

Principal Investigator

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Employment History

Present	Director, Singapore Cancer Syndicate
Present	Professor of Medicine, National University of Singapore, Special Advisor to the Vice Chancellor
Present	Executive Director, Genome Institute of Singapore
1996-2001	Director, Division of Clinical Sciences, National Cancer Institute, Bethesda, MD
1995-1996	Professor, Departments of Medicine, Epidemiology, Biochemistry and Biophysics.
1995-1996	Chief, Division of Medical Genetics, School of Medicine
1992-1996	Director, Specialized Program of Research Excellence in Breast Cancer (NIH Designated)
1993-1995	Associate Professor, Departments of Medicine and Epidemiology and Biochemistry, University of North Carolina at Chapel Hill
1987-1993	Assistant Professor in Medicine and Oncology, School of Medicine University of North Carolina at Chapel Hill

Research Interests

The historical focus of my group has been the integrated investigation of genes controlling the biology of human breast cancer. Primarily centered on gene discovery and functional validation both biologically and clinically, we were among the first to clone and to elucidate the function of previously new tyrosine kinases such as AXL, JAK3, FAK, and RAK to cancer biology. Moreover, we determined that the overexpression and amplification of another tyrosine kinase, HER-2, is a predictive marker for dose and chemotherapeutic selection to obtain optimal therapeutic response. More recently, we have used expression genomics, focusing on the transcripts, to expedite this discovery and to uncover overarching biological truths in breast cancer biology and treatment.

Currently, our work is divided into three main sectors; First, we are studying the genome-wide control strategy of the estrogen receptor (ER). We have found that the ER status is the most important determinant of the expression profile of a breast cancer. Our work determined the complete list of direct ER targets, and found that the ER control elements (EREs) are distributed throughout the gene and not in only the 5' cis-regulatory domains. Using these precise mining methods, we are redefining the functional ERE and, in conjunction with the proteomics group, systematically identifying all possible ER cofactors bound to specific EREs. The outcome will have significance in dissecting the very complex control network by estrogen and estrogen analogs and inhibitors clinically in use. Our second program, in collaboration with Lance Miller and Yu Qiang, is the clinical genomic assessment of breast cancers to uncover genetic determinants of tumor biology and therapeutic response. To this end, we have identified clear

prognostic and therapeutic markers in human breast cancers relevant in clinical decision making, and have uncovered specific sub-pathways that when perturbed, will dramatically alter the efficacy of cancer therapeutics. Our final program, in conjunction with YiJun Ruan and Chialin Wei, is to map the complete oncotranscriptome using advanced cloning and sequencing technologies. Our final goal is to assess all the possible transcriptional components of breast cancer cells, and to determine their control network so as to functionally manipulate biological outcome.

Academic Qualifications

1983-1987 Postdoctoral Fellow - Dept. of Microbiology, University of California at San Francisco, CA (Dr. J. Michael Bishop)
1982-1985 Hematology Fellowship, University of California San Francisco, Moffitt Hospital
1980-1982 Oncology Fellowship, Stanford University
1979-1980 Residency, Barnes Hospital - Washington University, St. Louis
1978-1979 Internship, Barnes Hospital - Washington University, St. Louis
1973-1978 Stanford University, M.D. 1969-1973 Stanford University, B.S. Chemistry, Psychology

Selected Publications

1. Chin-Yo Lin, Anders Strom, Vinsensius Berlian Vega, Say Li Kong, Ai Li Yeo, Jane S Thomsen, Wan Ching Chan, Balraj Doray, Dhinoth K Bangarusamy, Adaikalavan Ramasamy, Liza A Vergara, Suisheng Tang, Allen Chong, Vladimir B Bajic, Miller Lance D, Jan-Ake Gustafsson, Liu Edison Tak-Bun, (Epub 2004) "Discovery of estrogen receptor alpha target genes and response elements in breast tumor cells" . *Genome Biol.* Aug 12 5(9) . R66
2. Miller Lance D, Smeds J, George J, Vega VB, Vergara L, Ploner A, Pawitan Y, Hall P, Klaar S, Liu Edison Tak-Bun, Bergh J, (2005) "An expression signature for p53 status in human breast cancer predicts mutation status, transcriptional effects and patient survival". Under review in PNAS
3. A. Bimbo, Jia, Yonghui, Siew Lay Poh, Radha Krishna Murthy, Karuturi, Nicole den Elzen, Xu Peng, Liling Zheng, Matthew O'Connell, Liu Tak Bun, Edison, Mohan Balasubramanian, Liu Jian Hua, (2005) "Systematic Deletion Analysis of Fission Yeast Protein Kinases" . *Eukaryotic Cell.* 4(4) . (A Bimbo and Jia Yonghui are co-first authors)
4. X. Peng, K. M. Karuturi, Miller Lance D, Lin K, Jia Yonghui, Kondu P, L. Wang, L. Wong, Liu Edison Tak-Bun, M. Balasubramanian, Liu Jian-Hua, (2005) "Identification of cell cycle-regulated genes in fission yeast" . *Mol. Biol. Cell.* 16 . 1026-1042 . (X Peng and K.M.Karuturi are co-first authors)
5. Wei Chia Lin, Takumi Miura, Robson Paul, Lim Sai Kiang, Xiu-qin Xu, Mathia Yu-Chuan Lee, Gupta Sanjay, Stanton, Lawrence W, Yongquan Luo, Jacqui Schmitt, Scott Thies, Wei Wang, Irina Khrebtukova, Daixing Zhou, Liu Tak Bun, Edison, Ruan Yijun, Mahendra Rao, Lim Bing, (2005) "Transcriptome Profiling of Murine and Human ES

