Recent studies have pushed PolyU to the leading edge of cancer research with alternative treatment methods.

理大在癌病另類療法的最新研究中，取得突破性進展。

Hope for cancer healing

癌症治療 再現曙光

Cancer is one of the leading causes of death worldwide, outpacing the effects of AIDS, tuberculosis and malaria. A serious problem for the medical sciences, it is responsible for between seven and eight million deaths each year, with that number expected to rise to 10 million by 2020. There has long been an obvious need to deal with this situation, but current forms of treatment are often limited in their effects. Radiation therapy and chemotherapy have drastic side effects, and surgery is only helpful in those few cases that are detected early.

Fortunately, researchers at PolyU have recently made major breakthroughs that offer hope for effective alternative treatments. Ranging from the use of an African mushroom extract as a food supplement and compounds that target proliferating cancer stem cells to drugs that starve cancer cells of an essential nutrient, teams from the Department of Applied Biology and Chemical Technology have been offering new hope that this deadly disease might yet be tamed.

癌症是導致全球人口死亡的主因之一，較愛滋病、結核和瘧疾的影響更深更遠。每年因癌病致死的人數達七至八百萬，這個數字預計到二零二零年將上升至一千萬，確實是醫學上一個嚴峻的問題。這個情況一直以來都備受關注，但目前不同癌症療法的效用都有所局限。放射治療和化療有很強的副作用，而手術亦只適用於少數及早發現的病例中。

最近，理大研究人員鑽研有效的另類療法，並取得重大的突破。應用生物及化學科技學系的研究團隊，從非洲虎奶菇提取物製成保健食品，更研發針對腫瘤幹細胞繁殖的化合物，以及開發消耗癌細胞生長所需養料的藥物。這些成果令人鼓舞，為戰勝致命癌魔燃點了新的希望。

Mycelia
菌絲體

Mature fruiting bodies
成熟的子實體

Mushroom extract inhibits breast cancer

The most recent breakthrough has solved a vexing problem in the use of selenium for cancer treatment. Selenium is a trace element essential for human health that has drawn attention from researchers around the world for its excellent bio-availability, low toxicity and strong anti-tumour activity. Yet these characteristics are only apparent at the nanoscale, and selenium nanoparticles clump together very easily. The challenge, then, has been to stabilize the particles so they retain their scale.

Dr Wong Ka-hing, Assistant Professor at the PolyU's Department of Applied Biology and Chemical Technology and Associate Director of the Food Safety and Technology Research Centre, solved this problem with a novel approach. He successfully prepared highly stable, size-controllable selenium nanoparticles that are water dispersable using a polysaccharide protein complex extracted from the African tiger milk mushroom. The added benefit of the process is that it can be achieved using a simple food grade redox (oxidation-reduction) system.

Looked from a slightly different angle, Dr Wong has developed a method that promises to deliver ultimate products that can be consumed as food or health supplements. This will obviously make them more appealing as anti-cancer treatments, given their ease of use and potential for wide availability. Ultimately, that could lead to governments reducing the now spiralling cost of cancer treatments in public healthcare systems.

Dr Wong's preliminary study found that the stabilized selenium nanoparticles could significantly inhibit the growth of breast cancer cells by apoptosis, or cell death. Recently, he reported even more promising results. "By using different mushroom polysaccharide-protein complexes as the stabilizer", he said, "the resulting selenium nanoparticles exhibit strong in vitro anti-tumour activity against different kinds of cancer cell lines".

In the next stage of his research, Dr Wong will evaluate the anti-cancer activity of the stabilized selenium nanoparticles on small animals, and elucidate the underlying mechanism of their growth-inhibition effects on breast cancer cells. He will also be looking to determine at how many of its developmental stages the African tiger milk mushroom could be used for cancer research. With this in mind, PolyU has partnered with the city government of Zhaoqing in Guangdong and a commercial mushroom farm to grow the mushroom in large enough quantities to support further research.

