Curriculum vitae

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現任(Current position)

2019/02-presernt 國立嘉義大學 生命科學院 微生物免疫與生物藥學系 副教授

Associate Professor at Department of Microbiology, Immunology and Biopharmaceuticals, College of Life Science, National Chiayi University

2003/02-2019/01 國立嘉義大學 生命科學院 微生物免疫與生物藥學系 助理教授

Assistant Professor at Department of Microbiology, Immunology and Biopharmaceuticals, College of Life Science, National Chiayi University.

2013/08-present 國立嘉義大學 生命科學院 檢驗分析及技術推廣服務中心 微生物與分子檢驗組組長(102/08—

Manager of Laboratory Microbial and Molecular Diagnosis, Analytical and Technical Service Center, NCYU.

學歷(Education)

1998/04 日本 國立東京大學 農學生命科學研究所 博士

Ph.D. from Graduate School of Agricultural and Life Sciences, Faculty of Agriculture, The University of Tokyo, Japan.

1994/06 國立台灣大學農業化學所碩士

MS. from Department of Agricultural Chemistry, National Taiwan University, Taiwan, ROC.

1992/06 國立台灣大學 農業化學系 學士

BS. from Department of Agricultural Chemistry, National Taiwan University, Taiwan, ROC.

經歷(Vita)

2001/10-2003/01 生展生物科技股份有限公司 研究發展部 副理

Assistant Manager of Department of Research and Development, Syngen Biotech Co., Ltd, Taiwan, ROC.

2000/05-2001/09 台糖公司 產品開發處 工程師

Engineer, Department of Product Development, Taiwan Sugar Corporation, Taiwan, ROC.

1999/10-2000/04 台糖公司研究所 產程開發系 副研究員
Assistant Researcher, Department of Process Development, Taiwan Sugar Research Institute, Taiwan, ROC.

1998/08-1999/09 國家衛生研究院 癌症研究組 博士後研究
Postdoctor at The Division of Cancer Research, NHRI, Taiwan, ROC.

榮譽/獲獎(Honor/Award):

2018 榮獲 107 年度國科會補助大專校院獎勵特殊優秀人才
The Reward for Excellent Researcher in University from NSC of 108

2016 榮獲 105 年度國立嘉義大學教學肯定獎
The Lecture Recognition Award of 2016, National Chiayi University

2014 榮獲 103 年度國立嘉義大學產學合作績效獎金全校第 3 名
The 3th Place of Industry-University Cooperation Performance in NCYU

2014 榮獲 103 年度國立嘉義大學服務傑出獎
The Teacher Service Excellent Award of 2014, National Chiayi University

