

8. Biographical Sketches

姓 名 (in Chinese) 施嘉和	ID No. (身份証或護照字號)		
Name (in Print) Chiaho Shih	Date of Birth		
Signature <i>Chiaho Shih</i>	Sex	X Male <input type="checkbox"/> Female	
Education / Training (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
Institution and location	Degree	Year (s)	Field of study
National Taiwan University	B.S.	1969-1973	Microbiology
MIT, Cambridge, Mass.	Ph.D.	1975-1982	Oncogene/Cancer
Mass Gen Hospital/Harvard Medical School	Postdoc	1982-1985	Molecular Virology

Note: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order: previous positions, concluding with your present position. List any honors. Include present membership on any government and/or public advisory committee.

1986 - 1992 Assistant Professor (Tenure Track), Department of Biochemistry and Biophysics, School of Medicine, University of Pennsylvania, Philadelphia, PA

1992 – 2000 Associate Professor (with Tenure), Department of Pathology School of Medicine, University of Texas Medical Branch (UTMB), Galveston, TX

2000 - 2008 Professor (with Tenure), Dept of Pathology, UTMB,
1992 - 1997 NIH Research Career Development Award (RCDA)
2002 Chief Meeting Organizer, 2002 International Meeting of Molecular Biology of Hepatitis Viruses, Asilomar Conference Center, CA

2006 - 2008 Member, International Committee on Taxonomy of Viruses (ICTV), Hepadnaviridae study group

Advisory Committee: Served on several study sections in Taiwan NSC, NHRI, NRPGM and USA NIH. Reviewers for grants of Hong Kong, Singapore, and Japan/South Africa. Ad hoc reviewers of academic promotions and recruitment for universities in Taiwan and USA.

2007 - present Professor, Adjunct appointment, Yang-Ming Univ. and National Defense Medical Center, Taiwan,

2007 - present Advisory Board, Development Center of Biotechnology (DCB), Taiwan

2007 - present Distinguished Research Fellow, IBMS, Academia Sinica

2010 - present Review Editorial Board, Frontiers in Virology,

B. Selected peer-reviewed publications (in chronological order, including patent and technology transfer).

Representative Publications

Sun, T.T., Shih, C., and Green, H. (1979). "Keratin Cytoskeletons in Epithelial Cells of Internal Organs". Proc. Nat. Acad. Sci. 76: 2813-2817.

Shih, C., Shilo, B., Goldfarb, M.P., Dannenberg, A., and Weinberg, R.A. (1979). "Passage of Phenotypes of Chemically Transformed Cells via Transfection of DNA and Chromatin". Proc. Nat. Acad. Sci. 79: 5714-5718. (total citations 415, 11-04-2011)

Shih, C., Padhy, L.C., Murray, M., and Weinberg, R.A. (1981). "Transforming Genes of Carcinomas and Neuroblastoma Introduced into Mouse Fibroblasts". Nature 290: 261-264. (total citations 651, 11-04-2011)

Murray, M.J., Shilo, B.Z., Shih, C., Cowing, D., Hsu, H.W., and Weinberg, R.A. (1981). "Three Different Human Tumor Cell Lines Contain Different Oncogenes". Cell 25: 355-361.

Padhy, L.C., Shih, C., Cowing, D., Finkelstein, R.J., and Weinberg, R.A. (1982). "Identification of a Phosphoprotein Specifically Induced by the Transforming DNA of Rat Neuroblastoma". Cell 28: 865-871.

Shih, C. and Weinberg, R.A. (1982). "Isolation of a Transforming Sequence from a Human Bladder Carcinoma Cell Line". Cell 29: 161-169. (total citations 739, 11-04-2011)

Parada, L.F., Tabin, C.J., Shih, C., and Weinberg, R.A., (1983). "Human EJ Bladder Carcinoma Oncogene is Homologue of Harvey Sarcoma Virus ras Gene". Nature 297: 474-479.

Martinville, B., Giacalone, J., Shih, C., Weinberg, R.A., and Francke, Uta. (1983). "Oncogene from Human EJ Bladder Carcinoma is Located on the Short Arm of Chromosome 11". Science 219: 498-501.

Lun, H., Isselbacher, K.J., Wands, J.R., Goodman, H.M., Shih, C., and Quarone, A. (1984). "Establishment and Characterization of a New Human Hepatocellular Carcinoma Cell Line". In Vitro 20: 493-504.

