule de Cassia. — Manioc de Cayenne, Latr.

- 食用山藥有，野生和人工栽培，又區分長山藥與短山藥。
- 長山藥和短山藥因生長環境不同，所以長出來的形狀也不相同。
- 自古中醫學的“淮山”就是將山藥的根去皮乾燥或清蒸後乾燥所製成。
- 山藥被認為是東方草藥或功能性食品，所以生產量和消費量增加，一些農業合作社也和食品公司合作，銷售山藥粉。
- 某些山藥研究報告，提到“蒸過、乾燥”的山藥其黏液和蛋白質含量都比生山藥低，但是甘露糖含量卻比生山藥高。

- 體外實驗證明山藥黏液中的多醣具有消除重金屬的作用。
- 山藥黏液能抑制血管中ACE酶的作用，達到降低血壓的效果。
- 已知山藥黏液，除了增進免疫系統，更具有去除重金屬的能力及抑制ACE酶的效果。
- 山藥黏液可刺激腸道淋巴結“培氏斑”的細胞增殖，並可誘導產生抗體IgA。



# 材料與方法



# 山藥黏液的製備

## 一. 新鮮山藥

- ① 購買市面上的短山藥
  - ② 將短山藥清洗乾淨，切成薄片(0.5 cm)
  - ③ 浸泡95°C~100°C的熱水兩小時
  - ④ 先以棉布做第一層過濾，清除殘餘雜質，獲得濾液
  - ⑤ 濾液再通過真空過濾，獲取純淨的萃取物
- 短山藥有82.1%的水分、1.52%粗蛋白、0.48%粗脂肪、0.23%粗纖維、0.88%粗灰分、16.94%可溶性固形物

## 二. 山藥粉

- ① 購買山藥粉
- ② 加水至10%濃度
- ③ 離心分離，取得上清液
- ④ 進行熱水萃取
- ⑤ 使用硫酸銨或乙醇消除蛋白質與 $\alpha$ -澱粉酶
- ⑥ 通過透析後，再使用離子交換樹脂可得到更多醣類
- ⑦ 並以PAS染色檢測醣的含量
- ⑧ 萃取物和黏多醣的產物，再使用旋轉蒸發器(EYELA)濃縮後，保存於 $-20^{\circ}\text{C}$

# 人參萃取物的製備

- ① 購買6年以上新鮮人參，以 $0^{\circ}\text{C} \sim 5^{\circ}\text{C}$ 低溫保存
- ② 接著洗淨人參，切成薄片
- ③ 再用 $95^{\circ}\text{C} \sim 100^{\circ}\text{C}$ 熱水浸泡2小時，樣本:水=1:40
- ④ 使用棉布作為第一層的過濾，濾液再經過真空過濾後並拿至旋轉蒸發器(EYELA)進行，濃縮、乾燥步驟。(存於 $-20^{\circ}\text{C}$ ，以便後續實驗)



# 雙歧桿菌的製備

- ① 購買-日本雙歧基金會的雙歧桿菌M101-4
- ② 培養於37°C含5%乳糖的MSR的培養基中
- ③ 繪製生長曲線
- ④ 將培養基的菌，並以4°C離心15min，收集細胞
- ⑤ 倒掉上清液加入『Hank's緩衝溶液』稀釋，再測懸浮液中菌的濃度
- ① 再以95°C熱水泡30min，保存於-20°C





# 淋巴細胞增殖

## 一. 實驗組

- ① 購買8週大的雄性小鼠，馴化1週
- ② 並從小鼠後肢，尾部注射50  $\mu\text{g}$ 的BSA(牛血清蛋白)
- ③ 2週後解剖小鼠，取出淋巴結組織
- ④ 再用RPMI1064培養基，培養成淋巴細胞懸浮液
- ⑤ 並以Trypan blue染色，計算活細胞的濃度
- ⑥ 注入於96孔培養板中，每孔放入 $4 \times 10^5$ 濃度細胞懸浮液
- ⑦ 分別加入3種試劑，每種試劑均包含1，5，25  $\mu\text{g}/\text{ml}$ 三種濃度

# 淋巴細胞增殖

## 二. 對照組

- LPS(脂多醣)-B cell有絲分裂的促進劑  
濃度:0.1, 1, 10  $\mu\text{g/mL}$
- Con A(刀豆蛋白A)-T cell有絲分裂促進劑  
濃度:1, 2, 4  $\mu\text{g/mL}$
- 雙歧桿菌  
濃度: $10^6$ ,  $10^7$ ,  $10^8$  Cell/mL
- 用MTT檢測法和分光光度計(吸光值570nm)測細胞增殖的倍數

