

is ineffective. Studies have thus far failed to show the effectiveness of finasteride in the treatment of female androgenetic alopecia.

[0006] There are significant differences between male androgenetic alopecia and female androgenetic alopecia. Apart from the different baldness patterns, male and female alopecia follow a different mechanism. In men, alopecia is related to the normal high androgen levels in males, combined with an underlying sensitivity of the hair roots to androgens. Women, however, have roughly 10 times lower androgen levels than men, and the absolute amount of androgen is a less significant factor than the increased sensitivity of the hair roots to androgens.

[0007] Among various individuals, whether male or female, there is a broad variability in the response of different people to various hair loss treatments. This variability is presumed to be a result of genetic factors contributing to variable enzyme activity in the follicles, making a one- size-fits-all approach difficult to achieve. It would therefore be advantageous to be able to have an effective diagnostic and treatment method where patients could be selected and treated on the basis of criteria such as enzyme activity, which would identify some people as being likely to benefit from treatment by minoxidil and other drugs, while identifying other individuals in which treatment is not likely to be effective. Previous methods of predicting response to minoxidil are explained in United States Patent No. 8,691,518. However, there still existed a need to predict response to oral forms of minoxidil versus topical forms of minoxidil.

BRIEF SUMMARY

[0008] The disclosures described here relate to systems and methods for predicting oral and/or topical form minoxidil response in the treatment of androgenetic alopecia, which in one example may be based on a colorimetric assay. Various examples are possible, a number of which are exemplified here. In particular, variations in hair follicle minoxidil sulfotransferase activity may be used to predict the efficacy of minoxidil for the treatment of androgenetic alopecia.

[0008a] In one aspect, there is provided a method for predicting response to minoxidil, the method comprising:

measuring gene, genetic, and/or enzymatic activity in a sample of a patient to generate an activity value indicative of a biochemical activation response to minoxidil;

comparing the activity value to a standardized activity value; and
predicting a response to minoxidil treatment based on the comparison.

[0008b] In another aspect, there is provided a method for selecting a treatment for a human subject suffering from androgenetic alopecia, the method comprising:

measuring gene, genetic activity, and/or enzymatic in a sample of a patient to generate an
activity value indicative a biochemical activation response to minoxidil;

comparing the activity value to a standardized activity value;

predicting a response to minoxidil treatment based on the comparison; and

prescribing a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine as the androgenetic alopecia treatment.

[0009] In one example of the present disclosure, there is provided a method for selecting a treatment for a subject suffering from androgenetic alopecia, comprising obtaining a sample of one or more hair follicles, or a scalp biopsy, from the subject; performing an assay to measure minoxidil sulfotransferase activity in the sample, thereby generating an activity

value indicative of the minoxidil sulfotransferase activity level in the sample; comparing the activity value to one or more standardized activity values, each standardized activity value representing either high or low expected minoxidil response for hair re-growth or retention for a class of patients including the subject, thereby producing an indication of either high or low expected minoxidil response for hair re-growth or retention for the subject at a particular dosage of minoxidil; and presenting the indication to the subject. Optionally, the indication of high or low expected minoxidil response for hair re-growth or retention is used to select oral or topical minoxidil treatment.

[0010] In another example, there is provided a composition of matter for performing an assay comprising about 30 to about 70 mM potassium phosphate buffer (pH 6.5); about 3 to about 7 mM magnesium chloride; about 15 to about 25 μ M adenosine 3',5'-diphosphate (PAP) or adenosine 3'-phosphate, 5'-phosphosulfate (PAPS); about 3 to about 7 mM p-nitrophenyl sulfate; and about 0.07 to about 0.13 mM minoxidil.

[0011] In another example, there is provided a kit comprising a transparent container with a lid, comprising the above composition for performing an assay; a buffer container comprising about 0.20 M to about 0.30 M Tris-HCl, pH 8.7; and means for mixing the contents of the buffer container with the contents of the apparatus.

