RESEARCH SUBJECT CONSENT FORM

TITLE: Single center, prospective, blinded, non-selection study to validate a non-invasive preimplantation genetic test (niPGT-A) for embryo aneuploidy in the spent blastocyst media (SBM) for clinical outcome.

PROTOCOL NO.: NGG001
WCG IRB Protocol #20214749

SPONSOR: NextGen Genetics

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STUDY RELATED PHONE NUMBER(S): 408-503-6484

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research.

Why is this research being done?

The purpose of this research is to further investigate noninvasive PGT-A (niPGT-A) and its feasibility as a clinical test.

What should I know about this research?

- Taking part in this research is voluntary.
- If you don't understand, ask questions.

How long will I be in this research?

We expect that taking part in this research will last until transfer of any/all embryo(s) deemed appropriate by you and your IVF physician following standard PGT-A and reported outcome from those transfer(s) (i.e., pregnant or not pregnant).

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, you can demonstrate your interest in participating by signing this consent form. Once consented, your IVF group will be

notified, and following embryo biopsy, samples of the spent culture media collected and sent to NextGen Genetics laboratory.

Could being in this research hurt me?

In agreeing to participate in this research, no part of your IVF and PGT-A cycle is expected to be impacted.

Will being in this research benefit me?

It is not expected that you will personally benefit from this research. Possible benefits to others include the possibility of having noninvasive PGT-A as an option for future patients.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

What should I know about this research?

- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to further investigate noninvasive PGT-A (niPGT-A).

Extra or missing chromosomes, also called chromosomal aneuploidies, are highly associated with spontaneous miscarriages in human pregnancies, and can prevent implantation or result in abnormal offspring. The study and selection of embryos prior to transfer is a key step for the success of infertility treatments in assisted reproduction. At present, trophectoderm biopsy plus next generation sequencing (NGS) is the most common approach to determine the chromosomal status of preimplantation embryos, what is called Preimplantation Genetic Testing for Aneuploidy (PGT-A). This process requires specific equipment and trained personnel that add cost and risks. Thus, the development of a non-invasive technique is sought as an alternative.

It has been reported in previous studies that the liquid the embryo is cultured in contains traces of embryonic cell free DNA (cfDNA) that reflects the DNA of the embryo. This liquid is called the culture media, and once embryo culture is complete, it is “spent culture media”. Typically, this media is discarded after the embryo is done

growing in it. Other studies show a range of concordance between results when comparing the DNA from this spent culture media to that of the trophectoderm biopsy used in standard PGT-A.

The main objective of this project is to validate a new non-invasive method for PGT-A, based on improved collection and analysis of the culture media to achieve higher rates of sensitivity and specificity and to decrease the effect of some inherent difficulties of sample collection and testing.

Test Method and Design

This is a prospective, analytical, observational study, in which spent culture media will be collected from embryos coming from patients who already have PGT-A as part of their care plan and scheduled to have trophectoderm biopsy. To determine the chromosomal status of the embryos, the trophectoderm biopsy will be analyzed by PGT-A, where biopsy is required to obtain the sample and then is sequenced by NGS.

For this study, your IVF group will be using intracytoplasmic sperm injection (ICSI), as well as making sure the oocytes are thoroughly cleaned of other cells prior to fertilization. Any cells obtained during this cleaning will be collected and used as a reference sample. It is crucial to remove all other cells from the oocyte to minimize the risk of extraneous DNA.

The culture medium where the embryos are grown from either day 1 (D1) of development until biopsy or day 3 of development (D3) until biopsy will be collected (on D5 or later). This study design imposes a small change in the standard protocols of embryo handling but will not involve any change in the treatment offered to the patient. The analysis of the spent culture media will follow the new protocol we aim to develop and will not be part of the PGT-A results. The media samples collected are not returnable.

NextGen Genetics will receive PGT-A media samples for analysis that have been deidentified and uniquely numbered. Samples are shipped frozen. The spent culture media samples will be analyzed using Next Generation Sequencing (NGS) with a modified protocol (VeriSeq, Illumina) or (ReproSeq, Thermofisher) to look for aneuploidies. Validation for NGS has been performed on single cell samples (S. Bono. at all Prenatal diagnosis 2015, 35, 938-944). About 200 subjects will take part in this research.

