

CURRICULUM VITAE

James Jea-Huang Huang, Ph.D.

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CAREER OBJECTIVE

Use cutting edge recombinant DNA and molecular biology technique to generate essential research reagents, novel diagnostic biochemicals, and potential therapeutical compounds. Special research interest in the area of anti-cancer, anti-aging, and anti-inflammation. Make drugs to improve the quality of life.

BACKGROUND SUMMARY

Results-oriented proactive senior research scientist with 15 years of industrial experience and accomplishments. Exhibited strong leadership, creativity, and problem solving skills. Awarded with increasing responsibilities in the area of recombinant DNA technologies, protein engineering and purification, and biopharmaceuticals manufacturing. Extensive experience in gene cloning, high level expression, mutagenesis, strain improvement, cell banking, plasmid stability, process fermentation, assay development, product characterization, analytical testing, quality assurance and control, virus removal (biologics), gene therapy vectors manufacturing, ultrafiltration, GLP, GMP, and regulatory compliance.

PROFESSIONAL EXPERIENCE AND ACCOMPLISHMENTS

4-00- **Director, Virology Department, Puresyn, Inc., Malvern, PA 19355**
Responsible for overall process involved in up-stream and down-stream process development as well as final product characterization. Developed independent processes for column purification of Gene Therapy viral vectors: Adenovirus (Ad) and Adenovirus-Associated Virus (AAV). Verified and validated tandem column purification process for Adenovirus from scale of 1.0×10^{12} to 1.0×10^{15} particles/run. Established final product release testing criteria. Final Ad preparation demonstrated excellent recovery, purity and infectivity (moi in single digit number).

Developed High Performance Tangential Flow Filtration process for crude material preparation for column chromatography. Developed and

validated two-column purification process for AAV using Puresyn's proprietary PolyFlo resin in both Capture and Polishing Step.

8-98 **Assistant Director, Process and Assay Development, and GMP**
3-00 **manufacturing, Institute for Human Gene Therapy (IHGT), Department of Molecular and Cellular Engineering, University of Pennsylvania, Philadelphia, PA**

Certified and managed the cGMP viral vector production facility-Huuman Application Laboratory at IHGT. Developed production and purification scheme for both Adenovirus (Ad) and Adeno-Associated Virus (AAV). Identified, developed, and validated run parameters for bioreactor and column purification. QC assay development: identity test by genetic characterization, purity test by slot blot, silver stain, western blot and IEF, potency test by infection center assay and functional ELISA. GMP Human Application Laboratories' function: wrote SOPs, Production Batch Records and purified adenovirus and AAV via CsCl and column chromatography. Prepared Type II Drug Master File's Annual Report. Monitored In-house and Contract Testing Organization QC testing.

4/97- **Director, Process Development and Manufacturing**

8-98 Goodwin Biotechnology Incorporated, Plantation, FL33313

Supervised 8 Process and Manufacturing Scientists.

Developed, optimized and validated affinity purification protocols for IgM which won a manufacturing contract totaled ca. 2.2 million dollar.

Verified and validated IgG affinity purification processes (low LAL).

GMP manufacturing of Mab for Rx and Dx applications (50 gm scale).

Reengineered Mab: chimerized and humanized antibodies.

Implemented ELISA in-process testing for IgM and IgG.

Accelerated QA/QC test methods, SOPs and production batch records.

8/95- **Manager, Fermentation Technology and Process Purification**

4/97 Avitech Diagnostic, Inc., Malvern, PA 19355

Implemented expression systems and purification protocols for DNA bindase, resolvase, and bacterial streptavidin.

Optimized solid-phase assay for mismatch scanning system.

Audited, and supervised contract manufacturing facility.

Generated cell bank, developed and validated fermentation process for GLP fermentation (65L); purified DNA resolvase Endo VII.

Applied affinity chromatography to purify plant DNA resolvases.

12/93 Associate Director, Fermentation Technology and

-7/95 Head, Molecular Biology

Lexin Pharmaceutical Corporation, Horsham, PA 19044

Supervised 2 MS scientists.

Contributed to process fermentation and production functions.

Achieved in generating development candidates LEX032 and LEX026.

Constructed a high level expression vector for anti-chymotrypsin.

Improved product formation by clonal selection and education.

Prepared SOPs, test methods, batch records, and IND.

Supported QA/QC function, GMP compliance, assisted in assay development and establishing analytical tests for finished product.

Awarded SBIR grant; facilitated academic collaboration.

