human FHR-2 are found in the EMBL/GenBank Data Libraries under accession number BC022283. The FHR-2 gene sequence is found under GenBank accession number AL139418.

FHR-3 Gene

[0008] The FHR-3 gene is also known as *CFHR3*, *CFHL3*, *FHR3* and *HLF4*. The FHR-3 cDNA encodes a polypeptide 330 amino acids in length having a predicted molecular weight of 38 kDa (see Strausberg *et al.*, *Proc. Natl. Acad. Sci USA* 99:16899-16903). cDNA and amino acid sequence data for human FHR-3 are found in the EMBL/GenBank Data Libraries under accession number BC058009. The FHR-3 gene sequence is found under GenBank accession number AL049741.

FHR-4 Gene

[0009] The FHR-4 gene is also known as *CFHR4*, *CFHL4* and *FHR4*. The FHR-4 cDNA encodes a polypeptide 331 amino acids in length having a predicted molecular weight of 38 kDa (see Skerka *et al.*, 1991, *J. Biol. Chem.* 272:5627-5634). cDNA and amino acid sequence data for human FHR-4 are found in the EMBL/GenBank Data Libraries under accession number X98337. The FHR-4 gene sequence is found under GenBank accession numbers AF190816 (5' end), AL139418 (3' end) and BX248415.

FHR-5 Gene

[0010] The FHR-5 gene is also known as *CFHR5*, *CFHL5* and *FHR5*. The CFHR5 cDNA encodes a polypeptide 569 amino acids in length having an apparent molecular weight of 65 kDa (see McRae *et al.*, 2001, *J. Biol.Chem.* 276:6747-6754). cDNA and amino acid sequence data for human CFHR5 are found in the EMBL/GenBank Data Libraries under accession number AF295327. The 2821 base nucleotide sequence of the reference form of human *CFHR5* has GenBank accession number AF295327, and the polypeptide sequence has GenBank accession number AAK15619. The CFHR5 genomic sequence is found under GenBank accession numbers AL139418 (5' end) and AL353809 (3' end). The FHR-5 promoter is located 5' to the coding region of the CFHR5 gene.

BRIEF SUMMARY OF THE INVENTION

[0011] In one ~~aspect~~example, the ~~invention~~present disclosure provides a screening method for determining a human subject's propensity to develop a vascular disorder and/or age-related macular degeneration (AMD), involving analysis of a biological sample from the subject to detect the presence or absence of a deletion in chromosome 1 between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene, wherein the presence of a deletion is evidence

that the subject is at an increased risk of developing a vascular disorder and a decreased risk of developing AMD.

[0011a] In one aspect, there is provided an antibody that reduces the activity or amount of a gene product of the CFHR1 and/or CFHR3 genes, for use in the treatment of a subject having or at risk of developing AMD.

[0012] Examples of vascular disorders include aneurysms, such as abdominal aortic aneurysm (AAA) and brain intracranial aneurysm.

[0013] In one ~~embodiment~~example, the method comprises detecting the presence or absence of at least a portion of the complement Factor H-related 3 (*CFHR3*) gene. In a related ~~embodiment~~example the entire protein coding region of the *CFHR3* gene is deleted. In a related ~~embodiment~~example the entire *CFHR3* gene is deleted. In a related ~~embodiment~~example the entire *CFHR3* gene and the region between the *CFHR3* gene and complement Factor H-related 1 (*CFHR1*) gene are deleted.

[0014] In one ~~embodiment~~example, the method comprises detecting the presence or absence of at least a portion of the complement Factor H-related 1 (*CFHR1*) gene. In a related ~~embodiment~~example the entire protein coding region of the *CFHR1* gene is deleted. In a related ~~embodiment~~example the entire *CFHR1* gene is deleted. In a related ~~embodiment~~example the entire *CFHR1* gene and the region between the *CFHR1* gene and complement factor H-related 4 (*CFHR4*) gene are deleted. In a related ~~embodiment~~example the entire *CFHR1* gene and the region between the *CFHR1* gene and *CFHR3* gene are deleted.