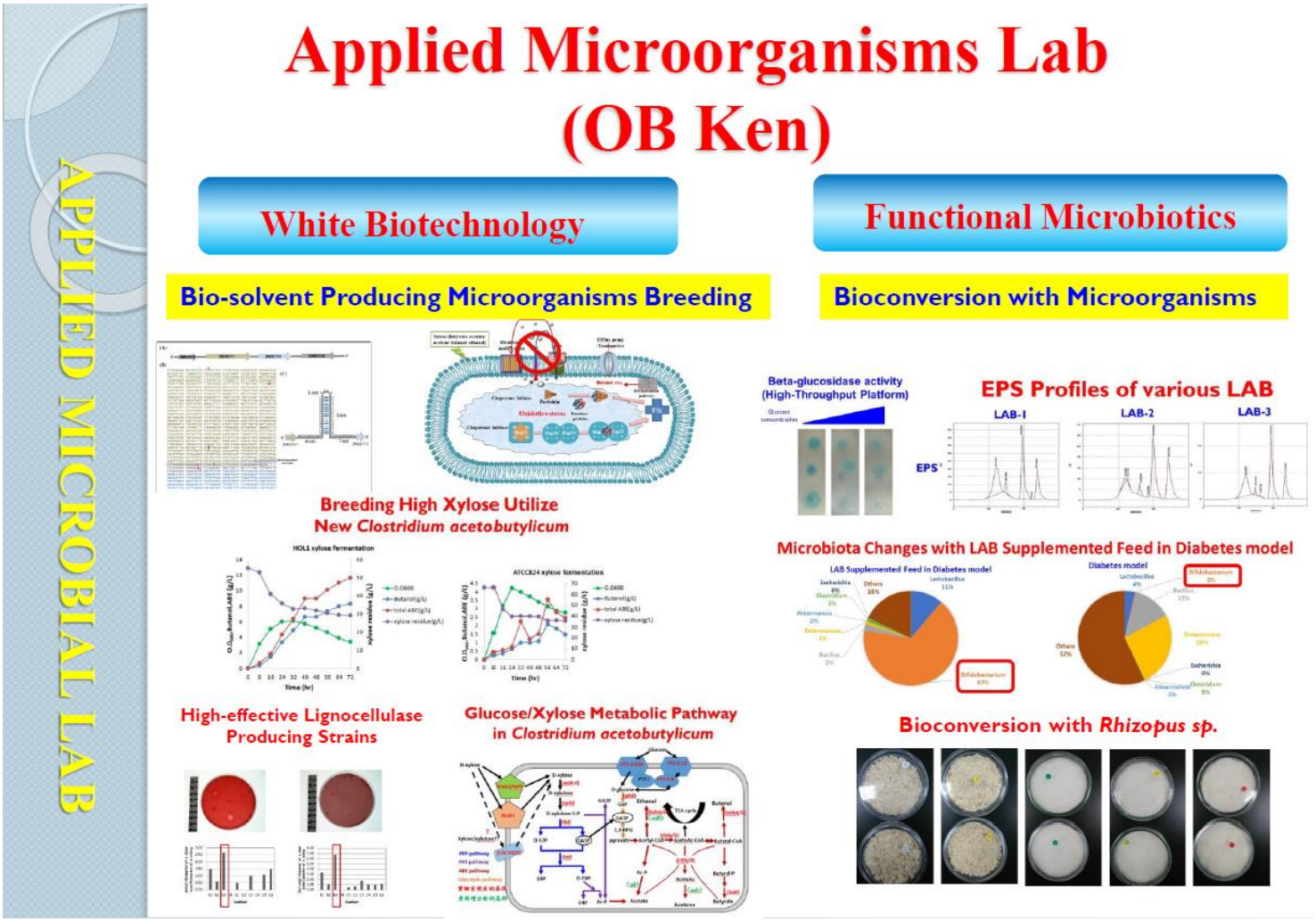
2010 榮獲 99 年度國科會補助大專校院獎勵特殊優秀人才
The Reward for Excellent Researcher in University from NSC of 100

2006 榮獲 95 學年度國立嘉義大學教學特優獎
The Lecture Excellent Award of 2006, National Chiayi University

研究專長(Research Area)

微生物學(Microbiology)、分子生物學(Molecular Biology)、蛋白質工程(Protein Engineering)、發酵學(Fermentation)

目前研究方向(Current Research Topics)



白色生物科技(White Biotechnology):

因氣候變遷以及日益嚴重的工業汙染，驅動尋找新的友善環境方式，取代現行的各種化學品。以生物科技方式，利用微生物與自然界物質進行轉換，生產對環境友善的綠色化學品，例如綠色化學生物農藥、纖維乙醇、纖維丁醇等為目前研究室嘗試的主要方向。

The worldwide awareness of sustainable environment, global climate change, urban air pollution, and security of future supply of energy carriers stimulates research for alternative fuels and related chemicals. Liquid (ethanol, biodiesel) or gaseous (methane or hydrogen) biofuels are derived from organic materials such as starch, oilseeds, or cellulose. Cellulose is the most abundant biopolymer in the world. Discarded cellulosic biomass derived from forestry and agriculture is potential feedstocks for the synthesis of biofuels.

1. 藥用微生物之菌種改良 (Improving pharmaceuticals or bio-pesticides producing bacteria)

放線菌因為其豐富且多樣性的二次代謝產物，已被廣泛的應用於人類用藥品開發、動物健康及植物保護等等用途。放線菌(Actinomycetes)中的鏈黴菌屬(Streptomyces)的代謝物生產分析的相關分析系統改進，在近年有相當快速的發展。我們實驗室以放線菌刺糖多孢菌 (Saccharopolyspora spinosa)為研究平台菌株。*S. spinosa* 生產之 spinosyn 的對環境高度友善、作用標的具高度選擇性，以及非標的生物低毒性，成為目前唯一能三度獲得 US-EPA Presidential Green Chemistry Challenge