9/91- Principal Research Investigator

12/93 Sterling Winthrop Immunoconjugates Division

Sterling Winthrop Inc., Sharon Hill, PA 19079

Supervised 1 MS and 2 BS scientists.

Contributed to large-scale cell culture and purification of ING-1 Mab antibody for therapeutic applications; followed cGMP guidelines.

Determined genetic stability, integrity(cDNA sequencing), and copy number of ING-1 plasmid in Master Cell Bank and Production Cells.

Participated in technology transfer, prepared SOP and Test Methods; wrote molecular biology section of ING-1's IND submission.

Succeeded in generating clinical trial candidates by expressing ING-1's antibody fragments (Fab, scFv and tandem repeat scFv), and by constructing bacterial DHFR-scFv(ING-1) fusion polypeptides.

Cloned, transfected and screened for stable and high-level ING-1 producing cell lines (genomic and cDNA constructs).

Developed inducible expression systems for yeast (GAL 1/10) and mammalian cells (DHFR).

9/88 - Senior Research Investigator

9/91 Sterling Winthrop Pharmaceuticals Group

Sterling Winthrop Inc., Collegeville, PA 19426

A successful project team leader: Stromelysin Inhibitor Project Team.

Supervised a Research Team of 5 Ph.D., and 10 MS and BS scientists.

Licensed key research reagents, expressed 45kDa stromelysin and constructed a functional 18kDa truncated form for biophysical study, validated high through-put assays for chemical files screening.

A skillful team builder: Molecular Expression and Purification.

Hired and supervised 1 Ph.D., and 2 MS scientists.

Established both microbial and mammalian expression systems.
Participated in a multi-faceted program directed toward the identification of disease-related genes (inflammation, immunology, cardiovascular, and cancer biology).

Implemented Molecular Biology Core Facility: PCR, DNA synthesizer, oligopeptide synthesizer, peptide sequencer, Fermentor, FPLC, HPLC.

Conducted PCR-directed unique single strand gene synthesis for PLA2. Succeeded in providing purified recombinant protein or reporter genes for inhibitors screening: TNF, PLA2, Stromelysin, ICAM, p56lck protein kinase, CD45 phosphatase, bFGF, HIV-intergrase. Determined critical structure-function relationships for SWPRD's protein molecular targets by site-directed mutagenesis. Supported SWPRD's rational drug design and screening.

7/85 - Principal Investigator

9/88 Immunology Department, Medical Product Development

E. I. duPont de Nemours & Co., Glenolden, PA 19036

A premier cloner in a multi-disciplinary IL-1 Research Group.

Supervised 2 MS and 5 BS scientists.

Expressed and purified to homogeneity in grams quantity of IL-1 β for inhibitors screening and biophysical study (CD, NMR, and X-ray crystallography).

Constructed and patented a series of IL-1 muteins that exhibited increased or decreased biological activity.

Carried out *in vivo* study to examine cytokines' anticancer activities.

Cloned and expressed a synthetic TNF gene; murine IL-1, and IL-3.

Assisted in constructing human monocyte cDNA library, and cloning of both forms of IL-1 and TNF cDNA.

6/84 - Senior Postdoctoral Fellow

7/85 Molecular Biology Department, Centocor, Inc., Malvern, PA 19355

A major contributor in a highly motivated **AIDS Task Force**.

Sequenced and expressed various domains of HTLV-III antigen (gag, env., and pol.) in *E. coli* and yeast.

Screened against panels of AIDS patient serum samples and defined the common epitopes for potential diagnostic and therapeutic applications.

1/82 - Research Associate

5/84 Laboratory of Renewable Resources Engineering

Department of Chemistry Engineering

Purdue University, West Lafayette, IN
Expressed E. coli xylose isomerase gene in Bacillus and yeast.
Cloned, sequenced and expressed yeast xylulose kinase in E. coli.
Built anaerobic growth chamber, and developed a novel cloning system for anaerobic methanogenic bacteria.

7/78 - **Graduate Research Assistant** - Nutrition Program
12/8 North Carolina State University, Raleigh, NC

9/77 - **Graduate Student** - Biochemistry Department
7/78 Kent State University, Kent, OH

8/75 - **Instructor** - Agriculture Chemistry Department
7/77 National Chung Hsing University, Taichung, Taiwan

7/73 - **Instructor** - National First Sergeant School, Taoyuang
7/77 (Served in the Army of R.O.C.)

9/71 - **Graduate Research Assistant** - Agri. Chem. Institute
6/73 National Taiwan University, Taipei, Taiwan, R.O.C.

