

isolated, for example, but not to be limited to a tissue sample, a sample of saliva, a cheek swab sample, blood, or other biological fluids that contain genomic DNA. In some embodiments, the sample comprises DNA. In some embodiments, the sample comprises RNA. In some embodiments, the identity of the nucleotide at the polymorphism in a patient is determined via genotyping. In some embodiments the genotyping is performed by PCR analysis, sequence analysis or LCR analysis. In some embodiments, the patient is identified as a patient with increased risk of progression of AMD (e.g. intermediate or advanced AMD such as wet (neovascular/exudative) AMD or geographic atrophy) when at least one allele comprising a nucleotide selected from the group consisting of a G nucleotide at the SNP rs4698775 is present, a G nucleotide at the SNP rs17440077 is present, an A nucleotide at the SNP rs10737680 is present, a G nucleotide at the SNP rs1329428 is present, a G nucleotide at the SNP rs429608 is present or the G nucleotide at the SNP rs2230199 is present. The patient is identified as being at increased risk of AMD progression if the patient has one or two copies of the G allele at rs4698775 or rs17440077 associated with CFI, or equivalent alleles thereof, at rs1329428 associated with CFH, or equivalent allele thereof, or at rs429608 associated with C2/CFB, or equivalent allele thereof, or at rs2230199 associated with C3, or equivalent allele thereof or one or two copies of the A allele at rs10737680 associated with CFH, or equivalent allele thereof. The patient is identified as being at decreased risk of AMD progression if the patient does not have one or two copies of the G allele at rs4698775 or rs17440077 associated with CFI, or equivalent alleles thereof, at rs1329428 associated with CFH, or equivalent allele thereof, at rs429608 associated with C2/CFB, or equivalent allele thereof, or at rs2230199 associated with C3, or equivalent allele thereof or one or two copies of the A allele at rs10737680 associated with CFH, or equivalent allele thereof.

[0011a] In one aspect, there is provided a method of predicting the progression rate of an age related macular degeneration (AMD) in a patient having AMD, the method comprising: determining the presence of at least two AMD-associated polymorphisms in a biological sample that has been obtained from the patient; (i) by providing a nucleic acid sample isolated from the biological sample; and (ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of single nucleotide polymorphism (SNP) rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

[0012] One embodiment of the disclosure provides methods of predicting progression of AMD (e.g. intermediate or advanced AMD such as wet (neovascular/exudative) AMD or geographic atrophy), the method comprising determining the genotype of a patient, wherein a patient who is determined to carry a risk allele (e.g. AMD-associated polymorphism) is identified as a patient with an increased risk of progression of AMD (e.g. intermediate or advanced AMD such as wet (neovascular/exudative) AMD or geographic atrophy). In some embodiments, increased risk of progression of AMD includes progression from early AMD to intermediate AMD and intermediate to advanced AMD. In some embodiments, the risk allele is the minor allele of a selected SNP. In some embodiments, the risk allele is the major allele of a selected SNP. In

one or two copies of the A allele at rs10737680 associated with CFH, or equivalent allele thereof. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/100. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/100. In one embodiment, the study eye in the patient has a BCVA better than 20/25 or worse than 20/400. In one embodiment, the BCVA was determined using ETDRS charts. In some embodiments, the antibody or antigen-binding fragment thereof is administered intravitreally. In some embodiments, the age-related macular degeneration is dry AMD. In some embodiments, the dry AMD is advanced dry AMD. In some embodiments, the advanced dry AMD is geographic atrophy. In some embodiments, the patient has a reduced mean change in geographic atrophy (GA) area following administration of the antibody as compared to control patients that do not receive the antibody treatment. In some embodiments, the mean change in GA area is determined by measurements of GA area via standard imaging methods (e.g. fundus autofluorescence (FAF) or color fundus photography (CFP)). In some embodiments, the age-related macular degeneration is early AMD or intermediate AMD. In some embodiments, the patient with early AMD or intermediate AMD has a reduction or delay in appearance of clinical signs (e.g. may include measuring the number and size of drusen (for early and intermediate AMD) and monitoring hypo- and hyperpigmentation associated with drusen (for intermediate AMD)). In some embodiments, the methods further comprise administering a second medicament to the subject. In some embodiments, the second medicament is VEGF inhibitor.

