A TIGER Visits Thailand

The first site visit for an international collaboration brings fresh perspectives on liver cancer.

(Photo: X. Wang, CCR)

Members of the TIGER-LC consortium at a clinical site in the Non Sang District

Of the two histological subtypes of liver cancer, hepatocellular carcinoma (HCC) is dominant throughout the world, except in Thailand, where cholangiocarcinoma (CCA) accounts for 70–80 percent of cases, particularly in the northeast province of Khon Kaen. One often proposed reason for this dubious distinction is the presence in this region of a parasite—a liver fluke, *Opisthorchis viverrini*, —whose eggs can be ingested with raw fish and develop into worms that persist in the liver for many years, causing inflammation and other complications which may eventually result in CCA.

The importance of this link is one of the many questions that are being addressed by the Thailand Initiative for Genomics and Expression Research in Liver Cancer (TIGER-LC), a collaboration between the Chulabhorn Research Institute in Thailand, CCR's Liver Cancer Research Group, and participating local institutions. The Initiative has enrolled more than 2,000 patients since 2012. In November 2014, members of the TIGER-LC consortium from the U.S. side, consisting of Anuradha Budhu, Ph.D., Staff Scientist, and Xin Wei Wang, Ph.D., Chief of the Liver Carcinogenesis Section in CCR's Laboratory of Human Carcinogenesis (LHC), along with Curtis Harris, M.D., Chief of LHC, Christopher Loffredo, Ph.D., Professor at Georgetown University Lombardi Comprehensive Cancer Center, and Robert Wiltrout, Ph.D., CCR Director, travelled for the first time to visit the local clinical sites where patients are being recruited.

"This provided us with a completely different perspective," said Wang. "We've read a lot of papers, but we couldn't have imagined a lot of the issues without seeing them first hand. For example, in Khon Kaen, we went to one of the major reservoirs located in the Non Sang District where the fish are caught. In the same locale, among 60,000 people who drink the same water and eat the same fish, one side of the village has a very high incidence of CCA; the other does not. It speaks to how detailed the analysis must be."

The visitors also learned about local campaigns to eradicate the liver fluke. Its lifecycle includes a snail that ingests the eggs from fecal matter before subsequently being ingested by fish. Local campaigns to control the snails include pesticides. "We have members of our group that can advise on these potent chemicals, some of which could be carcinogenic," said Wang. "We are including an analysis of chemical metabolites in urine to examine this link."

TIGER-LC grew out of a long-standing collaboration between the Chulabhorn Research Institute and NCI (See "Collaboration Reigns," *CCR connections* Vol. 4, No. 2). Ultimately, the initiative plans to enroll 5,000 people. The first of six proposed phases includes molecular profiling to establish biomarkers and genomic risk factors associated with HCC and CCA. The Chulabhorn Institute is responsible for coordinating patient recruitment with the five participating hospitals, and funding a national biobank and tissue repository. NCI is providing resources for data analysis and training.

"The study aims to be comprehensive," said Wang. "We want to analyze various etiologies including hepatitis, obesity, and dietary influences." As a result of the local visits, the group is also considering a dietary interventional study to see if local nutritional factors could quickly change the whole disease profile.

"I was humbled by our interactions with the local people," said Wang. "They were highly welcoming and wanted to help us in our efforts to help them."