AIChE 2002
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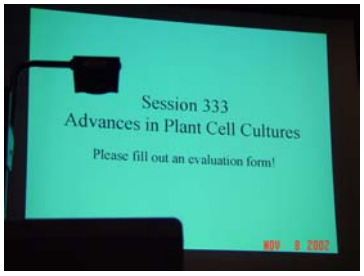
11•3 — 11•8
Indianapolis, IN

Nov 08, 2002

드디어 학회마지막 날이 되었습니다. 지난 일주일여동안 정신없이 달려와서인지 마지막날이라는 게 은근히 섭섭하고 아쉽기까지 합니다. 어제도 말씀드린 바와 같이 학회가 막바지를 향해 가서인지 학회에 참석하는 화공인의 숫자는 확실히 줄었습니다. 자신이 관심있는 session 이 남아있는 일부를 제외하고는 이미 인디아나폴리스를 다들 떠났습니다. 학생들 발표가 가장 나중에 배치되어 있어서 특강이나 대가들의 강연을 들으려던 사람들도 이미 자신들의 직장으로 돌아간 것같습니다.



오늘 필자가 참석한 session 은 Advances in Metabolic Engineering 과 Advances in Plant Cell Culture 이었습니다. 올해 미국화공학회에서 두드러지는 특징은 metabolic engineering 와 proteomics 의 강세였습니다. 기술이 진보된 만큼 결과도 그 어느 때보다 풍성했었습니다. 특히, NSF 의 biofund 책임자인 박사는 각 session 을 돌아다니며 각 분야의 발표수준, 참여수준 등을 점검하느라 노구에도 불구하고 가장 바빠보였습니다.

먼저 Advances in Plant Cell Culture 의 동향에 대해 이야기를 해보죠. 모두 7 개의 발표가 준비되어 있었습니다. audience 중에는 미국 식물세포배양의 최고 권위자인 Cornell 의 Michael L. Shuler 교수는 참석하셨으나, 만날 수 있을 것으로 기대를 가졌던 Penn State 의 Wayne Curtis 교수는

참석하지 않았습니다. 발표를 한 학생들이 속한 group 을 보면 앞서 언급한 Michael L. Shuler 교수그룹, Penn State 의 Wayne Curtis 교수그룹, Rice 대학의 San Kai-Yu 박사그룹, Iowa State 의 Jacqueline Shanks 교수그룹, Shuler 교수의 제자인 North Eastern 대학의 Carolyn Lee-Parson 교수그룹이었습니다. Lee 교수와 UMass 의 Susan Roberts 교수는 Shuler 교수의 제자이므로 한데 묶어보면 크게 4 개 그룹에 Rutgers 의 Henrik Pedersen 교수를 더하여 5 개 그룹이 미국의 plant cell culture 연구를 가장 활발히 하고있고, 이끌고 있다고 보시면 무리가 없을 것같습니다. 사실 다른 연구 session 에 비하면 상당히 연구자수가 적고 세인들의 관심을 받지 못하고 있는 것 또한 사실입니다. 하지만, plant cell culture 는 향후 산업화에 있어서 타 분야가 도출할 수 없는 potential 과 흥미로운 연구영역이 많이 있으며 현재의 bottleneck 만 해결한다면 새로운 전기를 마련할 수 있을 것이라고 필자는 믿고 있습니다. 전날 poster 장에서 만나 이야기를 나누었던 Carolyn Lee 박사도 이에 전적으로 동의하였습니다만 넘어야 할 산은 아직 크고 거칩니다. 그 bottleneck 을 넘게하는 방법은 아마도 metabolic engineering 과 'omics'일 것이라는 것이 연구자들의 지배적인 의견입니다. Metabolic engineering 쪽으로 가장 활발하게 움직이려고 하는 그룹은 Iowa State 의 Shanks 교수그룹입니다. 故 Bailey 교수의 제자답게 metabolic flux analysis 에서 가장 선두그룹을 형성하고 있습니다. 아직 *E.coli* 나 *Saccharomyces* 에 비하면 초보적인 단계이고 연구성과도 이에 비하면 미미하지만 나름대로의 영역구축은 이미 마친 것으로 파악됩니다. session 에서 발표된 내용은 아래와 같습니다.