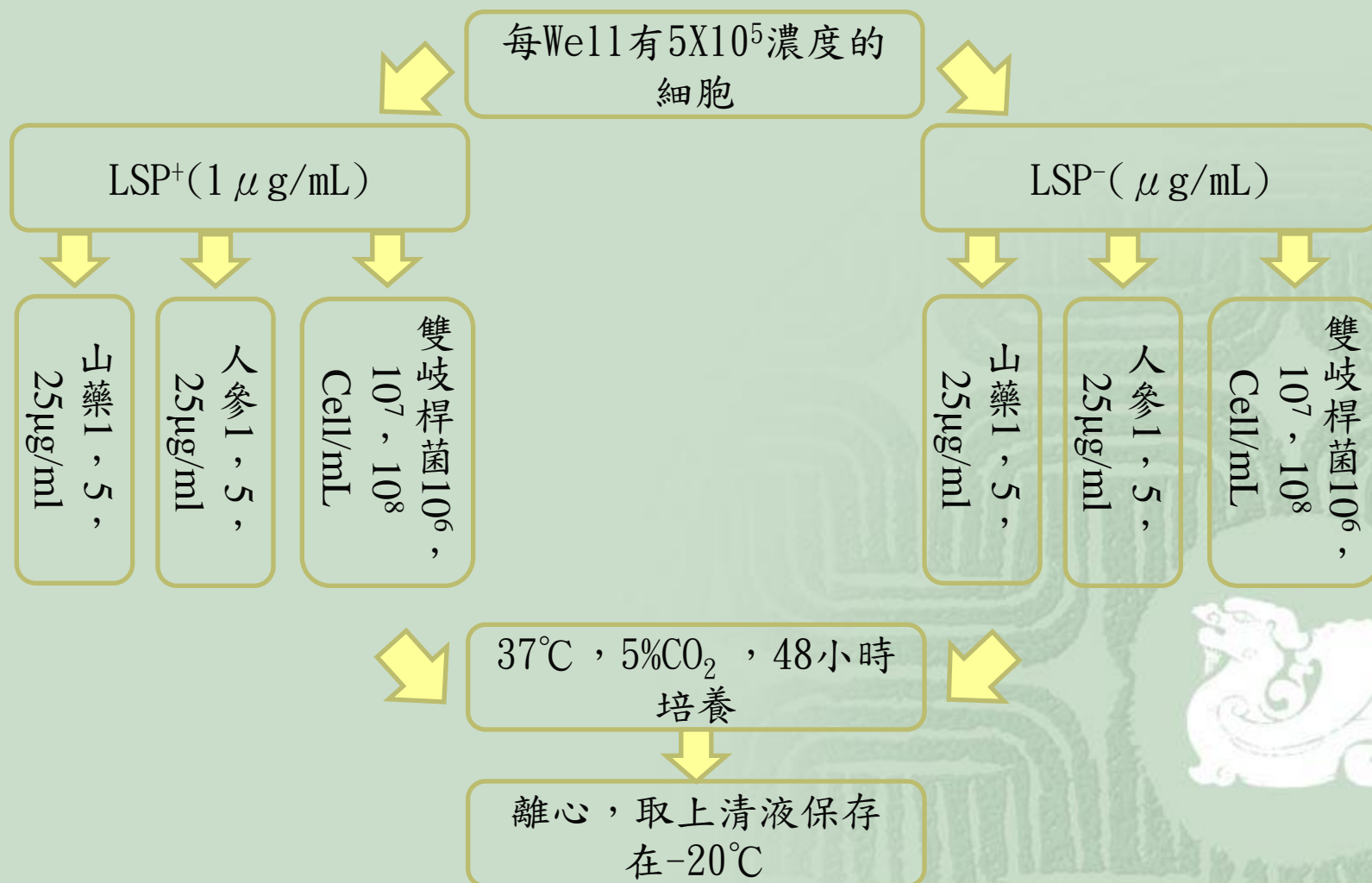
# 脾臟細胞和培氏斑細胞增殖

- ① 方法步驟與同上述淋巴細胞增殖實驗過程
- ② 在96孔培養板中，每孔放入 $5 \times 10^5$ 細胞濃度的懸浮液
- ③ 加入各五種試劑三種不同濃度，培養於 $37^\circ\text{C}$ ， $5\% \text{CO}_2$ ，48小時
- ④ 以MTT檢測計算細胞增殖的倍數



