＊梁毓津博士

發表期刊論文及研究

SELECTED PUBLICATIONS

1. **Liang YJ,** Ding Y. Steven B. Levery, Handa K, Hakomori SI: **Differential expression profiles of glycosphingolipids in human breast CSCs vs. Non-CSCs.** *Proc Natl Acad Sci U S A* 2013, **110:**4968-4973.
2. **Liang YJ,** Yang BC, Chen JM, Lin YH, Huang CL, Cheng YY, Hsu CY, Khoo KH, Shen CN, Yu J: **Changes in glycosphingolipid composition during differentiation of human embryonic stem cells to ectodermal or endodermal Lineages.** *Stem Cells* 2011, **29**:12, 1995-2004.
3. **Liang YJ,** Kuo HH, Lin CH, Chen YY, Yang BC, Cheng YY, Yu AL, Khoo KH, Yu J: **Switching of the core structures of glycosphingolipids from globo- and lacto- to ganglio-series upon human embryonic stem cell differentiation.** *Proc Natl Acad Sci U S A* 2010, **107:**22564-22569.
4. Chang HS, Lin CH, Yang CH, **Liang YJ,** Yu WC: **The human papillomavirus-16 (HPV-16) oncoprotein E7 conjugates with and mediates the role of the transforming growth factor-beta inducible early gene 1 (TIEG1) in apoptosis.** *Int J Biochem Cell Biol* 2010, **42:**1831-1839.
5. **Liang YJ,** Chang HS, Wang CY, Yu WC: **DYRK1A stabilizes HPV16E7 oncoprotein through phosphorylation of the threonine 5 and threonine 7 residues.** *Int J Biochem Cell Biol* 2008, **40:**2431-2441.
6. Chang HS, Lin CH, Yang CH, Yen MS, Lai CR, Chen YR, **Liang YJ,** Yu WC: **Increased expression of Dyrk1a in HPV16 immortalized keratinocytes enable evasion of apoptosis.** *Int J Cancer* 2007, **120:**2377-2385.
7. Wang CY, **Liang YJ,** Lin YS, Shih HM, Jou YS, Yu WC: **YY1AP, a novel co-activator of YY1.** *J Biol Chem* 2004, **279:**17750-17755.

CONFERENCE PAPER

1. **Liang, Y.J.**, Kuo, H.H., Lin, C.H., Chang, W.L., Yang, B.C., Cheng, Y.Y., Yu, A.L., Khoo, K.H., Yu, J, 2009, **"Glycome analysis during differentiation of human embryonic stem cell"**, paper presented at the *The 7th International Society*

for Stem Cell Research (ISSCR) annual meeting, Barcelona, Spain. July 8-11, 2009.

2. **Liang, Y.J.**, Kuo, H.H., Lin, C.H., Chang, W.L., Yang, B.C., Cheng, Y.Y., Yu, A.L., Khoo, K.H., Yu, J, 2011, **"Switching of the core structures of glycosphingolipids from globo- and lacto- to ganglio-series upon human embryonic stem cell differentiation"**, paper presented at *The Gordon Research Conference In Glycobiology*, Lucca (Barga), Italy. May 8 -13 , 2011.
3. **Liang YJ,** Ding Y. Steven B. Levery, Handa K, Hakomori SI**: "Selection of breast cancer stem cell specific markers by profiling glycosphingolipids between Breast non-CSCs and CSCs",** paper presented at *The Society for Glycobiology and the American Society for Matrix Biology*, San Diego, CA, USA. November 11-14, 2012.
4. **Liang YJ,** Yu, J, Hakomori SI**: "Selection of Stem Cells Specific Markers by Glycosphingolipidomics for Potential Use in Cancer Diagnosis and Therapy",** Oral presented at *2013 International Glycoforum in Wuxi*, Jiangnan University, China. September 16-17, 2013.

Research Interests

Glycosphingolipids (GSLs) consist of a ceramide moiety with one or several attached sugar units. They are localized primarily on the plasma membrane of animal cells, and function to mediate cell adhesion and signal transduction via lipid rafts. Many GSL species that are abundant in early embryogenesis, decline during development, and are expressed minimally in adult cells, have been found to reappear in tumor cells. Certain GSLs are highly expressed in human cancer cells and enhance tumor phenotypes, particularly cell proliferation, invasiveness, and motility. We recently analyzed GSL expression profiles of human embryonic stem cells (hESCs) and their differentiated counterparts. hESCs were found to contain specific GSL structures with potential application as surface markers for cancer diagnosis or therapy. In another study, we used an epithelial-mesenchymal transition (EMT) model to generate breast cancer stem-like cells from immortalized human mammary epithelial cells, and compared GSL expression profiles of cancer stem cells (CSCs) vs. non-CSCs. Gangliosides (*i.e.*, sialylated GSLs) GD2 and GD3 were found to be specifically enriched in a $CD44^{hi}/CD24^{lo}$ population of CSCs. CSC phenotypes such as mammosphere formation and migration ability were reversed when GD2 synthase (B4GALNT1) or GD3 synthase (*ST8SIA1*) were knocked down in breast cancer cell line lines. Our findings indicated that GD2/GD3 play an important

functional role in maintaining the CSC phenotype in human breast cancer. Gangliosides in combination with their interacting receptors/ adaptors are present in lipid rafts on the plasma membrane surface and are involved in regulation of signal transduction. There is increasing evidence for regulation of GSL expression by plasma membrane-associated glycohydrolases and glycosyltransferases. This type of regulation appears to be a rapid, essential mechanism for local control of ganglioside composition, membrane organization, and related signaling processes in response to external and internal stimuli.

The major aims of our studies are to: (1) identify the GD2/GD3 interacting molecules in lipid rafts of the cell membrane; (2) elucidate the regulation and function of GD2/GD3 interacting molecules; (3) elucidate the functional role of GD3 synthase (ST8SIA1) and GD2 synthase (B4GALNT1) in breast CSCs. Our results will clarify the functional organization of lipid rafts and the molecular mechanism underlying the signaling transduction pathways mediated by GD2/GD3 in breast CSCs. We expect that our findings will improve understanding of the role of GD2/GD3 in regulating CSC formation and maintenance, and lead to more effective molecular and pharmacological approaches to breast cancer therapy