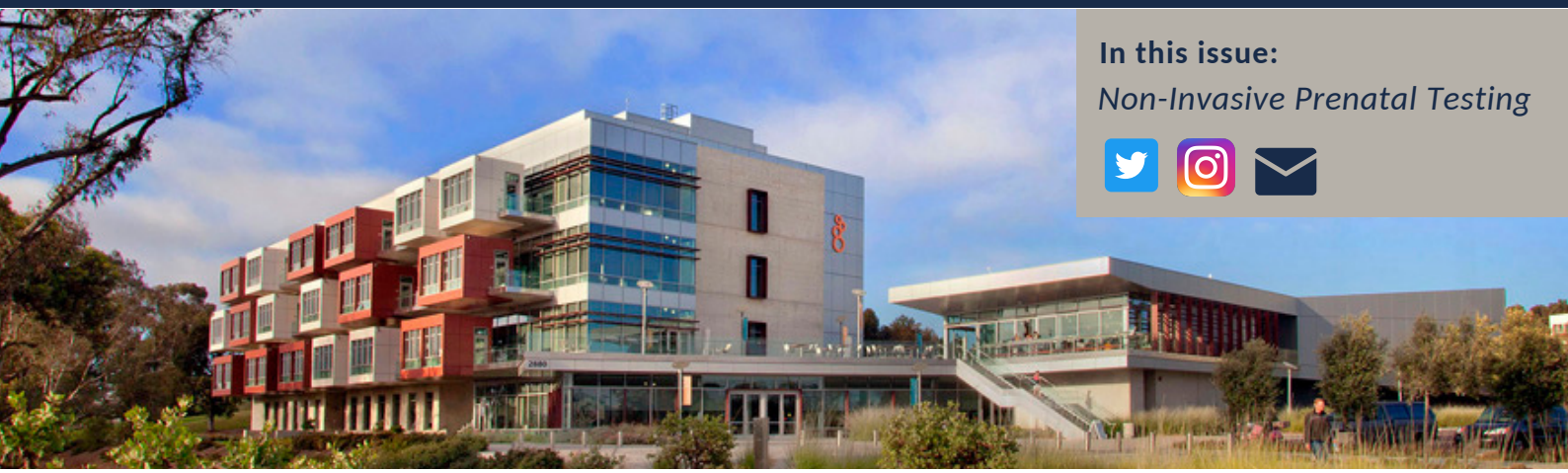
UC San Diego Health

Center for Perinatal Discovery

Community Newsletter - May 2022



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Center Updates & Events

Congratulations to the 2022-2023 Center for Perinatal Discovery Pilot Project Grant Recipients!

Dr. Kathleen Fisch

"Impact of aspirin resistance on adverse perinatal outcomes in high-risk pregnancies"

Dr. Priya Pantham

"Single-cell RNA Sequencing of Proximal Tubule Cells in Response to Placental Extracellular Vesicles in Preeclampsia"

Center for Perinatal Discovery Annual Symposium (google form) - Register Now!

Check out our upcoming monthly seminars (CPD Website)
First Wednesday of Every Month, 12:00 PM

In the News - Preeclampsia and Preterm Birth (leaps.org)
Learn about how scientists are trying to better understand preeclampsia and preterm birth.

If you are not already a CPD member and would like to receive this newsletter, please contact perinataldiscovery@health.ucsd.edu to be added to our mailing list.

Three Perspectives on Non-Invasive Prenatal Testing

Non-Invasive Prenatal Testing (NIPT) is a sensitive screening tool in prenatal testing that reveals information about a baby through its mother's blood. This tool is helpful in picking up abnormalities in the number of chromosomes a fetus has (called aneuploidies) or determining the sex of the baby.

While NIPT can provide valuable information to pregnant patients and their healthcare providers, it has also sparked controversy. Commercial testing offering detection of very specific and rare conditions, which is beyond standard medical practice, has become available. Most patients do not realize that the prevalence of a condition affects the predictive value for tests for that condition – in other words, the exact same test will have a lower positive predictive value when used in a population where the target disease is rarer compared to a population where the disease is more common. Because some parents may choose to end a pregnancy due to abnormal results, it is important that NIPT is regarded as a preliminary screening tool first and foremost. Parents are advised to undergo a diagnostic test called an amniocentesis if an abnormal result is found.

Researcher Perspective

Dr. Louise Laurent, Professor of Obstetrics, Gynecology and Reproductive Sciences at UC San Diego, was interviewed to explain how NIPT works, and its benefits and limitations.

The placenta is a unique organ formed during a pregnancy that helps deliver oxygen and nutrients to the baby. The placenta grows from the same cells as the baby, and sheds genetic information (DNA) into the mother's blood circulation.

"Because of this," Dr. Laurent explains, "NIPT allows us to sample the placental DNA that makes up approximately 4% to 12% of the DNA in the mother's blood sample, and the results will reflect the DNA of the baby." Occasionally, the amount of fetal DNA in a mother's blood sample is too low, and the laboratory will ask for another sample; if the amount of fetal DNA is too low in this second sample, the lab will not be able to provide a valid result.

NIPT can be used to test at three levels of genetic resolution: at the chromosome level; the microdeletion level; and the single-gene level.

The most common type of NIPT is performed on the chromosome level, and therefore is designed to detect aneuploidies. This type of test matches sequences of DNA found in the mother's blood to a list of known sequences on each of the 23 pairs of chromosomes that humans have. If there are a greater than expected number of sequences for a certain chromosome in the mother's blood, this will indicate that there is an extra copy of that chromosome. For example, if there are extra sequences for Chromosome 21, this indicates that the fetus may have Down Syndrome.