Dr Wong's research on the preparation of selenium nanoparticle with strong anti-tumour activity won him the Young Investigator Award at the 2011 International Conference on Food Factors in Taipei. In 2012, he received a Gold Medal and the Prize of the Chinese Delegation at the 40th International Exhibition of Inventions in Geneva. He holds a Chinese patent for this novel nanotechnology.

Dr Wong Ka-hing wins a Gold Medal and the Prize of the Chinese Delegation at the 40th International Exhibition of Inventions.
黃家興博士在第四十屆國際發明展中奪得金獎及中國代表團獎。

> By using different mushroom polysaccharide-protein complexes as the stabilizer, the resulting selenium nanoparticles exhibit strong in vitro anti-tumour activity against different kinds of cancer cell lines.
>
> 以不同菇類的多糖蛋白複合物作為穩定劑，其製造出來的納米硒粒子，能對不同類型的腫瘤細胞呈現高抗腫瘤活性。

虎奶菇提取物抑制乳腺癌

理大的最新突破，解決了利用「硒」作癌症治療的一個棘手問題。「硒」是一種人體健康必需的微量元素。由於納米硒具有生物可用度高、毒性低及抗腫瘤活性強等特質，因而成為世界各地科研人員熱衷探索的議題。然而，納米硒粒子很容易粘結在一起，而它的特性只顯現在納米尺度中。所以，要有效地穩定納米粒子以保持其尺度實在是一個挑戰。

理大應用生物及化學科技學系助理教授兼食物安全及科技研究中心副總監黃家興博士以一個嶄新方法解開了這個難題。他從非洲品種的虎奶菇中提取多糖蛋白複合物，在一個簡單的食品級氧化還原體系中，成功研製出具高穩定性、大小可控及可水溶的納米硒粒子。

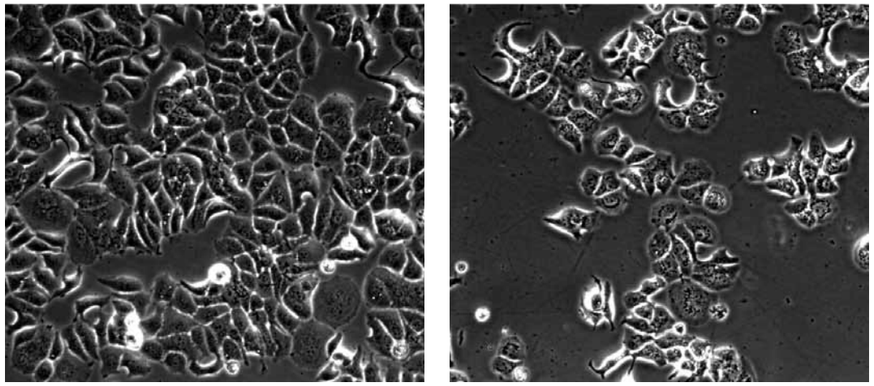
從另一個角度來看，黃博士其實開發了一種方法，可用以製造食品或保健產品。由於這些抗癌食品易於服用和可大量供應，預計將廣受歡迎。最終，這有助減低現時政府在公共醫療體系中為治療癌病所花費龐大的開支。

根據黃博士的初步研究，這些穩定化納米硒能高效地誘導乳腺癌細胞凋亡。最近，他再發現令人振奮的研究結果。他表示：「以不同菇類的多糖蛋白複合物作為穩定劑，其製造出來的納米硒粒子，能對不同類型的腫瘤細胞呈現高抗腫瘤活性。」

在研究的下一階段，黃博士將會評估穩定化納米硒在實驗動物身上的抗癌功效，以及探索其抑制乳腺癌細胞增長的背後機理。黃博士亦會探討虎奶菇在不同生長階段是否也可以用於抗癌研究。理大已與廣東省肇慶市政府及一所菇場達成合作協議，大量培植虎奶菇以供進一步研究之用。

黃博士這項製備抗腫瘤納米硒的研究，為他贏得於台北舉行的二零一一年國際食品保健因子大會上頒授的「青年科學家獎」。此外，這項研究亦於二零一二年在日內瓦舉行的第四十屆國際發明展中，奪得金獎及中國代表團獎。黃博士這項嶄新的納米技術擁有一項中國專利權。