[0012] As will be explained herein, examples can relate to a method for selecting a treatment for a human subject suffering from androgenetic alopecia. The method can involve obtaining a sample from the human subject. The sample can include one or more hairs that have been plucked from the human subject. The one or more hairs can include one or more hair follicles. The method can involve performing a colorimetric assay to measure minoxidil sulfotransferase activity in the sample, thereby generating an activity value indicative of the minoxidil sulfotransferase activity level in the sample. In some examples, the step of placing the sample in a reaction mixture can include use of an indicator dye and minoxidil. During the assay, the indicator dye can undergo a color change that correlates with the amount of minoxidil sulfotransferase activity level in the sample. The activity value can correlate with the color change. The method can involve comparing the activity value to one or more standardized activity values. Each standardized activity value can represent either high or low expected minoxidil response for hair re-growth or retention for a class of patients including the subject, thereby producing an indication of either high or low expected minoxidil response for hair re-growth or retention for the subject at a particular dosage of minoxidil. The method can involve presenting the indication to the human subject.

[0013] In some examples, the indication can be of high expected minoxidil response for hair re-growth or retention, and the particular dosage of minoxidil can be selected from the group consisting of approximately 2% topical solution, approximately 5% topical solution, approximately 2% topical foam, approximately 5% topical foam, approximately 0.625 mg, 1.25 mg, 2.5 mg tablet, and approximately 5 mg tablet.

[0014] In some examples, the assay can include the steps of: placing the sample in a reaction mixture containing about 50 mM potassium phosphate buffer with pH between about 6.5 and about 8.0, about 5 mM magnesium chloride, about 20 μ M adenosine 3',5'-diphosphate (PAP) or adenosine 3'-phosphate, 5'-phosphosulfate (PAPS), about 5 mM p-nitrophenyl sulfate and about 0.1 mM minoxidil; mixing the reaction mixture which contains the sample, such that a reaction is initiated; incubating the sample within the reaction mixture for a predetermined length; and stopping the reaction.

[0015] In some examples, the potassium phosphate buffer can have a pH of about 8.0.

[0016] In some examples, a basic buffer of about 0.25 M Tris-HCl, pH approximately 8.7 can be added to the reaction mixture to quench the assay and improve sensitivity of the assay.

[0017] In some examples, the reaction mixture can be incubated for about 30 minutes to about 24 hours at about 37° C.

[0018] In some examples, the sample within the reaction mixture can be incubated at room temperature.

[0019] In some examples, the reaction mixture can be incubated above room temperature to increase dye turnover and the signal strength of the colorimetric assay.

[0020] In some examples, the reaction mixture can be packaged in a capsule and dissolved in a solution along with the sample.

[0021] In some examples, the one or more standardized values can be one or more minoxidil sulfotransferase activity levels at which a statistical sample of other subjects show either high or low minoxidil response for hair re-growth or retention at the particular dosage of minoxidil.

[0022] In some examples, the step of presenting can include sending an electronic signal.

[0023] In some examples, the indicator dye can be p-nitrophenyl sulfate.

[0024] In some examples, the colorimetric assay can use 2-naphthol as a substrate, to improve the sensitivity or specificity of the assay.

[0025] In some examples, the sample can consist of one hair comprising one hair follicle that has been plucked from the human subject.

[0026] In some examples, the reaction time for the assay can be inversely correlated with the number of hair follicles in the reaction.

[0027] In some examples, the human subject with high minoxidil sulfotransferase activity can be prescribed a low dose of minoxidil and/or a decrease in the frequency of minoxidil application.

[0028] In some examples, the human subject with low minoxidil sulfotransferase activity can be prescribed a high dose of minoxidil and/or an increase in the frequency of minoxidil application.

[0029] In some examples, the human subject with low minoxidil sulfotransferase activity can be prescribed a stabilized form of minoxidil sulfate in the form of a cream, solution and/or gel.

[0030] In some examples, minoxidil sulfate can be stabilized in liposomes or microencapsulation.

[0031] In some examples, the assay can include a positive (reference) and negative (blank) control to compare to the sample.

