Improving Prenatal Testing

A DNA chip could make it easier to diagnose rare conditions while the patient is still in utero.

by **Rachel Kremen** December 1, 2008

Many pregnant women have their unborn children screened for genetic abnormalities, such as Down syndrome. But standard tests cannot identify all problems, and many extremely serious conditions go undetected until birth. In a new study, researchers from the Baylor College of Medicine in Houston used DNA chips to test unborn babies for more than 270 genetic syndromes. They found that this procedure provided a more detailed and accurate view of the fetus's genetic profile than the approach commonly used today.

Arthur Beaudet, who led the study with Cheung and is chair of Baylor's Department of Molecular and Human Genetics, says some parents want an early diagnosis so they can decide whether or not to terminate a pregnancy. Others simply want the information to prepare for their child's special needs.

The DNA chip used in the study performs a process known as array comparative genomic hybridization (aCGH), which involves looking for an abnormal number of copies of particular segments of DNA. Normally, humans have two copies of each segment. Having extra or missing copies can result in serious medical problems. Each DNA chip contains hundreds of single-stranded DNA segments, each embedded in a piece of glass at a precise location. The researchers then add single-stranded, fetal DNA segments, usually taken from amniotic fluid. These strands are labeled red. Single-stranded DNA reference segments, which act as a control group and are labeled green, are also added to the chip. Once the fetal and control strands are bound with the embedded DNA, the arrangement of colors on the chip is imaged and analyzed by a computer.

“Basically we measured the color signal intensity,” said Cheung. If the fetus has an extra copy of a particular segment of DNA, then the spot on the chip that corresponds to that DNA segment will appear more red than green. If the fetus is missing a DNA segment, the corresponding spot on the chip will appear more green than red. And if the fetus has the correct number of copies of the DNA segment, then the spot should appear yellow.

Beaudet says that aCGH is already used in pediatric medicine with great success, but it has only recently been investigated for prenatal diagnostics. While the Baylor study sample was small–only 300 cases–the researchers say it is the largest of its kind to date. In the study, published in the current issue of Prenatal Diagnosis, the researchers identified seven cases where the aCGH results provided new information about the risk of disease, including two cases that would otherwise have been missed.

"In general, it’s a great study,” said Dr. David Chitayat, head of the Prenatal Diagnostic and Medical Genetics Program at Mount Sinai Hospital in Toronto, Canada. “But we need to expand it.”

Most of the patients involved in the study sought out the testing because of advanced maternal age. Chitayat says he would like to see results for a wider array of patients. Chitayat was not involved in the Baylor study, but he’s working on another research project involving aCGH for prenatal diagnosis, and he hopes to publish the results soon.

As with any prenatal diagnostic testing, aCGH brings with it a host of questions about how much information is too much.

“The downside of aCGH is you pick up these copy-number variants that may or may not have clinical significance, and in the worst case [the impact] may be unknown,” says Diana Bianchi, professor of pediatrics, obstetrics, and gynecology at Tufts University School of Medicine and the editor in chief of Prenatal Diagnostics. Knowing that an unborn child has genetic abnormalities but not knowing how those might affect the child’s development could leave many parents scared and confused, Bianchi says.

Price is another factor that could impede the use of aCGH. Beaudet says that an array currently costs $1,600. That’s far more than a karyotype, which costs between $500 and $700. (The tests reported in the study were performed on a fee-for-service basis.) But Beaudet believes the price of an array could drop significantly if the volume of tests performed increases.

Currently, karyotyping and aCGH also require invasive procedures–either extracting amniotic fluid or going into placental tissue–to retrieve samples for testing, and miscarriage can result. “The next big breakthrough would be to be able to [test] a maternal blood sample or a maternal Pap smear,” says Beaudet, so th baby wouldn’t be put at risk. Several research teams are currently working on techniques for isolating cells that float around in a pregnant woman’s bloodsttream.