PROFESSIONAL AWARDS

Strathmore's Who's Who -- Member Elected 1998

SBIR Grant, Phase 1, NIH -- Lexin Pharmaceutical Corp. (1995)

Vision and Accomplishment Award -- Sterling Winthrop Inc. (1993)

Special Accomplishment Research Award -- DuPont and Co. (1988)

Outstanding Achievement in AIDS Research -- Centocor, Inc. (1984)

Dutch Gardner Memorial Scholarship -- North Carolina State University. (1981)

Graduate Research Assistantship -- North Carolina State University (1978-1981)

Outstanding Teaching and Research Award -- National Science Foundation, Taiwan, ROC. (1976)

Graduate Research Assistantship -- National Taiwan University
(1971-1973)

EDUCATION

- Ph. D., Microbiology/Biochemistry - May, 1982
 North Carolina State University, Raleigh, NC
- M.S., Agriculture Chemistry/ Applied Microbiology - June, 1973
 National Taiwan University, Taipei, Taiwan, R.O.C.
- B.S., Agriculture Chemistry/ Soil Microbiology - June, 1971
 National Chung Hsing University, Taichung Taiwan, R.O.C.

PATENT

Huang, J. J. High level expression in E. coli of soluble mature hIL-1
beta and derivatives with altered biological activity.
US. Patent # 5,047,505. September 10, 1991

GRANT

Recombinant Serpins for Coagulative Disorder, National Institute of
Health, National Heart, Lung, and Blood Institute.
Grant reference number: 1R43 HL54378-1. July 21, 1995

REGULATORY COMPLIANCE TRAINING

Overview of FDA's Requirement in Biopharmaceutical Industry.
October, 1994, Pennsylvania Business Campus, Horsham, PA
Speaker: James Fenno, VP Product Development, Sparta (Lexin)
Pharmaceutics, Inc.

General Lab GMP and cGMP Issues.
December, 1997, Airport Hilton, West Palm Beach, FL
Speaker: Jerry Lanese, Ph.D., Institute of Validation Technology

Quality Improvement Seminar Series.
January, 1998, Goodwin Biotechnology Inc. Plantation, FL
Speaker: Paulette Smariga, VP Regulatory Affairs and QA/QC

JAMES JEA-HUANG HUANG, Ph.D.

PUBLICATIONS

1. Huang, J.J. et al (2001)
Purification of Recombinant Adeno-Associated Virus Type 2 by Cation Exchange Chromatography.
(Manuscript in Preparation; SBIR Phase I Final Report and SBIR Phase II Grant Submission Submitted on April 15, 2001)
2. Huang, J.J. et al (2001)
A New Scalable Method for the Purification of Recombinant Adenovirus Vectors. Poster presentation at ASGT 4th Annual Meeting, Seattle, WA May 30-June 3, 2001
(Manuscript and SBIR Phase II Final Report in preparation.)
3. Gao, G.P., et al (2000)
Purification of Recombinant Adeno-associated Virus Vectors by Column Chromatography and its Performance *In Vivo*
Human Gene Therapy 11:2079-2091
- 1a. Huang, J.J. (1999)
Preparation of annual update to the following Type II Drug Master File #BB-MF 6264 "The Recombinant Adenovirus H5.010.RSV.TK", #BB-MF 7624 "Adenovirus H5.001.RSV.TK", and #BB-MF 6857 "The Recombinant Adenovirus H5.001.CB.CFTR"
- 1b. Huang, J.J. (1999)
Study Report: Purification Process Development and Final Product Formulation of Adeno-Associated Virus.
Institute for Human Gene Therapy, UPENN
4. Huang, J.J. (1998)
Purification of therapeutic grade IgM monoclonal antibodies using protein A and ion exchange chromatography.
GBI Process Development Report #1569703
3. Huang, J.J., and J. Crowley (1998)
Production of low LAL antibodies with protein A/G affinity and flow through ion exchange chromatography for therapeutic application.
GBI Process Development Report #1549701-07, 1909701

