Claims

1. A method to identify one or more pharmacogenomic biomarkers, which method comprises:

a) isolating DNA from archived clinical samples of at least two patients exhibiting different values in a relevant phenotype;

b) amplifying said isolated DNA;

c) obtaining high-density genotyping data of said amplified DNA by using a genome-wide genotype calling algorithm, wherein the call rate cut-off value of the genome-wide genotype calling algorithm is less than about 80%; and

d) performing association analysis based on said genotyping data and said different values in said relevant phenotype,

wherein said pharmacogenomic biomarker(s) are identified.

2. ~~The method of claim 1,~~ A method to identify one or more pharmacogenomic biomarkers, which method comprises:

a) isolating DNA from archived clinical samples of at least two patients exhibiting different values in a relevant phenotype;

b) amplifying said isolated DNA;

c) obtaining high-density genotyping data of said amplified DNA; and

d) performing association analysis based on said genotyping data and said different values in said relevant phenotype,

wherein said pharmacogenomic biomarker(s) are identified, and wherein the archived clinical samples are selected from the group consisting of plasma samples, serum samples, dried blood spots, urine samples, ~~tissue samples,~~ tumor cells, and buccal swabs.

3. The method of claim 1 or 2, wherein the archived clinical samples are plasma samples or serum samples.

4. The method according to any one of claims 1-3, wherein the isolated DNA is suboptimal genomic DNA.

5. The method according to any one of claims 1-4, wherein the amplification is whole-genome amplification (WGA), and the resulting DNA is whole-genome amplified DNA (wgaDNA).

6. The method according to any one of claims 1-5, wherein the high-density genotyping is whole-genome genotyping.

7. The method according to any one of claims 1-6, wherein the high-density genotyping is by using single nucleotide polymorphisms (SNPs).

8. The method according to any one of claims 1-7, wherein the high-density genotyping is array based, bead based, or high-throughput sequencing based.

9. The method according to any one of claims 1-8, wherein the genotyping data is obtained by using a genome-wide genotype calling algorithm, further comprising:

e) adjusting the call rate cut-off value of the genome-wide genotype calling algorithm.

~~10. The method of claim 9, wherein the genotype calls are made by using a call rate cut-off that is lower than a typical call rate cut-off used for whole-genome genotyping of high quality genomic DNA.~~

~~11~~10. The method of claim 9, wherein the call rate cut-off ~~used is about 50-95%~~ value of the genome-wide genotype calling algorithm is adjusted to include more of the archived clinical samples.

~~12~~11. The method according to any one of claims ~~1-11~~1-10, further comprising performing association analysis based on additional genotyping data using the identified pharmacogenomic biomarkers, wherein some or all of the archived clinical samples from step a) and/or additional clinical samples are used for the additional genotyping.

~~13~~12. The method of claim ~~12~~ 11, further comprising comparing the additional genotyping data obtained by using the verification genotype calling algorithm to the genotyping data obtained by using the genome-wide genotype calling algorithm.

~~14~~13. The method according to claim ~~12~~11 or ~~13~~12, wherein a subset of the pharmacogenomic biomarkers from step d) is identified, wherein the method is used for retrospective study of archived clinical samples from a previously conducted clinical trial.

~~15. A pharmacogenomic biomarker identified by the method of claim 14, for use to develop a companion diagnostic test.~~

~~16. A companion diagnostic test using a pharmacogenomic biomarker identified by the method of claim 14.~~

~~17~~14. A genotyping method using suboptimal genomic DNA samples, which method comprises:

a) receiving sequence information of said suboptimal genomic DNA samples by using a genome-wide genotype calling algorithm and/or a verification genotype calling algorithm;

b) optimizing an inclusion criterion based on said sequence information, wherein the inclusion criterion is the call rate cut-off value of the genotype calling algorithm, wherein the optimized call rate cut-off value is less than 90%; and

c) calculating genotypes based on said sequence information and said optimized inclusion criterion,

wherein the suboptimal genomic DNA samples are from archived clinical samples.

~~18~~15. The method of claim ~~17~~14, wherein the optimization is repeated multiple times to include and/or exclude samples.

~~19~~16. A computer readable medium comprising a plurality of instructions for a genotyping method using suboptimal genomic DNA samples, which comprises the steps of:

a) receiving sequence information of said suboptimal genomic DNA samples;

b) optimizing an inclusion criterion based on said sequence information using the method according to claim ~~17~~14 or ~~18~~15; and

c) calculating genotypes based on said sequence information and said optimized inclusion criterion.

~~20. A method to conduct GWAS using suboptimal genomic DNA.~~

17. The method of claim 14, wherein the suboptimal genomic DNA samples are from archived clinical samples selected from the group consisting of plasma samples, body fluids, circulating tumor cells, and buccal cells.

18. The method of claim 14, wherein the optimization comprises adjusting the call rate cut-off value to include more of the suboptimal genomic DNA samples.

19. A method to identify one or more pharmacogenomic biomarkers, which method comprises:

a) isolating DNA from archived clinical samples of at least two patients exhibiting different values in a relevant phenotype;

b) amplifying said isolated DNA;

c) obtaining high-density genotyping data of said amplified DNA by using a genome-wide genotype calling algorithm, wherein the call rate cut-off value of the genome-wide genotype calling algorithm is less than 95%; and

d) performing association analysis based on said genotyping data and said different values in said relevant phenotype,

wherein said pharmacogenomic biomarker(s) are identified,

wherein the archived clinical samples are selected from the group consisting of plasma samples, body fluids, circulating tumor cells, and buccal cells, and

wherein the isolated DNA is suboptimal genomic DNA.

20. The method of claim 19, wherein the archived clinical samples are plasma samples.

21. The method of claim 19 or 20, wherein the amplification is whole-genome amplification (WGA), and the resulting DNA is whole-genome amplified DNA (wgaDNA).

22. The method of any one of claims 19-21, further comprising adjusting the call rate cut-off value of the genome-wide genotype calling algorithm used in step c).

23. The method of any one of claims 19-22, wherein the call rate cut-off value of the genome-wide genotype calling algorithm is adjusted to include more of the archived clinical samples.

24. A genotyping method using suboptimal genomic DNA samples, which method comprises:

a) receiving sequence information of said suboptimal genomic DNA samples by using a genome-wide genotype calling algorithm and/or a verification genotype calling algorithm;

b) optimizing an inclusion criterion based on said sequence information, wherein the inclusion criterion is the call rate cut-off value of the genotype calling algorithm, wherein the optimized call rate cut-off value is less than 95%; and

c) calculating genotypes based on said sequence information and said optimized inclusion criterion,

wherein the suboptimal genomic DNA samples are from archived clinical samples selected from the group consisting of plasma samples, body fluids, circulating tumor cells, and buccal cells.

25. The method of claim 24, wherein the optimization comprises adjusting the call rate cut-off value to include more of the suboptimal genomic DNA samples.