[0015] In one ~~embodiment~~example, the method comprises detecting the presence or absence of at least a portion of the *CFHR3* gene and at least a portion of the *CFHR1* gene. In a related ~~embodiment~~example both the entire protein coding regions of the *CFHR3* and *CFHR1* genes are deleted. In a related ~~embodiment~~example the entire *CFHR3* and *CFHR1* genes are deleted.

[0016] In one ~~embodiment~~example, a deletion or a partial deletion of an intergenic sequence selected from: a) a sequence between the CFH gene and the CFHR3 gene; b) a sequence between the CFHR3 gene and the CFHR1 gene; c) a sequence between the CFHR1 gene and the CFHR4 gene. In yet another ~~embodiment~~example, at least a portion of the CFH gene is deleted (*e.g.*, at least a portion of exon 22 is deleted).

[0017] In one ~~embodiment~~example, the presence or absence of the deletion is detected by assaying for a gene product encoded in chromosome 1 between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene, where the absence of the gene product, or a reduced level of expression of the gene product, indicates the presence of deletion. In another ~~embodiment~~example, the presence or absence of a CFHR1 gene product and/or CFHR3 gene product is detected, where the absence of a gene product is indicative of a deletion. In one instance, the gene product is a protein. In another ~~embodiment~~example, detecting the presence or absence of a deletion is performed by analyzing a chromosome or nucleic acid (*e.g.*, DNA or RNA) from the subject.

[0018] In one ~~embodiment~~example the presence or absence of the deletion is detected by assaying for a truncated CFHR1 or CRHR3 gene product, where detection of a truncated gene product is indicative of a

deletion. In a preferred ~~embodiment~~example, the CFHR1 gene is partially deleted and expresses a truncated polypeptide gene product.

[0019] In one ~~embodiment~~example the subject has a genotype of T at position 1277 of the coding region of the *CFH* gene of the chromosome comprising the deletion.

[0020] The subject may be homozygous or heterozygous for deletions. Thus, in one ~~embodiment~~example, deletions are present in both chromosomes 1 of the subject.

[0021] The presence or absence of the deletion may be detected in a biological sample from a patient by, for example, analyzing a chromosome or nucleic acid (*e.g.*, DNA or RNA) sample from the subject. The presence or absence of the deletion also may be detected by, for example, determining the presence or absence of protein encoded by the (deleted) DNA in a biological sample from the subject, *e.g.*, a body fluid or tissue sample of the subject, by detecting a variant or truncated form of the CFHR1 or CFHR3 polypeptides in a body fluid or tissue sample of the subject, or by measuring the level of CFHR1 or CFHR3 polypeptides in a body fluid or tissue sample of the subject.

[0022] The biological sample is any sample taken from a patient that is suitable for use in the invention. Examples of biological samples that include body fluids include blood, serum, urine, cerebral spinal fluid (CSF) and saliva. In one embodiment, the body fluid is blood, serum or urine. Examples of biological samples that comprise tissue samples include a skin biopsy and a cheek scraping. In one ~~embodiment~~example, the tissue sample is a skin biopsy.

[0023] Proteins (amount or presence) may be detected, for example, using an immunoassay such as a sandwich immunoassay, a competitive immunoassay, a radioimmunoassay, fluorophore-labelled immunoassay, an ELISA or a Western blot. Mass spectroscopy also may be used. Variant proteins (amount or presence) may be detected, for example, using variant-specific antibodies. Truncated proteins (amount or presence) may be detected, for example, by a difference in the size of the protein by Western blot analysis or mass spectroscopy.

[0024] In certain ~~embodiments~~examples, the method comprises in the detecting step determining the presence of a deletion, for example, a deletion in a *CFHR1* or *CFHR3* gene, or the absence or a reduction of corresponding gene product (e.g., the amount or activity of the gene product) indicating a higher risk of the subject developing a vascular disorder.

[0025] In other ~~embodiments~~examples, the method comprises in the detecting step determining the absence of a deletion, for example, the presence of a *CFHR1* or *CFHR3* gene, or the presence or an increase of the corresponding gene product (e.g., the amount or activity of the gene product) indicating a lower risk of the subject developing a vascular disorder.

