

藥物化學實驗

電子資源使用成果心得報告

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指導教授：吳建德 教授

Scifinder

Background knowledge

● 包含資料庫

- CAPlus (Chemical Abstracts Plus Database, 1907-)
- The CAS REGISTRY (1957-)
- CASREACT (Chemical Reactions Database, 1907-)
- CHEMLIST (Regulated Chemicals Listing Database, 1979-)
- CHEMCATS (Online Chemical Catalogs File, 最新版)
- MEDLINE (MEDlars onLine, 1958-)
- *其中我們可以在前面六個資料庫中進行整合查詢

● 檢索角度

- Explore Reference：能夠查到世界各國的專利以及科學、醫学期刊
- Explore Substance：有機無機物質的查詢，NMR 圖譜的查詢
- Explore Reaction：如何合成，單一步驟及多步驟的反應機轉

Explore Reference

● 輸入欲檢索字眼：「Gene therapy AAV-GAD Parkinson」



Research Topic

Author Name

Company Name

Document Identifier

Journal

Patent

Tags

Research Topic

gene therapy AAV GAD parkinson

Search

Examples:
The effect of antibiotic residues on dairy products
Photocyanation of aromatic compounds

←可以根據你要搜尋的主題
做選擇唷~本次是依照主題
(Research topic)

Saved Answer Set
KMP Alert Resu
NEW SciPlann

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Import

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No profiles exist

- 當輸入字眼越詳細，系統能幫你篩選出更專一性的文章；另外，選擇包含觀念(concept)的結果，能夠得到更完整的文獻。

Research Topic Candidates

Research Topic Candidates	References
10 references were found containing both of the concepts "gene therapy AAV" and "GAD parkinson".	10
4804 references were found containing the concept "gene therapy AAV".	4804
84 references were found containing the concept "GAD parkinson".	84

Get References

- 進入之後右邊有資料的分析，本次選擇「CA concept heading」

Research Topic "Gene therapy AAV-GAD Parkinson" > references (10) > Safety and tolerability of gen...

Get Substances Get Reactions Get Related Tools Send to SciPlanner

1 Selected Save Print Export

select All Sort by: Accession Number Answers per Page [20] Display:

Analysis Refine

Analyze by: CA Concept Heading

Click bar to view only those references within the current answer set

Gene therapy	7
Viral vectors	7
Brain	5
Parkinson disease	5
Human	4

將分析拉到下方，點選 show more 可得到更完整的分析

Antiparkinsonian agents	2
Gene	2
Parkinson's disease	2
Adenosine receptor antagonists	1
Behavior	1
Combination chemotherapy	1

show more

● 進入文章後下方有很精華的重點整理

Section cross-reference(s): 3

Concepts

- Adeno-associated virus
- Gene therapy
- Human
- Viral vectors

gene therapy involving transfer of adeno-assocd. virus borne glutamic acid decarboxylase gene into subthalamic nucleus was safe and well tolerated in patient with advanced Parkinson's disease

Brain

subthalamic nucleus; gene therapy involving transfer of adeno-assocd. virus borne glutamic acid decarboxylase gene into subthalamic nucleus was safe and well tolerated in patient with advanced Parkinson's disease

Substances

9024-58-2 Glutamic acid decarboxylase

gene therapy involving transfer of adeno-assocd. virus borne glutamic acid decarboxylase gene into subthalamic nucleus was safe and well tolerated in patient with advanced Parkinson's disease

Pharmacological activity; Therapeutic use; Biological study; Uses

● 進入文章後可點選右上角「Export」輸出成 PDF 文件

Export

For:

Citation Manager

- ☐ Citation export format (*.ris)
- ☐ Quoted Format (*.txt)
- ☐ Tagged Format (*.txt)

Offline review

- ☒ Portable Document Format (*.pdf)
- ☐ Rich Text Format (*.rtf)
- ☐ Answer Keys (*.txt)

Saving locally

- ☐ Answer Key eXchange (*.akx)

Details:

File Name: *

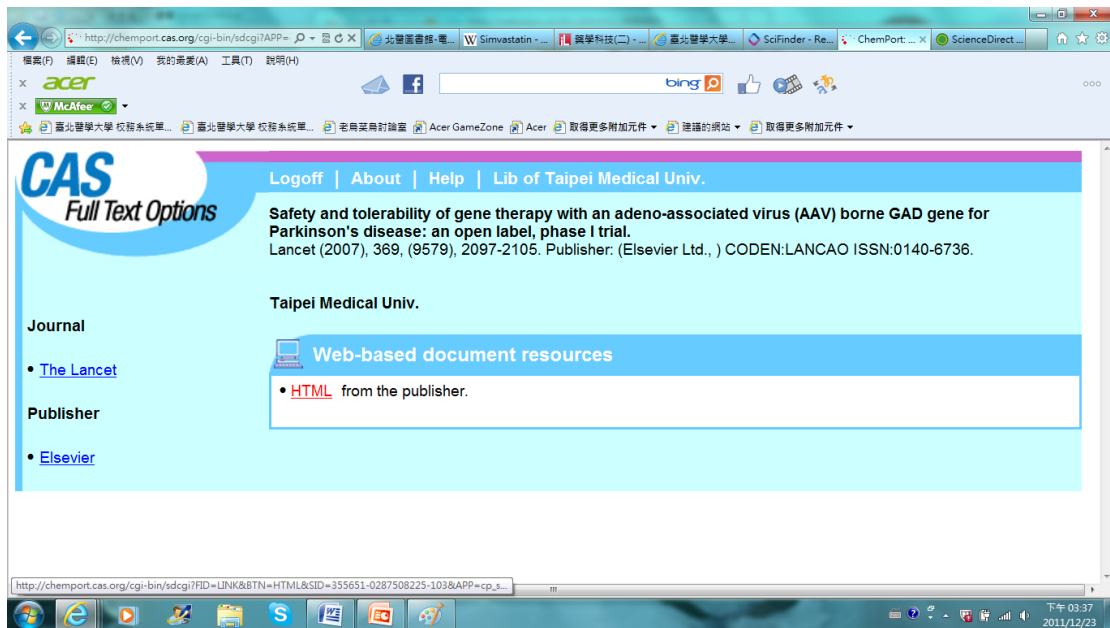
Reference_12_23_2011_154320

Include:

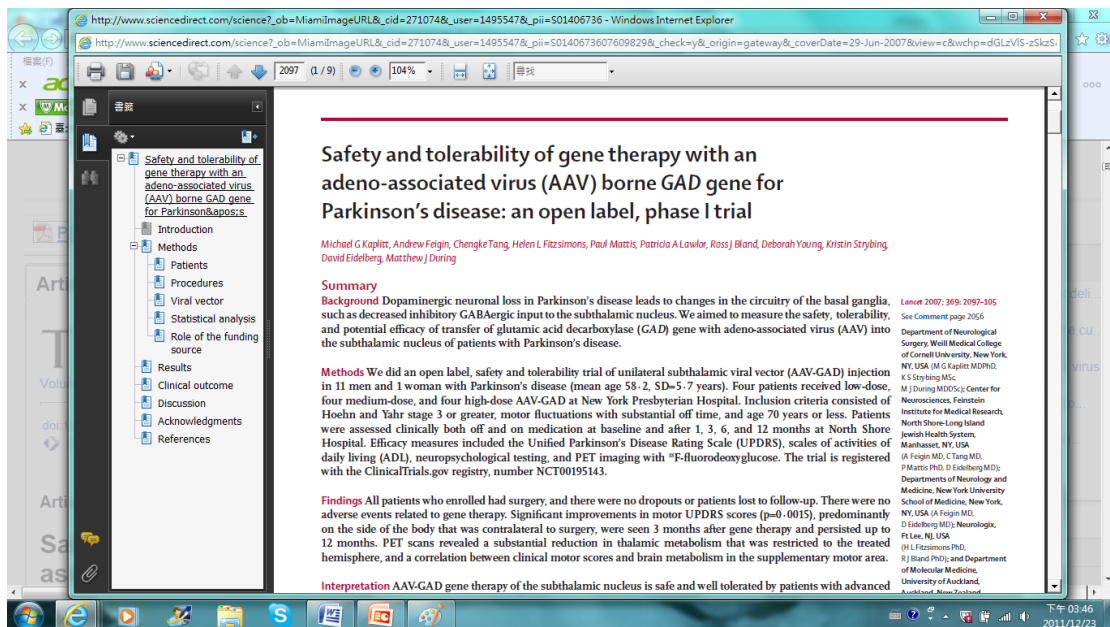
- ☒ Substances
- ☒ Concepts
- ☒ Task History
- ☒ Tags
- ☒ Comments