# 巨噬細胞及細胞因子的產生

- 購買自美國細胞培養中心的RAW264.7細胞



# 巨噬細胞及細胞因子的產生

- ① 檢測細胞因子
- ② 把0.1M碳酸氫鈉稀釋過的溶液分別加入 $1\ \mu\text{g}/\text{ml}$  IL-6和TNF- $\alpha$ 抗體， $4^{\circ}\text{C}$ ，放隔夜。
- ③ 用0.01M PBS，0.2% Tween 20(PBST)清洗三次。
- ④ 加 $300\ \mu\text{g}$  3%的BSA溶液，靜置30min。
- ⑤ 再利用PBST洗滌3次，以防止非特異性結合。
- ⑥ 加等量的6N- $\text{H}_2\text{SO}_4$ ，並於分光光度計(吸光值450nm)測出細胞因子的含量。



# 結果與討論



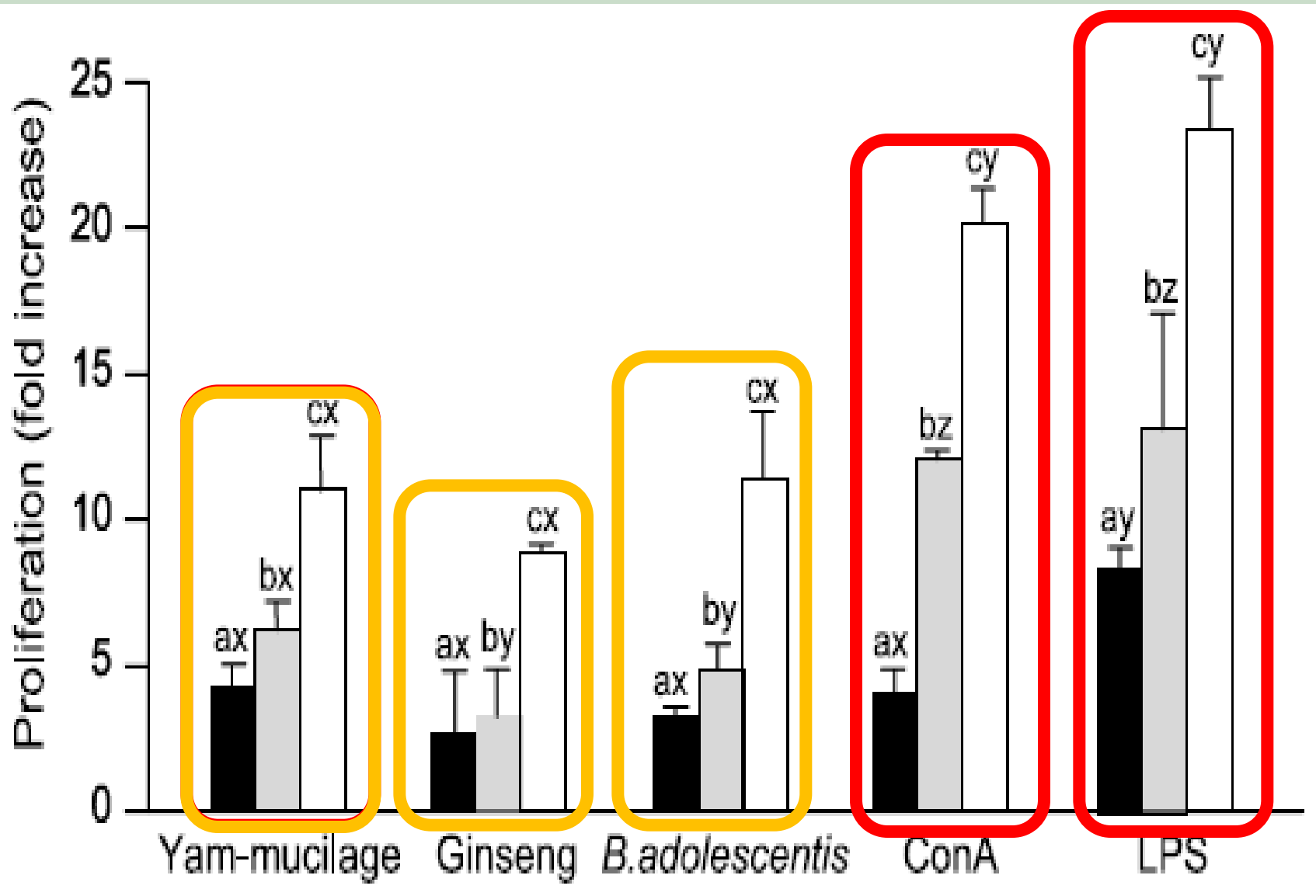


圖1，顯示五種添加物對於以BSA(牛血清蛋白)培養的小鼠淋巴結細胞數目增加的倍率

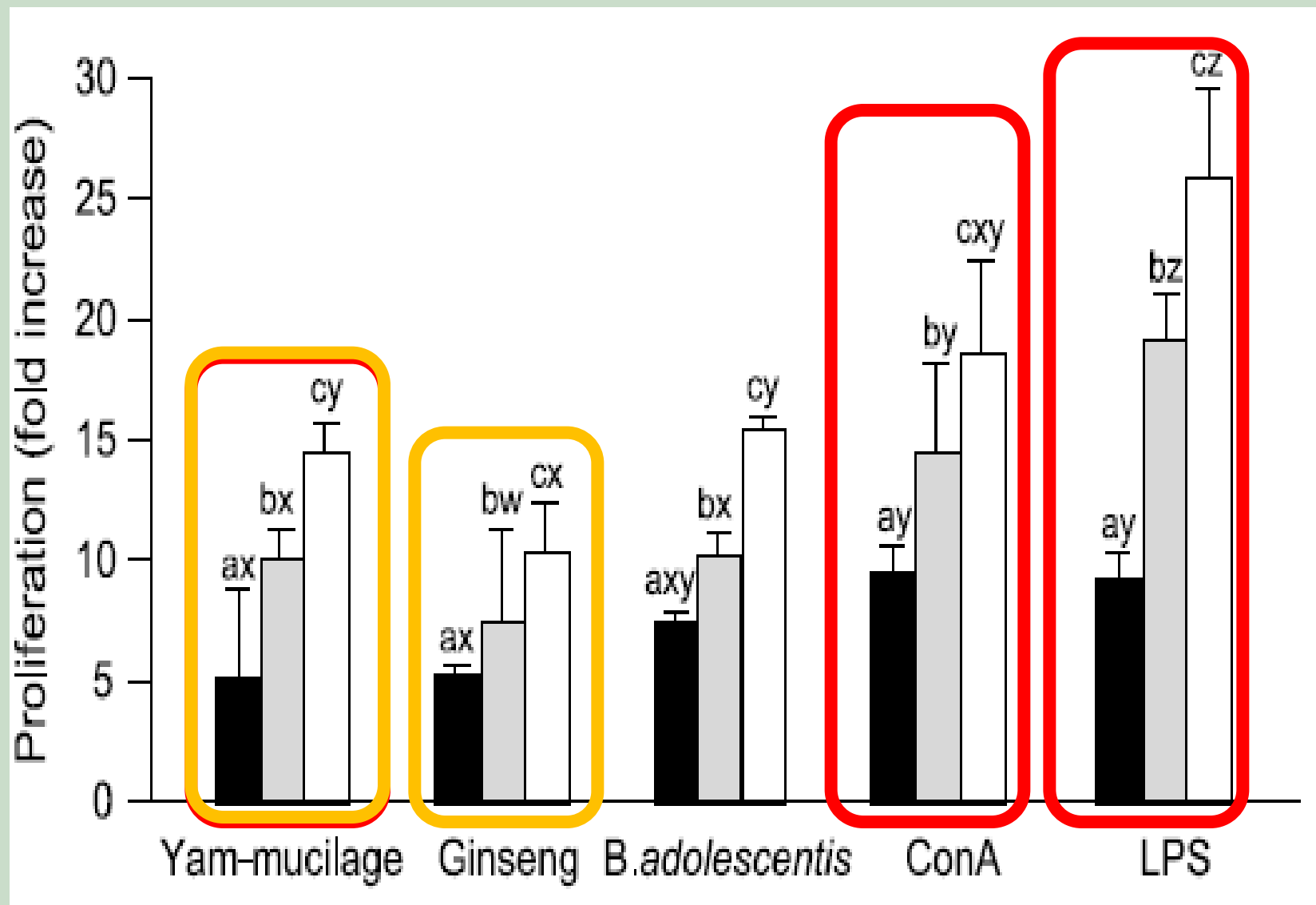