[0026] In another ~~embodiment~~example, the method comprises in the detecting step determining the presence of a deletion, for example, a deletion in a *CFHR1* or *CFHR3* gene, or the absence or a reduction

of the corresponding gene product (e.g., the amount or activity of the gene product) indicating a lower risk of the subject developing AMD.

[0027] In yet another example~~embodiment~~, the method comprises in the detecting step determining the absence of a deletion, for example, the presence of a *CFHR1* or *CFHR3* gene, or the presence or an increase of the corresponding gene product (e.g., the amount or activity of the gene product) indicating a higher risk of the subject developing AMD. The increase in gene product, for example, can be at least 10%, at least 20%, at least 50%, or more.

[0028] In certain example~~embodiments~~, the method further comprises detecting at least one other genetic variant or biomarker indicative of AMD and/or vascular disease. Genetic variants that may be detected in the invention include genetic variants of complement factor H (*CFH*) gene, *HTRA1* gene, complement factor B (BF) gene and/or the complement component 2 (C2) gene. In an example~~embodiment~~, the genetic variants include one or a plurality of polymorphic sites, such as those described herein.

[0029] In another example~~aspect~~, the present disclosure~~invention~~ provides a method for treating a subject having (i.e., exhibiting symptoms of), or is at risk for developing, a vascular disorder, by administering a CFHR1 polypeptide and/or a CFHR3 polypeptide to the subject. The polypeptide may be a full-length CFHR1 polypeptide or a fragment or portion thereof. The polypeptide may be a full-length CFHR3 polypeptide or a fragment or portion thereof.

[0029a] In another aspect, there is provided the use of an antibody that reduces the activity or amount of a gene product of the CFHR1 and/or CFHR3 genes for the manufacture of a medicament for the treatment of a subject having or at risk of developing AMD.

[0030] In another example, there is~~aspect the invention~~ provided a pharmaceutical composition comprising a CFHR3 protein or fragment thereof and at least one pharmaceutically effective excipient. In another example, there is~~aspect the invention~~ provideds a pharmaceutical composition comprising a CFHR1 protein or fragment thereof and at least one pharmaceutically effective excipient.

[0030a] In another aspect, there is provided a pharmaceutical composition comprising an anti-CFHR3 antibody that specifically binds to CFHR3; and a pharmaceutically acceptable carrier wherein the antibody is monoclonal.

[0030b] In another aspect, there is provided a pharmaceutical composition comprising an anti-CFHR1 antibody that specifically binds to CFHR1; and a pharmaceutically acceptable carrier, wherein the antibody of monoclonal.

[0031] In another example, the present disclosure~~aspect the invention~~ provides the use of a protein comprising the gene product of at least a portion of the CFHR3 and/or CFHR1 gene for the preparation of a medicament for the treatment of a vascular disorder.

[0032] In another example, the present disclosure~~aspect the invention~~ provides gene therapy vectors comprising nucleic acid encoding a CFHR3 or CFHR1 protein, or fragment thereof. The vector may include a promoter that drives expression of the *CFHR3* or *CFHR1* gene in multiple cell types. Alternatively, the vector may include a promoter that drives expression of the *CFHR3* or *CFHR1* gene only in specific cell types, for example, in cells of the retina or in cells of the kidney. In a related example~~aspect~~ pharmaceutical compositions are provided containing a gene therapy vector encoding a CFHR3 or CFHR1 protein or fragment thereof and a pharmaceutically acceptable excipient.

[0033] In another example, the present disclosure~~aspect the invention~~ provides a method of treating a subject having (i.e., exhibiting symptoms of), or susceptible to developing, age-related macular degeneration (AMD), by administering an agent that reduces the expression of the *CFHR1* and/or *CFHR3* genes or reduces the

activity or amount of a gene product of the *CFHR1* and/or *CFHR3* genes. Agents include antisense RNA, siRNA or ribozyme that reduces expression of the *CFHR1* and/or *CFHR3* genes. In a related example~~aspect~~ the level of protein is reduced, for example by using plasmaphoresis or antibody-based inhibition, for example, using an anti-CFHR1 antibody and/or an anti-CFHR3 antibody.

