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(71) Applicant: THE PROCTER & GAMBLE COMPANY

[US/US]; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US).

(72) Inventors: VELASQUEZ, Juan, Esteban;

One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). TREJO, Amy, Violet; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). BREYFOGLE, Laurie, Ellen; One Procter & Gamble Plaza, Cincinnati, Ohio 45202

(US). HENRY, James, Patrick; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). DOBROZSI, Douglas, Joseph; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). PENNER, Gregory, Allen; NeoVentures Biotechnology Inc., 516 Colborne St., London, Ontario N6B 2T5 (CA).

(74) Agent: KREBS, Jay A.; c/o THE PROCTER & GAMBLE COMPANY, Global IP Services, One Procter & Gamble Plaza, C9, Cincinnati, Ohio 45202 (US).

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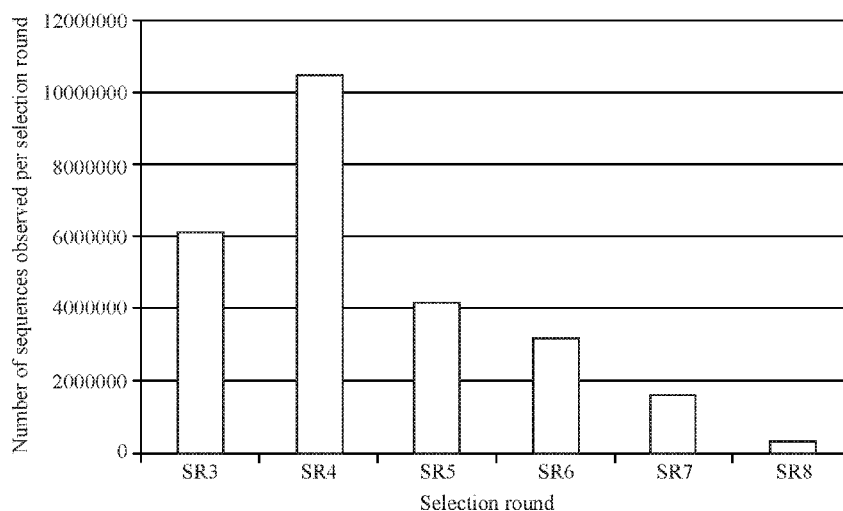


Figure 1

(57) Abstract: The present invention is directed to an aptamer composition comprising at least one oligonucleotide consisting of: deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof; wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*.



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APTAMERS FOR PERSONAL CARE APPLICATIONS

FIELD OF INVENTION

The present invention generally relates to nucleic acid aptamers that have a high binding
5 affinity and specificity for fungi of the genus *Malassezia*. This invention also relates to the use of
such aptamers as delivery vehicles of active ingredients to the scalp and the skin.

BACKGROUND OF THE INVENTION

Aptamers are short single-stranded oligonucleotides, with a specific and complex three-
10 dimensional shape, that bind to target molecules. The molecular recognition of aptamers is based
on structure compatibility and intermolecular interactions, including electrostatic forces, van der
Waals interactions, hydrogen bonding, and π - π stacking interactions of aromatic rings with the
target material. The targets of aptamers include, but are not limited to, peptides, proteins,
nucleotides, amino acids, antibiotics, low molecular weight organic or inorganic compounds, and
15 even whole cells. The dissociation constant of the complexes of aptamers and the corresponding
target materials typically varies between micromolar and picomolar levels, which is comparable to
the affinity of antibodies to their antigens. Aptamers can also be designed to have high specificity,
enabling the discrimination of target molecules from closely related derivatives.

Aptamers are usually designed in vitro from large libraries of random nucleic acids by
20 Systematic Evolution of Ligands by Exponential Enrichment (SELEX). The SELEX method was
first introduced in 1990 when single stranded RNAs are selected against low molecular weight
dyes (Ellington, A.D., Szostak, J. W., 1990. Nature 346: 818-822). A few years later, single
stranded DNA aptamers and aptamers containing chemically modified nucleotides are also
described (Ellington, A.D., Szostak, J.W., 1992. Nature 355: 850-852; Green, L.S., et al., 1995.
25 Chem. Biol. 2: 683-695). Since then, aptamers for hundreds of microscopic targets, such as cations,
small molecules, proteins, cells, or tissues have been selected. A compilation of examples from the
literature is included in the database at the website: [http://www.aptagen.com/apramer-
index/apramer-list.aspx](http://www.aptagen.com/apramer-index/apramer-list.aspx). However, a need still exists for aptamers that selectively bind to fungi of
the genus *Malassezia*, including *M. globosa*. These aptamers could be used to effectively deliver
30 active ingredients, such as anti-fungal agents, to the scalp or the skin.

SUMMARY OF THE INVENTION

In this invention, we have demonstrated the use of SELEX for the selection of aptamers against strains of the genus *Malassezia* and the use of such aptamers for the delivery of active ingredients to the scalp or the skin.

5 In the present invention, an aptamer composition is provided. The aptamer composition may comprise at least one oligonucleotide consisting of deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof, wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*.

10 In the present invention, an aptamer composition is provided. The aptamer composition may comprise at least one oligonucleotide selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4.

15 In the present invention, the aptamer composition may comprises at least one oligonucleotide comprising one or more motifs selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103.

 In the present invention, a personal care composition is provided. The personal care composition may comprise at least one nucleic acid aptamer, wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*.

20 In the present invention, a method for delivering one or more personal care active ingredients to the scalp or the skin is provided. The method may comprise administering a personal care composition comprising at least one nucleic acid aptamer and one or more personal care active ingredients, wherein said at least one nucleic acid aptamer and said one or more personal care active ingredients are covalently or non-covalently attached, and wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*.

25 In the present invention, a method for delivering one or more personal care active ingredients to the scalp of the skin is provided. The method may comprise administering a personal care composition comprising at least one nucleic acid aptamer and one or more nanomaterials, wherein said at least one nucleic acid aptamer and said one or more nanomaterials are covalently or non-covalently attached, wherein said at least one nucleic acid aptamer has a binding affinity
30 for one or more fungi species from the genus *Malassezia*, and wherein said one or more nanomaterials comprise one or more personal care active ingredients.

BRIEF DESCRIPTION OF THE DRAWING FIGURES

For a more complete understanding of the disclosure, reference should be made to the following detailed description and drawing Figures.

5 FIGURE 1. Total number of sequences on each selection round.

FIGURE 2. The enrichment trajectories of the top twenty sequences in terms of copy number across different selection rounds.

FIGURE 3. Binding of different aptamers to *M. globosa* as demonstrated by qPCR analysis.

10 FIGURE 4. Comparison of Ct values with different aptamers assessed for binding to *M. globosa*.

FIGURE 5. Motif analysis of random region of aptamer Mg-1.

FIGURE 6. The predicted secondary structures of aptamer Mg-1 and its conserved motifs.

FIGURE 7. Motif analysis of random region of aptamer Mg-2.

FIGURE 8. Predicted secondary structure of aptamer Mg-2.

15 FIGURE 9. Alignment of exemplary sequences with at least 90% nucleotide sequence identity that are identified during the selection process.

FIGURE 10. Alignment of exemplary sequences with at least 70% nucleotide sequence identity that are identified during the selection process.

20 FIGURE 11. Alignment of exemplary sequences with at least 50% nucleotide sequence identity that are identified during the selection process.

DETAILED DESCRIPTION OF THE INVENTION

I. DEFINITIONS

25 As used herein, the term “aptamer” refers to a single stranded oligonucleotide or a peptide that has a binding affinity for a specific target.

As used herein, the term “nucleic acid” refers to a polymer or oligomer of nucleotides. Nucleic acids are also referred as “ribonucleic acids” when the sugar moiety of the nucleotides is D-ribose and as “deoxyribonucleic acids” when the sugar moiety is 2-deoxy-D-ribose.

30 As used herein, the term “nucleotide” usually refers to a compound consisting of a nucleoside esterified to a monophosphate, polyphosphate, or phosphate-derivative group via the hydroxyl group of the 5-carbon of the sugar moiety. Nucleotides are also referred as “ribonucleotides” when the sugar moiety is D-ribose and as “deoxyribonucleotides” when the sugar moiety is 2-deoxy-D-ribose.

As used herein, the term “nucleoside” refers to a glycosylamine consisting of a nucleobase, such as a purine or pyrimidine, usually linked to a 5-carbon sugar (e.g. D-ribose or 2-deoxy-D-ribose) via a β -glycosidic linkage. Nucleosides are also referred as “ribonucleosides” when the sugar moiety is D-ribose and as “deoxyribonucleosides” when the sugar moiety is 2-deoxy-D-ribose.

As used herein, the term “nucleobase”, refers to a compound containing a nitrogen atom that has the chemical properties of a base. Non-limiting examples of nucleobases are compounds comprising pyridine, purine, or pyrimidine moieties, including, but not limited to adenine, guanine, hypoxanthine, thymine, cytosine, and uracil.

As used herein, the term “oligonucleotide” refers to an oligomer composed of nucleotides.

As used herein, the term “identical” or “sequence identity,” in the context of two or more oligonucleotides, nucleic acids, or aptamers, refers to two or more sequences that are the same or have a specified percentage of nucleotides that are the same, when compared and aligned for maximum correspondence, as measured using sequence comparison algorithms or by visual inspection.

As used herein, the term “substantially homologous” or “substantially identical” in the context of two or more oligonucleotides, nucleic acids, or aptamers, generally refers to two or more sequences or subsequences that have at least 40%, 60%, 80%, 90%, 95%, 96%, 97%, 98% or 99% nucleotide identity, when compared and aligned for maximum correspondence, as measured using sequence comparison algorithms or by visual inspection.

As used herein, the term “epitope” refers to the region of a target that interacts with the aptamer. An epitope can be a contiguous stretch within the target or can be represented by multiple points that are physically proximal in a folded form of the target.

As used herein the term “binding affinity” may be calculated using the following equation: Binding Affinity = Amount of aptamer bound to one or more fungi species / Total amount of aptamer incubated with the one or more fungi species.