[0013a] In another aspect, there is provided a method of identifying a patient having AMD as more likely to respond to a therapy comprising an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising: determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient; (i) by providing a nucleic acid sample isolated from the biological sample; and (ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele. In another aspect, there is provided use of an anti-factor D antibody, or antigen-binding fragment thereof in the manufacture of a medicament for treating a patient who has been identified as a patient having AMD who is more likely to respond to a therapy comprising the anti-factor D antibody, or antigen-binding fragment thereof, according to the method described herein.

[0014] A further embodiment of the disclosure provides methods of identifying a degenerative disease patient (e.g. AMD patient) who may benefit from and/or respond to treatment with an anti-factor D antibody, the method comprising determining the genotype of a patient, wherein a patient who is determined to carry a risk allele is identified as a patient who may benefit from treatment with an anti-factor D antibody or antigen-binding fragment thereof. In some embodiments, the method further comprises selecting the therapy comprising an anti-factor D antibody, or antigen-binding fragment thereof. In some embodiments, the antibody is lampalizumab. In one embodiment, the degenerative disease is an ocular degenerative disease. In one embodiment, the ocular degenerative disease is age-related macular degeneration. In some embodiments, the risk allele is the minor allele of a selected SNP. In some embodiments, the risk allele is the major allele of a selected SNP. In

delay in appearance of clinical signs (e.g. may include measuring the number and size of drusen (for early and intermediate AMD) and monitoring hypo- and hyperpigmentation associated with drusen (for intermediate AMD)).

[0014a] In another aspect, there is provided a method of optimizing therapeutic efficacy of treatment of a patient having AMD with an anti-factor D antibody, or antigen binding fragment thereof, the method comprising: determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient; (i) by providing a nucleic acid sample isolated from the biological sample; and (ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

[0015] Another embodiment of the disclosure provides methods of optimizing therapeutic efficacy for treatment of a degenerative disease (e.g. AMD), the method comprising determining the genotype of a patient, wherein a patient who is determined to carry a risk allele (e.g. AMD-associated polymorphism) is more likely to respond to treatment with the anti-factor D antibody, or antigen-binding fragment thereof or antigen-binding fragment thereof. In one embodiment, the degenerative disease is an ocular degenerative disease. In one embodiment, the ocular degenerative disease is age-related macular degeneration. In some embodiments, the antibody is lampalizumab. In some embodiments, the risk allele is the minor allele of a selected SNP. In some embodiments, the risk allele is the major allele of a selected SNP. In some embodiments, the risk allele may be a CFI risk allele, a CFH risk allele, a C2 risk allele, a CFB allele and/or a C3 risk allele. In some embodiments, the risk allele is a CFI risk allele. In some embodiments, the CFI risk allele is the rs4698775:G allele, or equivalent allele thereof or comprises a G at the selected SNP rs4698775, or comprises an alternate SNP in linkage disequilibrium to rs4698775. In some embodiments, the alternate SNP comprises a minor allele or the allele which resides on the same haplotype of the risk allele of the selected SNP rs4698775. In some embodiments, the CFI risk allele is the rs17440077:G allele, or equivalent allele thereof or comprises a G at the selected SNP rs17440077, or comprises an alternate SNP in linkage disequilibrium to rs17440077. In some embodiments, the alternate SNP comprises a minor allele or the allele which resides on the same haplotype of the risk allele of the selected SNP rs17440077. In some embodiments, the CFH risk allele is the rs10737680:A allele, or equivalent allele thereof, or comprises an A at the selected SNP rs10737680, or comprises an alternate SNP in linkage disequilibrium to rs10737680. In some embodiments, the alternate SNP comprises a minor allele or the allele which resides on the same haplotype of the risk allele of the selected SNP rs10737680. In some embodiments, the CFH risk allele is the rs1329428:G allele, or equivalent allele thereof, or comprises an G at the selected SNP rs1329428, or comprises an alternate SNP in linkage disequilibrium to rs1329428. In some embodiments, the alternate SNP comprises a minor allele or the allele which resides on the same haplotype of the risk allele of the selected SNP rs1329428. In some embodiments, the C2 risk allele is the rs429608:G allele, or equivalent allele thereof, or comprises a G at the selected SNP

