

Workshop on the Etiology of Hepatocellular Carcinoma in the United States

In April, DCEG sponsored a workshop on the etiology of hepatocellular carcinoma (HCC) in the United States. The workshop, funded by the NIH Office of Rare Diseases Research, sought to assemble investigators of U.S. based cohort studies in order to form a HCC pooling project. The workshop was motivated by the recent increase in incidence of HCC in the United States. **Katherine A. McGlynn, Ph.D.**, a senior investigator in the Hormonal and Reproductive Epidemiology Branch, was the workshop organizer.

Dr. McGlynn opened the workshop by presenting an overview of the epidemiology of HCC in the United States. She noted that HCC, with an incidence rate of roughly 6.0 per 100,000 persons, is not a common tumor among the general U.S. population. HCC incidence, however, has been increasing for several decades. Between 1999 and 2006 in the U.S., liver cancer experienced the second greatest annual percent increase in incidence (2.3%) and the single greatest annual percent increase in mortality (2.0%) of all major cancers. These increases are particularly worrisome as liver cancer has an extremely poor prognosis. At only 13% among whites and 9% among blacks, liver cancer's 5-year survival rate is the third worst among major cancers. In high-rate liver cancer areas, such as eastern Asia and sub-Saharan Africa, the great majority (80%) of liver cancer is associated with either chronic infection with hepatitis B virus (HCV), chronic infection with hepatitis C virus (HCV) and/or consumption of foodstuffs contaminated with aflatoxin B₁. In low rate areas such as the U.S., a smaller proportion of liver cancer is explained by known risk factors.

Presentations on a number of novel HCC hypotheses were then made. **Ellen Chang, Ph.D.** of the Northern California Cancer Center discussed the evidence that sunlight exposure and vitamin D might be inversely related to the development of HCC. Dr. Chang also discussed the use of nonsteroidal anti-inflammatory drugs and HCC. Dr. Chang's presentation was followed by that of **Christina Persson, Ph.D.**, a postdoctoral fellow in the Hormonal and Reproductive Epidemiology Branch, who discussed the possible role of reproductive factors, hormones and hormonal medications in ameliorating the risk of HCC among women. **Fatma M. Shebl, M.D., Ph.D.**, a postdoctoral fellow in the Infections and Immunoepidemiology Branch, discussed the role of chronic inflammation in HCC. Dr. Persson then discussed the links between pesticide exposure and HCC and Dr. McGlynn reviewed the evidence that type II diabetes and related morbidities, such as obesity and metabolic syndrome, are precursor conditions for HCC. **Neal Freedman, Ph.D.**, a tenure-track investigator in the Nutritional Epidemiology Branch and **Rashmi Sinha, Ph.D.**, a senior investigator in the Nutritional Epidemiology Branch, led a round-table discussion of dietary risk factors for HCC.

As a result of the workshop, the HCC pooling project has been joined by 16 cohort studies from the NCI Cohort Consortium. Studies currently involved in the project are the NIH-AARP study, the Agricultural Health Study, the Breast Cancer Detection Demonstration Project Follow-up Study, the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, the U.S. Radiologic Technologists Cohort, the ACS Cancer

Prevention Study, the Health Professionals Follow-up Study, the Physicians' Health Study, the Nurses' Health Study, the Women's Health Study, the California Teachers' Study, the CLUE study, the Black Women's Health Study, the Iowa Women's Health Study, the NYU Women's Health Study and the Women's Health Initiative. All studies are providing questionnaire data for analysis, and studies that collected biosamples are providing serum. Approximately 1500 HCCs have developed among all cohort participants.