Session Schedule

2:00 PM	Introduction
2:05 PM	Metabolic Engineering of the Indole Pathway in Catharanthus roseus Hairy Roots **Abstract**: *Catharanthus roseus* produces a wide variety of indole alkaloids including the anti-cancer drugs vincristine and vinblastine. Due to the commercial value of these compounds, several studies have focused on the characterization of enzymes and cloning of genes necessary for the production of indole alkaloids. The current literature indicates a complicated network involving numerous cellular compartments, several differentiated cell types, and developmentally controlled expression levels. In our laboratories, we are interested in the metabolic engineering of the indole pathway and its subsequent effect on indole alkaloid biosynthesis in *C. roseus* hairy roots. Hairy roots have a number of advantages over cell cultures including increased genetic stability and substantially higher alkaloid content. Previous feeding studies in our laboratories have suggested that the indole pathway is limiting for alkaloid production during late exponential growth of hairy roots. Based on these observations, our current metabolic engineering efforts focus on two vital genes within this pathway: an *Arabidopsis* feedback resistant anthranilate synthase alpha subunit (ASa) and *C. roseus*

	tryptophan decarboxylase (TDC). It is believed that, by controlling the level and timing of the expression of these genes, alkaloid flux can be increased without the observed negative growth effects when tryptophan pools are depleted or the early growth defects in the presence of elevated tryptophan levels. In our laboratory, we have shown that we can generate transgenic hairy roots expressing GFP driven by a glucocorticoid inducible promoter. Furthermore, the promoter exhibits the desirable characteristics of low basal expression, high inducibility, and a dosage dependent expression. It also should provide an improved negative control for data analysis by eliminating the problem of clonal variation. This inducible promoter, which allows controlled overexpression of ASa and TDC, will enable the study of metabolic effects specific to developmental stage. The current study focuses on metabolic engineering of the indole pathway in *C. roseus* hairy roots. In addition to a negative control line, lines with inducible expression of ASa, TDC, and ASa+TDC have been generated, adapted to liquid, and confirmed by Northern blot. The metabolic characterization of the various lines and the effects of induction on secondary metabolism will be discussed.
2:25 PM	Development of a Stoichiometric Model for Metabolic Flux Analysis of Catharanthus Roseus Hairy Roots **Abstract:** Metabolic flux analysis (MFA), or the quantification of all steady state intracellular metabolic fluxes in a biochemical reaction network, is a valuable tool in metabolic engineering. A relatively low-cost technique of implementing MFA is by using a stoichiometric model coupled with extracellular metabolite measurements. In this work, we report the development and application of a such a model for *Catharanthus roseus* hairy roots, as well as experimental work toward obtaining the biomass composition of the hairy roots, which is a vital component of the model. Such a comprehensive mathematical treatment of cellular metabolism for plant cell culture is rarely reported in the literature. The model developed includes all key biochemical reactions in primary and intermediate metabolism - glycolysis, pentose phosphate pathway, tricarboxylic acid cycle, anaplerotic pathways and the shikimate pathway. In metabolic flux analysis, underdetermined systems (such as the one under consideration) that have lesser available measurements than the number of fluxes to be determined also require an objective function, which needs to be maximized to obtain the flux distribution. In this work, we used maximization of plant biomass as the objective function, for 21-day old *C. roseus* hairy roots undergoing balanced growth. We also report experimental work on obtaining the biomass composition of *C. roseus* hairy roots, which is crucial to the model because of the above objective function. Preliminary results indicate that the protein, lipid and starch percentages are 3.9%, 2.6% and 3.1% of the dry weight respectively. In addition, the individual composition of the proteinogenic amino acids as well as of indole alkaloids, glucose polymers, nucleotides, and other biomass components such as lignins, suberins, etc. will be reported. We will also report a metabolic flux map for central carbon metabolism in *C. roseus* hairy roots, based on the stoichiometric model developed, extracellular metabolite measurements, and the biomass composition obtained.
2:45 PM	Factors Affecting the Stability of *Taxus* Suspension Culture for Production of Secondary Metabolites **Abstract:** Methyl jasmonate is known to be a potent elicitor of Taxol production in *Taxus* cultures. In this study, 5 different *Taxus* cell lines were treated with methyl jasmonate on day 7, and their growth and productivity of Taxol were compared with non-elicited cultures. Derivative subcultures from these treatments, transferred from 14-day old cultures, were also evaluated for growth and Taxol production. Fresh cell density of non-elicited culture was typically 2 times higher