Award 獎項的殺蟲藥劑。我們希望透過不同體學的資訊參數導入，可以更完善的預測出影響代謝的關鍵基因，對於工業用菌種改良，提供更完善的策。實驗室嘗試建立並加以驗證，希望可以可藉此強化放線菌株菌種優化之效果。此外，近年來也在代謝通量模擬系統的逐漸成形後，配合合成生物學的概念、對於基因剔除、基因放大、外源性基因導入等定向基因工程育種方式，提升至事先預測評估的模型建立。因此實驗室也嘗試將外源性基因導入、內源性基因放大以及基因剔除等，同步進行菌種改良、並透過建立的刺糖多孢菌代謝預測模式，進行驗證。

Actinomycetes produce a vast diversity of secondary metabolites of clinical and biotechnological importance, in particular antibiotics. Recent developments in metabolic engineering, sysnthetic and systems biology have opened new opportunities to exploit Actinomycetes secondary metabolism, but achieving industry-level production without time-consuming optimization has remained challenging. Genome-scale metabolic modelling has been shown to be a powerful tool to guide metabolic engineering strategies for accelerated strain optimization, and several generations of models of Actinomyces metabolism have been developed for this purpose. Spinosyns are novel macrolides, consist of a 21-carbon tetracyclic lactone containing forosamine and tri-O-methyl rhamnose, produced by the actinomycete Saccharopolyspora spinosa. Spinosyns are promising biopesticides worldwide and have been widely used in agriculture as potent insect control agents and animal health products because of theirs high efficiency against target insects and environment-friendly characteristics. We would like to apply an integrated system biology approach to characterize the metabolic landscape of *S. spinosa* and to identify a list of potential metabolic engineering targets of the overproduction of the secondary metabolites in this microorganism.

2. 新型纖維分解酵素生產菌種開發(Developing innovative cellulolytic enzymes producing bacteria)

纖維素有效的分解，為利用纖維素的第一個關鍵步驟。我們陸續自白蟻腸道、梅花鹿糞便、牛瘤胃等處，篩選各種對於纖維素分解具有競爭力細菌進行深入研究及應用。

As the primary and rate-limiting step involved in waste degradation, cellulose breakdown is an important step in the development of strategies to treat cellulosic biomass. We isolated various bacteria from termite guts, stool of Formosan sika deer, and cow rumen, and then investigated the various extracellular cellulo/xylano-lytic enzymes profiles and the regulation mechanisms.

3. 耐性纖維乙醇生產細菌改良(Improving stress-tolerant bio-ethanol producing bacteria)

運動發酵單胞菌(*Zymomonas mobilis*)轉換糖質生產酒精，由於具有較傳統酵母菌更好的醣類利用率及產率，近年來逐漸受到燃料用酒精工業生產的重視。我們建立新式的人工變異快速篩選平台，篩選具有特定耐性的 *Z. mobilis*。亦透過染色體序列分析，希望了解耐性的分子調控機轉，未來可應用於開發其他工業用微生物的耐性提升。

Zymomonas mobilis is the most efficient ethanol producer among the candidates with the production of 1.5-1.9 mol ethanol from each mol glucose, and the production rate is 3-5 folds higher than that of Saccharomyces cerevisiae. We developed a high-throughput screening platform could effectively selected targeted mutated bacteria. By NGS analysis, we also elucidated the molecular regulated mechanism of stress tolerant.

4. 耐性纖維丁醇生產細菌改良(Improving stress-tolerant bio-butanol producing bacteria)

利用 clostridia 進行Acetone-Butanol-Ethanol (ABE)的混合型溶劑生產是其中的一個選項。

我們實驗室以 *Clostridium acetobutylicum* 作為研究材料，除透過變異處理已選育出溶劑快速生產的菌株外，我們亦導入外源性修護性蛋白，可有效提升菌株對於溶劑的耐性，也探討該菌株對於不同碳源利用的分子機轉。希望了解耐性、糖質利用以及溶劑生產等分子調控機轉，可提供工業用菌的使用。

Clostridia naturally possess pathways that allow the conversion of sugar into solvents, known as acetone-butanol-ethanol (ABE) fermentation. Through artificial mutagenesis, we got a highly solvent-producing strain. We also introduced exogenous heat-shock proteins into the mutant to investigated the effects on enhancing solvent-tolerance. We are also interested in the mechanisms of regulating multiple-carbon utilization.