圖2，顯示山藥黏液促進脾臟細胞增殖的倍率



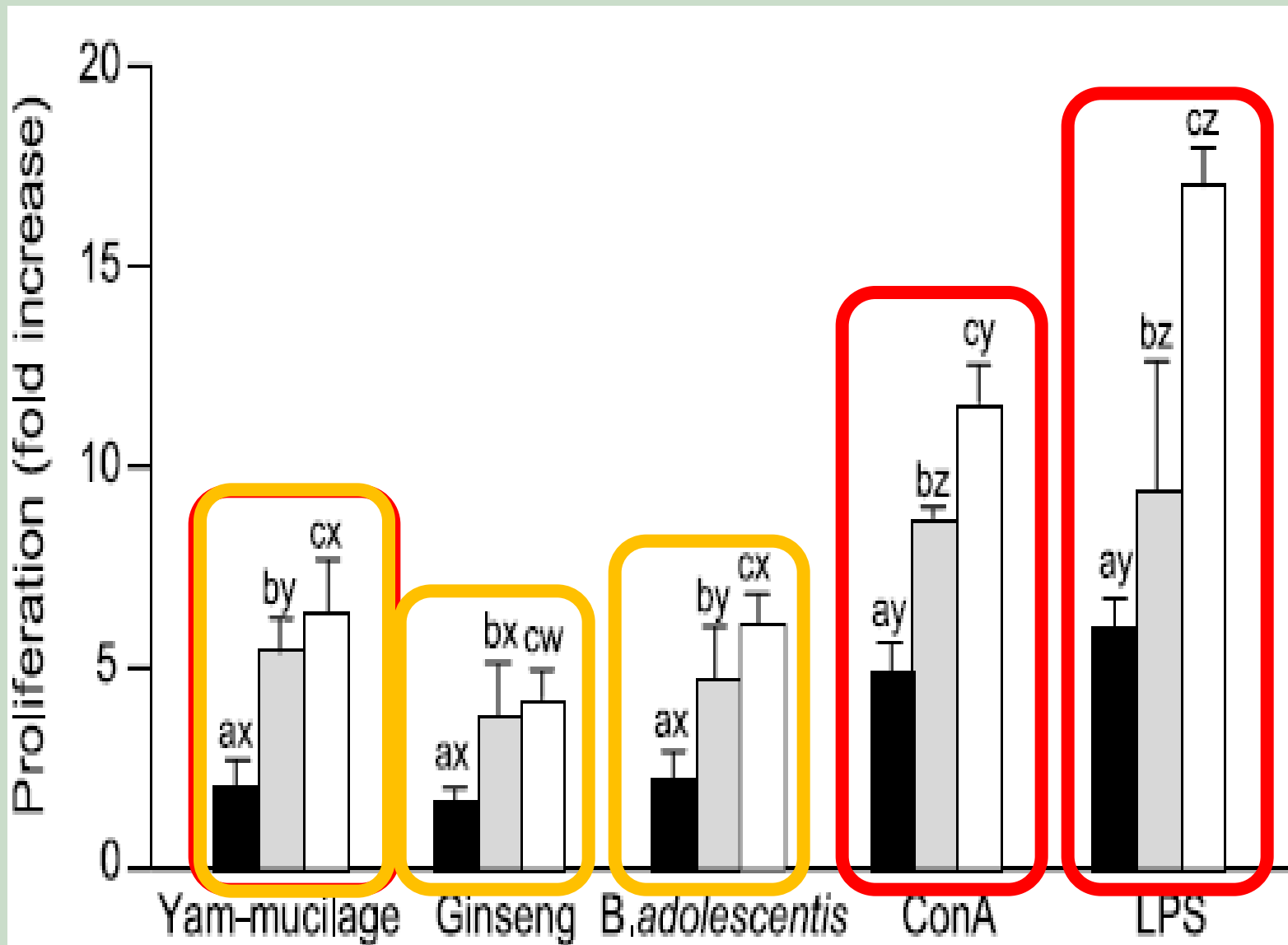


圖3，顯示山藥黏液促進培氏斑細胞增殖的倍率

**Table 1.** Effect of mucilage fraction from yam on TNF- $\alpha$  production by LPS-stimulated (LPS+) and unstimulated (LPS-) RAW 264.7 cells