	than that of elicited culture, while Taxol productivity was usually enhanced by 3 fold when *Taxus* cell lines were elicited. Subcultures derived from elicited cultures were less viable, but there was no enhancement of production of Taxol. High-producing cultures grew slower and died faster than low-producing counterparts. The elicited mother culture retained production of high amounts of Taxol, while the elicited daughter culture lost that ability upon subculture. We tested whether signal materials, which might be generated during culture, could be involved in the production of Taxol, and be diluted upon subculture by preparing 8 replicate flasks by mixing all inoculum prior to every subculture, and another 8 replicate flasks were obtained by single lineage subculture. The average cell densities and the variations from both replicate sets of flasks were statistically identical. The average Taxol production from the replicate flasks with mixing was 2 times higher than that from the replicate flasks without mixing, but the variations were statistically identical. Although mixing enhanced the production of Taxol, it did not reduce the variation among replicate flasks. After one additional single lineage subculture, the average Taxol production from the single lineage ones was a little bit higher. In conclusion, there appears to be inherent variability within the cell populations that is the major contributor to variation in secondary metabolite production.
3:05 PM	A Plant Tissue Culture Based System for High Level Transient Expression of Heterologous Proteins **Abstract:** Production of heterologous proteins in plants is an inexpensive alternative to transgenic animals and bacterial culture. However, the time involved in generating transgenic plants to produce material for testing and characterization can be significant. We are developing a transient gene expression system in plant tissue culture to decrease the time required for this process. An intron-containing GUS reporter gene is being used to optimize gene expression. The reporter is transferred to the plant tissue during co-culture with Agrobacterium tumefaciens. The gene of interest is transcribed transiently in the nucleus prior to integration in the chromosome. Large variation in protein expression has been observed between cell and root culture, which is also species and clone dependent. To increase protein expression, transgenic plant tissue has been developed containing an inducible viral replicase. The reporter gene has been modified to be amplified by this viral replicase. It is anticipated that the replicase function will augment the number of gene copies available to the cell, resulting in increased production from the transgene. Ongoing work involves determining if additional viral functions can increase expression. The potential for implementing this approach in bioreactors to rapidly produce protein will be presented.
3:25 PM	Break
3:35 PM	Resin Addition Strategies for Enhancing the Production and Recovery of Alkaloids from Catharanthus Roseus Cultures **Abstract:** Low volumetric productivity is a major factor impeding the commercialization of plant cell cultures for the production of secondary metabolites. In this paper, our goal was to manipulate *in situ* product adsorption using Amberlite XAD-7 and other resins to maximize alkaloid formation and recovery while minimizing the adsorption of nutrients and alkaloid precursors from *Catharanthus roseus* suspensions. The effect of a temporary resin incubation period, the duration of resin addition, and the resin type on the production and recovery of ajmalicine and serpentine were investigated. The production of ajmalicine and serpentine from *C. roseus* cultures using XAD-7 was successfully enhanced by 50-300% with the resin addition treatments compared to the controls. While production was enhanced over the controls, the overall combined production of ajmalicine and serpentine was not significantly different **between**

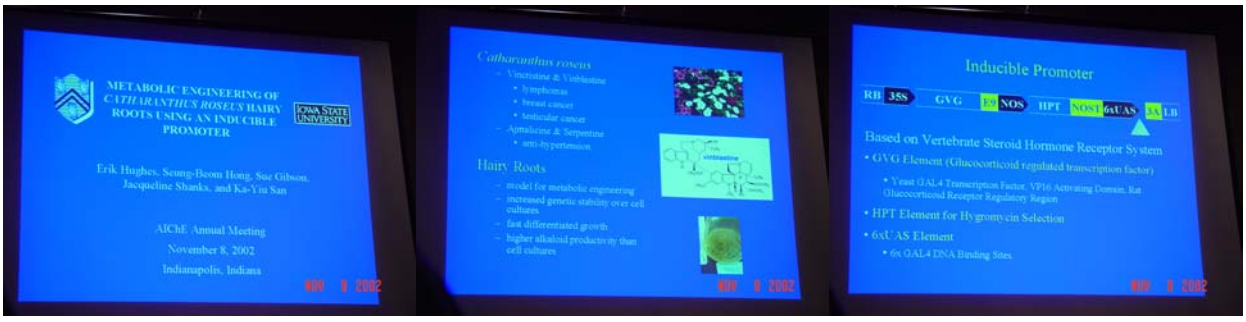
	the resin addition treatments. The effect of a temporary incubation period was investigated by adding XAD-7 resin to suspensions for seven days, starting on either day 0 or day 7. After a 14-day culture period, the addition of XAD-7 to cultures on day 0 yielded similar concentrations of ajmalicine and serpentine compared to cultures with XAD-7 addition on day 7. However, the later addition of XAD-7 favored a higher ajmalicine to serpentine ratio compared with the earlier addition of XAD-7. The earlier addition of resin resulted in higher extracellular recoveries for both ajmalicine and serpentine than with the later addition of XAD-7. The duration of XAD-7 addition (continuous incubation for 8 days versus two separate 24-hour incubation periods) resulted in comparable concentrations of ajmalicine and serpentine. However, the continuous presence of XAD-7 resulted in higher ajmalicine to serpentine ratios and higher total recoveries of ajmalicine and serpentine compared to the 24-hour incubations with XAD-7. The effect of resin type on alkaloid production and recovery was investigated using Amberlite XAD-7, C_2, C_4, C_8, SI-1, and SCX resins. The highest ajmalicine accumulation was achieved in suspensions with XAD-7, C_2, and C_4 addition, with a two-fold increase over that of the controls. The highest serpentine level was achieved in the suspensions with C_2 and C_8 addition, with a 54% increase over the control cultures. The highest percent recovery of ajmalicine and serpentine was obtained with C_4 and XAD-7 resin.
3:55 PM	Recovering a Histidine-Tagged Protein from Tobacco Extract (Absent)
4:15 PM	Purification of Ricin B From Hairy Root Culture Medium by Aqueous Two-phase Extraction **Abstract:** Ricin B is the non-toxic galactose-binding subunit of ricin, which is one of the most potent plant-derived cytotoxic proteins known to exist. Ricin B has been tested for utility in mucosal vaccine delivery and adjuvancy. It is expressed in tobacco hairy root culture and secreted into the culture medium. However, the secreted ricin B product is degraded by secreted proteases in a certain period of time. How to effectively recover the protein product in a timely fashion is thus extremely important. Aqueous two-phase extraction (ATPE) was chosen as the method of study because the culture medium does not need to be processed before protein separation and the protein partition equilibrium is reached rapidly. Two different PEG/salt/water systems, PEG/potassium phosphate and PEG/sodium sulphate, were first studied for favorable ricin B (in water) partitioning into the top phase. The results showed that the partition coefficients of Ricin B were much greater in PEG/sodium sulphate systems. On the other hand, studies on secreted native proteins (from non-transgenic hairy root culture medium) showed that the overall partition coefficients were greater than one but much smaller than those of ricin B under the same system conditions (PEG/sodium sulphate systems). Statistical analysis indicated that different factors (PEG molecular weight, concentration, sodium sulphate concentration, and NaCl concentration) have different impact on the partitioning of ricin B and native proteins. This provided opportunities for system optimization for the best separation between ricin B and secreted native proteins. ATPE was shown to hold promising future in initial recovery/purification and stabilization of ricin B from hairy root culture.
4:35 PM	Close