Shih, C., Burke, K., Zeldis, J., Wands, J., Isselbacher, K.J., Chou, M.J., Yang, C.S., Lee, C.S., and Goodman, H.M. (1987). "Tight Clustering of Human Hepatitis B Virus Integration Sites in Hepatomas Near a 'Triple-Stranded' Region". J. Virol. 61: 3491-3498.

Shih, C., Li, L.S., Roychoudhury, S., and Ho, M.H. (1989). "In Vitro Propagation of

- Human Hepatitis B Virus in a Rat Hepatoma Cell Line". *Proc. Natl. Acad. Sci. USA* 86: 6223-6327.
- Roychoudhury, S. and Shih, C. (1990). "cis-Rescue of a Mutated Reverse Transcriptase Gene of Human Hepatitis B Virus by Creation of an Internal ATG". *J. Virol.* 64: 1063-1069.
- Pei, D. and Shih, C. (1990). "Transcriptional Activation and Repression by a Cellular DNA-binding Protein C/EBP". *J. Virol.* 64: 1517-1522.
- Shih, C., Yu, M.Y.W., Li, L.S., and Shih, J.W.K. (1990). "Hepatitis B Virus Propagated in a Rat Hepatoma Cell Line is Infectious in a Primate Model". *Virology* 179: 871-873.
- Ou, J., Bao, H., Shih, C., and Tahara, S.M. (1990). "Preferred Translation of Human Hepatitis B Virus Polymerase From Core Protein But Not Precore Protein-specific Transcript". *J. Virol.* 64: 4578-4581.
- Hosono, S., Lee, C.S., Chou, M.J., Yang, C.S., and Shih, C. (1991). "Molecular Analysis of the p53 Alleles in Primary Hepatocellular Carcinomas and Cell Lines". *Oncogene* 6: 237-243.
- Faruqi, A., Roychoudhury, S., Greenberg, R., Israel, J., and Shih, C. (1991). "Replication Defective Missense Mutations Within the Terminal Protein and Spacer/intron Regions of the Polymerase Gene of Human Hepatitis B Virus". *Virology* 183: 764-768.
- Pei, D. and Shih, C. (1991). "An 'Attenuator Domain' is Sandwiched by Two Distinct Transactivation Domains in the Transcription Factor C/EBP". *Mol. Cell. Biol.* 11: 1480-1487.
- Roychoudhury, S., Faruqi, A., and Shih, C. (1991). "Pregenomic RNA Encapsulation Analysis of Eleven Missense and Nonsense Polymerase Mutants of Human Hepatitis B Virus". *J. Virol.* 65: 3617-3624.
- Hosono, S., Chou, M.J., Lee, C.S., and Shih, C. (1993). "Infrequent Mutation of p53 Gene in Hepatitis B Virus Positive Primary Hepatocellular Carcinomas". *Oncogene* 8: 491-496.
- Wu, K.J., Wilson, D.R., Shih, C. and Darlington, G.J. (1994). "The Transcription Factor HNF1 Acts With C/EBP- α Synergistically Activate the Human Albumin Promoter Through a Novel HNF1 Protein Domain". *J. Biol. Chem.* 269: 1177-1182.
- Yuan, T.-T., Faruqi, A., Shih, J.W.K., and Shih, C. (1995). "The Mechanism of Natural Occurrence of Two Closely-linked HBV Precore Predominant Mutations". *Virology* 211:144-156.