patient has a BCVA better than 20/25 or worse than 20/400. In one embodiment, the BCVA was determined using ETDRS charts. In some embodiments, the antibody or antigen-binding fragment thereof is administered intravitreally. In some embodiments, the age-related macular degeneration is dry AMD. In some embodiments, the dry AMD is advanced dry AMD. In some embodiments, the advanced dry AMD is geographic atrophy. In some embodiments, the patient has a reduced mean change in geographic atrophy (GA) area following administration of the antibody as compared to control patients that did not receive the antibody treatment. In some embodiments, the mean change in GA area is determined by measuring GA area via standard imaging methods (e.g. fundus autofluorescence (FAF) or color fundus photography (CFP)). In some embodiments, the age-related macular degeneration is early AMD or intermediate AMD. In some embodiments, the patient with early AMD or intermediate AMD has a reduction or delay in appearance of clinical signs (e.g. may include measuring the number and size of drusen (for early and intermediate AMD) and monitoring hypo- and hyperpigmentation associated with drusen (for intermediate AMD)). In some embodiments, the methods further comprise administering a second medicament to the subject. In some embodiments, the second medicament is VEGF inhibitor.

[0015a] In another aspect, there is provided a method of predicting responsiveness of an AMD patient to treatment with an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising: determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient; (i) by providing a nucleic acid sample isolated from the biological sample; and (ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

[0016] Even another embodiment of the disclosure provides methods of predicting responsiveness of a degenerative disease (e.g. AMD) patient to treatment with an anti-factor D antibody or antigen-binding fragment thereof, the method comprising determining the genotype of the patient, wherein a patient who is determined to carry a risk allele is identified as a patient who has an increased risk for AMD progression (e.g. GA progression) and is more likely to respond to treatment with the anti-factor D antibody or antigen-binding fragment thereof. In one embodiment, the degenerative disease is an ocular degenerative disease. In one embodiment, the ocular degenerative disease is age-related macular degeneration. In some embodiments, the antibody is lampalizumab. In some embodiments, the risk allele is the minor allele of a selected SNP. In some embodiments, the risk allele is the major allele of a selected SNP. In some embodiments, the risk allele (e.g. AMD-associated polymorphism) may be a CFI risk allele, a CFH risk allele, a C2 risk allele, a CFB risk allele and/or a C3 risk allele. In some embodiments, the risk allele is a CFI risk allele. In some embodiments, the CFI risk allele is the rs4698775:G allele, or equivalent allele thereof or comprises a G at the selected SNP rs4698775, or comprises an alternate SNP in linkage disequilibrium to rs4698775. In some embodiments, the alternate SNP comprises a

is more likely to benefit from treatment comprising an anti-factor D antibody, or antigen-binding fragment thereof when at least one allele comprising a nucleotide selected from the group consisting of a G nucleotide at the SNP rs4698775 is present, a G nucleotide at the SNP rs17440077 is present, an A nucleotide at the SNP rs10737680 is present, a G nucleotide at the SNP rs1329428 is present, a G nucleotide at the SNP rs429608 is present or the G nucleotide at the SNP rs2230199 is present. The patient is identified as being at increased risk of AMD progression if the patient has one or two copies of the G allele at rs4698775 or rs17440077 associated with CFI, or equivalent allele thereof, at rs1329428 associated with CFH, or equivalent allele thereof, at rs429608 associated with C2/CFB, or equivalent allele thereof, or at rs2230199 associated with C3, or equivalent allele thereof or one or two copies of the A allele at rs10737680 associated with CFH, or equivalent allele thereof. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/100. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/100. In one embodiment, the study eye in the patient has a BCVA better than 20/25 or worse than 20/400. In one embodiment, the BCVA was determined using ETDRS charts. In some embodiments, the antibody or antigen-binding fragment thereof is administered intravitreally. In some embodiments, the age-related macular degeneration is dry AMD. In some embodiments, the dry AMD is advanced dry AMD. In some embodiments, the advanced dry AMD is geographic atrophy. In some embodiments, the age-related macular degeneration is early AMD or intermediate AMD. In some embodiments, the patient with early AMD or intermediate AMD has a reduction or delay in appearance of clinical signs (e.g. may include measuring the number and size of drusen (for early and intermediate AMD) and monitoring hypo- and hyperpigmentation associated with drusen (for intermediate AMD)). In some embodiments, the methods further comprise administering a second medicament to the subject. In some embodiments, the second medicament is VEGF inhibitor.