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- 欲得全文，可以點上方「Get Full context」後進入此網頁，可得知北醫是否有買這篇文章，有的話您將有權限可以閱讀整篇文章。

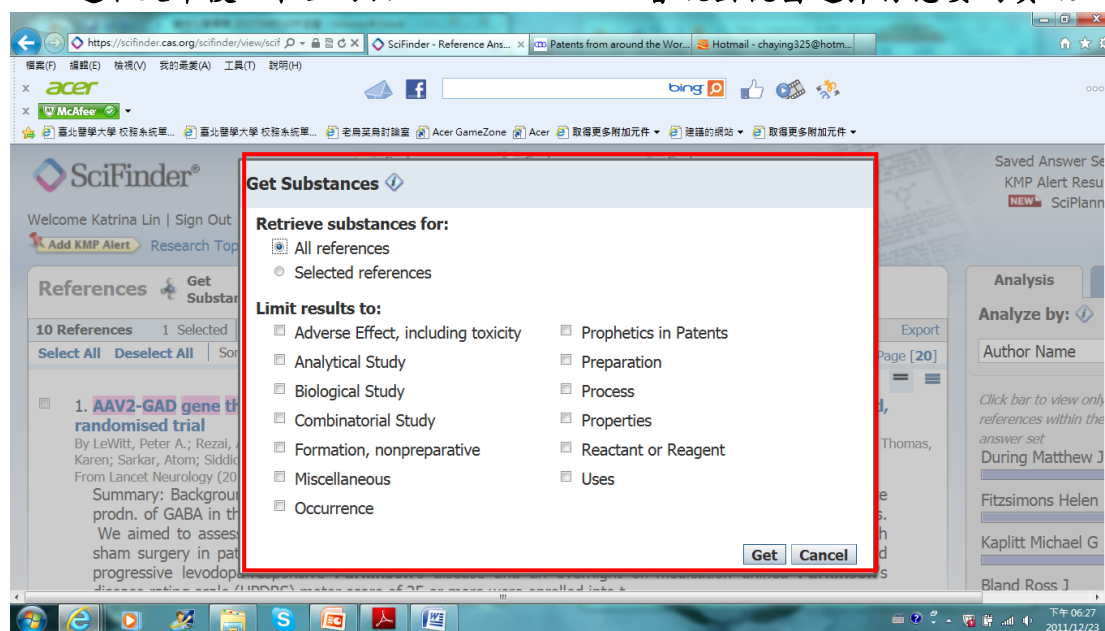


- 點入 HTML 進入全文網頁後，可以點選 PDF 檔案，以方便閱讀

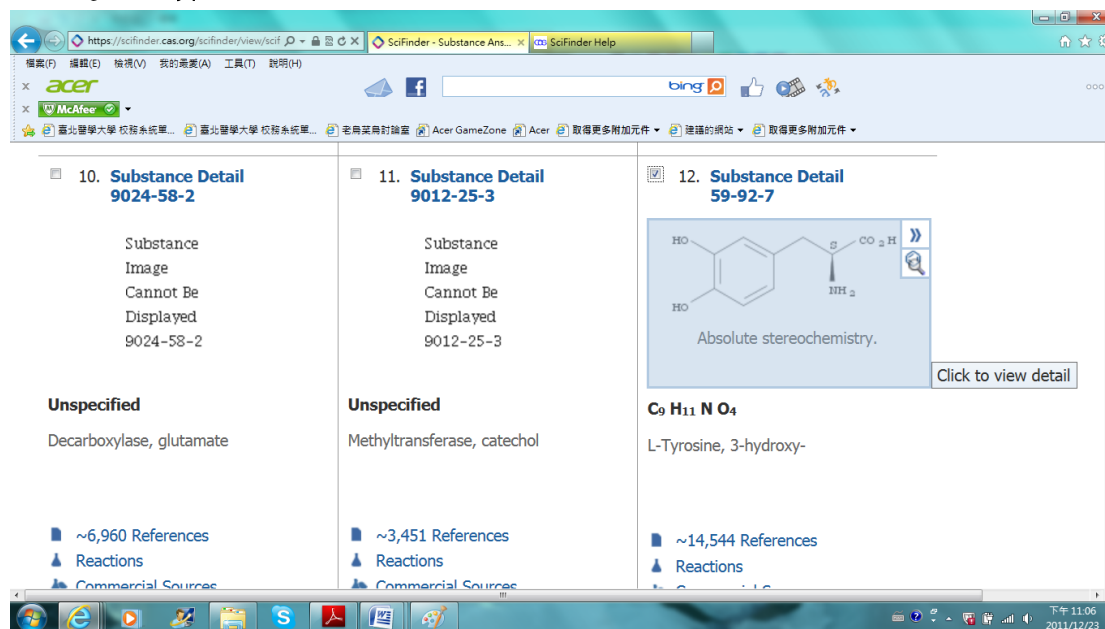


Explore Substance

- 選取文章後，在上方點"Get substance"會跳出視窗選擇你想要的資訊



- 選取物質



- 點入之後有一連串的資訊可以任您挑選，使用上很方便

Document Types: Book, Conference, Dissertation, Journal, Patent, Preprint, Report

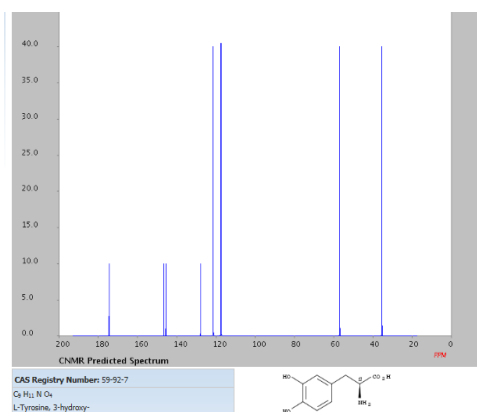
CAS Role	Patents	Nonpatents	Nonspecific Derivatives from Patents	Nonspecific Derivatives from Nonpatents
Analytical Study	✓	✓	✓	✓