[0032] In some examples, the color change can be visually discernible. In some examples, assay can be performed in a transparent container.

[0033] In some examples, generating an activity value can be performed by comparing the discernible color after the color change to a reference color card.

[0034] In some examples, the colorimetric assay can be performed in a transparent container, and generating an activity value is performed by measuring the absorbance at approximately 405 nm with a spectrophotometer.

[0035] Another exemplary example can relate to a method for predicting response to minoxidil. The method can involve measuring gene, genetic, and/or enzymatic activity in a sample of a patient to generate an activity value indicative of a biochemical activation response to minoxidil. The method can involve comparing the activity value to a standardized activity value. The method can involve predicting a response to minoxidil treatment based on the comparison.

[0036] In some examples, measuring gene or enzymatic activity can include: measuring SULT1A1 gene expression, a SULT1A1 gene variant expression, and/or SULT1A1 enzymatic activity in the sample; measuring SLC22A9 gene expression, SCL22A9 gene variant expression, SLC22A9 transport activity from a hair cell in the sample, and/or SLC22A9 transporter activity; measuring AABC3 gene expression and/or AABC3 gene

variant expression in the sample; and/or measuring blood flow in the patient (e.g., the patient's scalp).

[0037] In some examples, the SLC22A9 transport activity from a hair cell can be measured using a standard substrate uptake assay with known substrates (e.g., fluorescent substrates, radionuclear substrates, etc.).

[0038] In some examples, the minoxidil treatment can be oral minoxidil.

[0039] In some examples, predicting a response to minoxidil treatment can involve:

- when the gene, genetic, and/or enzymatic activity relates to SULT1A1: estimating that the patient will respond to oral minoxidil when the activity value is lower than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value;
- when the gene, genetic and/or SLC22A9 transporter activity relates to SLC22A9: estimating that the patient will respond to oral minoxidil when the activity value is higher than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is lower than a threshold standardized activity value;
- when the gene and/or genetic activity relates to AABC3: estimating that the patient will respond to oral minoxidil when the activity value is lower than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value.

[0040] In some examples, measuring blood flow of the patient (e.g., the patient's scalp) can involve Doppler velocitometry. Predicting a response to minoxidil treatment can involve: estimating that the patient will respond well to oral minoxidil when the Doppler velocity is lower than a threshold value; and estimating that the patient will not respond well to oral minoxidil when the Doppler velocity is higher than the threshold value.

[0041] In some examples, when the gene, genetic, and/or enzymatic activity relates to SULT1A1: estimating that the patient will respond well to oral minoxidil when the activity value is lower than a threshold standardized activity value that is within a range from 0.37 to 0.4, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value that is within a range from 0.37 to 0.4.

[0042] In some examples, the minoxidil treatment can be treatment for androgenetic alopecia.

[0043] In some examples, the method can involve generating plural activity values indicative of the biochemical activation response to minoxidil, and comparing the plural activity values to plural standardized activity values.

[0044] In some examples, the response to minoxidil treatment can be increased or improved hair growth or hair retention.

[0045] In some examples, predicting a response to minoxidil treatment can involve estimating a biochemical activation response based on a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine.

[0046] In some examples, the standardized activity value can pertain to biochemical activation response to minoxidil associated with hair growth or hair retention for a class of individuals.

[0047] In some examples, the standardized activity value can pertain to biochemical activation response to minoxidil associated with hair growth or hair retention at which a statistical sample of subjects show high or low minoxidil response for a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine.

[0048] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of a patient can involve obtaining one or more hair follicles and/or one or more scalp biopsies as the sample.

[0049] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of a patient can occur before, during, and/or after the patient is being administered a minoxidil treatment.

[0050] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of a patient can occur 1 to 14 days prior to the patient being administered a minoxidil treatment.

[0051] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of a patient can be performed via an assay device.

[0052] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of a patient can be performed via a colorimetric assay device.

[0053] In some examples, predicting the response to minoxidil treatment can involve implementation of a neural network.