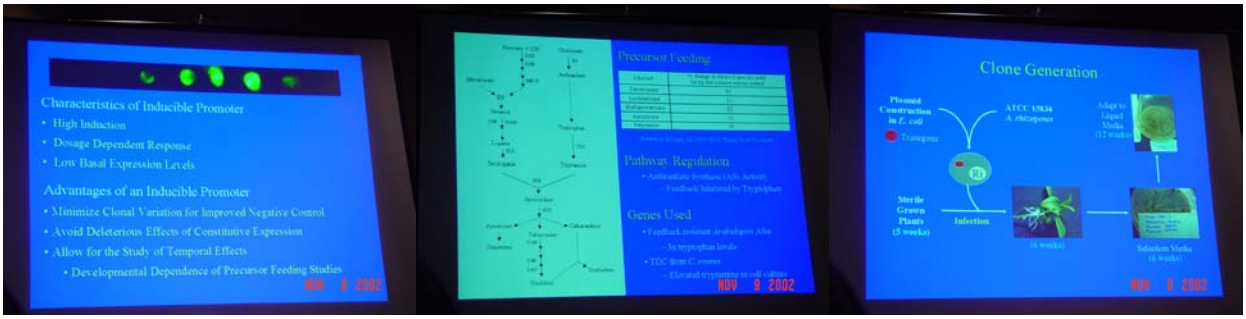
미국 내 plant cell culture group 의 두드러진 특징은 대부분 *Cathranthus roseus* 의 연구를 하고 있다는 사실입니다(talk: 3 편, poster: 3 편) . 식물 추출물 중 가장 비싼 가격을 보이는 vincristine 과 vinblastine 때문임은 쉽게 짐작이 갑니다. 이들 compound 의 생산이 미치는 impact 는 비단 plant cell culture 부분에만 그치는 것은 결코 아닐 것입니다. 따라서, 목표를 가장 까다로운 것에 둠으로써

연구개발의 성공시 얻을 수 있는 성과를 극대화하겠다는 전략으로 보입니다. 아시다시피 이들 compound 는 식물세포배양에서뿐만 아니라 식물체 자체에서도 생산량이 매우 소량인 것으로 알려져 있습니다. 따라서, 이들에 대한 metabolic flux 를 열러줄 수 있는 방법의 개발은 매우 중요한 의미를 지니고 있다고 볼 수 있죠.

첫 발표는 Rice 대학의 San Kai-Yu 그룹에서 하였습니다. 아주 童顔으로 이쁘게 생긴 모범생같은 미국학생이 발표를 하더군요.(필자주. 남자였습니다. 男!子!) Rice 대학의 생화학과, 그리고 Iowa State 대학의 Shanks 교수와의 공동연구였습니다. 반갑게도 Rice 대학의 생화학과에는 한국인 post-doc 의 성함(홍승범 박사)이 보이더군요. 전체적인 collaboration 의 구도는 rice 대학 생화학과에서 gene 의 cassette 이나 기타 molecular work 을 하고 화공과에서 이들을 가지고 식물체에 gene 을 삽입하여 culture 를 하며 data 를 도출하는 일을 하며 Shanks group 이 이들 실제 data 를 가지고 metabolic flux analysis 를 하면서 다음 작업에 대한 guideline 을 제시해 주는 것으로 나타났습니다.

