Project Name:	AI Fibrosis Treatment	**Start Date:**	2024-03-04
Project Number:	2402	**Completion Date:**	2024-09-30

Project Details:

Scientific or Technological Objectives:

Measurement	Current Performance	Objective	Has results?
System to identify risk (%)	90	99.5	Yes
develop anti fibrotic eye drop (0= no / 1 = yes)	0	1	Yes
Reduce Post Inflammation (%)	60	90	Yes

Applicant developed a new anti-fibrotic drug, Compound X, that effectively reduces scarring around a microstent implantation site in glaucoma patients at high risk of PI after microstent implant surgery without the undesirable side effects of drug A. In connection with this invention, the applicant filed a patent application disclosing Compound X and describing how it may be topically administered in eye drop form after microstent implant surgery.

The applicant also discovered that PI is a polygenic condition, meaning that it results from the interaction of multiple genes rather than any single gene. Using standard methodologies, the applicant conducted a large-scale genome wide association (GWA) study on PI in glaucoma patients and identified 37 informative single-nucleotide polymorphisms (SNPs) that have a statistically significant association with PI. The application defines “informative SNPs” as the 37 SNPs identified in the GWA study. These informative SNPs serve as genetic markers for the genes that give rise to PI.

Field of Science/Technology:

Pharmacogenomics, gene-based therapeutics (3.04.04)

Project Details:

Intended Results:	Develop new processes, Develop new materials, devices, or products
Work locations:	Research Facility
Key Employees:	
Evidence types:	

Scientific or Technological Advancement:

Uncertainty #1: Technological uncertainty

Glaucoma is a leading cause of blindness globally. The most common form is open angle glaucoma, in which irreversible vision loss results from cell and optic nerve damage caused largely by poor drainage of aqueous humor from the eye. Depending on condition severity and the timing of the diagnosis, treatment can include lifestyle adjustments, pharmaceutical eye drops, laser eye surgery, or drainage device implants to facilitate healthy drainage.

While newer drainage devices, such as microstents, are more comfortable than earlier drainage devices, post-surgery scarring and inflammation due to fibrosis remain issues. Commonly prescribed anti-fibrotic drugs, such as drug A, can reduce scarring but do so non-specifically while causing more inflammation (“post-implantation inflammation” or “PI”) that further damages the eye.

The most significant underlying key variables are:

treatments - drops, microstints, surgery, modelling SNPs - AI (unresolved), drop formulation

Technology or Knowledge Base Level:

Activity #1-1: Screening method AI based - Ineligible (Fiscal Year 2024)

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Methods of experimentation:

[Claim 1] A post-surgical fibrosis treatment method comprising:
(a) collecting and genotyping a sample from a glaucoma patient to a provide a genotype dataset;
(b) identifying the glaucoma patient as at high risk of post-implantation inflammation (PI) based on a weighted polygenic risk score that is generated from informative single-nucleotide polymorphisms (SNPs) in the genotype dataset by an ezAI model that uses multiplication to weight corresponding alleles in the dataset by their effect sizes and addition to sum the weighted values to provide the score; and
(c) administering an appropriate treatment to the glaucoma patient at high risk of PI after microstent implant surgery.

From the GWA study data, the applicant developed a polygenic risk score (PRS) model by classic clumping and thresholding methods to provide a weighted PRS. As is known in the art, a PRS is a single value estimate of an individual's relative risk for a given phenotype or condition based on the individual's genotype.

In brief, after collecting a sample from a patient, the sample is sequenced and genotyped to provide a genotype dataset. Alleles in the genotype dataset corresponding to informative SNPs selected from the GWA study are identified, tallied, and weighted (using effect sizes derived from GWA study summary statistics as weights). A PRS is then generated as a sum of the weighted values. Sample collection, sequencing, and genotyping for the purposes of providing a genotype dataset may be carried out by conventional methods known in the art.

The applicant also discloses a computer-implemented machine learning model (referred to as "the ezAI model" for the purposes of this disclosure) and its clinical applications.

Given an input of a patient's genotype dataset, the ezAI model calculates a weighted PRS from informative SNPs in the dataset—using multiplication to weight corresponding alleles in the dataset by their effect sizes and addition to sum the weighted values.

Using the same weights and informative SNPs, the ezAI model improves upon the base PRS model by determining a risk score and providing a classification in less time.

Results:

- System to identify risk : 97 % (73% of goal)

The specification discloses a method of identifying glaucoma patients at high risk of PI using this PRS model. An identification of a patient as being at high risk of PI is made by ranking a weighted PRS once the score has been generated.

The application defines a "glaucoma patient at high risk of PI" as a glaucoma patient having a weighted PRS in the top quartile of PRS values when ranked against reference PRS values established during PRS model development.