[0054] In some examples, measuring gene, genetic, and/or enzymatic activity in the sample of the patient can involve obtaining one or more hair follicles and/or one or more scalp biopsies

as the sample, and measuring gene, genetic, and/or enzymatic activity in the sample of the patient is performed via an assay device, wherein the method involves: placing the one or more hair follicles or one or more scalp biopsies in a reaction mixture containing potassium phosphate buffer, magnesium chloride, adenosine 3',5'-diphosphate (PAP) or adenosine 3'-phosphate,5'-phosphosulfate (PAPS), p-nitrophenyl sulfate, and minoxidil; mixing the reaction mixture; incubating the reaction mixture for a predetermined length; and stopping the reaction.

[0055] Another exemplary examples can relate to a method for selecting a treatment for a human subject suffering from androgenetic alopecia. The method can involve measuring gene, genetic and/or enzymatic activity in a sample of a patient to generate an activity value indicative of a biochemical activation response to minoxidil. The method can involve comparing the activity value to a standardized activity value. The method can involve predicting a response to minoxidil treatment based on the comparison. The method can involve prescribing a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine as the androgenetic alopecia treatment.

[0056] In some examples, measuring gene, genetic, and/or enzymatic activity can include: measuring SULT1A1 gene expression, SULT1A1 gene variant expression, and/or SULT1A1 enzymatic activity in the sample; measuring SLC22A9 gene expression, SCL22A9 gene variant expression, SLC22A9 activity from a hair follicle in the sample, and/or SLC transporter activity; measuring AABC3 gene expression and/or AABC3 gene variant expression in the sample; and/or measuring blood flow in the patient.

[0057] In some examples, prescribing the minoxidil dosage amount, the minoxidil dosage frequency, and/or the minoxidil dosage routine can involve prescribing oral minoxidil minoxidil.

[0058] In some examples, measuring blood flow of the patient (e.g., the patient's scalp) can involve Doppler velocitometry. Predicting a response to minoxidil treatment can involve: estimating that the patient will respond well to oral minoxidil when the Doppler velocity is lower than a threshold value; and estimating that the patient will not respond well to oral minoxidil when the Doppler velocity is higher than the threshold value.

[0059] In some examples, predicting a response to minoxidil treatment can involve:

- when the, gene, genetic and/or enzymatic activity relates to SULT1A1: estimating that the patient will respond to oral minoxidil when the activity value is lower than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value;

- when the gene, genetic and/or SLC22A9 transporter activity from the hair cell relates to SLC22A9: estimating that the patient will respond to oral minoxidil when the activity value is higher than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is lower than a threshold standardized activity value;
- when the gene and/or genetic activity relates to AABC3: estimating that the patient will respond to oral minoxidil when the activity value is lower than a threshold standardized activity value, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value.

[0060] In some examples, when the gene, genetic, and/or enzymatic activity relates to SULT1A1: estimating that the patient will respond well to oral minoxidil when the activity value is lower than a threshold standardized activity value that is within a range from 0.37 to 0.4, and estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value that is within a range from 0.37 to 0.4.

BRIEF DESCRIPTION OF THE DRAWINGS

[0061] The accompanying drawings, which are incorporated into this specification, illustrate one or more exemplary embodiments of the inventions disclosed herein and, together with the detailed description, serve to explain the principles and exemplary implementations of these inventions. One of skill in the art will understand that the drawings are illustrative only, and that what is depicted therein may be adapted based on the text of the specification or the common knowledge within this field.

[0062] In the drawings, where like reference numerals refer to like reference in the specification:

[0063] FIG. 1 is a flowchart showing a method of analyzing one or more hair follicles and providing a result.

[0064] FIG. 2 shows an example of a computerized system for conducting or analyzing an assay to test hair follicles and providing a result.

[0065] FIG. 3 shows a flow diagram of minoxidil sulfonation.

