**American Society for Reproductive Medicine 2019 Scientific Congress & Expo**
***October 12 to 16, 2019 ● Philadelphia, PA, USA***

**Title:**

# DO INFERTILE PATIENTS WHO TEST POSITIVE FOR GROWTH DIFFERENTIATION FACTOR 9 (GDF9) POLYMORPHISM C447T EXHIBIT AN ALTERED RESPONSE TO CONTROLLED OVARIAN HYPERSTIMULATION (COH)?

**Authors:**

Jenna Friedenthal, MD[1,2], Dmitry Gounko, MA[2], Joseph A. Lee, BA[2], Teresa A. Cacchione, MS, CGC[2] and Alan B Copperman, MD[1,2]

**Affiliations:**

1. Icahn School of Medicine at Mount Sinai, Klingenstein Pavilion 1176 Fifth Avenue 9th Floor New York, New York, United States, 10029

2. Reproductive Medicine Associates of New York, 635 Madison Ave 10th Floor New York, New York, United States, 10022

## Objective:

GDF9 is a protein coding gene responsible for promoting granulosa cell proliferation while inhibiting FSH-induced steroidogenesis [1]. GDF9 also potentiates the final stages of follicle growth and supports metabolic cascades such as sterol biosynthesis. Single nucleotide polymorphisms (SNPs) in GDF9 are associated with an increased risk for primary ovarian insufficiency and diminished ovarian reserve [2].Fertilome®, a multigene panel test, reports GDF9 SNPs as part of a multigene targeted sequencing panel and is often suggested in poor responding patients. We sought to evaluate ovarian stimulation outcomes in patients who tested positive for the GDF9 SNP C447T.

## Design:

Retrospective cohort study

## Materials and Methods:

The study included patients at a single academic center who underwent COH and Fertilome® testing from 2016 to 2018. Cases included patients who screened positive for the GDF9 SNP

C447T. Control cases included patients who screened negative. Patients testing positive for a Fragile X premutation or abnormal karyotype were excluded. Our primary outcome was number of oocytes retrieved. Secondary outcomes were number of metaphase II (MII) oocytes, number of fertilized oocytes, blastulation rate, and euploidy. Data were analyzed using student's t-test, with $p<0.05$ considered significant.

**Results:**

A total of 96 patients who underwent 214 COH cycles and Fertilome® testing were assessed in the study. A total of 80 patients (170 cycles) tested positive for the GDF9 SNP C447T, while 16 patients (44 cycles) tested negative for the GDF9 SNP. Although there was a difference in BMI between groups (23.59 vs 21.42, P = 0.0005), no differences in age or AMH were observed. We demonstrated no differences in the total number of oocytes retrieved or MII oocytes. Last, there was no difference in the fertilization, blastulation, or embryo euploidy between groups.

**Conclusion:**

A majority of patients who experienced poor response to IVF stimulation tested positive for the GDF9 SNP C447T. However, the presence of the SNP did not affect oocyte retrieval count or MII maturation. Thus, although the GDF9 gene may be important in follicular development and maturation, detection of SNP C447T is not associated with worse outcomes during COH. Patients can be reassured that testing positive for the SNP C447T does not translate to impaired ovarian stimulation and oocyte retrieval outcomes.

| | GDF SNP positive | | GDF9 SNP negative | | |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | p-value |
| Oocytes retrieved | 12.70 | 7.72 | 11.30 | 6.50 | 0.27 |
| MII oocytes | 9.27 | 5.65 | 8.18 | 5.30 | 0.25 |
| Fertilized oocytes | 6.86 | 5.23 | 5.72 | 5.03 | 0.20 |
| Blastocysts | 4.57 | 4.51 | 3.86 | 4.82 | 0.36 |
| Blastulation rate (%) | 60.82 | 31.49 | 55.88 | 38.3 | 0.38 |
| Euploidy (%) | 45.97 | 36.87 | 47.62 | 39.57 | 0.85 |