- Hosono, S., Tai, P.-C., Wang, W., Ambrose, M., Hwang, D.G.-Y., Yuan, T.-T., Peng, B.-H., Yang, C.-S., Lee, C.-S., and Shih, C. (1995). "Core Antigen Mutations of Human Hepatitis B Virus in Hepatomas Accumulate in MHC Class II-restricted T Cell Epitopes". *Virology* 212:151-162.
- Shih, C., Tai, P.-C., Whitehead, W., Hosono, S., Lee, C.-S., and Yang, C.-S. (1996). "Hepatitis B and C viruses and liver cancer". In: Bertino, J.R. eds. *Encyclopedia of Cancer*. Vol. II: 824-834, Academic Press.
- Tai, P.-C., Banik, D., Lin, G.-I., Pai, S., Pai, K., Lin, M.-H., Yuoh, G., Che, S., Hsu, S.H., Chen, T.-C., Kuo, T., Lee, C.-S., Yang, C.-S., Shih, C. (1997). Novel and frequent mutations of hepatitis B virus coincide with an MHC class I-restricted T cell epitope of the surface antigen. *J. Virol.* 71: 4852-4856.
- Yuan, T.T., Lin, M.H., Chen, D.S., and Shih, C. (1998). A defective interference-like phenomenon of human hepatitis B virus in chronic carriers. *J. Virol.* 72: 578-584.
- Yuan, T.T., Qiu, S.M., and Shih, C. (1998). Functional characterization of naturally-occurring variants of human hepatitis B virus containing the core internal deletion mutation. *J. Virol.* 72: 2168-2176.
- Yuan, T.T., Sahu, G. K., Whitehead, W. E., Greenberg, R., and Shih, C. (1999). The Mechanism of an "Immature Secretion" Phenotype of a Highly Frequent Naturally Occurring Missense Mutation at Codon 97 of Human Hepatitis B Virus Core Antigen. *J Virol* 73: 5731-5740.
- Yuan, T.T., Tai, P.C., and Shih, C. (1999). Subtype-independent immature secretion and subtype-dependent replication deficiency of a highly frequent naturally occurring mutation of human hepatitis B virus core antigen. *J. Virol.* 73: 10122-10128.
- Le Pogam S., Yuan T.T., Sahu G.K., Chatterjee S., and Shih, C. (2000). Low secretion phenotype of human hepatitis B virus virions caused by two independent, naturally occurring mutations (P5T and L60V) in the capsid protein. *J. Virol.* 74: 9099-9105.
- Yuan T.T. and Shih, C. (2000). A Frequent Naturally Occurring Mutation P130T of Human Hepatitis B Virus Core Antigen Is Compensatory for the Immature Secretion Phenotype of Another Frequent Variant F97L. *J. Virol.* 74:4929-4932.
- Sahu, G.K., Tai, P.C., Banerjee, S., Lin, M.H., Tennant, B., Gerin, J., and Shih, C. (2002). Out-of-frame vs. in-frame core internal deletion (CID) variants of human and woodchuck hepatitis B viruses. *Virology* 292:35-43 (Epub in December, 2001).
- Tai, P.-C., Suk, F.M., Gerlich W., Neurath R., and Shih, C. (2002). Hypermodification of an internally deleted middle envelope (M) protein of frequent and predominant hepatitis B virus variants. *Virology* 292:44-58 (Epub in December, 2001) (featured on frontcover).
- Le Pogam S. and Shih, C. (2002). Regulation of Hepatitis B Virus Virion Secretion Mediated Through a Putative Intermolecular Interaction between Core and the PreS1 Domain of the Large Envelope Protein. *J. Virol.* 76:6510-6517. (recommended by facultyof1000.com)
- Suk F.M., Lin M.H., Newman M., Pan S., Chen S.H., Liu J.D., and Shih, C. (2002). Replication Advantage and Host Factor Independent Phenotypes Attributable to a Common Naturally Occurring Capsid Mutation (I97L) in Human Hepatitis B Virus. *J. Virol.* 76:12069-12077.
- Shih, C. (2003). Functional Significance of Naturally Occurring Hepatitis B Virus Variants. In S. Locarnini and C.L. Lai eds. *Human Virus Guides- Human Hepatitis*