DETAILED DESCRIPTION

CLAIMS

WHAT IS CLAIMED IS:

1. A method for predicting response to minoxidil, the method comprising:
measuring gene, genetic, and/or enzymatic activity in a sample of a patient to generate
an activity value indicative of a biochemical activation response to minoxidil;
comparing the activity value to a standardized activity value; and
predicting a response to minoxidil treatment based on the comparison.
2. The method of claim 1, wherein:
measuring gene, genetic, and/or enzymatic activity includes:
measuring SULT1A1 gene expression, a SULT1A1 gene variant expression,
and/or SULT1A1 enzymatic activity in the sample ;
measuring SLC22A9 gene expression, SCL22A9 gene variant expression,
SLC22A9 transporter activity from a hair cell in the sample, and/or
measuring SLC22A9 transporter activity;
measuring AABC3 gene expression and/or AABC3 gene variant expression in
the sample; and/or
measuring blood flow in the patient; or
predicting a response to minoxidil treatment involves:
when the gene, genetic, and/or enzymatic activity relates to SULT1A1:
estimating that the patient will respond to oral minoxidil when the
activity value is lower than a threshold standardized activity value;
and
estimating that the patient will not respond well to oral minoxidil when
the activity value is higher than a threshold standardized activity
value;
when the gene, genetic, and/or SLC22A9 transporter activity from the hair cell
relates to SLC22A9:
estimating that the patient will respond to oral minoxidil when the
activity value is higher than a threshold standardized activity

value; and
estimating that the patient will not respond well to oral minoxidil when
the activity value is lower than a threshold standardized activity
value; and
when the gene and/or genetic activity relates to AABC3:
estimating that the patient will respond to oral minoxidil when the
activity value is lower than a threshold standardized activity value;
and
estimating that the patient will not respond well to oral minoxidil when
the activity value is higher than a threshold standardized activity
value; or
predicting a response to minoxidil treatment involves estimating the biochemical
activation response based on a minoxidil dosage amount, a minoxidil dosage
frequency, and/or a minoxidil dosage routine, or
predicting a response to minoxidil treatment involves implementation of a neural
network.

3. The method of claim 1, wherein:
the minoxidil treatment is oral minoxidil.
4. The method of claim 1, wherein:
measuring blood flow of the patient involves Doppler velocitometry;
predicting a response to minoxidil treatment involves:
estimating that the patient will respond well to oral minoxidil when the Doppler
velocity is lower than a threshold value; and
estimating that the patient will not respond well to oral minoxidil when the
Doppler velocity is higher than the threshold value.
5. The method of claim 1, wherein measuring SLC22A9 transport activity from the hair cell
involves use of an uptake assay.
6. The method of claim 1, wherein when the gene, genetic, and/or enzymatic activity relates
to SULT1A1:

estimating that the patient will respond well to oral minoxidil when the activity value is lower than a threshold standardized activity value that is within a range from 0.37 to 0.4; and

estimating that the patient will not respond well to oral minoxidil when the activity value is higher than a threshold standardized activity value that is within a range from 0.37 to 0.4.

7. The method of claim 1, wherein:
the minoxidil treatment is treatment for androgenetic alopecia.
8. The method of claim 1, comprising:
generating plural activity values indicative of the biochemical activation response to minoxidil; and
comparing the plural activity values to plural standardized activity values.
9. The method of claim 1, wherein:
the response to minoxidil treatment is increased or improved hair growth or hair retention.
10. The method of claim 1, wherein:
the standardized activity value pertains to biochemical activation response to minoxidil associated with hair growth or hair retention for a class of individuals, or
the standardized activity value pertains to biochemical activation response to minoxidil associated with hair growth or hair retention at which a statistical sample of subjects show high or low minoxidil response for a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine.
11. The method of claim 1, wherein:
measuring gene, genetic, and/or enzymatic activity in the sample of a patient involves obtaining one or more hair follicles and/or one or more scalp biopsies as the sample; or
measuring gene, genetic, and/or enzymatic activity in the sample of a patient occurs before, during, and/or after the patient is being administered a minoxidil treatment; or

measuring gene, genetic, and/or enzymatic activity in the sample of a patient is performed via an assay device; or