As used herein, the term “motif” refers to the sequence of contiguous, or series of contiguous, nucleotides occurring in a library of aptamers with binding affinity towards a specific target and that exhibits a statistically significant higher probability of occurrence than would be expected compared to a library of random oligonucleotides. The motif sequence is frequently the result or driver of the aptamer selection process.

II. APTAMER COMPOSITIONS

Nucleic acid aptamers are single-stranded oligonucleotides with specific secondary and tertiary structures, that can bind to targets with high affinity and specificity. In the present invention, an aptamer composition may comprise at least one oligonucleotide consisting of
5 deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof, wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*. In the present invention, said one or more fungi species may be selected from the group consisting of *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*,
10 *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof. In the present invention, said one or more fungi species may be selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.

In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 50% nucleotide
15 sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 70% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected
20 from the group consisting of oligonucleotides with at least 90% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of
25 oligonucleotides containing at least 10 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides containing at least 20 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer
30 composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides containing at least 40 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of

oligonucleotides containing at least 60 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides containing at least 70 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides containing at least 80 contiguous nucleotides from sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100. A non-limiting example of oligonucleotides with at least 90% nucleotide sequence identity to SEQ ID NO 59 is SEQ ID NO 73. Non-limiting examples of oligonucleotides with at least 90% nucleotide sequence identity to SEQ ID NO 6 are SEQ ID NO 66, SEQ ID NO 74, SEQ ID NO 85, and SEQ ID NO 86. Non-limiting examples of oligonucleotides with at least 90% nucleotide sequence identity to SEQ ID NO 5 are SEQ ID NO 23, SEQ ID NO 91, SEQ ID NO 92, and SEQ ID NO 95 (see Figure 9).

In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 50% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 70% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4. In the present invention, said aptamer composition may comprise at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 90% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4. Non-limiting examples of oligonucleotides with at least 50% nucleotide sequence identity to SEQ ID NO 2 are SEQ ID NO 84, SEQ ID NO 47, SEQ ID NO 17, SEQ ID NO 19, SEQ ID NO 25, SEQ ID NO 44, SEQ ID NO 49, SEQ ID NO 10, SEQ ID NO 30, SEQ ID NO 54, SEQ ID NO 29, SEQ ID NO 26, SEQ ID NO 35, SEQ ID NO 53, SEQ ID NO 22, SEQ ID NO 31, and SEQ ID NO 28 (see Figure 11). Non-limiting examples of oligonucleotides with at least 70% nucleotide sequence identity to SEQ ID NO 4 are SEQ ID NO 20, SEQ ID NO 58, SEQ ID NO 72, SEQ ID NO 80, SEQ ID NO 43, SEQ ID NO 64, SEQ ID NO 65, and SEQ ID NO 71 (see Figure 10).

In the present invention, said at least one oligonucleotide comprises one or more motifs selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103. In the present invention, said aptamer composition may comprise at least one oligonucleotide comprising a sequence of nucleotides with at least 70% nucleotide sequence identity to sequences
5 selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103. In the present invention, said aptamer composition may comprise at least one oligonucleotide comprising a sequence of nucleotides with at least 80% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103. In the present invention, said aptamer composition may comprise at least one oligonucleotide
10 comprising a sequence of nucleotides with at least 90% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103.

Chemical modifications can introduce new features into the aptamers such as different molecular interactions with the target, improved binding capabilities, enhanced stability of oligonucleotide conformations, or increased resistance to nucleases. In the present invention, said
15 at least one oligonucleotide of said aptamer composition may comprise natural or non-natural nucleobases. Natural nucleobases are adenine, cytosine, guanine, thymine, and uracil. Non-limiting examples of non-natural nucleobases are hypoxanthine, xanthine, 7-methylguanine, 5,6-dihydrouracil, 5-methylcytosine, 5-hydroxymethylcytosine, thiouracil, 1-methylhypoxanthine, 6-methylisoquinoline-1-thione-2-yl, 3-methoxy-2-naphthyl, 5-propynyluracil-1-yl, 5-methylcytosin-1-yl, 2-aminoadenin-9-yl, 7-deaza-7-iodoadenin-9-yl, 7-deaza-7-propynyl-2-aminoadenin-9-yl, phenoxazinyl, phenoxazinyl-G-clam, bromouracil, 5-iodouracil, and mixtures thereof.
20 thereof.

Modifications of the phosphate backbone of the oligonucleotides can also increase the resistance against nuclease digestion. In the present invention, the nucleosides of said
25 oligonucleotides may be linked by a chemical motif selected from the group comprising natural phosphate diester, chiral phosphorothionate, chiral methyl phosphonate, chiral phosphoramidate, chiral phosphate chiral triester, chiral boranophosphate, chiral phosphoroselenoate, phosphorodithioate, phosphorothionate amidate, methylenemethylimino, 3'-amide, 3' achiral phosphoramidate, 3' achiral methylene phosphonates, thioformacetal, thioethyl ether, fluorophosphate, and mixtures thereof. In the present invention, the nucleosides of said
30 oligonucleotides may be linked by natural phosphate diesters.

In the present invention, the sugar moiety of the nucleosides of said oligonucleotides may be selected from the group comprising ribose, deoxyribose, 2'-fluoro deoxyribose, 2'-O-methyl

ribose, 2'-O-(3- amino)propyl ribose, 2'-O-(2-methoxy)ethyl ribose, 2'-O-2-(N,N-dimethylaminoxy)ethyl ribose, 2'-O-2-[2-(N,N-dimethylamino)ethyloxy]ethyl ribose, 2'-O-N,N-dimethylacetamidyl ribose, N-morpholinophosphordiamidate, α -deoxyribofuranosyl, other pentoses, hexoses, and mixtures thereof.

5 In the present invention, said derivatives of ribonucleotides or said derivatives of deoxyribonucleotides may be selected from the group comprising: locked oligonucleotides, peptide oligonucleotides, glycol oligonucleotides, threose oligonucleotides, hexitol oligonucleotides, altritol oligonucleotides, butyl oligonucleotides, L-ribonucleotides, arabino oligonucleotides, 2'-fluoroarabino oligonucleotides, cyclohexene oligonucleotides, phosphorodiamidate morpholino
10 oligonucleotides, and mixtures thereof.

In the present invention, the nucleotides at the 5'- and 3'- ends of said at least one oligonucleotide may be inverted. In the present invention, at least one nucleotide of said at least one oligonucleotide may be fluorinated at the 2' position of the pentose group. In the present invention, the pyrimidine nucleotides of said at least one oligonucleotide may be fluorinated at the
15 2' position of the pentose group. In the present invention, said aptamer composition may comprise at least one polymeric material, wherein said at least one polymeric material is covalently linked to said at least one oligonucleotide. In the present invention, said at least one polymeric material may be polyethylene glycol.

In the present invention, said at least one oligonucleotide may be between about 10 and
20 about 200 nucleotides in length. In the present invention, said at least one oligonucleotide may be less than about 100 nucleotides in length. In the present invention, said at least one oligonucleotide may be less than about 50 nucleotides in length.

In the present invention, said at least one oligonucleotide may be covalently or non-covalently attached to one or more personal care active ingredients. In the present invention, said
25 one or more personal care active ingredients may be selected from the group comprising antifungal agents, cooling agents, natural extracts, peptides, enzymes, and mixtures thereof. Suitable personal care active ingredients include any material that is generally considered as safe and that provides benefits to the skin, the scalp, or the hair.

Examples of conditions these actives address include, but are not limited to, dandruff,
30 seborrhoeic dermatitis, tinea versicolor (pityriasis versicolor), and pityrosporum folliculitis. In the present invention, said one or more personal care active ingredients may be selected from the group consisting of antifungal agents. In the present invention, said one or more personal care active

ingredients may be selected from the group consisting of zinc pyrithione, piroctone olamine, ketoconazole, and selenium disulfide.

In the present invention, said at least one oligonucleotide may be non-covalently attached to said one or more personal care active ingredients via molecular interactions. Examples of
5 molecular interactions are electrostatic forces, van der Waals interactions, hydrogen bonding, and π - π stacking interactions of aromatic rings.

In the present invention, said at least one oligonucleotide may be covalently attached to said one or more personal care active ingredients using one or more linkers or spacers. Non-limiting examples of linkers are chemically labile linkers, enzyme-labile linkers, and non-cleavable linkers.

10 Examples of chemically labile linkers are acid-cleavable linkers and disulfide linkers. Acid-cleavable linkers take advantage of low pH to trigger hydrolysis of an acid-cleavable bond, such as a hydrazone bond, to release the active ingredient or payload. Disulfide linkers can release the active ingredients under reducing environments. Examples of enzyme-labile linkers are peptide
15 linkers that can be cleaved in the presence of proteases and β -glucuronide linkers that are cleaved by glucuronidases releasing the payload. Non-cleavable linkers can also release the active ingredient if the aptamer is degraded by nucleases.

In the present invention, said at least one oligonucleotide may be covalently or non-covalently attached to one or more nanomaterials. In the present invention, said at least one oligonucleotide and said one or more personal care active ingredients may be covalently or non-
20 covalently attached to one or more nanomaterials. In the present invention, said one or more personal care active ingredients may be carried by said one or more nanomaterials. Non-limiting examples of nanomaterials are gold nanoparticles, nano-scale iron oxides, carbon nanomaterials (such as single-walled carbon nanotubes and graphene oxide), mesoporous silica nanoparticles, quantum dots, liposomes, poly (lactide-co-glycolic acids) nanoparticles, polymeric micelles,
25 dendrimers, serum albumin nanoparticles, and DNA-based nanomaterials. These nanomaterials can serve as carriers for large volumes of personal care active ingredients, while the aptamers can facilitate the delivery of the nanomaterials with the actives to the expected target.

Nanomaterials can have a variety of shapes or morphologies. Non-limiting examples of shapes or morphologies are spheres, rectangles, polygons, disks, toroids, cones, pyramids,
30 rods/cylinders, and fibers. In the context of the present invention, nanomaterials usually have at least one spatial dimension that is less than about 100 μm and more preferably less than about 10 μm . Nanomaterials comprise materials in solid phase, semi-solid phase, or liquid phase.