The disclosure teaches that determining patient risk using a weighted PRS as disclosed and accordingly customizing treatment lends to better prognosis after implant surgery.

Limitation (b) also recites "a weighted PRS that is generated from informative SNPs in the genotype dataset by an ezAI model that uses multiplication to weight corresponding alleles in the dataset by their effect sizes and addition to sum the weighted values to provide the score."

this limitation requires a mathematical calculation. Namely, an arithmetic calculation (multiplication to weight alleles by their effect sizes and addition to sum the weighted values) is required to generate a weighted risk score. Limitation (b) hence recites a "mathematical calculation" and so falls into the "mathematical concepts" grouping of abstract ideas.

For instance, given a genotype dataset, a physician would identify, tally, and weight alleles corresponding to informative SNPs present in the dataset by their effect sizes, then sum the resulting values to generate a risk score. See MPEP 2106.04(a)(2), subsection I.C.

This limitation also falls into the "mental process" grouping because it requires an assessment of the genotype dataset in order to identify informative SNPs in evaluating patient risk. Moreover, the recited mathematical calculation is simple enough that it can be practically performed in the human mind.

Even if most humans would use a physical aid, like a pen and paper or a calculator, to make such calculations, the use of a physical aid would not negate the mental nature of this limitation.

Conclusion:

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The data gathering activities in limitation (a) are recited at a high level of generality and have been recognized by the courts as being routine laboratory techniques (analyzing DNA to provide sequence information or to detect allelic variants is conventional in the art); MPEP 2106.05(d), subsection II.

The specification otherwise only describes carrying out sample collection and genotyping by conventional methods.

Consequently the additional elements individually or in combination do not provide an inventive concept;

While the disclosure states that “the ezAI model improves upon the base PRS model by determining a risk score and providing a classification in less time,” there is no improvement to the functioning of a computer nor to any other technology.

At best, the claimed combination amounts to an improvement to the abstract idea of determining patient risk rather than to any technology. See MPEP 2106.05(a). Thus, even when considering the elements in combination, claim 1 as a whole does not integrate the recited exception into a practical application. (Step 2A, Prong Two: NO).

The claim is not eligible.

AUTHORS NOTE: THESE LIMITS RELATE TO RESULTS GENERATED BY THE AI SYSTEM INSTEAD OF ISSUES WHICH INVOLVED / REQUIRED "SIGNIFICANT INPUT" FROM THE HUMAN RESEARCHER.

Activity #1-2: Custom eyedrops - Eligible despite AI result (Fiscal Year 2024)

Methods of experimentation:

[Claim 2] The method of claim 1, wherein the appropriate treatment is Compound X eye drops.

From the GWA study data, the applicant developed a polygenic risk score (PRS) model by classic clumping and thresholding methods to provide a weighted PRS. As is known in the art, a PRS is a single value estimate of an individual’s relative risk for a given phenotype or condition based on the individual’s genotype.

In brief, after collecting a sample from a patient, the sample is sequenced and genotyped to provide a genotype dataset. Alleles in the genotype dataset corresponding to informative SNPs selected from the GWA study are identified, tallied, and weighted (using effect sizes derived from GWA study summary statistics as weights).

A PRS is then generated as a sum of the weighted values. Sample collection, sequencing, and genotyping for the purposes of providing a genotype dataset may be carried out by conventional methods known in the art.

Results:

- develop anti fibrotic eye drop: 1 0= no / 1 = yes (100% of goal) -- Successful product
- Reduce Post Inflammation: 93 % (110% of goal)

An abstract idea is used to identify the patient as belonging to a specific patient population (glaucoma patients at high risk of PI), and the patient is then administered a treatment (Compound X eye drops instead of any common anti-fibrotic treatment, such as drug A, after microstent implant surgery) that is particular to that specific patient population (glaucoma patients at high risk of PI).

Relying on the determination of patient risk to administer Compound X eye drops to glaucoma patients at high risk of PI after microstent implant surgery is therefore a particular treatment for a medical condition such that the claim as a whole integrates the judicial exception into a practical application. See MPEP 2106.04(d)(2). (Step 2A, Prong Two: YES).

Conclusion:

The claim is eligible.

AUTHORS NOTE: USE OF AI RESULTS TO CREATE NEW PRODUCT WHICH IS ELIGIBLE FOR PATENT.

AUTHORS NOTE: THE PATENT RULES PROVIDE ELIGIBILITY AS A RESULT OF IMPROVING A "PRODUCT" (DEVELOPMENT OF THE NEW EYE DROP FORMULATION) .

IN THE CASE OF LIFE SCIENCES THIS MAY PROVIDE SOME LESSONS FOR SR&ED RELATED CLAIMS - I.E. FOCUS ON NEW/IMPROVED PRODUCTS VS. PROCESSES?

Significant variables addressed: drop formulation, treatments - drops, microstints, surgery

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