功能性微生物開發(Investigating Functional Microorganisms):

益生菌/食藥用真菌開發(Investigating Probiotcs and Food & Medical Fungi for bioconversion)

乳酸菌經常作為發酵蔬菜及乳製品的主要菌種。傳統釀造使用的 *Aspergillus oryza, Rhizopus oligospora, Monascus ruber* 以及藥用真菌 *Ganoderma tsugae, Cordyceps militaris* 等。由於這些微生物的生理代謝能力，可以將許多天然物中的多酚類及胺基酸類進行轉換，進而成為更具有生理活性的物質。本實驗室建立快速篩選平台，篩選具有高多醣生產能力、高 GABA 生產能力、新型胜肽生產能力的菌株，除探索生理分子機制的特異性之外，亦應用於新型食品的開發。

Lactic acid bacteria (LAB) are used as fermentation starters in vegetable and dairy products and influence the pH and flavors of foods. *Aspergillus oryza, Rhizopus oligospora, Monascus ruber* have been widely used in fermented food process, *on the other hand, Ganoderma tsugae, Cordyceps militaris* are also taken as medicines used in Orient countries. Existing functional substances have been assessed as fermentation substrates for better component bioavailability or other functions. Representative materials that were bio-converted using LAB and these food-medical fungi have been reported and include minor ginsenosides, γ-aminobutyric acid, equol, aglycones, bioactive isoflavones, genistein, and daidzein, among others. Fermentation mainly involves polyphenol and polysaccharide substrates and is conducted using bacterial strains. We have investigated various characteristics of LAB and fungi to convert polyphenols in oybean milk, okara to potential bioactive compounds.

研究計畫 (Research financial aid and proposed project)

A. 科技部研究計畫(Grants from Ministry of Science and Technology)：

I. 計畫主持人 (Project Investigator)

計畫名稱 (執行期間) Title (Year)	計畫編號 Code	經費 Budget	狀態 Status
以混成淋巴球反應及表現重組螢光蛋白 T 細胞株建立微生物生產新型免疫抑制藥物篩選系統(2003/10~2004/07)	92-2312-B-415-001	500,000	核准 Granted
提昇細菌生產生質酒精之效率：改善 *Zymomonas mobilis* 對醋酸壓力之應變系統（96/08-99/07-99/07/31）	96-2313-B-415-011-MY3	3,046,000	核准 Granted
高效率纖維素及半纖維素之分解酵素複合體相關研究(I)（2009/01/01 ~ 2009/12/31）	98-2623-E-415-001-ET	721,000	核准 Granted
高效率纖維素及半纖維素之分解酵素複合體相關研究(II)（2010/01/01 ~ 2010/12/31）	NSC 99-2623-E-415-001-ET	620,000	核准 Granted
研究利用抗氧化壓力之應變系統改善溶劑毒性對丙酮丁醇梭桿菌生產丁醇效率之影響(2010/08/01 ~ 2012/07/31)	NSC 99-2313-B-415-004-MY2	2,040,000	核准 Granted
探討以梭狀芽孢桿菌的丁醇耐受性機制，應用於生物反應器中生產高濃度丁醇之可行性(2014/08/01 ~2017/07/31)	103-2221-E-415-026-MY3	2,660,000	核准 Granted
探討具丁醇耐受性之梭狀芽孢桿菌利用多重碳源於纖維床生物反應器生產高濃度丁醇之製程模擬及開發(2017/08/01 ~2018/07/31)	106-2221-E-415-018-	880,000	核准 Granted
以整合性代謝工程技術評估提升刺糖多孢菌生產賜諾司類植物保護劑之機制及其應用性(2018/08/01 ~2019/07/31)	107-2313-B-415-005-	830,000	執行中 Current grant