Aptamers can also be peptides that bind to targets with high affinity and specificity. These peptide aptamers can be part of a scaffold protein. Peptide aptamers can be isolated from combinatorial libraries and improved by directed mutation or rounds of variable region mutagenesis and selection. In the present invention, said aptamer composition may comprise at least one peptide or protein; wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*. In the present invention, said one or more fungi species may be selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof. In the present invention, said one or more fungi species may be selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.

III. METHODS OF DESIGNING APTAMER COMPOSITIONS

The method of designing nucleic acid aptamers known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX) has been broadly studied and improved for the selection of aptamers against small molecules and proteins (WO 91/19813). In brief, in the conventional version of SELEX, the process starts with the synthesis of a large library of oligonucleotides consisting of randomly generated sequences of fixed length flanked by constant 5'- and 3'- ends that serve as primers. The oligonucleotides in the library are then exposed to the target ligand and those that do not bind the target are removed. The bound sequences are eluted and amplified by PCR (polymerase chain reaction) to prepare for subsequent rounds of selection in which the stringency of the elution conditions is usually increased to identify the tightest-binding oligonucleotides. In addition to conventional SELEX, there are improved versions such as capillary electrophoresis-SELEX, magnetic bead-based SELEX, cell-SELEX, automated SELEX, complex-target SELEX, among others. A review of aptamer screening methods is found in (1) Kim, Y. S. and M. B. Gu, "Advances in Aptamer Screening and Small Molecule Aptasensors", *Adv. Biochem. Eng. Biotechnol.*, 2014 140:29-67 (Biosensors based on Aptamers and Enzymes) and (2) Stoltenburg, R., et al. (2007) "SELEX-A (r)evolutionary method to generate high-affinity nucleic acid ligands" *Biomol. Eng.* 2007 24(4): 381-403, the contents of which are incorporated herein by reference. Although the SELEX method has been broadly applied, it is neither predictive nor standardized for every target. Instead, a method must be developed for each particular target in order for the method to lead to viable aptamers.

Despite the large number of selected aptamers, SELEX has not been routinely applied for the selection of aptamers with binding affinities towards macroscopic materials and surfaces. For the successful selection of aptamers with high binding affinity and specificity against macroscopic materials, the epitope should be present in sufficient amount and purity to minimize the enrichment of unspecifically binding oligonucleotides and to increase the specificity of the selection. Also, the presence of positively charged groups (e.g. primary amino groups), the presence of hydrogen bond donors and acceptors, and planarity (aromatic compounds) facilitate the selection of aptamers. In contrast, negatively charged molecules (e.g. containing phosphate groups) make the selection process more difficult. Unexpectedly, the inventors have found that SELEX can be used for the design of aptamers with high binding affinity and specificity for species of the genus *Malassezia*.

Selection Library

In SELEX, the initial candidate library is generally a mixture of chemically synthesized DNA oligonucleotides, each comprising a long variable region of n nucleotides flanked at the 3' and 5' ends by conserved regions or primer recognition regions for all the candidates of the library. These primer recognition regions allow the central variable region to be manipulated during SELEX in particular by means of PCR.

The length of the variable region determines the diversity of the library, which is equal to 4^n since each position can be occupied by one of four nucleotides A, T, G or C. For long variable regions, huge library complexities arise. For instance, when $n=50$, the theoretical diversity is 450 or 1030, which is an inaccessible value in practice as it corresponds to more than 105 tons of material for a library wherein each sequence is represented once. The experimental limit is around 1015 different sequences, which is that of a library wherein all candidates having a variable region of 25 nucleotides are represented. If one chooses to manipulate a library comprising a 30-nucleotide variable region whose theoretical diversity is about 1018, only 1/1000 of the possibilities will thus be explored. In practice, that is generally sufficient to obtain aptamers having the desired properties. Additionally, since the polymerases used are unreliable and introduce errors at a rate on the order of 10^{-4} , they contribute to significantly enrich the diversity of the sequence pool throughout the SELEX process. One candidate in 100 will be modified in each amplification cycle for a library with a random region of 100 nucleotides in length, thus leading to the appearance of 1013 new candidates for the overall library.

In the present invention, the starting mixture of oligonucleotides may comprise more than about 106 different oligonucleotides and more preferably between about 1013 to about 1015

different oligonucleotides. In the present invention, the length of the variable region may be between about 10 and about 100 nucleotides. In the present invention, the length of the variable region may be between about 20 and about 60 nucleotides. In the present invention, the length of the variable region may be about 40 nucleotides. Random regions shorter than 10 nucleotides may be used, but may be constrained in their ability to form secondary or tertiary structures and in their ability to bind to target molecules. Random regions longer than 100 nucleotides may also be used but may present difficulties in terms of cost of synthesis. The randomness of the variable region is not a constraint of the present invention. For instance, if previous knowledge exists regarding oligonucleotides that bind to a given target, libraries spiked with such sequences may work as well or better than completely random ones.

In the design of primer recognition sequences, care should be taken to minimize potential annealing among sequences, fold back regions within sequences, or annealing of the same sequence itself. In the present invention, the length of primer recognition sequences may be between about 10 and about 40 nucleotides. In the present invention, the length of primer recognition sequences may be between about 12 and about 30 nucleotides. In the present invention, the length of primer recognition sequences may be between about 18 and about 26 nucleotides, i.e., about 18, 19, 20, 21, 22, 23, 24, 25 or 26 nucleotides. The length and sequence of the primer recognition sequences determine their annealing temperature. In the present invention, the primer recognition sequences of said oligonucleotides may have an annealing temperature between about 60°C and about 72°C.

Aptamers can be ribonucleotides (RNA), deoxynucleotides (DNA), or their derivatives. When aptamers are ribonucleotides, the first SELEX step may consist in transcribing the initial mixture of chemically synthesized DNA oligonucleotides via the primer recognition sequence at the 5' end. After selection, the candidates are converted back into DNA by reverse transcription before being amplified. RNA and DNA aptamers having comparable characteristics have been selected against the same target and reported in the art. Additionally, both types of aptamers can be competitive inhibitors of one another, suggesting potential overlapping of interaction sites.

New functionalities, such as hydrophobicity or photoreactivity, can be incorporated into the oligonucleotides by modifications of the nucleobases before or after selection. Modifications at the C-5 position of pyrimidines or at the C-8 or N-7 positions of purines are especially common and compatible with certain enzymes used during the amplification step in SELEX. In the present invention, said oligonucleotides may comprise natural or non-natural nucleobases. Natural nucleobases are adenine, cytosine, guanine, thymine, and uracil. Non-limiting examples of non-

natural nucleobases are hypoxanthine, xanthine, 7-methylguanine, 5,6-dihydrouracil, 5-5-methylcytosine, 5-hydroxymethylcytosine, thiouracil, 1-methylhypoxanthine, 6-methylisoquinoline-1-thione-2-yl, 3-methoxy-2-naphthyl, 5-propynyluracil-1-yl, 5-methylcytosin-1-yl, 2-aminoadenin-9-yl, 7-deaza-7-iodoadenin-9-yl, 7-deaza-7-propynyl-2-aminoadenin-9-yl, phenoxazinyl, phenoxazinyl-G-clam, 5-bromouracil, 5-iodouracil, and mixtures thereof. Some non-natural nucleobases, such as 5-bromouracil or 5-iodouracil, can be used to generate photo-crosslinkable aptamers, which can be activated by UV light to form a covalent link with the target.

In the present invention, the nucleosides of said oligonucleotides may be linked by a chemical motif selected from the group comprising natural phosphate diester, chiral phosphorothionate, chiral methyl phosphonate, chiral phosphoramidate, chiral phosphate chiral triester, chiral boranophosphate, chiral phosphoroselenoate, phosphorodithioate, phosphorothionate amidate, methylenemethylimino, 3'-amide, 3' achiral phosphoramidate, 3' achiral methylene phosphonates, thioformacetal, thioethyl ether, fluorophosphate, and mixtures thereof. In the present invention, the nucleosides of said oligonucleotides may be linked by natural phosphate diesters.

In the present invention, the sugar moiety of the nucleosides of said oligonucleotides may be selected from the group comprising ribose, deoxyribose, 2'-fluoro deoxyribose, 2'-O-methyl ribose, 2'-O-(3-amino)propyl ribose, 2'-O-(2-methoxy)ethyl ribose, 2'-O-2-(N,N-dimethylamino)ethyl ribose, 2'-O-2-[2-(N,N-dimethylamino)ethyloxy]ethyl ribose, 2'-O-N,N-dimethylacetamidyl ribose, N-morpholinophosphordiamidate, α -deoxyribofuranosyl, other pentoses, hexoses, and mixtures thereof.

In the present invention, said derivatives of ribonucleotides or said derivatives of deoxyribonucleotides may be selected from the group comprising locked oligonucleotides, peptide oligonucleotides, glycol oligonucleotides, threose oligonucleotides, hexitol oligonucleotides, altritol oligonucleotides, butyl oligonucleotides, L-ribonucleotides, arabino oligonucleotides, 2'-fluoroarabino oligonucleotides, cyclohexene oligonucleotides, phosphorodiamidate morpholino oligonucleotides, and mixtures thereof.

When using modified nucleotides during the SELEX process, they should be compatible with the enzymes used during the amplification step. Non-limiting examples of modifications that are compatible with commercial enzymes include modifications at the 2' position of the sugar in RNA libraries. The ribose 2'-OH group of pyrimidine nucleotides can be replaced with 2'-amino, 2'-fluoro, 2'-methyl, or 2'-O-methyl, which protect the RNA from degradation by nucleases.

Additional modifications in the phosphate linker, such as phosphorothionate and boranophosphate, are also compatible with the polymerases and confer resistance to nucleases.

In the present invention, at least one nucleotide of said oligonucleotides may be fluorinated at the 2' position of the pentose group. In the present invention, the pyrimidine nucleotides of said oligonucleotides may be at least partially fluorinated at the 2' position of the pentose group. In the present invention, all the pyrimidine nucleotides of said oligonucleotides may be fluorinated at the 2' position of the pentose group. In the present invention, at least one nucleotide of said oligonucleotides may be aminated at the 2' position of the pentose group.

