Use of Proteomics for Ovarian Ca Spurs Debate

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S
ystematic bias in the design of several
underlying studies raises doubt over
whether serum proteomics, a permeating
research field that has shown promise in
early detection of ovarian cancer, can act as a
useful complement to the current standard of
care, a spectrum that includes pelvic examina-
tions and transvaginal ultrasounds.

Several researchers are investigating
whether serum proteomics can function as a
useful tool in the early detection of ovarian
cancer. The approach involves measuring
differences in the levels of proteins in
serum samples from ovarian cancer patients
and healthy controls. If such differences can
be validated and reproduced, serum proteo-
mics may provide an alternative method for
discriminating between ovarian cancer pa-
tients and healthy controls.

The researchers, both of the University
of Texas M.D. Anderson Cancer Research
Center, Houston, have been unable to re-
produce the high sensitivity and specifi-
city rates reported in a 2003 study of the

The problem, said Keith A. Baggerly,
Ph.D. and Kevin R. Coombes, Ph.D., lies not in
the fundamental concept—that cancer-shed
proteins in serum may be able to identify
patients who have even very early-stage
cancer—but in the way the data sets
were processed in both the 2002 and 2004
studies.

In a letter to the editor, Dr. Baggerly
contented that a better decoding of the
mass spectrometry data may be necessary to
distinguish between patients with ovarian
cancer and healthy controls.

“We’re not saying proteomics doesn’t work. It may very well work. But these data sets can’t be used to say this approach works,’’ Dr. Baggerly said in an interview. “It may very well work. But these data sets can’t be used to say this approach works.’’

The method involves using mass spec-
trometry to display proteins in serum as a
series of peaks and valleys of varying
strength. A computer-driven mathematical
algorithm finds unique patterns associated
with ovarian cancer, two independent bio-
statistics studies found.

The researchers then chose 18 random
protein peaks from the same regions of
spectral data as Dr. Zhu’s peaks. The ran-
dom peaks separated cancer samples from
controls up to 56% of the time, depending on
the strength of the signals used.

Because the pattern of protein
expression was inconsistent between the
data sets, they concluded, the values
did not represent biologically
important changes in the serum of ovarian
cancer patients.

“We ran all the controls on one day and
all the cancers on the next day,” Dr.
Baggerly said. “This is the worst kind of
design when you are using a machine that
can be subject to external factors,’’ such as
changes in calibration or mechanical
degradation.

In fact, he said, a June 2004 study in
which Dr. Petricoin participated also suf-
f ered from just such a problem (Endoc. Re-
l. Cancer 2004;11:163-78). This study
used a different mass spectrometer, which
began to break down on day 3 of running.

“We would be surprised if the experi-
mental design could be repeated under
these conditions” Dr. Baggerly said. “We
cannot detect whether the cancer
expression was inconsistent between the
data sets, they concluded, the values
did not represent biologically
important changes in the serum of ovarian
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The problem, Dr. Baggerly
asserts, is that Dr. Zhu
processed the serum samples in a nonrandomized way that
likely inflated their results.

“If we cannot reproduce the high sen-
sitivity and specificity rates reported in a
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households, the expected difference in the
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