Treatment	Dose ( $\mu\text{g}$ or cells/ml)	TNF- $\alpha$ Relative change <sup>1)</sup> (fold control)	
		LPS+ <sup>2)</sup>	LPS- <sup>2)</sup>
Yam-mucilage	1	0.9 $\pm$ 0.2 <sup>Aa</sup>	15.6 $\pm$ 2.1 <sup>Ab</sup>
	5	1.6 $\pm$ 1.2 <sup>Ba</sup>	39.7 $\pm$ 2.8 <sup>Bb</sup>
	25	1.7 $\pm$ 0.4 <sup>Ba</sup>	60.1 $\pm$ 4.0 <sup>Cb</sup>
Ginseng	1	1.2 $\pm$ 0.4 <sup>Aa</sup>	0.1 $\pm$ 1.9 <sup>Ab</sup>
	5	1.8 $\pm$ 1.1 <sup>Ba</sup>	21.7 $\pm$ 2.8 <sup>Bb</sup>
	25	1.0 $\pm$ 0.6 <sup>Aa</sup>	50.1 $\pm$ 6.2 <sup>Cb</sup>
<i>B. adolescentis</i>	10 <sup>6</sup>	1.1 $\pm$ 0.2 <sup>Aa</sup>	10.4 $\pm$ 1.9 <sup>Ab</sup>
	10 <sup>7</sup>	2.3 $\pm$ 1.0 <sup>Ba</sup>	42.1 $\pm$ 2.5 <sup>Bb</sup>
	10 <sup>8</sup>	1.8 $\pm$ 0.6 <sup>Aa</sup>	71.3 $\pm$ 4.4 <sup>Cb</sup>

表1，檢測巨噬細胞裡TNF- $\alpha$ 細胞因子的產生倍率

**Table 2.** Effect of mucilage fraction from yam on IL-6 production by LPS-stimulated (LPS+) and unstimulated (LPS-) RAW 264.7 cells

Treatment	Dose ( $\mu\text{g}$ or cells/mL)	IL-6 Relative change <sup>1)</sup> (fold control)	
		LPS+ <sup>2)</sup>	LPS- <sup>2)</sup>
Yam-mucilage	1	$2.3 \pm 0.4^{Aa}$	$2.3 \pm 0.5^{Aa}$
	5	$2.2 \pm 0.2^{Aa}$	$3.8 \pm 1.0^{Bb}$
	25	$1.8 \pm 0.2^{Ba}$	$9.1 \pm 2.1^{Cb}$
Ginseng	1	$1.8 \pm 0.7^{Aa}$	$2.1 \pm 0.8^{Ab}$
	5	$1.1 \pm 0.9^{Ba}$	$2.8 \pm 1.0^{Bb}$
	25	$0.7 \pm 0.6^{Ca}$	$7.6 \pm 1.0^{Cb}$
<i>B. adolescentis</i>	$10^6$	$3.3 \pm 1.6^{Aa}$	$2.4 \pm 0.6^{Ab}$
	$10^7$	$2.1 \pm 0.7^{Aa}$	$4.9 \pm 1.1^{Bb}$
	$10^8$	$1.9 \pm 1.1^{Ba}$	$12.8 \pm 1.6^{Cb}$

表2，為檢測巨噬細胞裡IL-6細胞因子的產生倍率

# 討論

- Con A(刀豆蛋白A)-T cell有絲細胞分裂因子促進劑。
- LPS(脂多醣)-B cell有絲細胞分裂因子的促進劑。
- Con A和LPS有絲分裂效果相較於山藥黏液低，但高於人參。
- 已知人參萃取物裡的成分，例如皂苷、多醣等，不但可促進B細胞和T細胞的增殖，也可促進從小鼠脾臟細胞和淋巴結細胞分離的B細胞和T細胞的增殖。



- 已知從雙歧桿菌裡面的細胞壁或細胞質取得的多醣類，也具有免疫功能。
- 本研究中，山藥黏液在促進免疫系統細胞增殖的效果，以及增殖模式與LPS類似，因此被認為可能具有特定B細胞有絲分裂原的功能。
- 山藥黏液具有直接刺激巨噬細胞產生細胞因子的能力。



# 結論

- 近來有相關植物源免疫活性之研究頻傳，如桔梗萃取物能幫助小鼠產生殺手細胞對抗腫瘤…等。
- 因此將山藥黏液發展為保健食品或藥材，來預防可能因老化或疾病造成免疫活性下降，是指日可待的。

