GUEST SEMINAR

Discovery of the Molecular Linkage between Cell Survival in Circulation and Resistance to Doxorubicin in Metastatic Breast Cancer Cells

by

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Time: 2:00pm
Venue: LTH

Abstract
Metastasis is the biggest challenge in cancer treatment as metastatic tumor cells often develop resistance to anticancer drugs such as doxorubicin and paclitaxel. As a result, over 90% of cancer patients die of metastasis. Metastasis is a process by which cancer cells migrate from the primary tumor through the circulatory system to the metastatic sites. Once tumor cells enter the bloodstream, these circulating tumor cells (CTCs) can be destroyed by physical disruption, anoikis due to detachment from the extracellular matrix, or immuno-elimination. As metastatic CTCs must withstand the impacts of hemodynamic shear force before they can reach the secondary tumor site, we hypothesized that metastatic CTCs should have higher survival in the circulation than the non-metastatic CTCs. To test this hypothesis, we engineered metastatic MDA-MB-231-C3 and non-metastatic MCF7-C3 cells, both of which can produce a caspase sensor for real-time detection of apoptosis. We also developed three model systems including a microfluidic system, zebrafish and mouse tumor models.

Using these systems, we found that metastatic 231-C3 cells could better resist shear force-induced apoptosis than non-metastatic MCF7-C3 cells because they had higher level of a particular driver protein. We also found that there is a positive correlation between the level of this driver protein, and the abilities of metastasis and resistance to doxorubicin. We think this identified driver protein can serve as a new marker for more accurate diagnosis of metastasis and drug resistance. It can also serve as a new therapeutic target for preventing metastasis and reducing drug resistance.

Biography
Prof. Kathy Qian Luo received both Bachelor and Master degree in Biology from Peking University and Ph.D. degree in Molecular Biology from University of British Columbia in Canada. She then worked as a Postdoctoral Fellow at California Institute of Technology in USA for three years before joined Hong Kong University of Science and Technology in 1998. Prof. Luo is now an Associate Professor in the School of Chemical and Biomedical Engineering at Nanyang Technological University in Singapore. Prof. Luo has done significant research works in the areas of cell cycle regulation, apoptosis, metastasis, anti-cancer drug discovery, nano-medicine and microfluidic research. She has published over 80 top quality journal articles and conference papers with total citations of 1,399 and h-index of 22. She obtained 5 granted patents: 3 from USA, 1 from China, 1 from Singapore and filed 7 international patents. At NTU of Singapore, as a principal investigator, she obtained a total funding of S$2,466,542 (HK$14,799,252) in the last 5.5 years.

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