Biological Study	✓	✓	✓	✓
Combinatorial Study			✓	
Formation, Nonpreparative	✓	✓	✓	✓
Miscellaneous	✓	✓	✓	
Occurrence	✓	✓		✓
Preparation	✓	✓	✓	✓
Process	✓	✓	✓	✓
Properties	✓	✓	✓	✓
Prophetic in Patents	✓			
Reactant or Reagent	✓	✓	✓	✓
Uses	✓	✓	✓	✓

Predicted Properties: Biological Chemical Density Lipinski and Related Spectra Structure-related Thermal

←可以看到上方有討論各項性質的專利文獻
而下方有在專利中屬於“預測性”的一些物質

下方還可以觀看 NMR 的圖譜!!

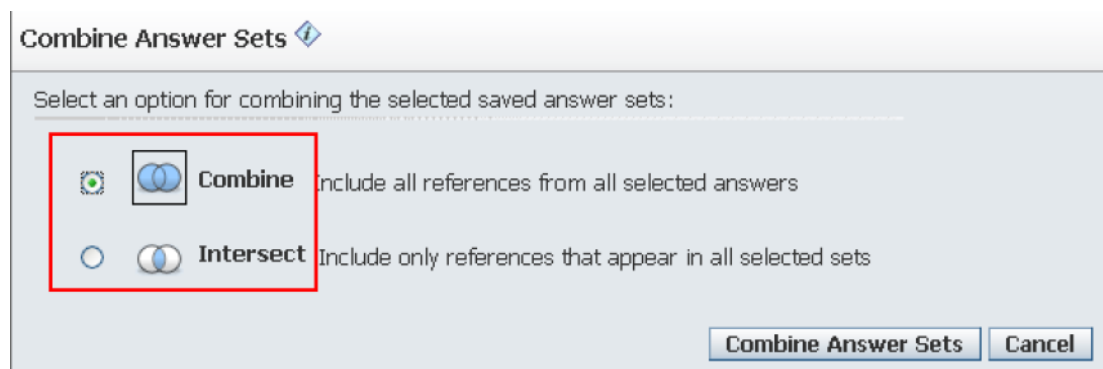
Spectra Properties	Value	Condition	Note	Top
Carbon-13 NMR Spectrum	See spectrum		(36)	
Proton NMR Spectrum	See spectrum		(36)	