Another approach, recently described as two-dimensional SELEX, simultaneously applies in vitro oligonucleotide selection and dynamic combinatorial chemistry (DCC), e.g., a reversible reaction between certain groups of the oligonucleotide (amine groups) and a library of aldehyde compounds. The reaction produces imine oligonucleotides, which are selected on the same principles as for conventional SELEX. It is thus possible to identify for a target hairpin RNA modified aptamers that differ from natural aptamers.

A very different approach relates to the use of optical isomers. Natural oligonucleotides are D-isomers. L-analogs are resistant to nucleases but cannot be synthesized by polymerases. According to the laws of optical isomerism, an L-series aptamer can form with its target (T) a complex having the same characteristics as the complex formed by the D-series isomer and the enantiomer (T') of the target (T). Consequently, if compound T' can be chemically synthesized, it can be used to perform the selection of a natural aptamer (D). Once identified, this aptamer can be chemically synthesized in an L-series. This L-aptamer is a ligand of the natural target (T).

Selection Step

Single stranded oligonucleotides can fold to generate secondary and tertiary structures, resembling the formation of base pairs. The initial sequence library is thus a library of three-dimensional shapes, each corresponding to a distribution of units that can trigger electrostatic interactions, create hydrogen bonds, etc. Selection becomes a question of identifying in the library the shape suited to the target, i.e., the shape allowing the greatest number of interactions and the formation of the most stable aptamer-target complex. For small targets (dyes, antibiotics, etc.) the aptamers identified are characterized by equilibrium dissociation constants in the micromolar range, whereas for protein targets K_d values below 10⁻⁹ M are not rare.

Selection in each round occurs by means of physical separation of oligonucleotides associated with the target from free oligonucleotides. Multiple techniques may be applied

(chromatography, filter retention, electrophoresis, etc.). The selection conditions are adjusted (relative concentration of target/candidates, ion concentration, temperature, washing, etc.) so that a target-binding competition occurs between the oligonucleotides. Generally, stringency is increased as the rounds proceed in order to promote the capture of oligonucleotides with the highest affinity. In addition, counter-selections or negative selections are carried out to eliminate oligonucleotides that recognize the support or unwanted targets (e.g., filter, beads, etc.).

The SELEX process for the selection of target-specific aptamers is characterized by repetition of five main steps: (1) binding of oligonucleotides to the target, (2) partition or removal of oligonucleotides with low binding affinity, (3) elution of oligonucleotides with high binding affinity, (4) amplification or replication of oligonucleotides with high binding affinity, and (5) conditioning or preparation of the oligonucleotides for the next cycle. This selection process is designed to identify the oligonucleotides with the greatest affinity and specificity for the target material.

In the present invention, a method of designing an aptamer composition may comprise the step of contacting: a) a mixture of oligonucleotides, b) a selection buffer, and c) a target material selected from the group consisting one or more fungi species from the genus *Malassezia*. In the present invention, said one or more fungi species may be selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof. In the present invention, said one or more fungi species may be selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof. In the present invention, said mixture of oligonucleotides may comprise oligonucleotides selected from the group consisting of deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof.

SELEX cycles are usually repeated several times until oligonucleotides with high binding affinity are identified. The number of cycles depends on multiple variables, including target features and concentration, design of the starting random oligonucleotide library, selection conditions, ratio of target binding sites to oligonucleotides, and the efficiency of the partitioning step. In the present invention, said contacting step may be performed at least 5 times. In the present invention, said contacting step may be performed between 6 and 15 times. In the present invention, said method further may comprise the step of removing the oligonucleotides that do not bind said target material during said contacting step.

Oligonucleotides are oligo-anions, each unit having a charge and hydrogen-bond donor/acceptor sites at a particular pH. Thus, the pH and ionic strength of the selection buffer are important and should represent the conditions of the intended aptamer application. In the present invention, the pH of said selection buffer may be between about 2 and about 9. In the present invention, the pH of said selection buffer may be between about 5 and about 8.

Cations do not only facilitate the proper folding of the oligonucleotides, but also can provide benefits to the hair or the scalp. In the present invention, said selection buffer may comprise cations. Non-limiting examples of cations are Zn^{2+} , Cu^{2+} . In the present invention, said selection buffer may comprise divalent cations selected from the group comprising Zn^{2+} and Cu^{2+} .

In order for the aptamers to maintain their structures and function during their application, the in vitro selection process can be carried out under conditions similar to those for which they are being developed. In the present invention, said selection buffer may comprise a solution or suspension of a personal care composition selected from the group comprising shampoos, conditioning shampoos, pet shampoo, leave-in treatments, sprays, liquids, pastes, Newtonian or non-Newtonian fluids, gels, and sols. In the present invention, said selection buffer may comprise a solution of a shampoo chassis.

In the present invention, said selection buffer may comprise at least one surfactant. In the present invention, said at least one surfactant may be selected from the group consisting of anionic surfactants, amphoteric or zwitterionic surfactants, and mixtures thereof. Non-limiting examples of anionic surfactants are alkyl and alkyl ether sulfates or sulfonates, including ammonium lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, sodium lauryl sarcosinate, sodium lauroyl sarcosinate, lauryl sarcosine, cocoyl sarcosine, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauryl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate, sodium tridecyl benzene sulfonate, sodium dodecyl benzene sulfonate, sodium cocoyl isethionate and combinations thereof. Non-limiting amphoteric surfactants include those surfactants broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight or branched chain and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an

anionic group such as carboxy, sulfonate, sulfate, phosphate, or phosphonate, including cocoamphoacetate, cocoamphodiacetate, lauroamphoacetate, lauroamphodiacetate, and mixtures thereof. Non-limiting examples of zwitterionic surfactants include those surfactants broadly described as derivatives of aliphatic quaternaryammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight or branched chain, and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate or phosphonate, and betains.

In the present invention, said selection buffer may comprise at least one material selected from the group comprising: aqueous carriers, gel matrixes, silicone conditioning agents, organic conditioning materials, non-ionic polymers, deposition aids, rheology modifier / suspending agents, benefit agents, and mixtures thereof. Non-limiting examples of aqueous carriers are water and water solutions of lower alkyl alcohols and polyhydric alcohols, including ethanol, isopropanol, propylene glycol, hexylene glycol, glycerin, and propane diol. Non-limiting examples of gel matrixes include water solutions of fatty alcohols, including cetyl alcohol, stearyl alcohol, behenyl alcohol, and mixtures thereof. Non-limiting examples of silicone conditioning agents include dimethicones, dimethiconols, cyclic silicones, methylphenyl polysiloxane, and modified silicones with various functional groups such as amino groups, quaternary ammonium salt groups, aliphatic groups, alcohol groups, carboxylic acid groups, ether groups, sugar or polysaccharide groups, fluorine-modified alkyl groups, alkoxy groups, or combinations of such groups. Non-limiting examples of organic conditioning materials include hydrocarbon oils, polyolefins, fatty esters, fluorinated conditioning compounds, fatty alcohols, alkyl glucosides and alkyl glucoside derivatives, quaternary ammonium compounds, polyethylene glycols and polypropylene glycols having a molecular weight of up to about 2,000,000 including those with CTFA names PEG-200, PEG-400, PEG-600, PEG-1000, PEG-2M, PEG-7M, PEG-14M, PEG-45M and mixtures thereof. Non-limiting examples of non-ionic polymers include polyalkylene glycols, such as polyethylene glycols. Non-limiting examples of deposition aids include copolymers of vinyl monomers having cationic amine or quaternary ammonium functionalities with water soluble spacer monomers such as acrylamide, methacrylamide, alkyl and dialkyl acrylamides, alkyl and dialkyl methacrylamides, alkyl acrylate, alkyl methacrylate, vinyl caprolactone, and vinyl pyrrolidone; vinyl esters, vinyl alcohol (made by hydrolysis of polyvinyl acetate), maleic anhydride, propylene glycol, and ethylene glycol, cationic celluloses, cationic starches, and cationic guar gums. Non-limiting examples of rheology modifier / suspending agents include homopolymers based on acrylic acid, methacrylic acid or other related derivatives, alginic

acid-based materials, and cellulose derivatives. Non-limiting examples of benefit agents include brightening agents, strengthening agents, anti-fungal agents, anti-bacterial agents, anti-microbial agents, anti-dandruff agents, anti-malodor agents, perfumes, olfactory enhancement agents, anti-itch agents, cooling agents, anti-adherence agents, moisturization agents, smoothness agents, surface modification agents, antioxidants, natural extracts and essential oils, dyes, pigments, bleaches, nutrients, peptides, vitamins, enzymes, chelants, and mixtures thereof.

Negative selection or counter-selection steps can minimize the enrichment of oligonucleotides that bind to undesired targets or undesired epitopes within a target. In the present invention, said method of designing an aptamer composition may further comprise the step of contacting: a) a mixture of oligonucleotides, b) a selection buffer, and c) one or more undesired targets. Methods for negative selection or counter-selection of aptamers against unbound targets have been published in WO201735666, the content of which is incorporated herein by reference.

In the present invention, the method of designing an aptamer composition may comprise the steps of: a) synthesizing a mixture of oligonucleotides; b) contacting: i. said mixture of oligonucleotides, ii. a selection buffer, and iii. a target material selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof, to produce a target suspension; c) removing the liquid phase from said target suspension to produce a target-oligonucleotide mixture; d) contacting said target-oligonucleotide mixture with a washing buffer and removing the liquid phase to produce a target-aptamer mixture; and e) contacting said target-aptamer mixture with an elution buffer and recovering the liquid phase to produce an aptamer mixture. In the present invention, said steps may be performed repetitively at least 5 times. In the present invention, said steps may be performed between 6 and 15 times.

