

cules in living cells, gene expression in particular, at the single-molecule level; and to develop new microscopy techniques for cellular imaging. Dr. Xie holds three patents and has published more than 70 journal articles. In 2003, he won the Raymond and Beverly Sackler Prize in the Physical Sciences

The nine recipients represent a broad spectrum of scientific disciplines, including quantitative and mathematical biology, pathogenesis, epidemiology and translational clinical research, molecular and cellular biology, integrative physiology, instrumentation, and bioengineering.

Applicants underwent a rigorous nomination and selection process to establish who among them appeared to hold the greatest potential for addressing critical scientific questions that would greatly impact biomedical science and health care. Nominees and applicants were expected to demonstrate a commitment to accepting considerable risk in addressing critically important scientific questions relevant to the mission of the NIH.

External evaluators representing a broad range of scientific disciplines screened approximately 1,000 nominations and recommended that a subset of 240 nominees be invited to submit award applications. Further review by

external evaluators resulted in the selection of 21 candidates, who were invited to the NIH for interviews and to present their ideas. The recommendations of the panel of external evaluators who interviewed the 21 candidates were considered by the Advisory Committee to the Director, NIH, and the NIH director.

The applicants were evaluated based on the following criteria: evidence of scientific innovation and creativity; testimony of intrinsic motivation, enthusiasm, and intellectual energy; and potential for scientific leadership and evidence of, or potential for, effective communication skills.

Hopkins Scientists Use Blood Proteins to Detect Ovarian Cancer

Johns Hopkins Kimmel Cancer Center researchers have designed a blood test to detect ovarian cancer using three proteins found in common in the blood of women with the disease. Their preliminary studies with the new test suggest a molecular signature exclusive to this deadly cancer, known for its ability to remain undetected and spread quickly.

The Hopkins test, described in the August 15, 2004, issue of *Cancer Research*, identifies the proteins as a truncated form of transthyretin, a fragment of ITIH4 and apolipoprotein A1, teased out with a rigorous evaluation of protein patterns present in blood samples from ovarian cancer patients at several US and international hospitals. Other research groups are evaluating ovarian cancer blood tests that use protein profiles consisting of tens of thousands of unidentified molecules.

This research was funded by the National Cancer Institute and CIPHERgen Biosystems of Fremont, California, which licensed the test.

The study, led by Daniel W. Chan, PhD, professor and director of the Biomarker Discovery Center, emphasizes that the test will not be commercially available for screening the population at large until completion of further validation studies in larger groups of patients. Even then, Chan notes, it is never going to be possible for a blood test to correctly diagnose 100% of can-

cerous tumors 100% of the time. They believe, however, that with some refinements, it may already have use for helping determine whether a pelvic mass is ovarian cancer.

In a systematic search to find the most promising blood proteins for their test, the Hopkins scientists conducted a multicenter study and used protein chip technology to screen 195 blood samples from two groups of ovarian cancer patients, healthy people, and patients with benign ovarian tumors. A sophisticated bioinformatics program was used to select proteins present at unusually high or low levels in ovarian cancer samples compared with normal patients or benign tumors. Samples in the two groups were analyzed separately to account for differences in patient populations and sample collection techniques. Then the researchers compared protein profile results in these two groups and ultimately narrowed the search for potential marker candidates to the three proteins, one of which (ITIH4) is commonly found at high levels in ovarian cancer and the other two at lower levels.

The new proteins were screened against a separate collection of blood samples from patients with normal and cancerous tissues. Of 23 patients with early-stage ovarian cancer, the three protein markers plus cancer antigen (CA) 125 correctly identified cancer

74% of the time (17 of 23) compared with 65% (15 of 23) with CA 125 alone. Although the sample size was too small for this difference to be statistically significant, the scientists conducted further studies, lowering the cutoff value for CA 125 to below current standards. The new test plus CA 125 and CA 125 alone detected 83% (19 of 23) of the cancers. In addition, the new test plus CA 125 correctly identified healthy samples 94% of the time (59 of 63) compared with 52% (33 of 63) for CA 125 alone.

To verify that the candidate markers were specific to ovarian cancer, the scientists also compared the results of the protein profiles with a separate group of blood samples from 142 Johns Hopkins ovarian, breast, colon, and prostate cancer patients and healthy people. Protein markers from these ovarian cancer samples matched those from the other two groups of blood samples. Breast, colon, and prostate cancer samples exhibited levels of the three proteins closer to those of normal patients, indicating that the markers may be exclusive to ovarian cancer.

The scientists will conduct further studies to map all three proteins to the genetic pathways linked to ovarian cancer development and combine the blood test with radiologic tools, such as ultrasonography. They also will search for more proteins to add to the current panel of markers.