Explore reaction

本次選取的 paper 中不具有這個資訊，不過這個使用上也很容易，只要把欲合成 product 以及原料放上去，便可依照 solvent 來幫你分類所有的反應，同樣的也能很方便的在每個反應上做連結。現在還有一個功能是 similar reaction，可以依照相似程度的不同選取適合的反應。

- 最後，我們可以將文獻、物質、反應，分別的 combined 起來蒐集的整體資料就會很完善。



使用成果主題報告

- **Topic : Gene therapy of Parkinson disease**

Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne GAD gene for Parkinson's disease: an open label, phase I trial

By: Kaplitt, Michael G.; Feigin, Andrew; Tang, Chengke; Fitzsimons, Helen L.; Mattis, Paul; Lawlor, Patricia A.; Bland, Ross J.; Young, Deborah; Strybing, Kristin; Eidelberg, David; During, Matthew J.

- **Abstract**

Dopaminergic neuronal loss in Parkinson's disease leads to changes in the circuitry of the basal ganglia, such as decreased inhibitory GABAergic input to the subthalamic nucleus. We aimed to measure the safety, tolerability, and potential efficacy of transfer of glutamic acid decarboxylase (GAD) gene with adeno-assocd. virus (AAV) into the subthalamic nucleus of patients with Parkinson's disease. We did an open label, safety and tolerability trial of unilateral subthalamic viral vector (AAV-GAD) injection in 11 men and 1 woman with Parkinson's disease (mean age 58.2, SD = 5.7 years). Four patients received low-dose, four medium-dose, and four high-dose AAV-GAD

at New York Presbyterian Hospital. Inclusion criteria consisted of Hoehn and Yahr stage 3 or greater, motor fluctuations with substantial off time, and age 70 years or less. Patients were assessed clin. both off and on medication at baseline and after 1, 3, 6, and 12 mo at North Shore Hospital. Efficacy measures included the Unified Parkinson's Disease Rating Scale (UPDRS), scales of activities of daily living (ADL), neuropsychol. testing, and PET imaging with 18F-fluorodeoxyglucose. The trial is registered with the registry, no. All patients who enrolled had surgery, and there were no dropouts or patients lost to follow-up. **There were no adverse events related to gene therapy. Significant improvements in motor UPDRS scores** ($p = 0.0015$), predominantly on the side of the body that was contralateral to surgery, were seen 3 mo after gene therapy and persisted up to 12 mo. PET scans revealed a substantial redn. in thalamic metab. that was restricted to the treated hemisphere, and a correlation between clin. motor scores and brain metab. in the supplementary motor area. AAV-GAD gene therapy of the subthalamic nucleus is safe and well **tolerated by patients with advanced Parkinson's disease**, suggesting that in-vivo gene therapy in the adult brain might be safe for various neurodegenerative diseases.

- 心得討論：這次我想得知的主題是 New treatment of Parkinson disease，一開始使用 Scifinder 直接輸入後發現找到的東西不勝枚舉，於是我先利用 google 做大範圍的查詢，找到了關於 Parkinson disease 有關的新療法，這包含了：Deep brain stimulation、Gene therapy(AAV-GAD gene transfer into STN, AAV-AADC Gene Transfer Into the Putamen)另為一種則是火紅的 Cell-based therapy(stem cell)最後我選擇了基因療法裡 AAV-GAD 到 Scifinder 作進一步的查詢。其實我還看了蠻多篇文章，我就以我看所有資料作為我的心得總結，這個新的基因療法主要是利用 Adenovirus vector typeII 作為 GAD(glutamic acid decarboxylase)的載體，而我們都知道 GAD 的作用就是將 Glutamic acid 轉換成抑制性的神經傳導物質 GABA，這有益於改善 Parkinson 的病人過度活躍的 STN (一般我們會有電及刺激、燒灼、GABA 的注射來改善這些情形) 這個方法在很多論文中都顯示不具有毒性副作用，不過少數的案例中我有發現有些病人會有顱內出血(intracranial bleeding)的情形發生，可想而知，因為你把病毒打入腦袋中，危險的機率實在太大了，縱使 AAV type2 是美國 FDA 目前唯一允許的攜帶藥物的病毒載體，但對於要將之在人體上的應用，我想還有許多要努力的地方吧！不過在搜尋的過程中看見許多前輩設計療法的一些想法我覺得學習很多；但相對的要把一個想法真正變成上市使用的是少之又少，必須經過四期的臨床試