- Cells reveals Divergent Paths Required to Maintain the Stem Cell State" . *Stem Cells*. 23 . 166-185
6. Ng, Patrick Wei Pern, Wei Chia Lin, Sung, Wing Kin Ken, Chiu, Kuo Ping, Lipovich Leonard, Ang Chin Chin, Gupta Sanjay, Shahab Atif, Wong Chee Hong, Ridwan Azmi, Liu Tak-Bun Edison, Ruan Yijun, (2005) "Gene identification signature (GIS) analysis for transcriptome characterization and genome annotation" . *Nature Method*. 2 . 105-111
 7. Xu XQ, Emerald BS, Goh EL, Kannan N, Miller Lance D, Gluckman PD, Liu Edison Tak-Bun, Lobie PE, (2005) "Gene expression profiling to identify oncogenic determinants of autocrine human growth hormone (hGH) in human mammary carcinoma" . *J Biol Chem*. Apr 20 . Epub ahead of print
 8. Liu Jianjun, SL Lim, Ruan Yijun, Ling AE, Ng LF, C Drostein, Liu Edison Tak-Bun, Stanton Lawrence W, Hibberd Martin Lloyd, (2005) "SARS Transmission Pattern in Singapore Reassessed by Viral Sequence Variation Analysis" . *PLoS Med*. 2(2) . 162-168
 9. Reid, G., Metivier, R, Lin Chin-Yo, Denger S, Ibberson D, Ivacevic T, Brand H, Benes V, Liu Edison Tak-Bun, Gannon F, (2005) "Multiple mechanisms induce transcriptional silencing of a subset of genes, including oestrogen receptor alpha, in response to deacetylase inhibition by valproic acid and trichostatin A" . *Oncogene*. epublished May 2
 10. Vega VB, Bangarusamy DK, Miller Lance D, Liu Edison Tak-Bun, Lin CY, (2004 Jul 1) "BEARR: Batch Extraction and Analysis of cis-Regulatory Regions" . *Nucleic Acids Res*. 32: . W257-60
 11. Miller Lance D, McPhie P, Suzuki H, Kato Y, Liu Edison Tak-Bun, Cheng S-Y, (2004 Apr) "Multi-tissue gene expression analysis in a mouse model of thyroid hormone resistance" . *Genome Biol*. 5(5) . R31
 12. Peng X, Murthy Karuturi RK, Miller Lance D, Lin K, Jia Y, Kondu P, Wang L, Wong LS, Liu Edison Tak-Bun, Balasubramanian MK, Liu J, (2004) "Identification of Cell Cycle-regulated Genes in Fission Yeast" . *Mol Biol Cell*. Dec 22 . Epub ahead of print
 13. Wong Christopher Wing-Cheong, Albert, T.J, Vinsensius B Vega S, Norton, J.E., Cutler, D.J., Richmond, T.A, Stanton Lawrence W, Liu Edison Tak-Bun, Miller Lance D, (2004) "Tracking the Evolution of the SARS Coronavirus using Rapid, High-throughput, High-density Resequencing Arrays" . *Genome Research*. 14(3) . 398-405 . Featured on the cover of the journal.
 14. Ng, Lisa Fong-Poh, Wong MS, Koh, S., Ooi, E. E., Tang, K. F., Leong, H. N., Ling, A. E., Agathe, L. V., Tan, J., Liu Tak Bun, Edison, Ren Ee Chee, Ng, L. C., Hibberd, Martin Lloyd, (2004) "Detection of SARS CoV in blood of infected patients" . *J. Clin. Micro*. 42 . 347-350