첫 발표의 내용은 다음과 같습니다. Target compound 의 양이 워낙 작으므로 이들 생산에 관계되는 pathway 중 upregulation 하는 enzyme 의 생산을 자극함으로서 final compound 의 생산량을 증가시켜 보자는 것입니다. 구체적으로 언급하면 chorismate 에서 anthranilate 로의 step 에 관여하는 anthranilate synthase(AS)와 tryptophan 에서 trytamine 으로의 step 에 관여하는 TDC 의 생산을 증가시켜 이 부분이 traffic 을 증가시켜보고자 inducible gene cassette 을 만들어 식물체 삽입한 후 hairy root 를 만들었고 이들에서의 target compound 의 생산량을 check-up 하여 metabolic concentration 의 변화를 관찰하였습니다. 이미 이런 시도는 여러 연구그룹에서(화공파트가 아니라도) 시도된 바 있어서 연구의 참신성은 다소 떨어졌습니다만 전체적인 연구의 진행도나 logic 은 박사과정학생수준으로 볼 때 우수하였다고 평가할 수 있었습니다. 아마 collaboration 을 하기때문에 다소 수준이 향상되었다고 그 이유를 가늠할 수 있을 것같습니다. 내용은 다음 slide 에서 참고하시죠.




Characteristics of Inducible Promoter
• High Induction
• Dosage Dependent Response
• Low Basal Expression Levels
Advantages of an Inducible Promoter
• Minimize Clonal Variation for Improved Negative Control
• Avoid Deleterious Effects of Constitutive Expression
• Allow for the Study of Temporal Effects
• Developmental Dependence of Precursor Feeding Studies
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Precursor Feeding
Pathway Regulation
Genes Used
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Clone Generation
Plasmid Construction in E. coli
Transgene
ATCC 15834
A. rhizogenes
Sterile Grown Plants (5 weeks)
Infection
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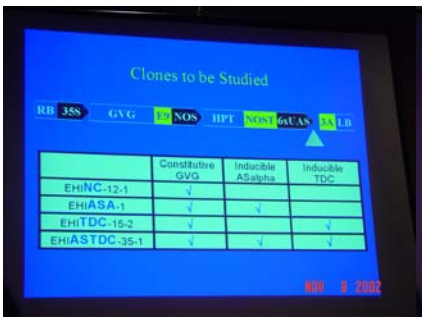
Clones to be Studied
RB 35S GVG F9 NOS HPT NOST 6xUAS 3A LB
Constitutive GVG
Inducible AS alpha
Inducible TDC
EHiNC-12-1
EHiASA-1
EHiTDC-15-2
EHiASTDC-35-1
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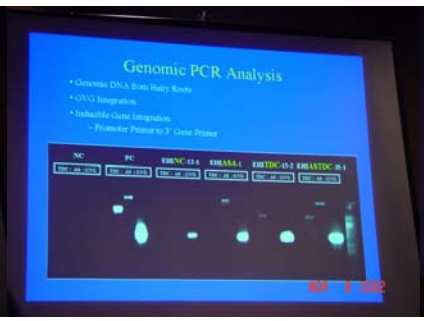
Genomic PCR Analysis
Genomic DNA from Hairy Roots
GVG Integration
Inducible Gene Integration
Promoter Primer to 3' Gene Primer
NC
PC
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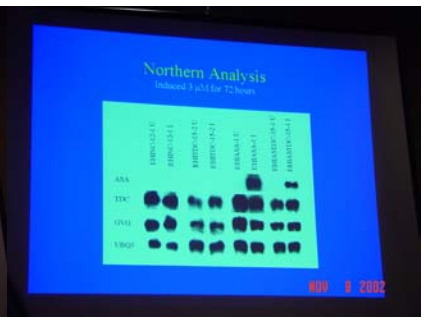
Northern Analysis
Induced 3 µM for 72 hours
ASA
TDC
GVG
UBQ9
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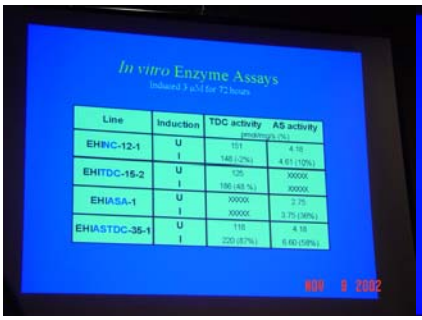
In vitro Enzyme Assays
Induced 3 µM for 72 hours
Line
Induction
TDC activity
AS activity
EHiNC-12-1
EHiTDC-15-2
EHiASA-1
EHiASTDC-35-1
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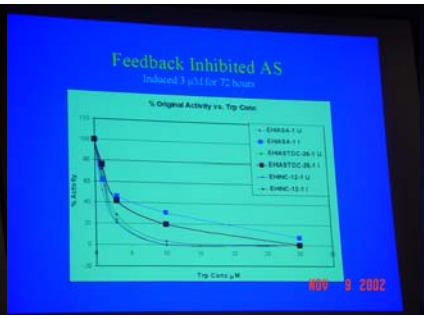
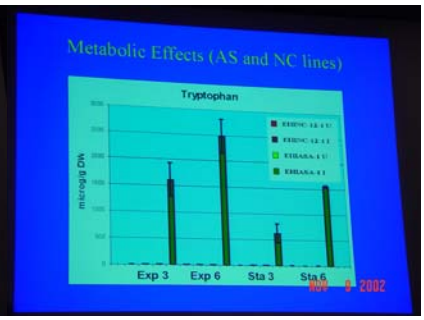
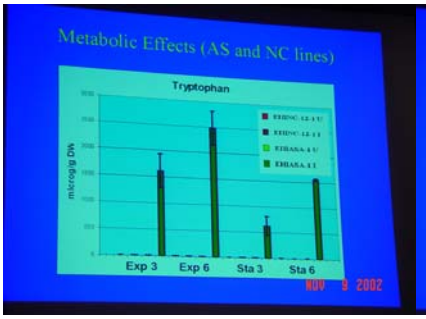
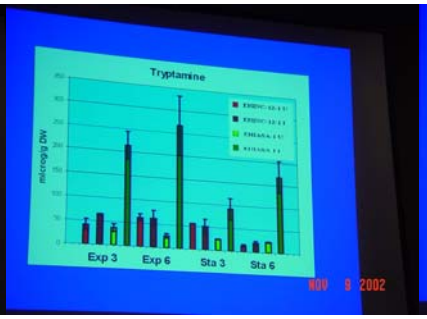
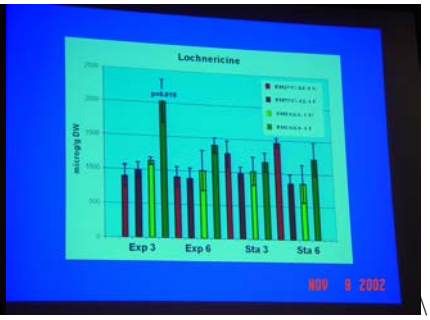