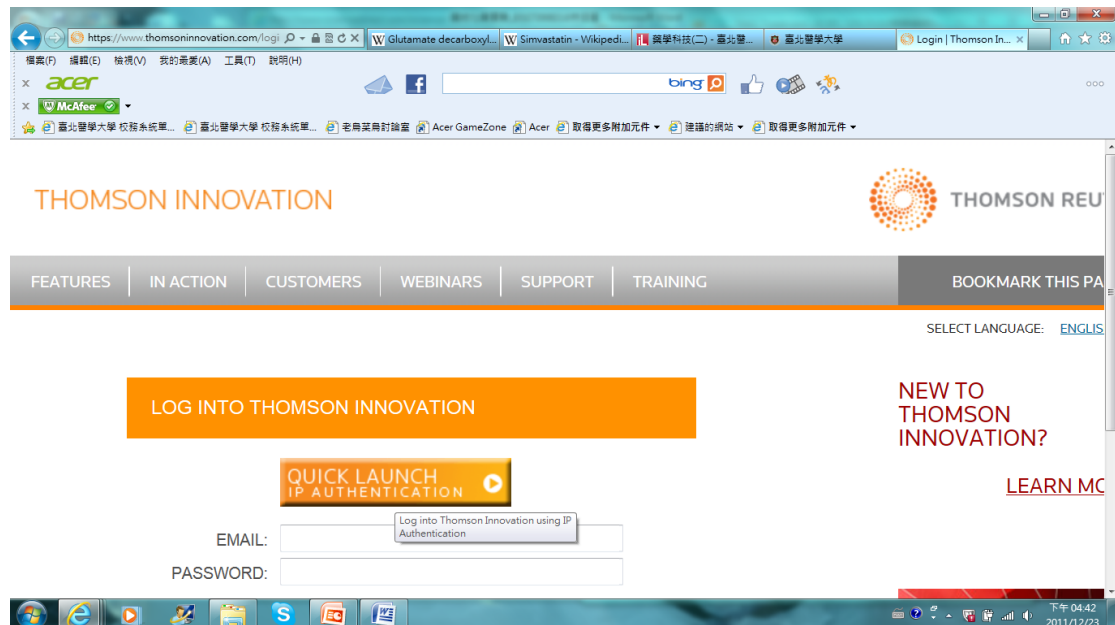
驗，花費的龐大的金額，背後必須要有一股很大的力量支撐著，縱使成功了拉上治療的舞台，很有可能因為上市後的不良反應，一生的心血全都付之一炬。真的著實打從心底佩服這些偉大的研究者呀!

對於 PD patient 當務之急，我想身為藥學系的我們應先教導病人對於 Parkinson disease 的用藥次序，以及最佳的心理建設，畢竟得到這種病一旦開始服用藥物，就必須終生服藥控制，除非到藥物真的無法控制，我們可能才會以新手術做為治療吧!