15. Vinsensius, B Vega S, Ruan Yijun, Liu Jianjun, Lee W.H., Wei Chia Lin, Su Yun S.T., Tang K.F., Zhang Tao, Lin S., Kolatkar, Prasanna R, Eong O.E., Ling A.E., Stanton, Lawrence W, Long P.M., Liu Tak Bun, Edison, (2004) "Mutational dynamics of the SARS corona virus in cell culture and human population." . BMC Infectious Diseases 4(1):32-40
16. Liu Tak Bun, Edison, Radha Krishna Murthy, Karuturi, (2004) "Microarrays and Clinical Investigations" . The New England Journal of MedicineThe New England Journal of Medicine . 350 . 1595-1597
17. Ng Fong-Poh Lisa, Hibberd, Martin Lloyd, Eng-Eong Ooi, Kin-Fai Tang, Neo Seok Ying, Tan, Hui Hui Jenny, Radha Krishna Murthy, Karuturi, Vinsensius, B Vega S, Jer-Ming Chia, Liu Tak Bun, Edison, Ren Ee Chee, (2004) "A human in vitromodel system for investigating genome-wide host responses to SARS coronavirus infection" . BMC Infectious Diseases. 4 . 34-45
18. Chia KS, Lee JJM, Cheung P, Cheung KH, Seielstad Mark, Wilcox MM, Liu Edison Tak-Bun, (2004) "Twin births in Singapore: a population-based study using the national birth registry" . Annals Academy of Medicine Singapore. 33 . 195-199
19. Wei Chia Lin, Ng, Patrick Wei Pern, Chiu, Kuo Ping, Chee Hong Wong, Chin Chin Ang, Lipovich Leonard, Liu Tak Bun, Edison, Ruan Yijun, (2004) "5' Long serial analysis of gene expression (LongSAGE) and 3' LongSAGE for transcriptome characterization and genome annotation" . Proc Natl Acad Sci. 101 (32) . 11701-6
20. Lin Chin-Yo, Strom, A., Vega, V.B., Kong, S.L, Thomsen J.S., Yeo, A.L., Doray, B., Chan, W.C, Bangarusamy, D.K., Tang, S, Chong, A., Bajic, V.B, Ramasamy, A, Vergara, L, Miller Lance D, Gustafsson, J.-A., Liu Edison Tak-Bun, (2004) "Estrogen receptor alpha target gene and response element discovery in breast tumor cells" . Genome Biology. 5 (9) . R66
21. Vega, V.B., Bangarusamy, D.K, Miller Lance D, Liu Edison Tak-Bun, Lin Chin-Yo, (2004) "BEARR: Batch extraction and analysis of cis-regulatory regions" . Nucleid Acid Res. 32 Web Server Issue . W257-60
22. Ruan Yijun, Le Ber P, Ng Huck Hui, Liu Edison Tak-Bun, (2004) "Interrogating the transcriptome" . Trends in Biotechnology. 22(1) . 23-30
23. Ruan Yijun, Wei Chia Lin, Thoreau Herve, Chia Jer-Ming, Lim Landri, Ng, Patrick Wei Pern, Zhang Tao, Chiu, Kuo Ping , Vinsensius, B Vega S, Liu Tak Bun, Edison, (2003) "Genome Sequence Analysis of Coronavirus Isolated from Singapore SARS Patients" . WHO SARS Aetiology Site
24. Ruan Yijun, Wei Chia Lin, Ling Ai Ee, Vinsensius, B Vega S, Thoreau Herve, Su Yun Se Thoe, Chia Jer-Ming, Ng, Patrick Wei Pern, Chiu, Kuo Ping, Lim Landri, Zhang Tao, Chan Kwai Peng, Lynette Oon Lin Ean, Ng Mah Lee, Leo Yee Sin, Ng, Lisa Fong-Poh,

- Ren Ee Chee, Stanton, Lawrence W, Long M. Philip, Liu Tak Bun, Edison, (2003)
"Comparative full-length genome sequence analysis of 14 SARS coronavirus isolates and common mutations associated with putative origins of infection" . *Lancet*. 361 (9371) . 1779-85
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 27. Miller Lance D, Long PM, Wong L, Mukherjee S, McShane LM, Liu Edison Tak-Bun, (2002 Nov) "Optimal gene expression analysis by microarrays" . *Cancer Cell*. 2(5) . 353-61
 28. Zhou Y, Gwadry FG, Reinhold WC, Miller Lance D, Smith LH, Scherf U, Kohn KW, Liu Edison Tak-Bun, Pommier Y, Weinstein JN, (2002 Mar) "Transcriptional regulation of mitotic genes by camptothecin-induced DNA damage: Microarray analysis of dose- and time-dependent effects" . *Cancer Res*. 62(6) . 1688-95
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 32. Laura Assersohn, L Gangi, Y Zhao, M Dowsett, R Simon, T Powles, Liu Tak Bun, Edison, (2002) "The feasibility of using fine needle aspiration from primary breast cancers for cDNA microarray analyses. (In press, Clin Cancer Res)"
 33. Jazaeri A, Boyd J, McShane L, Liu Tak Bun, Edison, (2002) "Expression profiling of ovarian cancers in BRCA1 and BRCA2 carriers. (In press, JNCI)"