Growing sclerotia
生長中的菌核



Inhibitor treatment on breast cancer cells (right picture) versus the control treatment (left picture)
抑制劑對抗乳腺癌細胞（右圖）與對照組（左圖）的比較

Research collaboration targets cancer stem cell growth

Another of the more difficult problem facing cancer researchers lies in determining how to halt the early proliferation of cancer cells. Cancer stem cells, otherwise known as cancer initiating cells, exist only in small numbers but can easily proliferate and self-renew. They resist chemotherapy and radiation therapy due to their differences in cell cycle regulation and DNA repair processes, and metastasise into a range of differentiated cancer cells that form tumours.

The lack of chemical inhibitors or other agents to halt this process inspired a PolyU team led by Dr Ye Tao, Associate Professor at the Department of Applied Biology and Chemical Technology, to conduct collaborative research with teams from the Peking University Shenzhen Graduate School and the Nevada Cancer Institute in the United States.

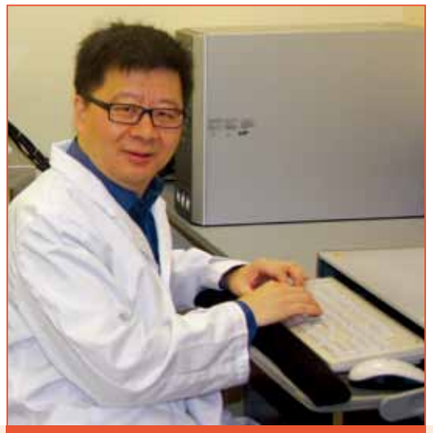
A leading scientist in the field of chemical biology, Dr Ye has been very successful in obtaining funding from the Research Grants Council and the Innovation and Technology Fund to carry out both basic and applied research. His anti-cancer drug discovery programme was also supported by the generous donation received from Fong Shu Fook Tong Foundation and Joyce M. Kuok Foundation. Under his guidance, the PolyU team worked on the search for inhibitors of LSD1, a histone demethylase that is highly expressed in a broad range of tumours. Of nine potential inhibitors developed, two – CBB1003 and CBB1007 – proved most successful. In tests of a variety of cell lines, the two compounds inhibited the growth of cancer stem cells but had only minimal effects on other cancer cells and normal cells.

According to Dr Ye, the new LSD1 inhibitors could be put to clinical use in three ways. They could first be used to treat malignant germ cell tumours such as teratomas, teratocarcinomas and embryonic carcinomas, all of which are usually treated through surgery or with cis-platinum. The drawback of these conventional methods is that after initial treatment, the tumours always become resistant to platinum drugs.

The inhibitors could also be used in stem-cell-based therapy. One of the difficulties posed by such therapy is that it tends to cause the formation of embryonic carcinomas, teratomas, or teratocarcinomas when embryonic and induced pluripotent stem cells incompletely differentiate in the organs of recipients. With LSD1 inhibitors selectively inhibiting these cancers, successful application of stem cell therapy could be ensured.

Dr Ye mentioned that the inhibitors will also be highly useful in selectively inhibiting the proliferation of cancer stem cells into other types of cells that cause organ-specific forms of cancer such as breast, ovarian, lung and brain cancer, and leukaemia. He said that further studies have indicated that the LSD1 inhibitors can also be used to inhibit the cancer stem cells that ultimately cause liver, gastric and kidney cancer.

Leading pharmaceutical companies such as Johnson & Johnson, Pfizer and Roche have shown great interest in further developing the new class of LSD1 inhibitors. The collaborative group's findings have also generated attention from the scientific community around the world. Part of the research work has already been published in *Cancer Research* and was highlighted by *Nature* (China) earlier this year.