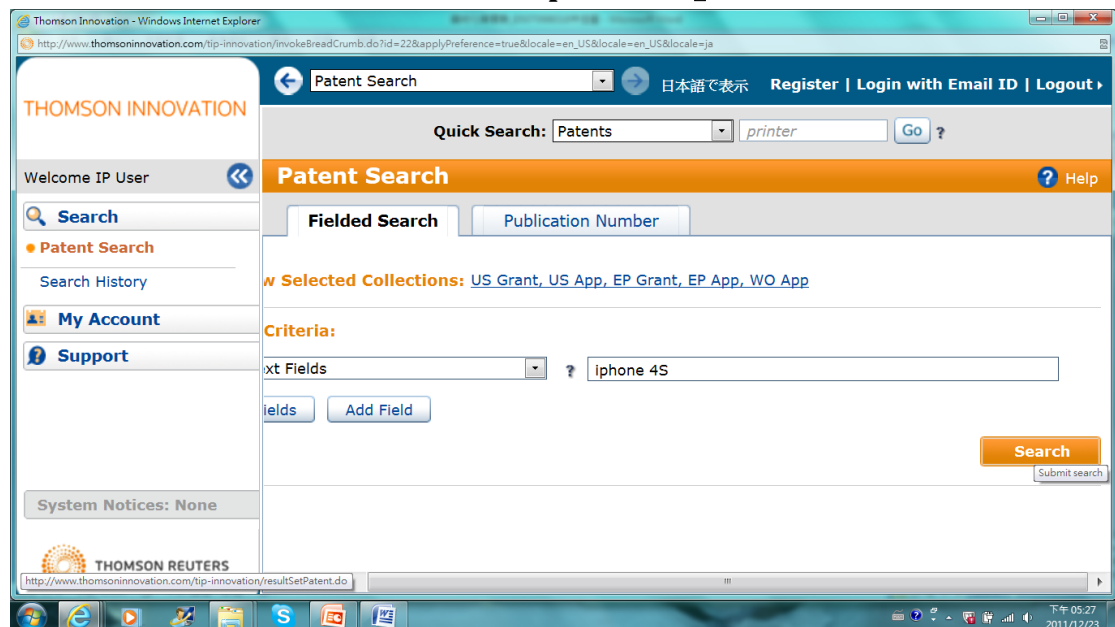
*附註: 這個軟體教過之後我就常常拿來當作寫報告最佳資料來源處，畢竟這是「evidence-based information」不同於以往 google 的結果千奇百怪，可惜的是不一定每次都能順利登入，全校只有兩個幸運兒呀!

Thomson innovation

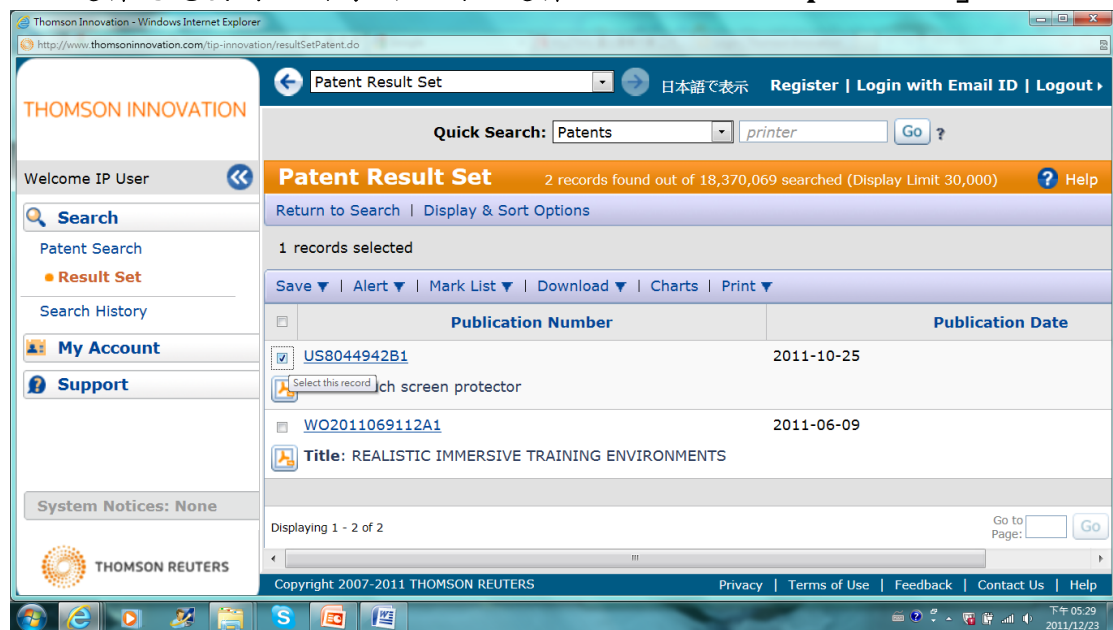
- 北醫網頁→行政單位→研究發展處→專利檢所平台→Quick launch 點入即可