II. 計畫共同主持人(Project Co-Investigator)

計畫名稱 (執行期間) Title (Year)	計畫編號 Code	經費 Budget	狀態 Status
植物化合物對內皮細胞保護作用的機轉(95/08-96/07）	95-2320-B-415-003	700,000	核准 Granted
萃取不同來源 β-glucan 降低雞蛋卵黃中膽固醇之影響（95/08-98/07）	95-2313-B-415-005-MY3	2,460,000	核准 Granted
花生白藜蘆醇及其衍生物預防老化相關疾病與延長壽命之探討－白藜蘆醇及其發酵衍生物對心血管疾病及神經退化性疾病之預防及保護作用探討(1/3) （95/08-96/07）	95-2321-B-415-002	1,235,000	核准 Granted
花生白藜蘆醇及其衍生物預防老化相關疾病與延長壽命之探討－白藜蘆醇及其發酵衍生物對心血管疾病及神經退化性疾病之預防及保護作用探討(2/3)（ 96/08-97/07）	96-2321-B-415-002	1,235,000	核准 Granted
花生白藜蘆醇及其衍生物預防老化相關疾病與延長壽命之探討－白藜蘆醇及其發酵衍生物對心血管疾病及神經退化性疾病之預防及保護作用探討(3/3)(97/08/01 ~99/02/28)	97-2321-B-415-002-	1,235,000	核准 Granted
輻射照射處理於農業之應用	108-NU-E-415-001-NU	1,380,000	執行中 Current grant
味噌品質提升與其菌相檢測受添加活性花生芽粉及發酵期間接種 Akkermancia muciniphila 影響之探討(1/2)	107-2320-B-415-003-	1,150,000	執行中 Current grant

III. 指導大專生專題研究計畫(Advisor of undergraduate research program)

計畫名稱 (執行期間)	計畫編號	經費	學生

Title (Year)	Code	Budget	Student
Bacillus subtilis var. natto HC- 3 血纖維蛋白溶解酵素之純化分析及活性提升之探討	NSC 94-2815-C-415 -011-B	47,000	蔡瑞蘭
藉由基因工程提升 *Zymomonas mobilis* 的酒精耐受性	105-2815-C-41 5-025-B	48,000	陳宜廷
探討過表現熱休克蛋白對 *Clostridium acetobutylicum* 蛋白表現的差異	105-2815-C-41 5-029-B	48,000	黃暘展
Evaluating the effect of chaperone for improving butanol productivity of Clostridium acetobutylicum	107-2813-C-41 5-079-B	48,000	胡景婇

B. 產學合作/農委會/校內計畫
(Industrial-University Cooperative / Council of Agriculture/In School Projects)

I. 計畫主持人 (Project Investigator)

計畫名稱 (執行期間) Title (Year)	計畫編號 Code	經費 Budget	狀態 Status
lovastatin 8'-(a-methylbutyryloxy)特異性酯解酵素之生產菌株篩選與其在藥物研發之應用	93 年度 國立嘉義大學	680,000	核准 Granted
微生物生物活性成分高效分離純化及活性檢測之技術平台之高效率活性多醣純化平台之建立(I)	93 年度 國立嘉義大學	40,000	核准 Granted
茯苓菌絲體功能性產品之開發-抗憂鬱(安神、助眠)、抗氧化(防老化)及抗發炎功能性篩選平台技術之開發 （2006/01-2006/12）	台糖公司研究所糖研-9503	750,000	核准 Granted
中草藥之抗氧化、抗老化生理活性測試 （2007/01-2007/12）	台糖公司研究所糖研-9603	630,000	核准 Granted
丁醇生產菌基因體研究分析(2009/06 ~ 2010/05)	中油公司 EEA9612001	850,000	核准 Granted
雜糧之醱酵機能性素材開發研究計畫(2009/05/ ~ 010/04)	農委會 98 研培-13.1-糧-01(c1)	603,000	核准 Granted
「丁醇生產菌菌種改良」委託研究(2010/08 ~ 2011/08)	中油公司 EEA0016002	880,000	核准 Granted
「功能性成分開發技術之建立」(2012/09~ 2013/08)	民間廠商	850,000	核准 Granted
建構具固碳能力之酪丁酸梭菌(2014/08~2015/12)	民間廠商	600,000	核准 Granted
功能性植物發酵飲品開發(2015/10-2016/07)	民間廠商	600,000	核准 Granted
新型發酵糖品開發(2017/04 -2018/08)	民間廠商	450,000	核准 Granted
微生物於植物性發酵食品之應用(2017/07/01-2018/10/31)	民間廠商	650,000	核准 Granted
微生物代謝物生產調節分子機制調控技術應用平台建立	民間廠商	1,680,000	執行中 Current grant