34. Miller Lance D, Park KS, Guo QM, Alkharouf NW, Malek RL, Lee NH, Liu Edison Tak-Bun, Cheng SY, (2001 Oct) "Silencing of Wnt signaling and activation of multiple metabolic pathways in response to thyroid hormone-stimulated cell proliferation" . *Mol Cell Biol.* 21(19) . 6626-39
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37. Dong G, Loukinova E, Chen Z, Gangi L, Liu Tak Bun, Edison, Van Waes C, (2001) "Molecular Profiling of Metastatic Tumor Progression of a Murine Squamous Cell Carcinoma by Differential Display and cDNA Microarray Reveals Dysregulated Expression of Genes Related to the Nuclear Factor- κ B Signal Pathway" . *Cancer Res.* 61(12):4797-808
38. Guo QB, Malek R, Kim S, Chiao C, He M, Ruffly M, Sanka K, Lee NH, Dang CV, Liu Tak Bun, Edison, (2001) "Identification of c-Myc Target Genes Using Rat cDNA Microarray, *Cancer Res.*" . 60(21):5922-8
39. Campbell M, Aprelikova, ON, van der Meer R, Woltjer RL, Yee, CJ, Liu Tak Bun, Edison, Jensen RA, (2001) "Construction and Characterization of recombinant adenoviruses expressing human BRCA1 or murine Brca1 genes." . *Cancer Gene Ther.* 8(3):231-9
40. Wang E, Miller Lance D, Ohnmacht GA, Liu Edison Tak-Bun, Marincola FM, (2000 April) "High fidelity mRNA amplification for gene profiling" . *Nature Biotechnology.* 18(4) . 457-9
41. Huang WY, Newman B, Millikan RC, Conway K, Hulka BS, Schell MJ, Liu Tak Bun, Edison, (2000) "Risk of breast cancer according to the status of HER2.neu oncogene amplification." . *Cancer Epidemiol Biomarkers Prev.* 9(1):65-71
42. Aprelikova O, Meissner E, Cotter S, Kuthiala A, Bessho M, Liu Tak Bun, Edison, (1999) "BRCA1 associated growth arrest is Rb dependent. BRCA1-associated growth arrest is RB-dependent." . *Proc Natl Acad Sci USA.* 96(21):11866-71
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48. Fridell YW, Jin Y, Quilliam LA, Burchert A, McCloskey P, Spizz G, Varnum B, Der C, Liu Tak Bun, Edison, (1996) "Differential activation of the Ras/extracellular-signal-regulated protein kinase pathway is responsible for the biological consequences induced by the Axl receptor tyrosine kinase." . *Mol Cell Biol.* 16(1):135-145
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55. O'Bryan J, Frye RA, Cogswell P, Kitch B, Neubauer A, Espinosa R, LeBeau M, Prokop C, Earp HS, Liu Tak Bun, Edison, (1991) "axl, a transforming gene isolated from primary human myeloid leukemia cells, encodes a novel receptor tyrosine kinase" . Mol Cell Biol. 11:5016-5031
56. Liu Tak Bun, Edison, Hjelle B, Bishop JM, (1988) "Transforming genes in Chronic Myelogenous Leukemia" . Proc. Natl. Acad. Sci. USA. 85:1952-1956
57. Liu Tak Bun, Edison, Hjelle B, Morgan R, Hecht F, Bishop JM, (1987) "Mutations of the Kirsten-ras proto-oncogene in human preleukemia" . Nature. 330:186-188
58. Miller Lance D, Liu Edison Tak-Bun, "Expression Profiling and Breast Cancer Biology". In Press in Breast Disease

Honors And Awards

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| 2000 | Rosenthal Award, AACR: for the discovery that HER-2 status determines response to adjuvant chemotherapy with doxorubicin. |
| 1999 | Elected-Board of Directors, American Association for Cancer Research |
| 1996 | 1996 Brinker International Award for Breast Cancer Research - Basic Research Award |
| 1995 | American Society of Clinical Investigation (Membership) |
| 1991-1996 | Leukemia Society Scholar |
| 1990-1993 | Komen Foundation Award for Breast Cancer Research (funding fellow salary) |
| 1990-1994 | Jefferson Pilot Award: University of North Carolina at Chapel Hill, Junior Faculty Award for Research Excellence |
| 1985-1988 | Clinical Investigator Award, National Cancer Institute, K08-CA01036-02, Preceptor: Dr. J. Michael Bishop. |
| 1983-1985 | Damon Runyan Cancer Fund Fellowship Preceptor: Dr. J. Michael Bishop (UCSF) |
| 1974 | Ford Foundation Fellowship for Intensive Studies in Chinese, Stanford University |
| 1973 | Phi Beta Kappa Stanford University 1972 National Science Foundation Fellowship in Chemistry 1972. |