In the present invention, the method of designing an aptamer composition may comprise the steps of: a) synthesizing a random mixture of deoxyribonucleotides comprising oligonucleotides consisting of: i. a T7 promoter sequence at the 5'-end, ii. a variable 40-nucleotide sequence in the middle, and iii. a conserved reverse primer recognition sequence at the 3' end; b) contacting: i. said random mixture of deoxyribonucleotides, ii. a selection buffer, and iii. a suspension of *M. globosa*, to produce a target suspension; c) removing the liquid phase from said target suspension to produce a hair-oligonucleotide mixture; d) contacting said hair-oligonucleotide mixture with a washing buffer and removing the liquid phase to produce a hair-aptamer mixture; e) contacting said hair-aptamer mixture with an elution buffer and recovering the liquid phase to produce a DNA aptamer mixture; f) amplifying said DNA aptamer mixture to

produce an enriched mixture of deoxyribonucleotides; and g) sequencing said enriched mixture of deoxyribonucleotides.

Post-Selection Modification

5 To enhance stability of the aptamers, chemical modifications can be introduced in the aptamer after the selection process. For instance, the 2'-OH groups of the ribose moieties can be replaced by 2'-fluoro, 2'-amino, or 2'-O-methyl groups. Furthermore, the 3'- and 5'- ends of the aptamers can be capped with different groups, such as streptavidin-biotin, inverted thymidine, amine, phosphate, polyethylene-glycol, cholesterol, fatty acids, proteins, enzymes, fluorophores, among others, making the oligonucleotides resistant to exonucleases or providing some additional
10 benefits. Other modifications are described in previous sections of the present disclosure.

Unlike backbone modifications which can cause aptamer-target interaction properties to be lost, it is possible to conjugate various groups at one of the 3'- or 5'- ends of the oligonucleotide in order to convert it into a delivery vehicle, tool, probe, or sensor without disrupting its
15 characteristics. This versatility constitutes a significant advantage of aptamers, in particular for their application in the current invention. In the present invention, one or more personal care active ingredients may be covalently attached to the 3'- end of said at least one oligonucleotide. In the present invention, one or more personal care active ingredients may be covalently attached to the 5'- end of said at least one oligonucleotide. In the present invention, one or more personal care
20 active ingredients may be covalently attached to random positions of said at least one oligonucleotide.

Incorporation of modifications to aptamers can be performed using enzymatic or chemical methods. Non-limiting examples of enzymes used for modification of aptamers are terminal deoxynucleotidyl transferases (TdT), T4 RNA ligases, T4 polynucleotide kinases (PNK), DNA
25 polymerases, RNA polymerases, and other enzymes known by those skilled in the art. TdTs are template-independent polymerases that can add modified deoxynucleotides to the 3' terminus of deoxyribonucleotides. T4 RNA ligases can be used to label ribonucleotides at the 3'- end by using appropriately modified nucleoside 3',5'-bisphosphates. PNK can be used to phosphorylate the 5'- end of synthetic oligonucleotides, enabling other chemical transformations (see below). DNA and
30 RNA polymerases are commonly used for the random incorporation of modified nucleotides throughout the sequence, provided such nucleotides are compatible with the enzymes.

Non-limiting examples of chemical methods used for modification of aptamers are periodate oxidation of ribonucleotides, EDC activation of 5'-phosphate, random chemical labeling methods, and other chemical methods known by those skilled in the art, incorporated herein.

During periodate oxidation, meta- and ortho-periodates cleave the C-C bonds between
5 vicinal diols of 3'-ribonucleotides, creating two aldehyde moieties that enable the conjugation of labels or active ingredients at the 3'- end of RNA aptamers. The resulting aldehydes can be easily reacted with hydrazide- or primary amine- containing molecules. When amines are used, the produced Schiff bases can be reduced to more stable secondary amines with sodium cyanoborohydride (NaBH₄).

10 When EDC activation of 5'-phosphate is used, the 5'-phosphate of oligonucleotides is frequently activated with EDC (1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride) and imidazole to produce a reactive imidazolide intermediate, followed by reaction with a primary amine to generate aptamers modified at the 5' end. Because the 5' phosphate group is required for the reaction, synthetic oligonucleotides can be first treated with a kinase (e.g. PNK).

15 Random chemical labeling can be performed with different methods. Because they allow labeling at random sites along the aptamer, a higher degree of modification can be achieved compared to end-labeling methods. However, since the nucleobases are modified, binding of the aptamers to their target can be disrupted. The most common random chemical modification methods involve the use of photoreactive reagents, such as phenylazide-based reagents. When the
20 phenylazide group is exposed to UV light, it forms a labile nitrene that reacts with double bonds and C-H and N-H sites of the aptamers.

Additional information about methods for modification of aptamers is summarized in Hermanson G. T., "Bioconjugate Techniques", pp. 969-1002, 2nd Edition, Academic Press, San Diego, 2008, the content of which is incorporated herein by reference.

25 After selection, in addition to chemical modifications, sequence truncations can be performed to remove regions that are not essential for binding or for folding into the structure. Moreover, aptamers can be linked together to provide different features or better affinity. Thus, any truncations or combinations of the aptamers described herein are incorporated as part of the current invention.

30 IV. APPLICATION OF APTAMER COMPOSITIONS IN PERSONAL CARE PRODUCTS

The aptamers of the current invention can be used in hair care compositions to provide one or more benefits.

SHAMPOO COMPOSITION

The hair care composition of the present invention can be a shampoo. The shampoo composition comprises from about .001% to about 1%, alternatively from about .01% to about 0.5%, alternatively from about 0.1% to about 0.3% of one or more aptamer.

5

A. DETERGENT SURFACTANT

The shampoo composition may comprise one or more detergent surfactants, which provides cleaning performance to the composition. The one or more detergent surfactants in turn may comprise an anionic surfactant, amphoteric or zwitterionic surfactants, or mixtures thereof.

10 Various examples and descriptions of detergent surfactants are set forth in U.S. Patent No. 6,649,155; U.S. Patent Application Publication No. 2008/0317698; and U.S. Patent Application Publication No. 2008/0206355, which are incorporated herein by reference in their entirety.

The concentration of the detergent surfactant component in the shampoo composition should be sufficient to provide the desired cleaning and lather performance, and generally ranges
15 from about 2 wt% to about 50 wt%, from about 5 wt% to about 30 wt%, from about 8 wt% to about 25 wt%, from about 10 wt% to about 20 wt%, about 5 wt%, about 10 wt%, about 12 wt%, about 15 wt%, about 17 wt%, about 18 wt%, or about 20 wt%.

Anionic surfactants suitable for use in the compositions are the alkyl and alkyl ether sulfates. Other suitable anionic surfactants are the water-soluble salts of organic, sulfuric acid
20 reaction products. Still other suitable anionic surfactants are the reaction products of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide. Other similar anionic surfactants are described in U.S. Patent Nos. 2,486,921; 2,486,922; and 2,396,278, which are incorporated herein by reference in their entirety.

Exemplary anionic surfactants for use in the shampoo composition include ammonium
25 lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, sodium lauryl sarcosinate, sodium lauroyl sarcosinate,
30 lauryl sarcosine, cocoyl sarcosine, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauryl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate, sodium tridecyl benzene sulfonate, sodium dodecyl benzene

sulfonate, sodium cocoyl isethionate and combinations thereof. The anionic surfactant may be sodium lauryl sulfate or sodium laureth sulfate.

Suitable amphoteric or zwitterionic surfactants for use in the shampoo composition herein include those which are known for use in shampoo or other personal care cleansing. Concentrations of such amphoteric surfactants range from about 0.5 wt% to about 20 wt%, and from about 1 wt% to about 10 wt%. Non-limiting examples of suitable zwitterionic or amphoteric surfactants are described in U.S. Patent Nos. 5,104,646 and 5,106,609, which are incorporated herein by reference in their entirety.

Amphoteric deterative surfactants suitable for use in the shampoo composition include those surfactants broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight or branched chain and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate, or phosphonate. Exemplary amphoteric deterative surfactants for use in the present shampoo composition include cocoamphoacetate, cocoamphodiacetate, lauroamphoacetate, lauroamphodiacetate, and mixtures thereof.

Zwitterionic deterative surfactants suitable for use in the shampoo composition include those surfactants broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight or branched chain, and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate or phosphonate. Zwitterionics such as betaines may be selected.

Non-limiting examples of other anionic, zwitterionic, amphoteric or optional additional surfactants suitable for use in the shampoo composition are described in McCutcheon's, Emulsifiers and Detergents, 1989 Annual, published by M. C. Publishing Co., and U.S. Patent Nos. 3,929,678, 2,658,072; 2,438,091; 2,528,378, which are incorporated herein by reference in their entirety.

The shampoo composition may also comprise a shampoo gel matrix, an aqueous carrier, and other additional ingredients described herein.

B. AQUEOUS CARRIER

The shampoo composition comprises an aqueous carrier. Accordingly, the formulations of the shampoo composition can be in the form of pourable liquids (under ambient conditions). Such compositions will therefore typically comprise an aqueous carrier, which is present at a level of at

least 20 wt%, from about 20 wt% to about 95 wt%, or from about 60 wt% to about 85 wt%. The aqueous carrier may comprise water, or a miscible mixture of water and organic solvent, and in one aspect may comprise water with minimal or no significant concentrations of organic solvent, except as otherwise incidentally incorporated into the composition as minor ingredients of other components.

The aqueous carriers useful in the shampoo composition include water and water solutions of lower alkyl alcohols and polyhydric alcohols. The lower alkyl alcohols useful herein are monohydric alcohols having 1 to 6 carbons, in one aspect, ethanol and isopropanol. The polyhydric alcohols useful herein include propylene glycol, hexylene glycol, glycerin, and propane diol.

CONDITIONER COMPOSITION

The hair care composition of the present invention can be a hair conditioner. The hair conditioner composition described herein comprises (i) from about .001% to about 1%, alternatively from about .01% to about 0.5%, alternatively from about 0.1% to about 0.3% of one or more aptamer. The conditioner composition may also comprise a conditioner gel matrix comprising (1) one or more high melting point fatty compounds, (2) a cationic surfactant system, and (3) a second aqueous carrier.