[0034] In another example, the present disclosure~~aspect the invention~~ provides a pharmaceutical composition comprising an anti-CFHR1 antibody and a pharmaceutically acceptable carrier. In one example~~embodiment~~, an anti-CFHR1 antibody specifically binds the amino-terminus of a CFHR1 polypeptide. In another example, the present disclosure~~aspect the invention~~ provides a pharmaceutical composition comprising an anti-CFHR3 antibody and a pharmaceutically acceptable carrier. In one example~~embodiment~~, an anti-CFHR3 antibody specifically binds the carboxyl-terminus of a CFHR3 antibody.

[0035] In another example, the present disclosure~~aspect the invention~~ provides a diagnostic kit for diagnosing susceptibility to a vascular disorder and/or AMD in a subject, comprising nucleic acid primers or probes that detect the presence or absence of a deletion in the DNA sequence between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene on human chromosome 1.

[0036] In another example, the present disclosure~~aspect the invention~~ provides a diagnostic device comprising nucleic acid primers or probes that detect the presence or absence of a deletion in the DNA sequence between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene on human chromosome 1 immobilized on a substrate, such as a microarray.

[0037] In another example, the present disclosure~~aspect the invention~~ provides a diagnostic kit for diagnosing susceptibility to a vascular disorder and/or AMD in a subject, comprising antibodies that detect the presence or absence of the complement Factor H-related 3 (CFHR3) protein, or variant or truncated forms thereof, and/or complement Factor H related 1 (CFHR1) protein, or variant or truncated forms thereof, in a body fluid or tissue sample of the subject.

[0038] In another example, the present disclosure~~aspect the invention~~ provides a drug screening method for screening for agents for use in treating a vascular disorder. The method involves a) combining (i) a cell that expresses CFHR3 and/or CFHR1 polypeptides; and (ii) a test agent; b) measuring the level of CFHR3 and/or CFHR1 polypeptides secreted into the medium; and c) comparing the level of CFHR3 and/or CFHR1 polypeptides secreted into the medium in the presence of the test agent with a reference value, said reference value being the level of CFHR3 and/or CFHR1 polypeptides secreted into the medium in the absence of the test agent, where a higher level of CFHR3 and/or CFHR1 polypeptides secreted into the medium in the presence of the test agent indicates the test agent may be useful for treating the vascular disorder.

[0039] In another example, the present disclosure~~aspect the invention~~ provides a method for identifying a CFH protein likely to protect against AMD development, by identifying a subject with a deletion in the DNA sequence between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene on human chromosome 1; determining the sequence of the *CFH* gene encoded by the gene contained in the chromosome containing the deletion; and determining the sequence of the protein encoded by the *CFH* gene, wherein said protein is different from wild-type CFH, said protein being a CFH protein likely to protect against AMD development. The present disclosure~~invention~~ also provides a protective CFH protein obtained using the method.

BRIEF DESCRIPTION OF THE FIGURES

[0040] Figure 1 is a diagram showing the organization of the regulators-of-complement-activation (RCA) gene cluster on chromosome 1q32 and the arrangement of approximately 60-amino acid domains known as short consensus repeats (SCRs) in complement Factor H (CFH), Factor H-Like 1 (CFHL1) and Factor H-Related 1, 2, 3, 4 and 5 (CFHR1, CFHR2, CFHR3, CFHR4 and CFHR5). CFH has 20 SCRs. The interacting partners with some of these SCRs has been determined and is shown on the top right (CRP, C reactive protein; Hep, heparin). Complement factor H-like 1 (CFHL1) is a splice isoform of CFH, while complement factor H-related proteins 1-5 (CFHR1-5) are each encoded by a unique gene (*CFHR1-5*). The SCRs of CFHR1-5 are similar to some of the SCRs in CFH, as denoted by the numbers in the ovals. For example, CFHR5 has 9 SCRs, with the first two being similar to SCRs 6 and 7 of Factor H and therefore having CRP and heparin binding properties. SCRs 5-7 of CFHR5 have the numbers 12-14 within the corresponding ovals because these SCRs are similar to SCRs 12-14 of Factor H and have C3b and heparin binding properties.