II. 計畫共同主持人 (Project Co-Investigator)

計畫名稱 (執行期間) Title (Year)	計畫編號 Code	經費 Budget	狀態 Status
利用混合型益生菌製造發酵完全飼料之技術開發 （95/01-95/12）	農委會 95AS-5.1.3-AD-U1	794,000	核准 Granted
利用混合型益生菌製造發酵完全飼料之技術開發 II-雞隻之應用(96/01-96/12）	農委會 96AS-2.1.3-AD-U1(11)	605,000	核准 Granted
開發富含伽瑪胺基丁酸(GABA)的雜糧類發酵機能性計畫(2011/01- 2011/12)	台灣區雜糧發展基金會 100-02-002	650,000	核准 Granted

應用富含伽瑪胺基丁酸(GABA)的乳酸菌發酵雜糧類機能性素材之產品開發技術評估(2012/01- 2012/12)	台灣區雜糧發展基金會	750,000	核准 Granted
經濟部在地型產業加值學界科專--高異黃酮非基改大豆之高加價值產品研發 3 年計畫	104-EC-17-A-18-S1-226	1400 萬	核准 Granted
農委會學界科專 --毛木耳全株分級利用之高加價值產品開發 3 年計畫	107/02-109/12	1470 萬	執行中 Current grant

學術著作(Academic Publication)

期刊論文(Referred articles)(first author, corresponding author*)

1. Wung BS, Hsu MC, Wu CC and **Hsieh CW.** Piceatannol upregulates endothelial heme oxygenase-1 expression via novel protein kinase C and tyrosine kinase pathways. Pharmacol. Res. 2006. 53(2):113-122. ***SCI***(2016 Impact factor: 4.48; Rank Factor: 31/257) (Cited by in Scopus: 49)
2. Wu CC, Hsu MC, **Hsieh CW**, Lin JB, Lai PH and Wung BS. Upregulation of heme oxygenase-1 by Epigallocatechin-3-gallate via the phosphatidylinositol 3-kinase/Akt and ERK pathways. Life Sci. 2006, May 15;78(25):2889-97. ***SCI*** (2016 Impact factor: 2.936; Rank Factor: 45/128) (Cited by in Scopus: 169)
3. Wung BS, Wu CC, Hsu MC, and **Hsieh CW .** 15-Deoxy- 12,14–prostaglandin J2 suppresses IL-6-induced STAT3 phosphorylation via electrophilic reactivity in endothelial cells. Life Sci. 2006, May 22;78(26): 3035-3042. ***SCI***. (2016 Impact factor: 2.936; Rank Factor: 45/128) (Cited by in Scopus: 16)
4. Wu CC, **Hsieh CW**, Lai PH, Lin JB, Liu YC and Wung BS. Upregulation of endothelial heme-oxygenase-1 expression through the activation of the JNK pathway by sublethal concentrations of acrolein. Toxicol. Appl. Pharmacol. 2006 Aug 1;214(3):244-52. ***SCI*** (2016 Impact factor: 3.791; Rank Factor: 15/92) (Cited by in Scopus: 72)
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33.

技術轉移(Technique transfer)

項次	成果名稱	移轉對象(名稱)	簽約日期
1	一種可生產功能性成分的微生物培養技術	OO 國際股份有限公司	102/ 12/25
2	一種可生產功能性成分的微生物培養技術	OO 食品有限公司	103/1/16
3	一種可生產功能性成分的微生物培養技術	OO 科技有限公司	108/04

專利(Patent)

1. 松杉灵芝活性物质、其制备法及其组合物
公開號　CN101904875 B　出版類型 授權
申請書編號　CN 200910203171　發佈日期　2012 年 10 月 24 日
申請日期　2009 年 6 月 3 日　優先權日期 2009 年 6 月 3 日
其他公開專利號　CN101904875A
發明人　翁炳孙, 谢佳雯, 魏钰珊　申請者　生展生物科技股份有限公司