[0016a] In another aspect, there is provided a method of determining the likelihood that an AMD patient benefits from treatment with an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient; (i) by providing a nucleic acid sample isolated from the biological sample; and (ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

[0017] Yet another embodiment of the disclosure provides methods for determining the likelihood that a AMD patient will benefit from treatment with an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising determining genotype of the patient, wherein a patient who carries a risk allele, is identified as a patient who has an increased risk of AMD progression and is more likely to respond to treatment with an anti-factor D antibody, or antigen-binding fragment thereof. In some embodiments,

greater than 55% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 50% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 45% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 40% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 35% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 30% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 25% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 20% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 15% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 10% reduction of change in GA area from baseline GA area. In one embodiment, the treatment results in greater than 5% reduction of change in GA area from baseline GA area. In one embodiment, the patient has geographic atrophy secondary to AMD. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/25 and 20/100. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/400. In one embodiment, the study eye in the patient has a BCVA between 20/50 and 20/100. In one embodiment, the study eye in the patient has a BCVA better than 20/25 or worse than 20/400. In one embodiment, the BCVA was determined using ETDRS charts. In one embodiment, the patient has not received any previous intravitreal treatment, retinal surgery or other retinal therapeutic procedures in the study eye.

[0026] In one embodiment, the disclosure provides a kit for genotyping in a biological sample from a degenerative disease patient, wherein the kit comprises oligonucleotides for polymerase chain reaction or sequencing for detection of a risk allele. In another aspect, there is provided a kit for determining the presence of at least two AMD-associated polymorphisms in a biological sample, comprising reagents and instructions for detecting the genotype of the biological sample for the presence of at least two AMD-associated polymorphisms, wherein the AMD-associated polymorphisms are the SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199. In one embodiment, the biological sample is a blood sample, saliva, cheek swab, tissue sample or a sample of bodily fluids. In one embodiment, the biological sample is a nucleic acid sample.

C2, CFB, C3 or CFH respectively, selected from the group consisting of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or the A genotype at the SNP rs10737680. In one embodiment, the anti-factor D antibody, or antigen-binding fragment thereof, comprises HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, HVRL3, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6.

[0028] In one embodiment of the disclosure, the anti-factor D antibody, or antigen-binding fragment thereof, comprises the variable heavy chain of SEQ ID NO: 7 and/or the variable light chain of SEQ ID NO: 8..

[0029] In one embodiment of the disclosure, the polymorphism is a CFI polymorphism. In one embodiment, the CFI polymorphism is present in combination with one or more additional polymorphisms selected from the group consisting of a CFH polymorphism, a C2 polymorphism, a C3 polymorphism or a CFB polymorphism.

[0030] In one aspect, there is provided the use of an agent that specifically binds to at least two AMD-associated polymorphisms, wherein the polymorphisms are SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199, for the manufacture of a diagnostic for diagnosing AMD. In one embodiment, the CFI allele is an equivalent allele thereof, the CFH allele is an equivalent allele thereof, the C2 allele is an equivalent allele thereof, the CFB allele is an equivalent allele thereof, or the C3 allele is an equivalent allele thereof. In one embodiment, the CFI allele comprises a G at the single nucleotide polymorphism (SNP) rs4698775 or rs17440077, the CFH allele comprises an A at the single nucleotide polymorphism (SNP) rs10737680 or a G at the single nucleotide polymorphism (SNP) rs1329428, the C2 allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, the CFB allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, and the C3 allele comprises a G at the single nucleotide polymorphism (SNP) rs2230199. In one embodiment, at least one polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping

platforms, molecular beacons, 5' nuclease reaction, Taqman assay, MassArray (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification. In one embodiment, at least one polymorphism is detected by amplification of a target region containing at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to at least one polymorphism and detecting the hybridization. In one embodiment, the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or one or two alleles of the A genotype at the SNP rs10737680 in the individual indicates an increased risk for degenerative disease progression. In one embodiment, a polymorphism that is in linkage disequilibrium with at least one single nucleotide polymorphism selected from the group consisting of single nucleotide polymorphism (SNP) rs4698775, rs17440077, rs10737680, rs1329428, rs429608, and rs2230199 is detected. In one embodiment, the degenerative disease is age related macular degeneration. In one embodiment, the age related macular degeneration is early, intermediate or advanced AMD. In one embodiment, the advanced AMD is geographic atrophy.

[0031] In one aspect, there is provided an in vitro use of an agent that binds to at least two AMD-associated polymorphisms, wherein the polymorphisms are SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199, for identifying a patient having an AMD likely to respond to a therapy comprising an anti-factor D antibody, or antigen binding fragment thereof, wherein the presence of said polymorphisms identifies that the patient is more likely to respond to the therapy. In one embodiment, the CFI allele is an equivalent allele thereof, the CFH allele is an equivalent allele thereof, the C2 allele is an equivalent allele thereof, the CFB allele is an equivalent allele thereof, or the C3 allele is an equivalent allele thereof. In one embodiment, the CFI allele comprises a G at the single nucleotide polymorphism (SNP) rs4698775 or rs17440077, the CFH allele comprises an A at the single nucleotide polymorphism (SNP) rs10737680 or a G at the single nucleotide polymorphism (SNP) rs1329428, the C2 allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, the CFB allele comprises a G at the single nucleotide

WHAT IS CLAIMED IS:

1. A method of predicting the progression rate of an age related macular degeneration (AMD) in a patient having AMD, the method comprising:

determining the presence of at least two AMD-associated polymorphisms in a biological sample that has been obtained from the patient;

(i) by providing a nucleic acid sample isolated from the biological sample; and

(ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of single nucleotide polymorphism (SNP) rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199; wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

2. A method of identifying a patient having AMD as more likely to respond to a therapy comprising an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising:

determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient;

(i) by providing a nucleic acid sample isolated from the biological sample; and

(ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199;

wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

3. A method for optimizing the therapeutic efficacy of the treatment of a patient having AMD with an anti-factor D antibody, or antigen binding fragment thereof, the method comprising:

determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient;

(i) by providing a nucleic acid sample isolated from the biological sample; and

(ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199;

wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

4. A method of predicting responsiveness of an AMD patient to treatment with an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising:

determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient;

(i) by providing a nucleic acid sample isolated from the biological sample; and

(ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199;

wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

5. A method for determining the likelihood that an AMD patient benefits from treatment with an anti-factor D antibody, or antigen-binding fragment thereof, the method comprising:

determining the presence of at least two AMD-associated polymorphism in a biological sample that has been obtained from the patient;

(i) by providing a nucleic acid sample isolated from the biological sample; and

(ii) detecting the genotype of the nucleic acid sample for the presence of the AMD-associated polymorphism of SNP rs4698775 and the AMD-associated polymorphism selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199;

wherein the SNPs rs4698775 and rs17440077 are a CFI risk allele, the SNPs rs10737680 and rs1329428 are a CFH risk allele, the SNP rs429608 is a C2 or CFB risk allele, and the SNP rs2230199 is a C3 allele.

6. The method of any one of claims 1 to 5, wherein the CFI allele comprises a G at the single nucleotide polymorphism (SNP) rs4698775 or rs17440077, the CFH allele comprises an A at the single nucleotide polymorphism (SNP) rs10737680 or a G at the single nucleotide polymorphism (SNP) rs1329428, the C2 allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, the CFB allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, and the C3 allele comprises a G at the single nucleotide polymorphism (SNP) rs2230199.

7. The method of any one of claims 1 to 6, wherein the biological sample is a blood sample, saliva, cheek swab, tissue sample or a sample of a bodily fluid.