[0041] Figure 2 shows regions of homology (genomic duplications) in the genes encoding CFH and the Factor H-related proteins. Exons are indicated as vertical lines. Regions labeled with the same letter (*e.g.*, A, A', and A") have substantially identical sequences.

[0042] Figure 3 shows a Western blot of serum proteins from seven patients using an anti-human CFH antibody. FHL-1, CFHR1 and CFHR2 indicate the positions of the truncated form of CFH, CFHR1 and CFHR2, respectively. The anti-human CFH antibody employed also cross-reacts with CFHR1 and CFHR2. No CFHR1 is detected in the serum of two patients (197-02 and 325-02) that have a homozygous deletion of the *CFHR3* and *CFHR1* genes, as determined by SSCP analysis and direct DNA sequencing.

[0043] Figure 4 shows a SSCP analysis of the *CFH*, *CFHR3* and *CFHR1* genes. 1, 2, 3, and 4 indicate four different SSCP patterns observed using primers from exon 22 of the *CFH* gene to PCR amplify DNA. SSCP patterns 1, 2 and 3 correspond to homozygous non-deletion or heterozygous

WHAT IS CLAIMED IS:

1. A screening method for determining a human subject's propensity to develop a vascular disorder and/or age-related macular degeneration (AMD) comprising:

analyzing a biological sample from the subject to detect the presence or absence of a deletion in the region of chromosome 1 between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene

wherein the presence of a deletion indicates the subject is at increased risk of developing a vascular disorder and is at decreased risk of developing AMD.

2. The method of claim 1 wherein the presence or absence of the deletion is detected by assaying for a gene product encoded in chromosome 1 between the 3' end of exon 22 of the complement factor H (*CFH*) gene and the 5' end of exon 1 of complement Factor H-related 4 (*CFHR4*) gene, where the absence of the gene product, or a reduced level of expression of the gene product, indicates the presence of deletion.

3. The method of claim 2 wherein the presence or absence of a CFHR1 gene product and/or a CFHR3 gene product is detected, where the absence of a gene product is indicative of a deletion.

4. The method of claim 2 wherein the gene product is a protein.

5. The method of claim 3 wherein entire protein coding region of the CFHR3 gene is deleted.

6. The method of claim 3 wherein entire protein coding region of the CFHR1 gene is deleted.

7. The method of claim 1 comprising detecting a deletion of an intragenic sequence selected from a sequence between the CFHR3 gene and the CFHR1 gene and a sequence between the CFHR1 gene and the CFHR4 gene.

8. The method of claim 1 wherein the subject is homozygous for the deletion.

9. The method of claim 1 wherein the biological sample is blood, serum, urine or a tissue sample.

10. The method of claim 4 wherein the detection step comprises detecting a gene product using an immunoassay or mass spectroscopy.

11. The method of claim 1 wherein the presence or absence of the deletion is detected by assaying for a truncated CFHR1 or CFHR3 gene product, where detection of a truncated gene product is indicative of a deletion.

12. The method of claim 1 wherein the step comprising detecting the presence or absence of a deletion is performed by analyzing a chromosome or nucleic acid from the subject.

13. The method of claim 12 wherein the nucleic acid is DNA or RNA.

14. The method of claim 1, wherein the vascular disorder is aneurysm.

15. The method of claim 1 wherein the subject has a genotype of T at position 1277 of the coding region of the *CFH* gene of the chromosome comprising the deletion.

16. The method of claim 1 further comprising detecting genetic variants of complement factor H (CFH) gene comprising detecting one or a plurality of polymorphic sites selected from the group consisting of:

a) any one or more of rs529825; rs800292; rs3766404; rs1061147; rs1061170; and rs203674;

b) any one of more of intron 2 (IVS2 or insTT); rs2274700; exon 10A; and rs375046;

c) one or both of rs529825 and rs800292;

d) one or more of rs1061147, rs1061170 and rs203674;

e) at least one of rs529825 and rs800292; and rs3766404; and at least one of rs1061147, rs1061170 and rs203674;

f) at least rs529825, rs800292, rs3766404, rs1061170, and rs203674;

g) exon 22 (R1210C); and

h) exon 22 (R1210C) and any of (a)-(g).