A. CATIONIC SURFACTANT SYSTEM

The conditioner gel matrix of the conditioner composition includes a cationic surfactant system. The cationic surfactant system can be one cationic surfactant or a mixture of two or more cationic surfactants. The cationic surfactant system can be selected from: mono-long alkyl quaternized ammonium salt; a combination of mono-long alkyl quaternized ammonium salt and di-long alkyl quaternized ammonium salt; mono-long alkyl amidoamine salt; a combination of mono-long alkyl amidoamine salt and di-long alkyl quaternized ammonium salt, a combination of mono-long alkyl amidoamine salt and mono-long alkyl quaternized ammonium salt.

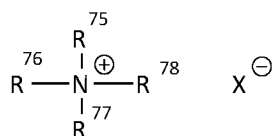
The cationic surfactant system can be included in the composition at a level by weight of from about 0.1% to about 10%, from about 0.5% to about 8%, from about 0.8 % to about 5%, and from about 1.0% to about 4%.

Mono-long alkyl quaternized ammonium salt

The monoalkyl quaternized ammonium salt cationic surfactants useful herein are those having one long alkyl chain which has about 22 carbon atoms and may be a C22 alkyl group. The remaining groups attached to nitrogen are independently selected from an alkyl group of from 1 to

about 4 carbon atoms or an alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 4 carbon atoms.

Mono-long alkyl quaternized ammonium salts useful herein are those having the formula (I):



(I)

wherein one of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ is selected from an alkyl group of 22 carbon atoms or an aromatic, alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 30 carbon atoms; the remainder of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ are independently selected from an alkyl group of from 1 to about 4 carbon atoms or an alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 4 carbon atoms; and X⁻ is a salt-forming anion such as those selected from halogen, (e.g. chloride, bromide), acetate, citrate, lactate, glycolate, phosphate, nitrate, sulfonate, sulfate, alkylsulfate, and alkyl sulfonate radicals. The alkyl groups can contain, in addition to carbon and hydrogen atoms, ether and/or ester linkages, and other groups such as amino groups. The longer chain alkyl groups, e.g., those of about 22 carbons, or higher, can be saturated or unsaturated. One of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ can be selected from an alkyl group of about 22 carbon atoms, the remainder of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ are independently selected from CH₃, C₂H₅, C₂H₄OH, and mixtures thereof; and X is selected from the group consisting of Cl, Br, CH₃OSO₃, C₂H₅OSO₃, and mixtures thereof.

Nonlimiting examples of such mono-long alkyl quaternized ammonium salt cationic surfactants include: behenyl trimethyl ammonium salt.

Mono-long alkyl amidoamine salt

Mono-long alkyl amines are also suitable as cationic surfactants. Primary, secondary, and tertiary fatty amines are useful. Particularly useful are tertiary amido amines having an alkyl group of about 22 carbons. Exemplary tertiary amido amines include: behenamidopropyldimethylamine, behenamidopropyldiethylamine, behenamidoethyldiethylamine, behenamidoethyldimethylamin. Useful amines in the present invention are disclosed in U.S. Patent 4,275,055, Nachtigal, et al. These amines can also be used in combination with acids such as *l*-glutamic acid, lactic acid, hydrochloric acid, malic acid, succinic acid, acetic acid, fumaric acid, tartaric acid, citric acid, *l*-glutamic hydrochloride, maleic acid, and mixtures thereof; and may be *l*-glutamic acid, lactic acid,

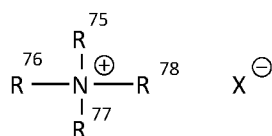
and/or citric acid. The amines herein can be partially neutralized with any of the acids at a molar ratio of the amine to the acid of from about 1 : 0.3 to about 1 : 2, and/or from about 1 : 0.4 to about 1 : 1.

5 Di-long alkyl quaternized ammonium salt

Di-long alkyl quaternized ammonium salt can be combined with a mono-long alkyl quaternized ammonium salt or mono-long alkyl amidoamine salt. It is believed that such combination can provide easy-to rinse feel, compared to single use of a monoalkyl quaternized ammonium salt or mono-long alkyl amidoamine salt. In such combination with a mono-long alkyl quaternized ammonium salt or mono-long alkyl amidoamine salt, the di-long alkyl quaternized ammonium salts are used at a level such that the wt% of the dialkyl quaternized ammonium salt in the cationic surfactant system is in the range of from about 10% to about 50%, and/or from about 30% to about 45%.

The di-long alkyl quaternized ammonium salt cationic surfactants useful herein are those having two long alkyl chains having about 22 carbon atoms. The remaining groups attached to nitrogen are independently selected from an alkyl group of from 1 to about 4 carbon atoms or an alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 4 carbon atoms.

Di-long alkyl quaternized ammonium salts useful herein are those having the formula (II):



(II)

wherein two of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ is selected from an alkyl group of from 22 carbon atoms or an aromatic, alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 30 carbon atoms; the remainder of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ are independently selected from an alkyl group of from 1 to about 4 carbon atoms or an alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to about 4 carbon atoms; and X⁻ is a salt-forming anion such as those selected from halogen, (e.g. chloride, bromide), acetate, citrate, lactate, glycolate, phosphate, nitrate, sulfonate, sulfate, alkylsulfate, and alkyl sulfonate radicals. The alkyl groups can contain, in addition to carbon and hydrogen atoms, ether and/or ester linkages, and other groups such as amino groups. The longer chain alkyl groups, e.g., those of about 22 carbons, or higher, can be saturated or unsaturated. One of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ can be selected from an alkyl group of from 22 carbon atoms, the remainder of R⁷⁵, R⁷⁶, R⁷⁷ and R⁷⁸ are

independently selected from CH₃, C₂H₅, C₂H₄OH, and mixtures thereof; and X is selected from the group consisting of Cl, Br, CH₃OSO₃, C₂H₅OSO₃, and mixtures thereof.

Such dialkyl quaternized ammonium salt cationic surfactants include, for example, dialkyl (C₂₂) dimethyl ammonium chloride, ditallow alkyl dimethyl ammonium chloride, dihydrogenated
5 tallow alkyl dimethyl ammonium chloride. Such dialkyl quaternized ammonium salt cationic surfactants also include, for example, asymmetric dialkyl quaternized ammonium salt cationic surfactants.

B. HIGH MELTING POINT FATTY COMPOUND

10 The conditioner gel matrix of the conditioner composition includes one or more high melting point fatty compounds. The high melting point fatty compounds useful herein may have a melting point of 25°C or higher, and is selected from the group consisting of fatty alcohols, fatty acids, fatty alcohol derivatives, fatty acid derivatives, and mixtures thereof. It is understood by the artisan that the compounds disclosed in this section of the specification can in some instances fall
15 into more than one classification, e.g., some fatty alcohol derivatives can also be classified as fatty acid derivatives. However, a given classification is not intended to be a limitation on that particular compound, but is done so for convenience of classification and nomenclature. Further, it is understood by the artisan that, depending on the number and position of double bonds, and length and position of the branches, certain compounds having certain carbon atoms may have a melting
20 point of less than 25°C. Such compounds of low melting point are not intended to be included in this section. Nonlimiting examples of the high melting point compounds are found in International Cosmetic Ingredient Dictionary, Fifth Edition, 1993, and CTFA Cosmetic Ingredient Handbook, Second Edition, 1992.

Among a variety of high melting point fatty compounds, fatty alcohols are suitable for use
25 in the conditioner composition. The fatty alcohols useful herein are those having from about 14 to about 30 carbon atoms, from about 16 to about 22 carbon atoms. These fatty alcohols are saturated and can be straight or branched chain alcohols. Suitable fatty alcohols include, for example, cetyl alcohol, stearyl alcohol, behenyl alcohol, and mixtures thereof.

High melting point fatty compounds of a single compound of high purity can be used.
30 Single compounds of pure fatty alcohols selected from the group of pure cetyl alcohol, stearyl alcohol, and behenyl alcohol can also be used. By "pure" herein, what is meant is that the compound has a purity of at least about 90%, and/or at least about 95%. These single compounds of high purity provide good rinsability from the hair when the consumer rinses off the composition.

The high melting point fatty compound can be included in the conditioner composition at a level of from about 0.1% to about 20%, alternatively from about 1% to about 15%, and alternatively from about 1.5% to about 8% by weight of the composition, in view of providing improved conditioning benefits such as slippery feel during the application to wet hair, softness and moisturized feel on dry hair.

C. AQUEOUS CARRIER

The conditioner gel matrix of the conditioner composition includes an aqueous carrier. Accordingly, the formulations of the conditioner composition can be in the form of pourable liquids (under ambient conditions). Such compositions will therefore typically comprise a second aqueous carrier, which is present at a level of from about 20 wt% to about 95 wt%, or from about 60 wt% to about 85 wt%. The aqueous carrier may comprise water, or a miscible mixture of water and organic solvent, and in one aspect may comprise water with minimal or no significant concentrations of organic solvent, except as otherwise incidentally incorporated into the composition as minor ingredients of other components.

The aqueous carriers useful in the conditioner composition include water and water solutions of lower alkyl alcohols and polyhydric alcohols. The lower alkyl alcohols useful herein are monohydric alcohols having 1 to 6 carbons, in one aspect, ethanol and isopropanol. The polyhydric alcohols useful herein include propylene glycol, hexylene glycol, glycerin, and propane diol.

LEAVE-ON TREATMENT

The hair care composition of the present invention can be leave-on treatment. The leave-on treatment composition described herein may comprise from about .001% to about 1%, alternatively from about .01% to about 0.5%, alternatively from about 0.1% to about 0.3% of one or more aptamer. The leave-on treatment may also comprise (1) one or more rheology modifiers and (2) an aqueous carrier.