2. 内皮細胞保護・閉鎖性動脈硬化予防効果を有するガノデルマ・ツガエの活性物質及びその組成物
この技術が特許化される前の公開公報はこちら
特許権者　生展生物科技股▲分▼有限公司発明者　魏▲ギョク▼珊 、謝佳▲ブン▼ 、翁炳孫
出願日　2009 年 6 月 10 日 （5 年 7 ヶ月経過）　出願番号　2009-139186
公開日　2010 年 12 月 24 日 （4 年 1 ヶ月経過）　公開番号　2010-285366
登録日　2012 年 7 月 20 日 （2 年 6 ヶ月経過）　登録番号　5044612

期刊審查(Journal Reviewer):

- Reviewer for Journal of Agricultural Science and Technology (2009/5)
- Reviewer for Journal of Agricultural and Food Chemistry (2010/2)
- Reviewer for Journal of Agricultural Science and Technology (2010/5)
- Reviewer for Poultry Science (2010/5)
- Reviewer for Bioorganic & Medicinal Chemistry. (2010/11)
- Reviewer for Journal of Zhejiang University-SCIENCE B. (2011/06)
- Reviewer for 花蓮農改場研究彙報 (2011/11)
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- Reviewer for Iranian Journal of Applied Animal Science (2012/11) IJAS-12-186
- Reviewer for Iranian Journal of Applied Animal Science (2012/11) IJAS-12-201
- Reviewer for Iranian Journal of Applied Animal Science (2013/02) IJAS-13-23
- Reviewer for Iranian Journal of Applied Animal Science (2013/03) IJAS-13-38
- Reviewer for Journal of Zhejiang University-SCIENCE B(2013/03) ZUSB-D-14-00092
- Reviewer for Livestock Science.(2013/04)
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- Reviewer for 南台學報(2019/03) A0402
- Reviewer for Biotechnology Journal International (2019/01) Ms_BJI_46808
- Reviewer for 屏東科技大學教師升等 (2019/04)
- Reviewer for Natural Product Journal (2019/03) BMS-NPJ-2019-27.

人才培育、研究團隊建立及服務方面的重要貢獻及成就

✧ 配合行政院勞工委員會職業訓練局九十二學年度辦理「大學及技專校院辦理就業學(課)程」，協助本校爭取設立『醫學生物技術就業模組課程』: 開設「生物醫藥產業趨勢」、「生物技術核心實驗」及「分子檢驗技術」。計獲補助 415,500 元/共同主持人。

✧ 配合行政院勞工委員會職業訓練局九十三學年度辦理「大學及技專校院辦理就業學(課)程」，協助本校爭取開設『醫學生物技術就業模組課程』:計 92 年度繼續開設「生物醫藥產業趨勢」、「生物技術核心實驗」及「分子檢驗技術」等課程，並新增「生物技術核心實驗」及「藥物合成與活性分析」課程。計獲補助 572,000 元/共同主持人。

✧ 獲 94 年度教育部顧問室「基礎科學前瞻性人才培育計畫」補助，協助辦理本校舉辦『高中職教師生命科學(微生物資源發展)研習會』/聯絡人獲 95 年度教育部顧問室「基礎科學前瞻性人才培育計畫」補助，協助辦理高中職教師生命科學(微生物資源發展)研習會/聯絡人。

✧ 指導學生獲得中國畜牧學會 94 年新人獎: Lin, X. L., Kho W. L., Hsieh C. W. andChen K. L. (2005) Poly- -glutamate-copper complex produced by Cu2+ and Bacillus natto secreted g-PGA. J. Chinese Soc. Ani. Sci. 34:117.

✧ 協助國立嘉義大學於 96 年 12 月取得「日本納豆激酶協會」頒發給台灣第一張「納豆激酶活性檢測認證實驗核可實驗室」證書。

✧ 協助執行 102-103 學年度教學卓越計畫-- F 主軸計畫之院特色人才培育計畫，開設 5 課程，包括: 「生技發展與產業應用講座」、「生技素材功能評估技術」、「生質量產單元操作」、「生技產品製程開發專題實作」及「生技專利法規與行銷管理講座」等。

✧ 勞動部勞動力發展署補助國立嘉義大學，105 年度生技產業人才培訓就業學程，擔任計畫主持人。

✧ 勞動部勞動力發展署補助國立嘉義大學，107 年度生技產業人才培訓就業學程，擔任一門課程主授老師。

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