"If people want to go down that path of prenatal testing, it should be presented as a choice, always a choice, and the intent and value of the test should be presented."

-Diana De Rosa, patient

Tests for microdeletions aim at detection of mutations that are smaller than chromosomes but bigger than single genes. Because the microdeletions that are tested for are generally rarer than the aneuploidies that are reported on, the predictive value of the microdeletion tests are correspondingly lower.

As the name suggests, a single gene analysis looks at only one gene at a time. The performance of this kind of test also depends on the prevalence of the condition that is being tested for. In addition, because single genes are very small, the amount of DNA corresponding to that gene in a mother's blood samples is very low, and this can decrease the performance of the test.

"NIPT is fairly new," says Dr. Laurent, "but it has changed OB practice a lot. Before NIPT was available, the only option for pregnant patients at moderate to high risk of fetal aneuploidy was amniocentesis, where we collect a small amount of amniotic fluid from around the baby to send to the lab. Amniocentesis is the most accurate approach to prenatal testing, but does involve a small risk of miscarriage, so many patient would prefer to start with a safer non-invasive method." UC San Diego was one of the sites that participated in the early clinical studies that established the accuracy of NIPT, and as it was phased into practice, it drastically reduced the number of amniocentesis procedures.

For general screening of low-risk pregnancies, the standard of care includes NIPT for the most common aneuploidies (Chromosomes 21, 18, and 13). Dr. Laurent emphasizes that even though the application of NIPT to detection of microdeletions or single-gene mutations is an active area of research, and is increasing in accuracy, it will remain very important to consider the clinical context before recommending one of these higher-resolution tests. This is because the predictive value of the same test is lower in a population where the disease is rarer.

Clinician Perspective

Some patients may have strong feelings when considering whether or not to receive an NIPT test, but considering the wide array of options that are possible, there can also be a lot of stress and deliberation in making the choice to undergo this kind of screening.

Lauren Korty is a prenatal genetic counselor at the Maternal Fetal Care and Genetics Clinic at UCSD. She has been a genetic counselor since 2007 and specializes in prenatal genetic counseling.

A large part of Korty's job is to review family histories, understand the probabilities of genetic abnormalities, and discuss the limitations and benefits of genetic testing to families. She has helped many patients through the decision to use prenatal testing and to understand the results. Ultimately some patients may opt to not move forward with NIPT, but the decision heavily weighs on what is best for the individual and what they are comfortable with.

"Ideally, I am able to provide reassurance to patients, especially those 35 or older who are at higher risk for genetic abnormalities," Lauren says, discussing the greatest impact her work has on her patients. All patients 35 or older are encouraged to use NIPT, but as of this year, the American College of OBGYN recommends that NIPT for aneuploidy screening is offered and recommended to all pregnant patients regardless of their risk levels.

When looking at NIPT for detection of microdeletions or single gene mutations, Lauren's approach is very individualized, and based on the individual baby and mother and their risks.
"For NIPT for microdeletions, most patients will get an accurate, negative result, which will be reassuring to them" says Lauren, "But with any screening test, there is a small chance of a false positive which may lead to unnecessary invasive testing." Korty stresses that it is important that if you do get a positive result through NIPT, you should meet with a genetic counselor, who will explain the result in detail, go over your options, and help you through the process of making decisions regarding your pregnancy.

Patient Perspective

Diana De Rosa is a patient with a unique perspective. She is a genetic counselor, and a patient over 35 who was referred to genetic counseling. She feels that being able to be counseled with her spouse on the ins and outs of NIPT was very beneficial.

De Rosa finds that the test is complicated if you begin including rare conditions, and doctors do not have the time to explain what every result means, so meeting with a genetic counselor is often the best option, especially if you get a result that is abnormal.

"You do not have to get lost in trying to understand what every result means, which is very reassuring," she says.

When it came to the decision to use NIPT, she initially thought she wanted to only do the basic aneuploidy test. However, as time went on, fear began to creep in. "My fear of being blindsided by an abnormality was maybe bigger than the stress of understanding all of the results," said De Rosa. She debated with her spouse about all of the outcomes and they decided to use a test called MateriniT Genome, offered at the time by the company Sequenom, which reports on more chromosome abnormalities.

While De Rosa and her spouse have no regrets about this process, she says that it is so important to think through what going through any sort of prenatal test means. "I wanted the full picture of what I was getting myself into," she said, "but pregnancy weeks are long, and if anything came up positive, it would be so difficult to have to wait to get an amniocentesis for conclusive results."

De Rosa stresses the importance of informed consent. “If people want to go down that path of prenatal testing, it should be presented as a choice, always a choice, and the intent and value of the test should be presented,” says De Rosa. “There is so much to stress about during a pregnancy, and it can be really devastating to have information like this.”

On the topic of commercial testing, she comments that the market driven world of commercial testing is not the same as a conversation with a doctor, and genetic tests are not subject to regulatory oversight the way medication or devices are. She feels that the industry can sometimes push what is offered and recommended ahead of evidence based practices, and the field is so fast moving that it is hard to regulate. As a patient and as a counselor, she recommends that anyone considering complex prenatal testing should talk to a genetic counselor to become more informed.

Overall, all three of our panelists judge that NIPT tests, especially NIPT tests for aneuploidies, are highly accurate, but it should be understood that they are screening tools. When used for detection of rare microdeletions or single-gene disorders, the rates of false positive results can be high. It is highly advised that a patient talks to a genetic counselor to weigh their options, including the types of results they may receive, before moving forward with an NIPT test.

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