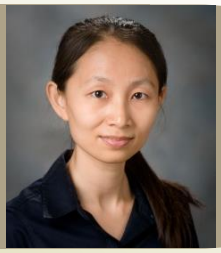
# Cancer Science Institute of Singapore

# SEMINAR ANNOUNCEMENT


## Li MA, Ph.D.

Assistant Professor, Department of Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center

## Determinants of Breast Cancer Progression

**Date:** **Thursday, 2 July 2015**

**Time:** **10:30am – 11:30am**

**Venue:** **LT 37, Level 3, Tahir Foundation Building (MD1)**
12 Science Drive 2, Singapore 117549


**Abstract:**

Deregulation of signaling pathways that control organ size, such as the Hippo-YAP pathway, can lead to tumor formation and metastatic progression. Combining high-throughput RNA sequencing, functional characterization, mechanistic studies, and clinical validation, we identified leukemia inhibitor factor receptor (LIFR) as a novel breast cancer metastasis suppressor downstream of the miR-9 microRNA and upstream of Hippo signaling (*Nature Medicine*, 2012). We found that LIFR suppresses metastasis by activating a Hippo kinase cascade leading to functional inactivation of the transcriptional co-activator YAP. We found that LIFR is downregulated in human breast cancer, and that loss of LIFR in non-metastatic stage I-III breast tumors is highly associated with poor metastasis-free, recurrence-free, and overall survival outcomes in approximately 1,000 patients. Recently, we generated *Lifr* conditional knockout mice and confirmed that Hippo signaling is indeed shut down in *Lifr*-deficient adult tissues and primary mouse embryonic fibroblast cells. We also found that liver-specific deletion of *Lifr* significantly increased liver size, and dramatically reduced survival and promoted liver tumorigenesis in a chemical-induced liver cancer model. We will continue to determine whether deletion of *Lifr* in the breast, liver, and other organs will promote organ growth, tumorigenesis, and metastasis.

We are also interested in the link between epithelial-mesenchymal transition (EMT), metastasis, and therapy resistance. EMT has been found to be associated with cancer stem cell properties such as radioresistance. Our lab recently discovered that it is not EMT itself that causes tumor radioresistance; instead, it is a specific EMT inducer, ZEB1, that regulates radiosensitivity. We identified ZEB1 as a central player in the key DNA damage response pathway linking ATM to CHK1 (*Nature Cell Biology*, 2014), and demonstrated the therapeutic utility of nanoparticle-encapsulated miR-205 (a microRNA that targets ZEB1) mimics as a tumor radiosensitizer in a preclinical model (*Nature Communications*, 2014). These findings shaped our understanding of the association between EMT, cancer stem cells, and radioresistance, and raised the caution that radiation treatment can lead to upregulation of ZEB1, downregulation of miR-205, and therapy-induced radioresistance. Based on our results, ZEB1-targeting agents, such as the miR-205 mimics, have the potential to be used as tumor radiosensitizers. Recently, a growing body of evidence, based on the work from many groups, has demonstrated that ZEB1 can promote radioresistance and resistance to various DNA-damaging chemotherapeutic agents, which is likely to contribute to tumor recurrence and metastatic relapse.


**Biography:**

Dr. Li Ma is an Assistant Professor at The University of Texas MD Anderson Cancer Center (her tenure and early promotion were approved and will take effect in September 2015). She received her bachelor's degree from Peking University in 2001. After completing her Ph.D. study at Sloan-Kettering Institute in 2006, she became a postdoctoral fellow at the Whitehead Institute and MIT. Dr. Ma joined the faculty of MD Anderson in 2010.

Dr. Ma conducted pioneering research on metastasis, therapy resistance, and regulation of key cancer proteins and pathways. She published seminal work in top journals including Cell, Nature, Nature Medicine, Nature Cell Biology, and Nature Biotechnology, with high volumes of citations (Web of Science, 4200 citations; Google Scholar, 5800 citations). Her achievements have been recognized by many prestigious awards, including the 2014 AAAS Martin and Rose Wachtel Award—an international recognition for outstanding work in the field of cancer research.