Feedback Inhibited AS
Induced 3 µM for 72 hours
% Original Activity vs. Trp Conc
% Activity
Trp Conc µM
NOV 9 2002


Metabolic Effects (AS and NC lines)
Tryptophan
microg/g DW
Exp 3
Exp 6
Sta 3
Sta 6
NOV 9 2002


Metabolic Effects (AS and NC lines)
Tryptophan
microg/g DW
Exp 3
Exp 6
Sta 3
Sta 6
NOV 9 2002


Tryptamine
microg/g DW
Exp 3
Exp 6
Sta 3
Sta 6
NOV 9 2002


Lochnericine
microg/g DW
Exp 3
Exp 6
Sta 3
Sta 6
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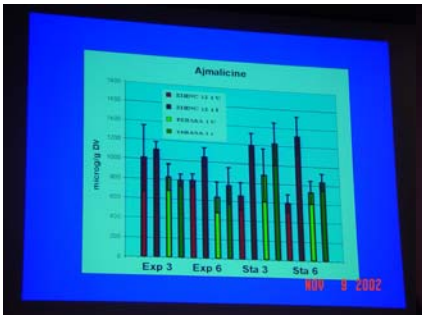
Ajmalicine
microg/g DW
Exp 3
Exp 6
Sta 3
Sta 6
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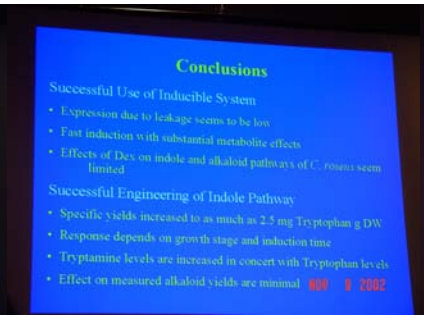
Conclusions
Successful Use of Inducible System
• Expression due to leakage seems to be low
• Fast induction with substantial metabolite effects
• Effects of Dex on indole and alkaloid pathways of C. roseus seem limited
Successful Engineering of Indole Pathway
• Specific yields increased to as much as 2.5 mg Tryptophan g DW
• Response depends on growth stage and induction time
• Tryptamine levels are increased in concert with Tryptophan levels
• Effect on measured alkaloid yields are minimal
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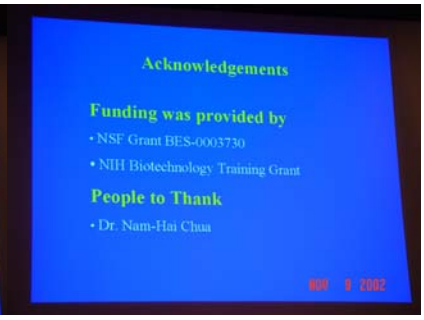
Acknowledgements
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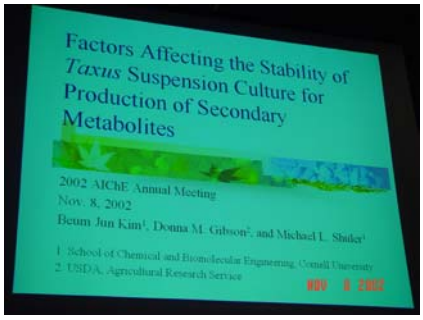
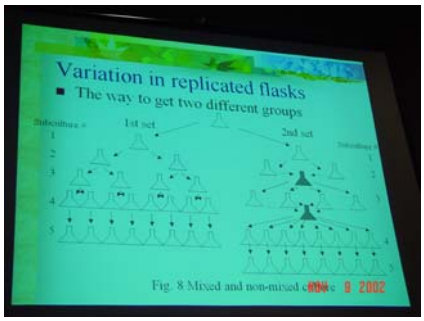
• NSF Grant BES-0003730
• NIH Biotechnology Training Grant
People to Thank
• Dr. Nam-Hai Chua
NOV 9 2002