17. The method of claim 1 further comprising detecting in a sample from the subject a macular degeneration-associated molecule selected from the group consisting of fibulin-3, vitronectin,

β-crystallin A2, β-crystallin A3, β-crystallin A4, β-crystallin S, glucose-regulated protein 78 kD (GRP-78), calreticulin, 14-3-3 protein epsilon, serotransferrin, albumin, keratin, pyruvate carboxylase, villin 2, complement 1 q binding protein/hyaluronic acid binding protein ("complement 1 q component"), amyloid A (al amyloid A), amyloid P component, C5 and CSb-9 terminal complexes, HLA-DR, fibrinogen, Factor X, prothrombin, complements 3,5 and 9, complement reactive protein (CRP), HLA-DR, apolipoprotein A, apolipoprotein E, antichymotrypsin, p2 microglobulin, thrombospondin, elastin, collagen, ICAM-1, LFA1, LFA3, B7, IL-1, IL-6, IL-12, TNF-alpha, GM-CSF, heat shock proteins, colony stimulating factors (GM-CSF, M-CSFs), and IL-10.

18. The method of claim 1 further comprising detecting in a sample from the subject genetic variants of the HTRA1 gene comprising detecting a polymorphic site selected from the group consisting of: at least one of rs10490924, rs11200638, rs760336, and rs763720.

19. The method of claim 1 further comprising detecting in a sample from the subject genetic variants of the complement factor B (BF) gene and/or the complement component 2 (C2) gene comprising detecting a polymorphic site selected from the group consisting of:

a) A or G at rs641153 of the BF gene, or R or Q at position 32 of the BF protein;

b) A or T at rs4151667 of the BF gene, or L or H at position 9 of the BF protein;

c) G or T at rs547154 of the C2 gene; and

d) C or G at rs9332379 of the C2 gene, or E of D at position 318 of the C2 protein.

20. A method of treating a subject having or at risk for developing a vascular disorder, comprising administering a CFHR1 polypeptide, a CFHR3 polypeptide, at least one portion of a CFHR1 and/or a CFHR3 polypeptide, or mixtures thereof, to the subject.

21. The method of claim 20 comprising administering a CFHR1 polypeptide.

22. The method of claim 21 comprising administering a full-length CFHR1 polypeptide.

23. The method of claim 20 comprising administering a CFHR3 polypeptide.

24. The method of claim 23 comprising administering a full-length CFHR3 polypeptide.

25. The method of claim 20 wherein the vascular disease is aneurysm.

26. A pharmaceutical composition comprising a CFHR3 protein or a fragment thereof and at least one pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising a CFHR1 protein or a fragment thereof and at least one pharmaceutically acceptable carrier.

28. A pharmaceutical composition comprising a gene therapy vector encoding a CFHR3 polypeptide or a fragment thereof and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition comprising a gene therapy vector encoding a CFHR1 polypeptide or a fragment thereof and a pharmaceutically acceptable carrier.

30. A method of treating a subject having or at risk of developing AMD comprising administering an agent that reduces the expression of the *CFHR1* and/or *CFHR3* genes or reduces the activity or amount of a gene product of the *CFHR1* and/or *CFHR3* genes.

31. The method of claim 30 wherein the agent is an antisense RNA, siRNA or ribozyme that reduces expression of the *CFHR1* and/or *CFHR3* genes.

32. The method of claim 30 comprising reducing the level of CFHR1 and/or CFHR3 gene product by plasmaphoresis.

33. The method of claim 30 comprising reducing the level of CFHR1 and/or CFHR3 gene product by administering an antibody to a CFHR1 protein and/or an antibody to a CFHR3 protein.

34. A pharmaceutical composition comprising an anti-CFHR1 antibody and a pharmaceutically acceptable carrier.

35. The pharmaceutical composition of claim 34 comprising an anti-CFHR1 antibody which binds the amino-terminus of a CFHR1 polypeptide.