A. RHEOLOGY MODIFIER

The leave-on treatment may include one or more rheology modifiers to adjust the rheological characteristics of the composition for better feel, in-use properties and the suspending stability of the composition. For example, the rheological properties are adjusted so that the composition remains uniform during its storage and transportation and it does not drip undesirably

onto other areas of the body, clothing or home furnishings during its use. Any suitable rheology modifier can be used. The leave-on treatment may comprise from about 0.01% to about 3% of a rheology modifier, alternatively from about 0.1% to about 1% of a rheology modifier,

The one or more rheology modifier may be selected from the group consisting of
 5 polyacrylamide thickeners, cationically modified polysaccharides, associative thickeners, and mixtures thereof. Associative thickeners include a variety of material classes such as, for example: hydrophobically modified cellulose derivatives; hydrophobically modified alkoxyated urethane polymers, such as PEG-150/decyl alcohol/SMDI copolymer, PEG-150/stearyl alcohol/SMDI copolymer, polyurethane-39; hydrophobically modified, alkali swellable emulsions, such as
 10 hydrophobically modified polypolyacrylates, hydrophobically modified polyacrylic acids, and hydrophobically modified polyacrylamides; hydrophobically modified polyethers. These materials may have a hydrophobe that can be selected from cetyl, stearyl, oleayl, and combinations thereof, and a hydrophilic portion of repeating ethylene oxide groups with repeat units from 10-300, alternatively from 30-200, and alternatively from 40-150. Examples of this class include PEG-
 15 120-methylglucose dioleate, PEG-(40 or 60) sorbitan tetraoleate, PEG-150 pentaerythrityl tetrastearate, PEG-55 propylene glycol oleate, PEG-150 distearate.

Non-limiting examples of additional rheology modifiers include acrylamide/ammonium acrylate copolymer (and) polyisobutene (and) polysorbate 20; acrylamide/sodium acryloyldimethyl taurate copolymer/ isohexadecane/ polysorbate 80; acrylates copolymer; acrylates/beheneth-25
 20 methacrylate copolymer; acrylates/C10-C30 alkyl acrylate crosspolymer; acrylates/steareth-20 itaconate copolymer; ammonium polyacrylate/Isohexadecane/PEG-40 castor oil; C12-16 alkyl PEG-2 hydroxypropylhydroxyethyl ethylcellulose (HM-EHEC); carbomer; crosslinked polyvinylpyrrolidone (PVP); dibenzylidene sorbitol; hydroxyethyl ethylcellulose (EHEC); hydroxypropyl methylcellulose (HPMC); hydroxypropyl methylcellulose (HPMC);
 25 hydroxypropylcellulose (HPC); methylcellulose (MC); methylhydroxyethyl cellulose (MEHEC); PEG-150/decyl alcohol/SMDI copolymer; PEG-150/stearyl alcohol/SMDI copolymer; polyacrylamide/C13-14 isoparaffin/laureth-7; polyacrylate 13/polyisobutene/polysorbate 20; polyacrylate crosspolymer-6; polyamide-3; polyquaternium-37 (and) hydrogenated polydecene (and) trideceth-6; polyurethane-39; sodium acrylate/acryloyldimethyltaurate/dimethylacrylamide;
 30 crosspolymer (and) isohexadecane (and) polysorbate 60; sodium polyacrylate. Exemplary commercially-available rheology modifiers include ACULYN™ 28, Klucel M CS, Klucel H CS, Klucel G CS, SYLVACLEAR AF1900V, SYLVACLEAR PA1200V, Benecel E10M, Benecel K35M, Optasense RMC70, ACULYN™33, ACULYN™46, ACULYN™22, ACULYN™44,

Carbopol Ultrez 20, Carbopol Ultrez 21, Carbopol Ultrez 10, Carbopol 1342, Sepigel™ 305, Simulgel™600, Sepimax Zen, and/or combinations thereof.

B. AQUEOUS CARRIER

5 The leave-on treatment may comprise an aqueous carrier. Accordingly, the formulations of the leave-on treatment can be in the form of pourable liquids (under ambient conditions). Such compositions will therefore typically comprise an aqueous carrier, which is present at a level of at least 20 wt%, from about 20 wt% to about 95 wt%, or from about 60 wt% to about 85 wt%. The aqueous carrier may comprise water, or a miscible mixture of water and organic solvent, and in
10 one aspect may comprise water with minimal or no significant concentrations of organic solvent, except as otherwise incidentally incorporated into the composition as minor ingredients of other components.

 The aqueous carriers useful in the leave-on treatment include water and water solutions of lower alkyl alcohols and polyhydric alcohols. The lower alkyl alcohols useful herein are
15 monohydric alcohols having 1 to 6 carbons, in one aspect, ethanol and isopropanol. The polyhydric alcohols useful herein include propylene glycol, hexylene glycol, glycerin, and propane diol.

pH

 The hair care composition of the present invention may have a pH in the range from about
20 2 to about 10, at 25°C. More preferably, the hair care composition may have a pH in the range of from about 2 to about 6, alternatively from about 3.5 to about 5, alternatively from about 5.25 to about 7.

ADDITIONAL COMPONENTS

25 The hair care composition described herein may optionally comprise one or more additional components known for use in hair care or personal care products, provided that the additional components are physically and chemically compatible with the essential components described herein, or do not otherwise unduly impair product stability, aesthetics or performance. Such additional components are most typically those described in reference books such as the CTFA
30 Cosmetic Ingredient Handbook, Second Edition, The Cosmetic, Toiletries, and Fragrance Association, Inc. 1988, 1992. Individual concentrations of such additional components may range from about 0.001 wt% to about 10 wt% by weight of the hair care compositions.

Non-limiting examples of additional components for use in the hair care compositions include conditioning agents, natural cationic deposition polymers, synthetic cationic deposition polymers, anti-dandruff agents, particles, suspending agents, paraffinic hydrocarbons, propellants, viscosity modifiers, dyes, non-volatile solvents or diluents (water-soluble and water-insoluble),
5 pearlescent aids, foam boosters, additional surfactants or nonionic cosurfactants, pediculocides, pH adjusting agents, perfumes, preservatives, proteins, skin active agents, sunscreens, UV absorbers, and vitamins.

1. Conditioning Agent

The hair care composition may comprise one or more conditioning agents. Conditioning
10 agents include materials that are used to give a particular conditioning benefit to hair. The conditioning agents useful in the hair care compositions of the present invention typically comprise a water-insoluble, water-dispersible, non-volatile, liquid that forms emulsified, liquid particles. Suitable conditioning agents for use in the hair care composition are those conditioning agents characterized generally as silicones, organic conditioning oils or combinations thereof, or those
15 conditioning agents which otherwise form liquid, dispersed particles in the aqueous surfactant matrix.

One or more conditioning agents are present from about 0.01 wt% to about 10 wt%, from about 0.1 wt% to about 8 wt%, and from about 0.2 wt% to about 4 wt%, by weight of the composition.

20

Silicone Conditioning Agent

The hair care compositions of the present invention may contain one or more silicone conditioning agents. Examples of the silicones include dimethicones, dimethiconols, cyclic silicones, methylphenyl polysiloxane, and modified silicones with various functional groups such
25 as amino groups, quaternary ammonium salt groups, aliphatic groups, alcohol groups, carboxylic acid groups, ether groups, epoxy groups, sugar or polysaccharide groups, fluorine-modified alkyl groups, alkoxy groups, or combinations of such groups. Such silicones may be soluble or insoluble in the aqueous (or non-aqueous) product carrier. In the case of insoluble liquid silicones, the polymer can be in an emulsified form with droplet size of about 10 nm to about 30 micrometers

30

Organic Conditioning Materials

The conditioning agent of the compositions of the present invention may also comprise at least one organic conditioning material such as oil or wax, either alone or in combination with

other conditioning agents, such as the silicones described above. The organic material can be nonpolymeric, oligomeric or polymeric. It may be in the form of oil or wax and may be added in the formulation neat or in a pre-emulsified form. Some non-limiting examples of organic conditioning materials include, but are not limited to: i) hydrocarbon oils; ii) polyolefins, iii) fatty esters, iv) fluorinated conditioning compounds, v) fatty alcohols, vi) alkyl glucosides and alkyl glucoside derivatives; vii) quaternary ammonium compounds; viii) polyethylene glycols and polypropylene glycols having a molecular weight of up to about 2,000,000 including those with CTFA names PEG-20 200, PEG-400, PEG-600, PEG-1000, PEG-2M, PEG-7M, PEG-14M, PEG-45M and mixtures thereof.

Additional Benefit Agents

The hair care composition may further comprise one or more additional benefit agents. The benefit agents comprise a material selected from the group consisting of anti-dandruff agents, anti-fungal agents, anti-itch agents, anti-bacterial agents, anti-microbial agents, moisturization agents, anti-oxidants, vitamins, lipid soluble vitamins, perfumes, brighteners, enzymes, sensates, attractants, dyes, pigments, bleaches, and mixtures thereof.

The hair care compositions of the present invention may be presented in typical hair care formulations. They may be in the form of solutions, dispersion, emulsions, powders, talcs, encapsulated, spheres, spongers, solid dosage forms, foams, and other delivery mechanisms.

The hair care compositions may be provided in the form of a porous, dissolvable solid structure, such as those disclosed in U.S. Patent Application Publication Nos. 2009/0232873; and 2010/0179083, which are incorporated herein by reference in their entirety. Accordingly, the hair care compositions comprise a chelant, a buffer system comprising an organic acid, from about 23% to about 75% surfactant; from about 10% to about 50% water soluble polymer; and optionally, from about 1% to about 15% plasticizer; such that the hair care composition is in the form of a flexible porous dissolvable solid structure, wherein said structure has a percent open cell content of from about 80% to about 100%.

The hair care compositions may be in the form of a viscous liquid comprising one or more aptomer, 20% surfactant and a polycarboxylate rheology modifier; wherein the polycarboxylate is specifically chosen to be effective at the high electrolyte levels resulting from the incorporation of the key buffer system and chelant used for this invention. Non-limiting examples include acrylates/C10-C30 alkyl acrylate crosspolymers such as Carbopol EDT2020, 1342, 1382, etc. from

Lubrizol. Rheology benefits of these actives may include stability, ease of dispensing, smoothness of spreading, etc.