Dr Ye Tao
葉濤博士

> "The newly developed inhibitors can inhibit the growth of cancer stem cells but has only minimal effects on other cancer cells and normal cells."
>
> 新開發的抑制劑能成功抑制腫瘤幹細胞的生長，但對其他癌細胞和正常細胞的影響則很微。

針對腫瘤幹細胞生長的協作研究

有關癌症研究的另一更大難題，是如何制止癌細胞早期的繁殖。腫瘤幹細胞（或稱腫瘤啟動細胞）數量雖然很少，但它們可以迅速繁殖和自我更新。由於幹細胞在細胞週期調控及基因損傷修復過程與正常的體細胞不同，因此它們對化療和放射治療具有較高的抵抗力。這些幹細胞還可成為腫瘤轉移的源頭。

現時缺乏化學抑製劑或其他可制止癌細胞繁殖的藥物，這啟發了理大應用生物及化學科技學系副教授葉濤博士帶領北京大學深圳研究生院和美國內華達癌症研究所的研究團隊，共同進行合作研究。

葉濤博士是化學生物學領域的權威科學家之一，並屢獲研究資助局和創新及科技基金撥款資助其基礎及應用研究。他的抗癌藥物研究項目同時也得到方樹福堂基金和郭謝碧蓉基金的捐贈支持。在他的領導下，理大團隊致力研究能高效對抗不同類別腫瘤的組蛋白去甲基酶LSD1的抑制劑。研究人員研製出九種有潛力的抑制劑，其中CBB1003及CBB1007兩種被證實最為有效。在各種腫瘤系的測試中顯示，這兩種複合物能成功抑制腫瘤幹細胞的生長，但對其他癌細胞和正常細胞的影響則很微。

葉博士說：「新開發的LSD1抑制劑可應用於三種臨床情況。首先，它們可用以治療惡性生殖系腫瘤，如畸胎瘤、畸胎癌及胚胎癌等。這些腫瘤一般以外科手術或順鉑治療，弊病是在首次治療後，通常都會產生順鉑抗性。」

這些抑制劑亦可用於幹細胞治療。這種治療的最大問題是，植入受體器官中的幹細胞或誘導性多能幹細胞不完全分化導致胚胎癌、畸胎瘤或畸胎癌的形成。LSD1抑制劑選擇性地抑制這些癌病，因此有助成功施行幹細胞治療。

葉博士指出，這些抑制劑有效地選擇性抑制其他主要器官腫瘤的腫瘤幹細胞，如乳腺癌、卵巢癌、肺癌、腦癌及白血病腫瘤等。進一步的研究結果顯示，這些LSD1抑制劑亦適用於抑制肝癌、胃癌和腎癌的腫瘤幹細胞。

大型製藥公司，包括強生、輝瑞和羅氏，對進一步發展新型LSD1抑製劑均很感興趣。合作團隊的研究結果亦引起了全球科學界別的關注。部分研究成果已刊載於《癌症研究》(Cancer Research)期刊，並於二零一二年初獲《自然（中國版）》(Nature China) 重點報導。

BCA-PEG20
藥物

A solid foundation

These two major breakthroughs have not occurred in isolation. In recent years PolyU has played a leading role in cancer research through efforts at the Department of Applied Biology and Chemical Technology in general and the Lo Ka Chung Centre for Natural Anti-Cancer Drug Development in particular.

Established in late 2006, the Centre carries out pioneering research into natural anti-cancer drugs, and contributes directly to the community by promoting educational training and scientific information on cancer-related discoveries. The Centre's research team itself has made two important discoveries – both related to the amino acid arginine.

Arginine is considered a conditionally essential amino acid, which means that the human body produces its own supply in most cases. Notable exceptions are premature babies, who need to receive it as a dietary supplement. Cancer cells fail to synthesize their own arginine and have to acquire arginine from the blood. The depletion of arginine in blood causes the arginine-dependent cancer cells to die while leaving the normal cells unharmed.

