In addition to looking exclusively at genomic information, by combining genetic information (e.g., polymorphisms, mutations, etc.) with phenotypic and/or environmental data, methods of the invention provide an additional level of clinical clarity. For example, polymorphisms in genes discussed below may provide information about a disposition toward premature ovarian failure. However, in certain cases, the clinical outcome may not be determinative unless combined with certain phenotypic and/or environmental information. Thus, methods of the invention provide for a combination of genetic predispositional analysis in combination with phenotypic and environmental exposure data in order to assess the potential for egg quality and viability; as well as the likelihood of continued viability as the woman ages.

In one example, a genetic predisposition to ovarian failure is determined, and an assessment of the impact of the genetic predisposition is made. If the genetic analysis is indeterminant, then the genetic data are combined with phenotypic and/or environmental data in order to inform the clinical indication. For example, if it is determined that a woman's egg cells produce a protein variant that is known to potentially cause an autoimmune response, that information may be combined with phenotypic data in order to determine whether an autoimmune response leading to premature ovarian failure is likely. If it is determined that an autoimmune response is likely, eggs can be harvested or ovaries can be preserved for later use.

Thus, in certain cases, genetic predisposition may be sufficient to make a diagnosis, but in other cases, the clinical outcome may not be clear based upon genetic analysis alone and the combination of genetic and phenotypic or environmental data must be used in order to assess the likelihood of ovarian failure and egg quality.

Certain aspects of the invention provide methods for assessing infertility in a mammal that involve conducting an assay to determine presence or absence of a mutation in a plurality of genes selected from Table 1 in which the presence of a mutation in at least two of those genes is indicative of poor egg quality or infertility. In particular embodiments, the assay is conducted on all of the genes from Table 1. Mutations detected according to the invention may be any type of genetic mutation. Exemplary mutations include a single nucleotide polymorphism, a deletion, an insertion, an inversion, other rearrangements, a copy number variation, or a combination thereof.

In one aspect, this invention provides a method for assessing infertility, the method comprising: conducting an assay on a sample obtained from a female subject to determine presence of at least one mutation in a plurality of genes selected from Table 1; determining

one or more phenotypic traits or environmental exposures of the female subject selected from Table 2; comparing the mutations and the phenotypic traits or environmental exposures of the female subject with a set of predictor variables that are correlated with infertility, wherein the predictor variables are weighted, comprise at least mutation present in one or more genes listed in Table 1 and at least one phenotypic trait or environmental exposure listed in Table 2, and are determined from an association analysis of genetic data obtained from an infertile patient population and an association analysis of phenotypic traits or environmental exposures of the infertile patient population; and using the comparison to determine infertility of the female subject.

In another aspect, this invention provides a method for assessing infertility, the method comprising: conducting an assay on a sample obtained from a female subject to determine one or more mutations in one or more genes of the female subject; determining one or more phenotypic traits or environmental exposures of the female subject; comparing the mutations and the phenotypic traits or environmental exposures of the female subject with a set of predictor variables that are correlated with infertility, wherein the predictor variables are weighted, comprise mutations present in one or more genes and phenotypic traits or environmental exposures, and are determined from an association analysis of genetic data obtained from an infertile patient population and an association analysis of phenotypic traits or environmental exposures of the infertile patient population, and; using the comparison to determine infertility of the female subject.

Any method of detecting genetic mutations is useful with methods of the invention, and numerous methods are known in the art. In certain embodiments, sequencing is used to

What is claimed is:

1. A method for assessing infertility, the method comprising:

conducting an assay on a sample obtained from a female subject to determine presence of at least one mutation in a plurality of genes selected from Table 1;

determining one or more phenotypic traits or environmental exposures of the female subject selected from Table 2;

comparing the mutations and the phenotypic traits or environmental exposures of the female subject with a set of predictor variables that are correlated with infertility, wherein the predictor variables are weighted, comprise at least mutation present in one or more genes listed in Table 1 and at least one phenotypic trait or environmental exposure listed in Table 2, and are determined from an association analysis of genetic data obtained from an infertile patient population and an association analysis of phenotypic traits or environmental exposures of the infertile patient population; and

using the comparison to determine infertility of the female subject.

2. The method according to claim 1, wherein the mutations are selected from the group consisting of: a single nucleotide polymorphism; a deletion; an insertion; a rearrangement; a copy number variation; and a combination thereof.

3. The method according to claim 1, wherein the assay comprises sequencing.

4. The method according to claim 3, wherein sequencing is sequencing-by-synthesis.

5. The method according to claim 1, wherein the assay is conducted on all of the genes from Table 1.

6. The method according to claim 1, wherein the sample is a tissue or body fluid.

7. The method according to claim 1, wherein prior to the conducting step, the method further comprises enriching the sample for the plurality of genes from Table 1.

8. A method for assessing infertility, the method comprising:

conducting an assay on a sample obtained from a female subject to determine one or more mutations in one or more genes of the female subject;

determining one or more phenotypic traits or environmental exposures of the female subject;

comparing the mutations and the phenotypic traits or environmental exposures of the female subject with a set of predictor variables that are correlated with infertility, wherein the predictor variables are weighted, comprise mutations present in one or more genes and phenotypic traits or environmental exposures, and are determined from an association analysis of genetic data obtained from an infertile patient population and an association analysis of phenotypic traits or environmental exposures of the infertile patient population, and;

using the comparison to determine infertility of the female subject.

9. The method according to claim 8, wherein the genes are maternal effect genes.

10. The method according to claim 9, wherein the maternal effect genes are from Table 1.

11. The method according to claim 8, wherein the assay comprises sequencing.

12. The method according to claim 11, wherein the mutations are selected from the group consisting of: a single nucleotide polymorphism; a deletion; an insertion; a rearrangement; a copy number variation; and a combination thereof.

13. The method according to claim 8, wherein the phenotypic traits or environmental exposures are selected from at least one trait in Table 2.

14. The method according to claim 8, wherein the sample is a tissue or body fluid.

15. The method according to claim 14, wherein prior to the conducting step, the method further comprises enriching the sample for one or more genes.