8. The method of claim 7, wherein the nucleic acid sample comprises DNA and/or RNA.

9. The method of claim 8, wherein the nucleic acid sample is amplified.

10. The method of claim 9, wherein the nucleic acid sample is amplified by a polymerase chain reaction.

11. The method of any one of claim 1-10, wherein at least one polymorphism is detected by polymerase chain reaction.

12. The method of any one of claims 1-10, wherein at least one polymorphism is detected by sequencing.

13. The method of any one of claims 1-10, wherein at least one polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5' nuclease reaction, Taqman assay, MassArray (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.
14. The method of any one of claims 1-10, wherein at least one polymorphism is detected by amplification of a target region containing at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to at least one polymorphism and detecting the hybridization.
15. The method of claim 1 wherein the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or one or two alleles of the A genotype at the SNP rs10737680 in the patient indicates an increased progression rate of the AMD.
16. The method of claim 6, wherein a polymorphism that is in linkage disequilibrium with at least one single nucleotide polymorphism selected from the group consisting of single nucleotide polymorphism (SNP) rs4698775, rs17440077, rs10737680, rs1329428, rs429608, and rs2230199 is detected.
17. The method of any one of claims 1-16 wherein the AMD is dry AMD.
18. The method of any one of claims 1-17, wherein the age related macular degeneration is early, intermediate or advanced AMD.
19. The method of claim 18, wherein the advanced AMD is geographic atrophy (GA).
20. The method of claim 1 wherein the genotype is detected by PCR using a set of oligonucleotides selected from SEQ ID NOs: 17-41 for respective alleles according to Table 9, and wherein the patient is identified as more likely to have increased progression rate when

the risk allele G at SNP rs4698775 for CFI allele is present along with at least one risk allele G at either SNP rs1329428 for CFH allele or SNP rs429608 for C2/CFB allele.

21. The method of claim 20, wherein the set of oligonucleotides include a forward primer selected from the group consisting of SEQ ID NOs. 17, 18, 25, 26, 34 and 35; a reverse primer selected from the group consisting of SEQ ID NOs. 19, 20, 27, 28, 36 and 37 and a labeled probe selected from the group consisting of SEQ ID NOs. 21-24, 29-33, and 38-41, according to Table 9.

22. The method of claim 21, wherein the genotype at rs4698775 (CFI) is detected using a forward primer of SEQ ID NO:17 or 18 combined with a reverse primer of SEQ ID NO:19 or 20 and a labeled probe selected from SEQ ID NOs. 21-24; the genotype at rs429608 (C2) is detected using a forward primer of SEQ ID NO:25 or 26 combined with a reverse primer of SEQ ID NO:27 or 28 and a labeled probe selected from SEQ ID NOs. 29-33; and the genotype at rs1329428 (CFH) is detected using a forward primer of SEQ ID NO:34 or 35 combined with a reverse primer of SEQ ID NO:36 or 37 and a labeled probe selected from SEQ ID NOs. 38-41.

23. The method of claim 2, wherein the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or one or two alleles of the A genotype at the SNP rs10737680 in the patient indicates an increased likelihood of response to an anti-factor D antibody treatment.

24. The method of any one of claims 2-23, wherein the anti-factor D antibody, or antigen-binding fragment thereof, comprises HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, HVRL3, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6.

25. The method of claim 24, wherein the anti-factor D antibody, or antigen-binding fragment thereof, comprises the variable heavy chain of SEQ ID NO:7 and/or the variable light chain of SEQ ID NO:8.

26. The method of claim 24 or 25, wherein the anti-factor D antibody, or fragment thereof is lampalizumab.

27. The method of claim 2, wherein the genotype is detected by PCR using a set of oligonucleotides selected from SEQ ID NOs: 17-41 for respective alleles according to Table 9, and wherein the patient is identified as more likely to respond to a therapy comprising anti-

factor D antibody, or an antigen-binding fragment thereof, when the risk allele G at SNP rs4698775 for CFI allele is present along with at least one risk allele G at either SNP rs1329428 for CFH allele or SNP rs429608 for C2/CFB allele.