With a keen awareness of this process, team members at the Centre jointly researched BCT-100, a new drug for liver cancer that depletes arginine with a natural human enzyme, with Bio-Cancer Treatment International Limited (BCT) at the laboratory stage. The drug, BCT-100, is currently under phase I/II clinical trials at Queen Mary Hospital, and the results have been encouraging so far. Generating extensive local and global attention, the breakthrough earned the team both a Gold Award and a Special Gold Award at the 33rd International Exhibition of Inventions in Geneva during 2005. Thereafter, BCT followed up on additional research and development. Submitted by BCT as its sole owner, BCT-100 has become Hong Kong's first Investigational New Drug (IND) approved by the US Food and Drug Administration (FDA). BCT-100 has been granted FDA approval in March 2012 for starting the clinical trial in the U.S. Phase I clinical study on liver cancer patients will be conducted in Loma Linda University in the fourth quarter of 2012.

Since the Centre's establishment, the team has continued investigating the use of arginine depletion under the leadership of Prof. Thomas Leung and Dr Thomas Lo. They have developed a second drug, BCA-PEG20, which represents a new paradigm for treating many types of cancer. This can be best understood through comparison with a similar drug under development, ADI-PEG 20.

Otherwise known as pegylated arginine deiminase, ADI-PEG 20 is being developed by a major multinational biopharmaceutical company. Like BCA-PEG20, it systematically depletes arginine from cancer cells. However, despite widespread publicity and promising clinical trials, the drug is limited in its effectiveness, with a relatively small selection of cancer types affected. This is where the new PolyU breakthrough becomes very important.

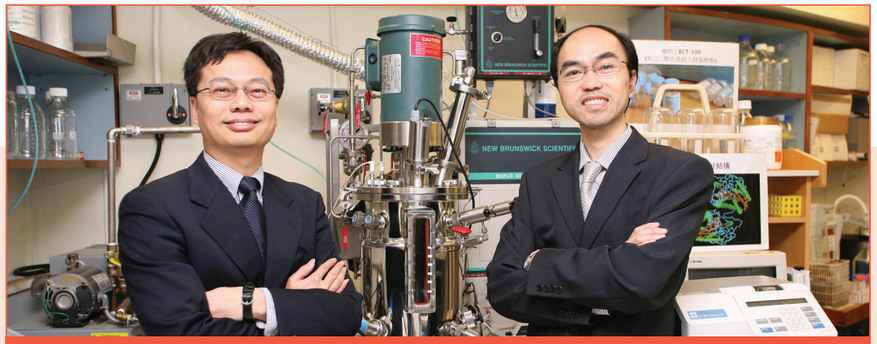
The team at the Lo Ka Chung Centre recently used state-of-the-art DNA technology and protein modification to formulate a similar drug with a significantly prolonged half-life. BCA-PEG20 is based on a special heat-stable arginase – an enzyme that converts arginine into ornithine and urea – and kills cancer cells that cannot be treated by ADI-PEG20. Pre-clinical findings so far suggest that the new drug kills cancer cells effectively and safely, dramatically expanding the usefulness of arginine depletion to a wide range of cancer types.

As the team put it when describing their research, BCA-PEG20 "brings a ray of hope to cancer patients".

For its efforts in developing the drug, the team was awarded the Prize of the State of Geneva and the Gold Medal with Jury's Commendation at the 37th International Exhibition of Inventions in 2009.

A year later, the team joined the SEED (Scientists to Entrepreneurs, Education and Development) competition, a life-sciences business plan competition sponsored and jointly organized by Roche, OrbiMed and McKinsey. Their business plan entitled "A new biological drug BCA-PEG20 for treating lung cancer and colorectal cancer" was one of 16 selected to go through to the final from a total of 77 submitted by leading scientists, researchers and entrepreneurs from throughout Greater China.

Dr Thomas Lo (left) and Prof. Thomas Leung
勞偉雄博士（左）及梁潤松教授



> BCA-PEG20 brings a ray of hope to cancer patients.
>
> BCA-PEG20為癌症病人帶來一線希望。

穩固的根基

其實，理大在癌症研究方面取得的突破並非偶然。近年，理大透過應用生物及化學科技學系和專注於抗癌研究的盧家聰天然抗癌藥物研發中心進行一系列的開發工作，在癌症研究範疇一直肩負起領導的角色。