4. Huang, J.J. (1997)
Process validation for virus removal and inactivation from spiked resins.
GBI Process Development Report #1389701, 1569703
5. Qoronfleh, M. W., S. K. Chowdhury. and B. Jones (1997)
Identification of new autolytic sites of recombinant truncated mature human fibroblast stromelysin by mass spectrometry
J. Peptide Res 49:612-619
6. Huang, J.J., and S. Jacob (1996)
Immobilized metal ion adsorption purification and characterization of recombinant DNA bindase HMP-1.
Avitech Study Report Series.
7. Huang, J.J. (1996)
Fermentation and purification of T4 bacteriophage DNA resolvase.
Avitech Study Report series.
8. Huang, J. J., and S. Sengha (1996)
Strain Improvement and characterization of MCB for the production of antichymotrypsin in *E. coli*.
Lexin Pharmaceuticals Research Report.
9. Qoronfleh, M. W., T. Ho, T. Banks, and R. Wahl (1996)
Mutagenesis of recombinant human fibroblast stromelysin C-terminus reveals the auto degradation pathway. Protein and Peptide Letters 3(4):233-240.
10. Huang, J.J., and C. Phillip (1995)
Mutagenesis, purification and characterization of LEX026, a bioengineered Serpin: a potential new class of drugs.
Lexin Pharmaceuticals Research Report.
11. Huang, J. J. (1995)
Clonal selection and generation of master cell bank for the production of biopharmaceutical LEX032 in *E. coli* (Lexin Study Report Series for IND submission)
12. Brake, P. G., et al., (1994)
Characterization of a recombinant cytosolic domain of CD45 phosphatase. Abstract. 10th International Conference on Methods in Protein Structure Analysis, Snowbird, Utah J. Protein Chemistry 13:524

13. Chowdhury, S. K., et al., (1994)
Electrospray ionization LC/MS and laser desorption mass spectrometric characterization of matrix-metalloproteinase: recombinant human fibroblast stromelysin. Abstract. ASMS Chicago, IL
14. Lischwe, M., R. C. Newton, J. J. Huang, and B. S. Larsen (1993)
Escherichia coli derived murine interleukin 1 beta with partially N[?]-acetylated. Protein Expression and Purification 4: 499-506.
15. Huang, J. J., V. Bushman, D. Kenney, and C. Shearman (1993)
Function expression of single chain Fv and Fab of a chimeric monoclonal antibody ING-1 in *E. coli* and yeast. (SRG Study Report #1114)
16. Huang, J. J., and C. Shearman (1993)
Mutagenesis and selection of recombinant human dihydrofolate reductase mutants exhibited improved trimethoprim binding affinity. (SRG Study Report #1115)
17. Huang, J. J., D. Willard, J. Koehn, and P. Gunguzlu (1992)
Arthritic synovial fluid PLA₂ : Novel synthesis of human gene and isolation of cDNA from placenta; molecular expression and refolding of the recombinant enzyme. (SRG Study Report #158)
18. Huang, J. J., S. Martin-Moe, K. Vastola, P. Brake and P. Gunguzlu (1992)
High-level expression in *E. coli* and affinity purification of recombinant human fibroblast stromelysin. (SRG Study Report #157)
19. Franken, P. A., L van den Berg, J. J. Huang, and G. H. de Hass (1992)
Purification and characterization of a mutant human platelet phospholipases A₂ expressed in *E. coli* - cleavage of a fusion protein with cyanogen bromide. Eur. J. Biochem. 203: 89-98.
20. Ciccarelli, R. B., P. Gunguzlu, J. J. Huang, C. Scott, and F. Oakes (1991)
Construction of HIV-1 **rev** and **nef** genes from DNA synthesis broths of entire top and bottom strands by PCR. Nucleic Acids Research 19: 6007-1013.
21. Pezzella, K. M., M. E. Neville, and J. J. Huang (1990)
In vivo inhibition of tumor growth of B16 melanoma by recombinant interleukin 1 β . Tumor inhibition parallels lymphocytes-activating factor activity of interleukin 1 β . Cytokine 2:357-362.
22. Zucali, J. R., J. Moreb, R. C. Newton, and J. J. Huang (1990)

Human N-terminal analogs of interleukin 1 β demonstrate altered binding and function in hematopoiesis. *Experimental Hematology* 18:1078-82.