28. The method of claim 27, wherein the set of oligonucleotides include a forward primer selected from SEQ ID NOs. 17, 18, 25, 26, 34 and 35; a reverse primer selected from the group consisting of SEQ ID NOs. 19, 20, 27, 28, 36 and 37 and a labeled probe selected from the group consisting of SEQ ID NOs. 21-24, 29-33, and 38-41, according to Table 9.

29. The method of claim 28, wherein the genotype at rs4698775 is detected using a forward primer of SEQ ID NO:17 or 18 combined with a reverse primer of SEQ ID NO:19 or 20 and a labeled probe selected from SEQ ID NOs. 21-24; the genotype at rs429608 (C2) is detected using a forward primer of SEQ ID NO:25 or 26 combined with a reverse primer of SEQ ID NO:27 or 28 and a labeled probe selected from SEQ ID NOs. 29-33; and the genotype at rs1329428 (CFH) is detected using a forward primer of SEQ ID NO:34 or 35 combined with a reverse primer of SEQ ID NO:36 or 37 and a labeled probe selected from SEQ ID NOs. 38-41.

30. A kit for determining the presence of at least two AMD-associated polymorphisms in a biological sample, comprising reagents and instructions for detecting the genotype of the biological sample for the presence of at least two AMD-associated polymorphisms, wherein the AMD-associated polymorphisms are the SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199.

31. The kit of claim 30 wherein the biological sample is a blood sample, saliva, cheek swab, tissue sample or a sample of bodily fluids.

32. The kit of claim 30 wherein the biological sample is one that has been obtained from a patient diagnosed with AMD.

33. The kit of any one of claims 30-32, wherein the AMD is dry AMD.

34. The kit of any one of claims 30-33, wherein the AMD is early, intermediate or advanced AMD.

35. The kit of claim 34, wherein the advanced AMD is geographic atrophy (GA).

36. A kit according to any one of claims 30-35, wherein the kit further comprises a package insert for determining whether a AMD patient is likely to respond to an anti-factor D antibody, or antigen binding fragment thereof.
37. A kit according to claim 30 wherein the kit is used to detect the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or two alleles of the A genotype at the SNP rs10737680.
38. The kit of claim 30, wherein the reagents comprise a set of oligonucleotides specific for detecting a polymorphism in CFI, C2, CFB, C3 or CFH allele.
39. A kit according to claim 38, wherein said set of oligonucleotides comprises a forward primer and a reverse primer suitable for amplifying a region of the CFI, C2, CFB, C3 or CFH gene comprising a polymorphism in CFI, C2, CFB, C3 or CFH respectively, selected from the group consisting of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or the A genotype at the SNP rs10737680.
40. The kit according to any one of claims 30-39, further comprising an oligonucleotide probe for detecting the polymorphism.
41. The kit according to any one of claims 30-40, wherein the reagents comprise a set of oligonucleotides selected from SEQ ID NOs: 17-41 for respective alleles according to Table 9.
42. The kit according to claim 41, wherein the reagents comprise (i) a forward primer of SEQ ID NO:17 or 18 combined with a reverse primer of SEQ ID NO:19 or 20 and a labeled probe selected from SEQ ID NOs. 21-24; (ii) a forward primer of SEQ ID NO:25 or 26 combined with a reverse primer of SEQ ID NO:27 or 28 and a labeled probe selected from SEQ ID NOs. 29-33; or (iii) a forward primer of SEQ ID NO:34 or 35 combined with a reverse primer of SEQ ID NO:36 or 37 and a labeled probe selected from SEQ ID NOs. 38-41.
43. The kit according to claim 42, wherein the reagents comprise a combination of (i)-(iii).
44. Use of an agent that specifically binds to at least two AMD-associated polymorphisms, wherein the polymorphisms are SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199, for the manufacture of a diagnostic for diagnosing AMD.
45. The use of claim 44, wherein the CFI allele comprises a G at the single nucleotide polymorphism (SNP) rs4698775 or rs17440077, the CFH allele comprises an A at the single nucleotide polymorphism (SNP) rs10737680 or a G at the single nucleotide polymorphism

(SNP) rs1329428, the C2 allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, the CFB allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, and the C3 allele comprises a G at the single nucleotide polymorphism (SNP) rs2230199:

46. The use of claim 44, wherein at least one polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5' nuclease reaction, Taqman assay, MassArray (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

47. The use of claim 44, wherein at least one polymorphism is detected by amplification of a target region containing at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to at least one polymorphism and detecting the hybridization.