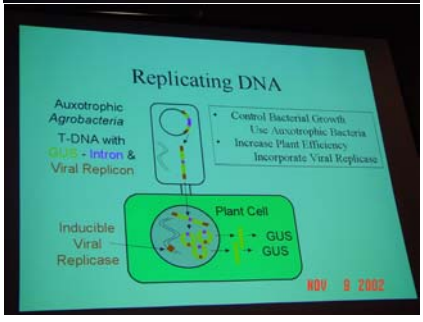
두번째 발표는 앞서 언급한 Iowa State 의 Shanks group 에서 MFA 에 대해 발표한 것이었습니다. 일부 pathway 에 대한 mapping 을 하였는데 slide 수가 너무 많이 이 지면에 모두 올리지 못함을 유감으로 생각합니다. 이 slide 뿐만 아니라 다른 발표자의 slide 자료가 필요하신 분은 개인적으로 필자에게 contact 해주시기 바랍니다.(shy4@postech.ac.kr)

세번째 발표는 Cornell 대학의 Shuler group 에서 발표하였습니다. 한국인 박사과정인 김범준씨가



발표를 하여 필자는 관심이 아주 많았습니다. 개인적인 친분이 이분과 있을 뿐만 아니라 taxol 에 대한 연구결과에서 더욱 그러하였습니다. 내용은 plant cell culture 를 하는 연구자에게는 공통적인 고민거리인 stability 문제를 다루고 있었습니다. 근본적인 원인이나 solution 을 제시한 것은 아니었으나 system 내의 signal compound 들과 high-producing cell line 의 subpopulation 이 주요 원인일 수 있다는 가설을 잘 증명하고 있었으며 아울러 epigenetic stability 와 apoptosis 가 원인일 수 있음을 설명하였습니다. 필자는 여전히 production stability 는 이 분야에서 화두가 될 수 밖에 없음이 안타까왔습니다. 이 문제때문에 80 년대 각광을 받을 수 있었던 plant cell culture 가 대규모 산업화로 연결되지 못하고 사양의 길을 걸었음을 돌이켜볼때 더욱 그러하였습니다. 김범준씨는 새로운 실험 idea 로 흥미로운 실험을 하여 좋은 결과를 도출하여서 더욱 눈길을 끌었습니다.