23. Back, O., R. C. Newton, J. J. Huang, and T. J. Linna (1989)
Systemic interleukin 1 administration suppresses arachidonic acid-induced ear oedema in the mouse. *British J. Dermatology* 121:701-703.
24. Newton, R. C., G. Sandlin, K. Pezzella, J. J. Huang, J. McKearn (1989)
Flow cytometric analysis of interleukin 1 administration on bone marrow population in mice. *J. Biol. Resp. Mod.* 8:155-169.
25. North, R. J., R. H. Neubauer, S. E. Loveless, and J. J. Huang (1988)
Interleukin 1 induced T cell-mediated regression of immunogenic murine tumors. *J. Exp. Medicine* 168:2031-2043.
26. Huang, J. J., R. Horuk, R. C. Newton, and Y. Lin (1988)
Mapping the receptor binding site of interleukin 1-beta. *Progress in Leukocyte Biology* 8:191-196.
27. Horuk, R., J. J. Huang, M. Covington, and R. C. Newton (1988)
Evidence for differences in the molecular properties of interleukin 1 receptors. *Progress in Leukocyte Biology* 8:179-184.
28. Huang, J. J., S. J. Rutledge, R. C. Newton, and Y. L. DeVries (1988)
Characterization of murine interleukin-1 beta: isolation, expression and purification. *J. Immunol.* 140:3838-3843.
29. Lin, Y., M. E. Neville, and J. J. Huang (1988)
Synthesis, expression and purification of human tumor necrosis factor. Abstract. Protein Society Meeting, Baltimore, MD
30. Stevis, P. E., J. J. Huang, and N. W. Y. Ho (1987)
Cloning of *Pachysolen tannophilus* xylulokinase gene by complementation in *E. coli*. *Appl. Environ. Microbiol.* 53:2975-2877.
31. Huang, J. J., R. C. Newton, R. Horuk, J. B. Metthew, Y. L. DeVries (1987)
Muteins of human interleukin-1 that show enhanced activities. *FEBS Letters* 223:294-298.
32. Horuk, R., J. J. Huang, M. Covington, and R. C. Newton (1987)
A biochemical and kinetic analysis of interleukin-1 receptor. *J. Biol. Chem.* 262:16275-16278.

33. Huang, J. J., R. C. Newton, K. Pezzella, and Y. Lin (1987)
High-level expression in *E. coli* of a soluble and fully active recombinant interleukin-1 beta. *Mol. Biol. Med.* 4:169-181.
34. Ghrayeb, J., I. Kato, S. McKinney, J. J. Huang, and N. T. Chang (1986)
Human T-cell Lymphotropic Virus Type-III (HTLV-III) core antigens:
Synthesis in *E. coli* and immunoreactivity with human sera. *DNA* 5:93-99.
35. Chang, N. T., J. J. Huang, J. Ghrayeb, and R. C. Gallo (1985)
HTLV-III peptide produced by recombinant DNA is immunoreactive with sera from patients with AIDS. *Nature* 315:151-154.
36. Chang, N. T., P. Chanda, D. Barone, and R. C. Gallo (1985)
Identification and expression of open reading frame DNA of HTLV-III. *Science* 228:93-96.
37. Ho, N. W. Y., H. C. Gao, J. J. Huang, P. E. Stevis, and G. T. Tsao (1985)
The development of a cloning system for *Candida* species. *Biotech. Bioeng. Symp.* 14:259-301.
38. Huang, J. J., and N. W. Y. Ho (1985)
Expression of *E. coli* xylose isomerase gene in *Bacillus*. *Biochem. Biophys. Res. Comm.* 126:1154-1160.
39. Stevis, P. E., J. J. Huang, G. C. Gao, and N. W. Y. Ho (1984)
Construction of a cloning vector for eukaryotic microorganism by using its DNA sequences capable of autonomous replication in yeast. *Abstract. Federal Proceeding* 43:1699
40. Ho, N. W. Y., P. Stevis, S. Rosenfeld, J. J. Huang, and G. T. Tsao (1983)
Expression of *E. coli* xylose isomerase gene by yeast promoter. *Biotech. Bioeng. Symp.* 13:245-250.
41. Huang, J. J., J. C. H. Shih, and S. C. Steinberger (1982)
Poultry Waste Digester: From the laboratory to the farm. In *Energy Conservation and Use of Renewable Energies in the Bioindustries*. Proc. 2d International Seminar, F. Vogt (ed.) Pergamon Press, Oxford.
42. Huang, J. J. (1982)
Microbiological Study of Methane Generation from Poultry Waste. Ph.D. Thesis, North Carolina State University, Raleigh, NC

43. Huang, J. J., and J. C. H. Shih (1981)
The potential of biological methane generation from chicken manure.
Biotech. Bioeng. Symp. 23:2307-2314.
44. Shih, J. C. H., and J. J. Huang (1980)
A laboratory study of methane production from broiler chicken litter.
Biotech. Bioeng. Symp. 10:317-323.
45. Huang, J. J. (1973)
Application of fluorescent antibody technique to define the mating
reaction of *Schizophyllum commune*. Master Thesis, National Taiwan
University, Taipei, R. O. C.

PUBLICATIONS IN CHINESE NOT LISTED.