盧家聰天然抗癌藥物研發中心於二零零六年成立，旨在研發具有抗癌療效的天然藥物，並透過提供有關癌症研究的教育培訓及科學資訊，對社會作出直接的貢獻。中心的研究團隊擁有兩項重要發現，它們均與精氨酸相關。

精氨酸是一種半必需氨基酸，人體通常可自行製造精氨酸，早產兒卻例外，需要以食物補充品形式攝取精氨酸。癌細胞無法自行製造精氨酸，因而依賴血液的供應。消耗血液中的精氨酸能導致這些依賴外源精氨酸的癌細胞死亡，同時人體正常細胞能維持正常功能而不受影響。

盧家聰天然抗癌藥物研發中心的研究團隊與康達醫藥科技有限公司（康達醫藥）在實驗室階段共同研發BCT-100，一種治療肝癌的新藥，以精氨酸酶誘導精氨酸耗竭作為治癌的新方法。這種藥物（BCT-100）現於瑪麗醫院進行第一及第二期的臨床試驗，效果令人鼓舞。這種新藥不但在本地及國際間受到廣泛關注，更於二零零五年在日內瓦舉行的第三十三屆國際發明展中獲得金獎及特別金獎。此外，其後康達醫藥繼續進行進一步的研究和開發，經康達醫藥提交申請，BCT-100成為首隻本港自主研發並通過美國食品藥品監督管理局批准臨床試驗申請的新藥。BCT-100於二零一二年三月獲美國食品藥品監督管理局批准，計劃於二零一二年第四季開始於美國洛瑪連達大學（Loma Linda University）進行第一期臨床研究。

中心自成立以來，研究團隊一直在梁潤松教授和勞偉雄博士領導下，致力鑽研精氨酸耗竭的用途。他們更研製出新一代的藥物BCA-PEG20，有效治療多種癌症。要理解這種新藥的機理，必先將它與正在開發中的同類藥物ADI-PEG 20作比較。

ADI-PEG 20（精氨酸脱亞胺酶）由一所跨國生物製藥公司研發，它跟BCA-PEG20一樣，可以系統性地耗竭癌細胞中的精氨酸。然而，即使經過廣泛的宣傳，以及臨床試驗結果令人滿意，這藥物只對少數癌病種類起着作用，藥效顯然非常局限。這卻成為了理大突破性發現的重點。

最近，盧家聰天然抗癌藥物研發中心的研究人員利用基因技術，再配合分子修飾技術，成功研製出一種延長了體內半衰期而近似ADI-PEG 20的藥物 — BCA-PEG20。它的主要成分是一種特殊的耐熱和穩定的精氨酸酶，是一種天然酵素，它的功能是將精氨酸分解成鳥氨酸和尿素等代謝物，並殺滅ADI-PEG 20所不能對抗的癌細胞。臨床前研究結果顯示，這種新的藥物有效且安全地殺滅癌細胞，更大幅擴展精氨酸耗竭的效用至不同類型的癌症。

研究團隊在介紹有關研究時指出，BCA-PEG20為癌症病人帶來一線希望。

在二零零九年的第三十七屆國際發明展中，該項突破性藥物奪得日內瓦州政府大獎及評審團特別嘉許金獎。

一年後，團隊參加了由羅氏（Roche）、沃脈德資本（OrbiMed）和麥肯錫公司（McKinsey）聯合主辦的SEED金種子大賽（SEED意思是「從科學家到企業家的教育和發展」），這是一個生命科學商業計劃書比賽。理大團隊的商業計劃書題為「一種嶄新用以治療肺癌和大腸癌的生物學藥物BCA-PEG20」，在七十七份大中華區內傑出科學家、研究人員和企業家提交的計劃書中，被挑選為進入總決賽的十六份計劃書之一。

Taken together, these four breakthroughs by PolyU researchers indicate the extent to which the University is pushing back the barriers to healthy living for all. In no better way could we enact the University's motto, "To learn and to apply, for the benefit of mankind".

以上四項理大研究人員的豐碩成果，代表着大學為改善人類健康生活而努力不懈，這正是我們彰顯大學校訓「開物成務 勵學利民」的最佳見證。