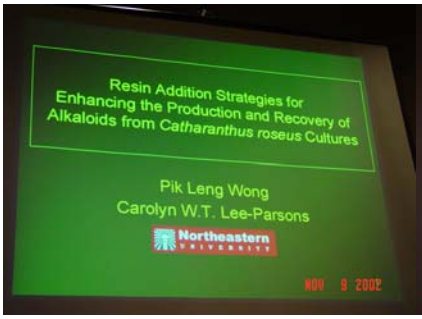


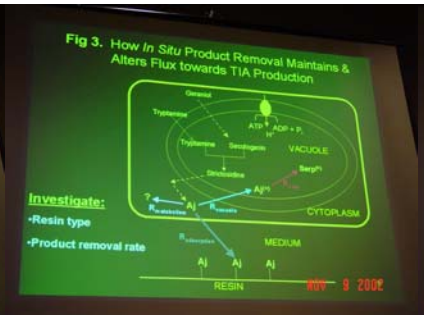


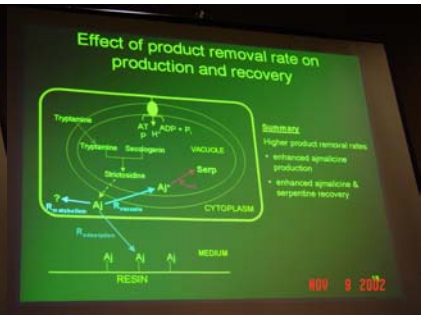
네번째는 필자가 관심을 가졌던 Penn State 의 Wayne Curtis 교수그룹에서 발표를 하였습니다. 아주 detail 하게 실험을 하여 결과를 보고한 것이 아니라 idea 와 방법을 제시했다는 차원으로 이해하는 것이 더욱 어울릴 듯 합니다. 다음 연구결과보고가 기대가 된다고나 할까요? 아니면 솔직하게 이번 발표는 그냥 그랬었다고 이야기를 해야할까요? (정치적으로 잘 처신해야 오래오래 몸보존하며 잘 산다고들 하던데…. 체질적으로 영….) 기대에는 미치지 못한 연구결과였습니다. 요지는 이렇습니다. Reactor 에 무지하게 잘 자라도록 식물세포를 배양하는 것은 자신이 있는데 문제는 이들 세포를 직접 transformation 하는 방법은

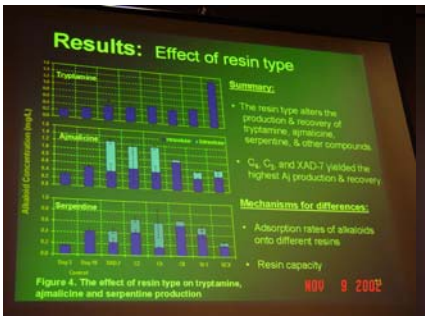
없을까? 또, transformation efficiency 를 높일 수 있는 방법은 없을까?하는 것이 이 연구의 시발점입니다. 결과는 직접 Agrobacterium 으로 transformation 을 하면 항상 이들의 overgrowth 가 문제인데 auxotroph 를 쓰면 좋더라.. 그리고 viral replicase 를 사용하니 efficiency 를 사용하니 efficiency 도 올라가더라입니다. 그런데 이들을 뒷받침해줄만한 data 가 상당히 부족했습니다. 필자가 다음 연구결과발표를 기대해야겠다고 언급한 이유가 여기에 있습니다.

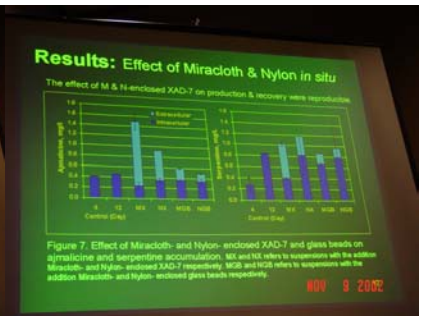
어제 이야기를 나누었던 Carolyn Lee 교수가 5 번째 발표였습니다. 아주 훌륭한 접근 방법이었다고 칭찬해 주고 싶은 logic 이었습니다. 아무래도 다른 발표는 박사과정학생이 하고 이 발표만 유독 교수가 직접 발표를 해서 그런지는 몰라도 다른 발표에 비해 논리적이고 세밀하게 접근하였음을 잘 설명해 주었습니다. 다만, 필자의 연구결과와 달랐던 점은 resin 으로 첨가한 XAD-7 이 전혀 cell growth 에 영향을 주지 않았다는 사실입니다. 필자의 경우 XAD-7 이 다량의 nutrient 를 adsorption 하여 early exponential growth stage 에 첨가를 하여도 growth 가 반으로 줄어들었으나 Lee 교수의 실험에서는 XAD-7 은 전혀 growth 에 영향을 미치지 않았습니다. 필자에게는 새로운 의문을 던진 결과였습니다. Stationary phase 에 넣어준다면 모를까….글쎄요.. 한번 더 생각해 봐야겠네요. 하지만 이를 제외하고는 아주 잘 짜여진 발표였습니다. 앞으로 Lee 교수의 연구활동을 기대해보아도 좋을것같습니다. 주요 결과들에 대해서만 선별적으로 언급하였습니다.

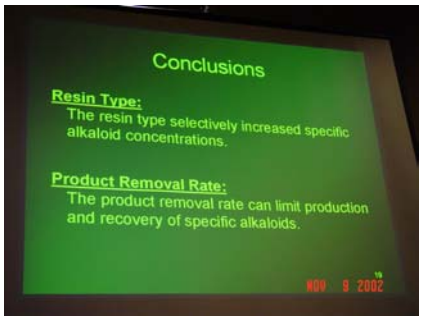












이 session 을 끝으로 일주일간의 AIChE Annual Meeting 이 막을 내렸습니다. 그간 필자가 나름대로 작성하여 송고하였던 보고서가 독자 여러분께 도움이 되었으면 합니다. 전체적인 흐름을 이해하시는데 도움이 되었으면 바램으로 작성된 것이니 소기의 목적이 달성되어진다면

필자로서는 더 이상 바랄 것이 없을 것입니다. 필자가 귀국한 후에는 전체적인 보고서를 요약 재작성하여 upload 하도록 하겠습니다.

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Indianapolis 에서 윤성용이었습니다.