- B Viruses. International Medical Press (IMP), London, UK. p. 23-41.
- Chua, P. K., Wen, Y.M., and Shih, C. (2003). Co-existence of Two Distinct Secretion Mutations (P5T and I97L) in Hepatitis B Virus Core Produces Wild Type Secretion. *J. Virol.* 77:7673-7676.
- Newman, M., Suk, F.M., Cajimat, M., Chua, P.K., and Shih, C. (2003). Stability and Morphology Comparisons of Self-assembled Virus-Like Particles from Wild Type and Mutant Human Hepatitis B Virus Capsid Proteins. *J. Virol.* 77:12950-12960.
- Shih, C. and Yuan, T.T. (2004). "A cis/trans Genetic Test for Pleiotropic Phenotypes Associated with a Frequent Naturally Occurring Mutation at Amino Acid 97 of HBV Core Protein". *Methods Mol Med.* 95:247-257.
- Shih, C. and Yuan, T.T. (2004). "A One-filter-three-probe Assay for Defective Interference (DI) Effects of Naturally-Occurring Core Internal Deletion (CID) Variants of Human Hepatitis B Virus". *Methods Mol Med.* 2004;95:151-163.
- Shih, C. and Tai, P.C. (2004). "Detection of Hypermodified Middle-Envelope (M) Proteins Secreted from Naturally Occurring HBV Variants Containing a preS2 Internal Deletion". *Methods Mol Med.* 95:165-173.
- Ning, B and Shih, C. (2004). Nucleolar Localization of Human Hepatitis B Virus Capsid Protein. *J. Virol.* 78:13653-13668.
- Le Pogam, S., Chua, P.K., Newman, M., and Shih, C. (2005). Exposure of RNA Templates and Encapsidation of Spliced Viral RNA are Influenced by the Arginine Rich Domain of Human Hepatitis B Virus Core Antigen (HBcAg 165-173). *J. Virol.* 79:1871-1887.
- Wang, Y.L., Shen, C.N., Lin, M.H., Tosh D. and Shih, C. (2005). Transdifferentiated Hepatocytes can Support Replication of Hepatitis B Virus. *J. Virol.* 79:13116-13128.
- Chua, P.K., Wang, Y.L., Lin, M.H., Masuda, T., Suk, F.M., and Shih, C. (2005). Reduced Secretion of Virions and Hepatitis B Virus (HBV) Surface Antigen of a Naturally Occurring HBV Variant Correlates with the Accumulation of the Small S Envelope Protein in the Endoplasmic Reticulum and Golgi Apparatus. *J. Virol.* 79:13483-13496.
- Chua, P.K., Lin M.H. and Shih C. (2006). Potent Inhibition of Human Hepatitis B Virus Replication by a Host Factor Vps4. *Virology* 354:1-6.
- Newman M, Chua PK, Tang FM, Su PY, Shih C. (2009). Testing an Electrostatic Interaction Hypothesis of Hepatitis B Virus Capsid Stability by Using an in vitro Capsid Disassembly/Reassembly System. *J. Virol.* 83:10616-10626.
- Chua PK, Tang FM, Huang JY, Suen CS, and Shih C. (2010). Testing the Balanced Electrostatic Interaction Hypothesis of Hepatitis B Virus DNA Synthesis by Using an In Vivo Charge Re-balance Approach. *J. Virol.* 84: 2340-2351 (Epub 2009, Dec. 16).
- Liu S, He J, Shih C, Li K, Dai A, Hong Zhou Z, Zhang J. (2010). Structural comparisons of hepatitis B core antigen particles with different C-terminal lengths. *Virus Research* 149:241-244.
- Shih, HH, Shih C, Wang HW, Su CW, Sheen, IJ and Wu JC. (2010). Pro-205 of Large Hepatitis Delta antigen and Pro-62 of Major Hepatitis B Surface Antigen influence the Assembly of Different Genotypes of Hepatitis D Virus. *J. Gen. Virol.* 91:1004-1012 (Epub 2009, Nov. 25).

- Li HC, Huang EY, Su PY, Wu SY, Yang CC, Lin YS, Chang WC, and **Shih C.** (2010). Nuclear Export and Import of Human Hepatitis B Virus Capsid Protein and Particles. *PLoS Pathogens* 6(10): e1001162.
- Wang CH, Davamani F, Sue SC, Lee SC, Wu PL, Tang FM, **Shih C**, Huang TH, Wu WG. (2010). Cell surface heparan sulfates mediated internalization of PWWP/HATH domain of HDGF via macropinocytosis to fine-tune cell signaling process involved in and its effect on fibroblast cell migration. *Biochem. J.* 433(1):127-138.
- Chen CC, Chang CM, Sun CP, Yu CP, Wu PY, Jeng KS, Hu CP, Chen PJ, Wu JC, **Shih C**, Gershwin ME, and Tao MH (2011). Use of RNA interference to modulate liver adenoma development in a murine model transgenic for hepatitis B virus. *Gene Therapy (in press)*.

PATENT:

- United States Patent 10-20-92, # 5,156,970
Methods of Viral Propagation and Gene Expression
Inventor: Chiaho Shih, Ph.D.
- United States Patent 11-09-99, # 5,980,901
Viral Defective Interfering Particles and Uses Thereof
Inventor: Chiaho Shih, Ph.D., Thomas Yuan, Ph.D.

C. Research Support.

08/01/2008 – 07/31/2011 (ongoing) **NSC, Taiwan**, "Testing the Charge Balance Hypothesis of Human Hepatitis B Virus". Principal Investigator.

11/01/2009 – 07/31/2011 (ongoing) **NSC, Taiwan**. "Evaluation of Lead Compounds against Hepatitis B Virus". Principal Investigator.

01/01/2010 – 12/31/2012 (ongoing) **NHRI, Taiwan**, "MicroRNA and Hepatitis B Virus in a Transdifferentiation System from Pancreas to Hepatocytes". Principal Investigator.

08/01/2010 – 07/31/2013 (ongoing) **NSC, Taiwan**. "To Develop an Animal Model for Enterovirus 71". Principal Investigator.