**Characterizing the Roles of COIL and WIPI1 in Breast Cancer Cells**

**Misan Lee**3, Grace Cheung3, Ranju Nair3, Susan J. Done1,2,3,4

Departments of 1Medical Biophysics and 2Laboratory Medicine and Pathobiology, University of Toronto; 3The Campbell Family Institute for Breast Cancer Research, Princess Margaret Hospital; 4Department of Pathology, Toronto General Hospital, University Health Network, Toronto, ON, Canada

Metastases, invasion of cancerous cells to different parts of the body, is a major cause of deaths from breast cancer. In previous aCGH study, we identified amplification of 17q22-23 region among three other genomic regions associated with metastases from analysis of thirty-three breast cancer samples from patients with invasive duct carcinomas; we have obtained 300 more samples, which will be used to further validate the amplification of the regions. Within 17q22-23, four genes that might contribute to metastases were identified: COIL, WIPI1, TMEM100, and SLC16A6. We are investigating these genes to identify a possible target gene for therapeutic treatment on metastases.

Through rtPCR analysis using seven different breast cancer cell lines normalized to non-tumorigenic epithelial cell line (MCF10A) to examine mRNA expressions of the four genes, we identified that only WIPI1and COIL were expressed in all breast cancer cell lines.

WIPI1 plays a role in autophagy and is up-regulated in a variety of tumor cells; in clinical data obtained from 298 breast cancer patients, high expression of WIPI1 was associated with higher chance of survival and lower chance of experiencing breast cancer relapse. Thus, it does not seem that WIPI1 directly contributes to malignity of tumor cells.

COIL is found in Cajal bodies (CBs) and as well as in a diffuse nucleoplasmic pool. The role of diffuse COIL is yet unclear, but CBs, involved in formation of macromolecular complexes and found in cells with high transcriptional activity, require COIL for proper formation and localization. Clinical data obtained from 245 breast cancer patients revealed that high expression of COIL resulted in lower chance of survival and higher chance of relapse into cancerous state. It may suggest involvement of COIL in constituting malignant cancers, in which case COIL may be a potential therapeutic treatment target.

Western blot that investigated protein composition revealed high expression of WIPI1 in highly invasive cell lines and high expression of COIL protein in cell lines with higher proliferation index. In order to characterize the role of the genes in cancer metastases, WIPI1 expression will be elevated in SKBR-3 that had lowest expression and knocked down in BT-549 that had highest expression of WIPI1; likewise, COIL will be over-expressed in SKBR-3 that had lowest expression and knocked down in MCF-7 that had highest expression of COIL protein. Then, the transfected cells will be assayed on their ability to migrate and proliferate, which is critical in metastatic abilities.