measuring gene, genetic and/or enzymatic activity in the sample of a patient is performed via a colorimetric assay device; or

measuring gene, genetic, and/or enzymatic activity in the sample of the patient involves obtaining one or more hair follicles and/or one or more scalp biopsies as the sample, and measuring gene, genetic, and/or enzymatic activity in the sample of the patient is performed via an assay device, the method comprising:

placing the one or more hair follicles or one or more scalp biopsies in a reaction mixture containing potassium phosphate buffer, magnesium chloride, adenosine 3',5'-diphosphate (PAP) or adenosine 3'-phosphate,5'-phosphosulfate (PAPS), p-nitrophenyl sulfate, and minoxidil;

mixing the reaction mixture;

incubating the reaction mixture for a predetermined length; and

stopping the reaction.

12. The method of claim 1, wherein:

measuring sulfotransferase activity in the sample of a patient occurs 1 to 14 days prior to the patient being administered a minoxidil treatment.

13. A method for selecting a treatment for a human subject suffering from androgenetic alopecia, the method comprising:

measuring gene, genetic activity, and/or enzymatic in a sample of a patient to generate an activity value indicative a biochemical activation response to minoxidil;

comparing the activity value to a standardized activity value;

predicting a response to minoxidil treatment based on the comparison; and

prescribing a minoxidil dosage amount, a minoxidil dosage frequency, and/or a minoxidil dosage routine as the androgenetic alopecia treatment.

14. The method of claim 13, wherein:

measuring gene, genetic, and/or enzymatic activity includes:

measuring SULT1A1 gene expression, SULT1A1 gene variant expression,

and/or SULT1A1 enzymatic activity in the sample;
measuring SLC22A9 gene expression, SCL22A9 gene variant expression
SLC22A9 transporter activity from a hair cell in the sample, and/or
SCL22A9 transporter activity;
measuring AABC3 gene expression and/or AABC3 gene variant expression in
the sample; and/or
measuring blood flow in the patient.

15. The method of claim 13, wherein:

prescribing the minoxidil dosage amount, the minoxidil dosage frequency, and/or the
minoxidil dosage routine involves prescribing oral minoxidil.

16. The method of claim 13, wherein.

measuring blood flow of the patient involves Doppler velocitometry;

predicting a response to minoxidil treatment involves:

estimating that the patient will respond well to oral minoxidil when the Doppler
velocity is lower than a threshold value; and
estimating that the patient will not respond well to oral minoxidil when the
Doppler velocity is higher than the threshold value.

17. The method of claim 13, wherein:

predicting a response to minoxidil treatment involves:

when the gene, genetic, and/or enzymatic activity relates to SULT1A1:

estimating that the patient will respond to oral minoxidil when the
activity value is lower than a threshold standardized activity value;
and

estimating that the patient will not respond well to oral minoxidil when
the activity value is higher than a threshold standardized activity
value;

when the gene, genetic and/or SLC22A9 transporter activity from the hair cell
relates to SLC22A9:

estimating that the patient will respond to oral minoxidil when the
activity value is higher than a threshold standardized activity

value; and
estimating that the patient will not respond well to oral minoxidil when
the activity value is lower than a threshold standardized activity
value; and
when the gene and/or genetic activity relates to AABC3:
estimating that the patient will respond to oral minoxidil when the
activity value is lower than a threshold standardized activity value;
and
estimating that the patient will not respond well to oral minoxidil when
the activity value is higher than a threshold standardized activity
value.

18. The method of claim 13, wherein when the gene, genetic and/or enzymatic activity relates to SULT1A1:
estimating that the patient will respond well to oral minoxidil when the activity value is
lower than a threshold standardized activity value that is within a range from
0.37 to 0.4; and
estimating that the patient will not respond well to oral minoxidil when the activity
value is higher than a threshold standardized activity value that is within a range
from 0.37 to 0.4.
19. The method of claim 13, wherein measuring SLC22A9 transport activity from the hair
cell involves use of an uptake assay.