48. The use of claim 44, wherein the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or one or two alleles of the A genotype at the SNP rs10737680 in the individual indicates an increased risk for AMD progression.

49. The use of claim 45, wherein a polymorphism that is in linkage disequilibrium with at least one single nucleotide polymorphism selected from the group consisting of single nucleotide polymorphism (SNP) rs4698775, rs17440077, rs10737680, rs1329428, rs429608, and rs2230199 is detected.

50. The use of any one of claims 44-49, wherein the AMD is dry AMD.

51. The use of any one of claims 44-50, wherein the age related macular degeneration is early, intermediate or advanced AMD.

52. The use of claim 51 wherein the advanced AMD is geographic atrophy.
53. In vitro use of an agent that binds to at least two AMD-associated polymorphisms, wherein the polymorphisms are SNP rs4698775 and a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608, and rs2230199, or a SNP that is in linkage disequilibrium with SNP rs4698775 and a SNP that is in linkage disequilibrium with a SNP selected from the group consisting of SNP rs17440077, rs10737680, rs1329428, rs429608 and rs2230199, for identifying a patient having an AMD likely to respond to a therapy comprising an anti-factor D antibody, or antigen binding fragment thereof, wherein the presence of said polymorphisms identifies that the patient is more likely to respond to the therapy.
54. The use of claim 53 wherein the CFI allele comprises a G at the single nucleotide polymorphism (SNP) rs4698775 or rs17440077, the CFH allele comprises an A at the single nucleotide polymorphism (SNP) rs10737680 or a G at the single nucleotide polymorphism (SNP) rs1329428, the C2 allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, the CFB allele comprises a G at the single nucleotide polymorphism (SNP) rs429608, and the C3 allele comprises a G at the single nucleotide polymorphism (SNP) rs2230199:
55. The use of claim 53 wherein at least one polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5' nuclease reaction, Taqman assay, MassArray (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.
56. The use of claim 53 wherein at least one polymorphism is detected by amplification of a target region containing at least one polymorphism, and hybridization with at least one

sequence-specific oligonucleotide that hybridizes under stringent conditions to at least one polymorphism and detecting the hybridization.

57. The use of claim 53 wherein the presence of one or two alleles of the G genotype at the SNP rs4698775, SNP rs17440077, SNP rs1329428, SNP rs429608 or SNP rs2230199 or one or two alleles of the A genotype at the SNP rs10737680 in the individual indicates an increased risk for AMD progression.

58. The use of claim 54 wherein a polymorphism that is in linkage disequilibrium with at least one single nucleotide polymorphism selected from the group consisting of single nucleotide polymorphism (SNP) rs4698775, rs17440077, rs10737680, rs1329428, rs429608, and rs2230199 is detected.

59. The use of any one of claims 53-58 wherein the AMD is dry AMD.

60. The use of any one of claims 53-59 wherein the age related macular degeneration is early, intermediate or advanced AMD.

61. The use of claim 60 wherein the advanced AMD is geographic atrophy.

62. Use of an anti-factor D antibody, or antigen-binding fragment thereof in the manufacture of a medicament for treating a patient who has been identified as a patient having an AMD who is more likely to respond to a therapy comprising the anti-factor D antibody, or antigen-binding fragment thereof, according to the method of claim 2.

63. The use of claim 62, wherein the anti-factor D antibody, or antigen-binding fragment thereof, comprises HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, HVRL3, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6.

64. The use of claim 62, wherein the anti-factor D antibody, or antigen-binding fragment thereof, comprises the variable heavy chain of SEQ ID NO:7 and/or the variable light chain of SEQ ID NO:8.

65. The use of claim 62, wherein the anti-factor D antibody, or fragment thereof is lampalizumab.

66. The use of any one of claims 62-65 wherein the AMD is dry AMD.

67. The use of any one of claims 62-66 wherein the age related macular degeneration is early, intermediate or advanced AMD.

68. The use of claim 67 wherein the advanced AMD is geographic atrophy.