36. A pharmaceutical composition comprising an anti-CFHR3 antibody and a pharmaceutically acceptable carrier.

37. The pharmaceutical composition of claim 36 comprising an anti-CFHR3 antibody which binds the carboxyl-terminus of a CFHR3 polypeptide.

38. A kit for conducting the screening method of claim 1 comprising reagents for detecting the presence or absence of a deletion in the DNA sequence between the 3' end of exon 22 of the *CFH* gene and the 5' end of exon 1 of the *CFHR4* gene on human chromosome 1 and/or the presence or absence of a CFHR1 and/or CFHR3 gene product.

39. A kit for conducting the screening method of claim 1 comprising an antibody that reacts preferentially with CFHR1 and/or CFHR3 protein, or a portion thereof.

40. A method of screening for agents for use in treating a vascular disorder, comprising:

a) combining

i) a cell that expresses CFHR3 and/or CFHR1 polypeptides; and

ii) a test agent;

b) measuring the level of expression of the CFHR3 and/or CFHR1 genes; and

c) comparing the level of CFHR3 and/or CFHR1 gene expression in the presence of the test agent with a reference value, said reference value being the level of CFHR3 and/or CFHR1 gene expression in the absence of the test agent,

wherein a higher level of CFHR3 and/or CFHR1 gene expression in the presence of the test agent indicates the test agent may be useful for treating the vascular disorder.

41. Use of a protein comprising the gene product of at least a portion of the CFHR3 gene for the preparation of a medicament for the treatment of a vascular disorder.

42. Use of a protein comprising the gene product of at least a portion of the CFHR1 gene for the preparation of a medicament for the treatment of a vascular disorder.

43. Use of an antibody that binds an epitope of CFHR1 for the preparation of a medicament for the treatment of age-related macular degeneration (AMD).

44. Use of an antibody that binds an epitope of CFHR3 for the preparation of a medicament for the treatment of age-related macular degeneration (AMD).

WHAT IS CLAIMED IS:

1. An antibody that reduces the activity or amount of a gene product of the CFHR1 and/or CFHR3 genes, for use in the treatment of a subject having or at risk of developing AMD.

2. Use of an antibody that reduces the activity or amount of a gene product of the CFHR1 and/or CFHR3 genes for the manufacture of a medicament for the treatment of a subject having or at risk of developing AMD.

3. The antibody for use as defined in Claim 1 or the use as defined in Claim 2, wherein the antibody is an antibody to a CFHR1 protein.

4. The antibody for use as defined in Claim 3 or the use as defined in Claim 3, wherein said antibody binds the amino-terminus of a CFHR1 polypeptide.

5. The antibody for use as defined in Claim 3 or the use as defined in Claim 3, wherein said treatment further comprises administering an antibody to a CFHR3 protein.

6. The antibody for use as defined in Claim 1 or the use as defined in Claim 2, wherein the antibody is an antibody to a CFHR3 protein.

7. The antibody for use as defined in Claim 6 or the use as defined in Claim 6, wherein said antibody binds the carboxyl-terminus of a CFHR3 polypeptide.

8. The antibody for use as defined in Claim 6 or the use as defined in Claim 6, wherein said treatment further comprises administering an antibody to a CFHR1 protein.

9. A pharmaceutical composition comprising an anti-CFHR1 antibody that specifically binds to CFHR1; and a pharmaceutically acceptable carrier, wherein the antibody of monoclonal.

10. The pharmaceutical composition of claim 9 wherein the antibody specifically binds an epitope between amino acids 1-143 of SEQ ID NO: 4 within the amino-terminus of a CFHR1 polypeptide.

11. A pharmaceutical composition comprising an anti-CFHR3 antibody that specifically binds to CFHR3; and a pharmaceutically acceptable carrier, wherein the antibody is monoclonal.

12. The pharmaceutical composition of claim 11 wherein the antibody specifically binds an epitope between amino acids 144-330 of SEQ ID NO: 6 within the carboxyl-terminus of a CFHR3 polypeptide.