Deidentified results from both trophectoderm biopsy and spent culture media will be compared. As trophectoderm biopsy is the current standard of care, these results will continue to be provided under the current testing protocol and considered the gold standard. This research will not interfere with those results or the transfer decisions between provider and patient, but elective single embryo transfer (eSET) based on current invasive PGT-A testing is a study requirement.

Confidential Reporting Practices

NextGen Genetics keeps test results confidential and is in compliance with all Health Insurance Portability and Accountability Act (HIPAA) regulations. NextGen Genetics will release your results only to your designated IVF physician or his or her designee unless otherwise directed by you (or a person legally authorized to act on your behalf) in writing, or as otherwise required by federal and state laws.

How long will I be in this research?

We expect that your part in this research will last until transfer of any/all embryo(s) deemed appropriate by you and your IVF physician following standard PGT-A has occurred and reported outcome from those transfer(s) (i.e., pregnant or not pregnant) sent to NextGen Genetics.

What happens to me if I agree to take part in this research?

- Spent culture media sample collection will happen at your IVF group and samples shipped to NextGen Genetics. You do not need to do anything differently than planned for your PGT-A cycle.
- Testing may be performed on any or all spent culture media samples received. These results will then be compared to the standard PGT-A results of this sample.
- Participating in this research will not affect your PGT-A testing ordered and performed by our clinical laboratory

This research involves the laboratory team being blinded to which patient sample they are studying. Your samples will be deidentified prior to NextGen Genetics reviewing, testing, or studying results. Testing will be performed via next generation sequencing, where the lab will study the DNA present in the spent culture media from the embryo. Results from this research will not be made known to you.

The principal investigator has a financial interest in the company that is sponsoring this research. Steps have been taken to ensure the integrity of all the data collected as well as ensure privacy of the participants. If you have any questions about this financial interest, please contact the study team.

What are my responsibilities if I take part in this research?

If you take part in this research, you will have no additional responsibilities during your standard PGT-A cycle. Following your cycle and transfer of any embryos, we will request follow-up data, such as but not limited to, whether there is a positive pregnancy test, and the results of any prenatal testing such as CVS or amniocentesis.

Could being in this research hurt me?

There are no anticipated risks from this research to you or any future pregnancy. For any questions regarding IVF and PGT-A for which you have consented to as part of your care and unrelated to this research, please address any questions to your clinical care team. Embryos appropriate for transfer will be determined via standard PGT-A protocol and results and transfer decisions will not be impacted by this study.

Will it cost me money to take part in this research?

There will be no cost to you to take part in this research

Will being in this research benefit me?

There are no direct benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, benefits to others include the possibility of noninvasive PGT-A as an option for their care. By participating, you are helping to give future patients more choice during their IVF cycle.

What other choices do I have besides taking part in this research?

You do not have to participate in this research. Your alternative is to decline to participate.

What happens to the information collected for this research?

Your private information and part of your medical record may be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsors
- People who work with the research sponsor
- WCG IRB, the Institutional Review Board (IRB) that reviewed this research

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or clientcare@wcgclinical.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

Can I be removed from this research without my approval?

The person in charge of this research may remove you from this research without your approval or notification. Possible reasons for removal may include if follow-up data is not available for your case, it is in your best interest, or the research is canceled.

What happens if I agree to be in this research, but I change my mind later?

If you decide to leave this research, contact the research team so that the investigator can address your request to remove your samples from the study. Your request will need to be documented in writing.

Will I be paid for taking part in this research?

You will not be paid for taking part in this research.

Patient Consent

I have read or have had read to me the complete consent form and have had the opportunity to ask questions that I might have about the testing, the risks and benefits and the alternatives prior to my informed consent.

I acknowledge that this niPGT-A testing with NextGen Genetics is not a replacement of the current gold standard of invasive PGT-A. Results from this study will not replace my PGT-A results. Results of this testing may be presented in aggregate at scientific or medical meetings or published in scientific journals or other publications, however, identity will not be disclosed.

Your signature documents your consent to take part in this research.

Patient:
Print: _____ Sign:_____ Date:_____

Partner(if applicable):
Print:_____ Sign:_____ Date:_____

Administrative Use Only:
Assigned Case ID: _____