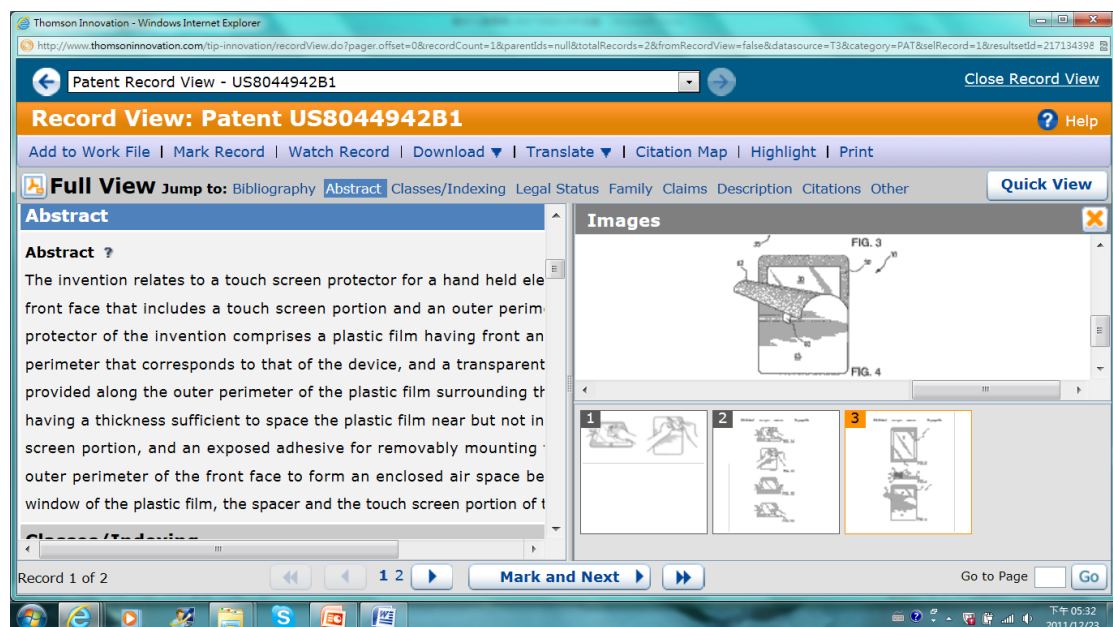
- 輸入欲檢索之項目；測試輸入「iphone 4S」



● 選擇您想要得知的專利；測試選擇「touch screen protector」



● 進入之後可以觀看到三種不一樣的專利圖片，也可以點選上面一列 Bibliography/Abstract/Classes/Indexing/Legal Status 等等詳細得知專利資訊。



上課內容補充

● 智慧財產權之專利權制度：

發明專利自申請日算起 20 年

新型專利自申請算起 12 年

新式樣專利自申請利算起 10 年

*注意：專利生效的起始日是由專利的公告日算起；但專利的終止日卻是從申請

日算起。

*表格整理：來源-根據專利法條例

	發明專利	新型專利	新式樣專利
定義	第十九條：「稱發明者，謂利用自然法則之技術思想之高度創作。」	第九十七條：「稱新型者，謂對物品之形狀、構造或裝置之創作或改良。」	第一百零六條：「Ⅰ稱新式樣者，謂對物品之形狀、花紋、色彩或其結合之創作。Ⅱ稱聯合新式樣者，謂同一人因襲其另一新式樣之創作且構成近似者。」
保護年限	第五十條：「Ⅲ發明專利權期限自申請日起算二十年屆滿。」	第一百條：「Ⅲ新型專利權期限自申請日起算十二年屆滿。」	第一百零九條：「Ⅲ新式樣專利權期限自申請日起算十年屆滿；聯合新式樣專利權期限與原專利權期限同時屆滿。」

使用心得：

還記得介紹者上課說到「**Read patent, not just paper**」這句話很有意思，對於在做新的藥物合成者而言，在有新的想法以前就必須先查詢是否有人成功的做過，並早先一步申請了專利。可惜的是，還記得上課的時候使用的介面具有有多功能，不過回到一般學校的系統上來使用卻發現功能簡略了許多，上課的時候操作的介面系統能夠聰明的經過交集、聯集幫你找到最合是最準確的專利，而這次在操作的時候，覺得找到的東西似乎有點少。此外，這個系統對於醫藥相關的專利似乎有限，當我輸入幾個藥名幾乎都沒找到，只能輸入一些比較新科技的東西(EX: ipad、iphone)來檢索，我想這是美中不足之處吧！

最後，我覺得上課教導我們使用檢索系統非常實用，不然以前的我都不知道學校有這麼多資源提供給我們，這些資源也都是花錢買來的，不用多可惜。況且好好利用它可以學到好多東西，謝謝老師。