The hair care compositions are generally prepared by conventional methods such as are known in the art of making the compositions. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, application of vacuum, and the like. The compositions are prepared such as to optimize stability (physical stability, chemical stability, photostability) and/or delivery of the active materials. The hair care composition may be in a single phase or a single product, or the hair care composition may be in a separate phases or separate products. If two products are used, the products may be used together, at the same time or sequentially. Sequential use may occur in a short period of time, such as immediately after the use of one product, or it may occur over a period of hours or days.

Diagnostic tool – Detectable Fungal Contamination

The aptamer of the present invention can be used in diagnostic methods for the detection of fungal contamination. The contaminations may be at the scalp, skin, foot, blood or other parts of the body. The aptamer of the present invention can be combined (covalently or not) with a detection agent such as fluorescent dye, a color dye, a pigment, an imaging agent, or another molecule or moiety that enables the presence of the specific fungus. After the complex of the fungus and the aptamer is formed, the detection of the complex may be directly apparent by the development of a color or other visible indication or it may need an analytical device to detect such as X-ray, spectroscopy, MRI, radionuclide methodology, etc. The separation of the native aptamer from the aptamer-fungus complex may be necessary or not.

The methodology of detecting the fungus enabled by the present invention can be very specific for the particular fungus as the aptamer is designed to bind the particular fungus selectively. Thus, the detection limits are expected to be very low. In addition, the methodology is relatively fast that common techniques that rely on culture of the fungus for its detection, which are very time consuming (at least a few hours or even days).

The diagnostic methods of the present invention can be used for the detection of the fungus in intravenous drugs or other drugs or in food sources or food preparations or in toys and other surfaces that may cause human or pet contamination. There are examples of severe health consequences, even deaths, which are caused by difficult-to-detect *Malassezia furfur* contamination of parenterals.

In the hair/scalp care field, the diagnostic method can involve detection of fungal infection using a kit, such as (a) a swab or (b) a woven substrate or (c) or nonwoven substrate or (d) comb, which comprise a region having an absorbing element comprising the aptamer and a detection agent for a simple and accurate detection of the fungus that causes dandruff. In the

5 feminine protection field, the diagnostic method can involve detection of fungal infection using a kit, such as a swab or a comb or another substrate comb that comprises the aptamer and a detection agent for a simple and accurate detection of the fungus that causes vaginal Candidiasis. In the feminine protection field and in the diaper field, the diagnostic method can involve

10 detection of fungal infection using a kit, such as a swab or a comb or another substrate comb that comprises the aptamer and a detection agent for a simple and accurate detection of the fungus that causes yeast infection.

EXAMPLES

The following examples illustrate non-limiting examples of the invention described herein.

15 The exemplified hair care compositions can be prepared by conventional formulation and mixing techniques. It will be appreciated that other modifications of the hair care compositions within the skill of those in the formulation art can be undertaken without departing from the spirit and scope of this invention. All parts, percentages, and ratios herein are by weight unless otherwise specified. Some components may come from suppliers as dilute solutions. The amount stated

20 reflects the weight percent of the active material, unless otherwise specified.

The following are non-limiting examples of hair care compositions described herein.

SHAMPOO COMPOSITION EXAMPLES

	Shampoo Example 1	Shampoo Example 2
Ingredients	wt%	wt%
Water Purified	Q.S to 100	Q.S to 100
Sodium Laureth-3 Sulfate	21.6	21.6
Sodium Lauryl Sulfate	34.5	34.5
Laureth-4	0.9	0.9
Dimethicone 330M cps	0.5	0.5
Glycol Distearate	1.5	1.5
Polyquaternium-6	0.32	0.32

MG1 Aptamer	0.01	0.001
Sodium Benzoate	0.27	0.27
Citric acid 50% Solution	0.52	0.52
Methylchloroisothiazolinone /methylisothiazolinone	0.035	0.035
Sodium chloride	1.66	1.66
Fragrance	0.65	0.65
DL-Panthenol 56% solution	0.05	0.05
Panthenyl Ethyl ether	0.03	0.03
Glycol Distearate	1.5	1.5

Additional Shampoo Examples

Ingredient	SH Ex 3	SH Ex 4	SH Ex 5	SH Ex 6	SH Ex 7	SH Ex 8	SH Ex 9
Sodium lauryl ether sulfate (SLE3S)		6	10	6	6	9	
Sodium cocoyl isethionate							8.5
Sodium lauryl sulfate (SLS)	1.5	7	1.5	7	7	6	
Sodium lauryl ether sulfate (SLE1S)	10.5						
Disodium laureth sulfosuccinate							8.5
Sodium lauryl sulfoacetate							2.5
Sodium Lauroyl Sarcosinate							0.75
Cocoamidopropyl Hydroxysultaine							1.5
Cocoamidopropyl Betaine	1	2	2	2	2	2	2
Coconut monoethanol amide (CMEA)		0.85		0.85			
Cetyl alcohol			1				
Stearyl alcohol			2				

MG1 Aptamer	0.1	0.01	0.001	0.1	0.01	.001	.01
Dimethicone	1	1	1	1	1		0.5
Ethylene glycol distearate (EGDS)	1.5	1.5	1.5	1.5	1.5		
Jaguar® C5001	0.25	0.25	0.15				
Synthetic Cationic Polymer AMT2				0.1			
Polydiallyldimethylammonium chloride (DADMAC)					0.1		
Excel Guar3						0.1	.15
pH	6	6	6	6	6	6	
Water-USP Purified & Minors	Q.S. to 100	Q.S. to 100	Q.S. to 100	Q.S. to 100	Q.S. to 100	Q.S. to 100	Q.S. to 100

1 Cationic polymer derived from a natural gum with low aqueous viscosity

2 Cationic synthetic copolymer

3 Cationic plant derived polymer

5 RINSE-OFF CONDITIONER FORMULATIONS

	Rinse-off Conditioner Ex 1	Rinse-off Conditioner Ex 2
Ingredients	Wt%	Wt%
Amodimethicone 10000 cps	0.50	0.50
Citric acid anhydrous	0.13	0.13
DL-Panthenol 56% solution	0.054	0.054
Panthenyl Ethyl ether	0.03	0.03
Perfume	0.50	0.50
Hydroxypropyl guar (Jaguar HP-105)	0.350	0.350
Quaternium-18	0.750	0.750
Steramidopropyl dimethylamine	1.00	1.00
Glyceryl stearate	0.25	0.25

Cetearyl alcohol and Polysorbate 60 Emulsion 1	0.50	0.50
Cetyl alcohol	1.20	1.20
Stearyl alcohol	0.80	0.80
Benzyl alcohol	0.40	0.40
Methylchloroisothiazolinone /methylisothiazolinone	0.033	0.033
MG1 Aptamer	0.01	0.001
Water Purified	QS to 100	QS to 100

1. Lipowax P from Lipo (looked in internet)

ADDITIONAL EXAMPLES OF RINSE-OFF HAIR CONDITIONING COMPOSITIONS

Components	Rinse-off Condition Ex. 3	Rinse-off Condition Ex. 4	Rinse-off Condition Ex. 5	Rinse-off Condition Ex. 6	Rinse-off Condition Ex. 7	Rinse-off Condition Ex. 8
Water-USP Purified & Minors	QS to 100%	QS to 100%	QS to 100%	QS to 100%	QS to 100%	QS to 100%
BTMS1	2.3	2.3	2.3	2.3	2.3	2.3
BTMAC2	-	-	-	-	-	-
Cetyl alcohol	1.1	1.1	1.1	1.1	1.1	1.1
Stearyl alcohol	2.8	2.8	2.8	2.8	2.8	2.8
Soy Oligomer3	1.0	-		-		-
Soy Oligomer Blend4	-	1.0	-		-	
Aminosilicone5	1.0	1.0	1.0	1.0	2.0	2.0
Perfume	0.5	0.5	0.5	0.5	0.5	0.5
Disodium EDTA	0.1	0.1	0.1	0.1	0.1	0.1
Panthenol	0.03	0.03	0.03	0.03	0.03	0.03
Panthenyl ethyl ether	0.03	0.03	0.03	0.03	0.03	0.03
MG1 Aptamer	0.1	0.001	0.01	0.1	0.001	.01
Benzyl Alcohol	0.4	0.4	0.4	0.4	0.4	0.4
Preservatives	0.03	0.03	0.03	0.03	0.03	0.03

Ingredients	Rinse-off Condition Ex. 9	Rinse-off Condition Ex. 10	Rinse-off Condition Ex. 11	Rinse-off Condition Ex. 12	Rinse-off Condition Ex. 13	Rinse-off Condition Ex. 14
Water-USP Purified & Minors	QS to 100%	QS to 100%	QS to 100%	QS to 100%	QS to 100%	QS to 100%
BTMS1	-	-	-	-	-	-
BTMAC2	2.8	2.8	2.8	2.8	2.8	2.8
Cetyl alcohol	1.8	1.8	1.8	1.8	1.8	1.8
Stearyl alcohol	4.6	4.6	4.6	4.6	4.6	4.6
Soy Oligomer3	-	-	0.75	-	-	-
Soy Oligomer Blend4	-	1.0	-	-	-	-
Aminosilicone5	1.0	-	0.75	1.5	2.0	2.0
Perfume	0.5	0.5	0.5	0.5	0.5	0.5
Disodium EDTA	0.1	0.1	0.1	0.1	0.1	0.1
Panthenol	0.03	0.03	0.03	0.03	0.03	0.03
Panthenyl ethyl ether	0.03	0.03	0.03	0.03	0.03	0.03
MG1 Aptamer	0.01	0.1	0.001	0.1	0.01	0.001
Benzyl Alcohol	0.4	0.4	0.4	0.4	0.4	0.4
Preservatives	0.03	0.03	0.03	0.03	0.03	0.03

Ingredients	Rinse-off Condition Ex. 15	Rinse-off Condition Ex. 16	Rinse-off Condition Ex. 17	Rinse-off Condition Ex. 18
Water-USP Purified & Minors	QS to 100%	QS to 100%	QS to 100%	QS to 100%
BTMS1	3.76	3.76	3.76	3.76
BTMAC2	-	-	-	-
Cetyl alcohol	1.3	1.3	1.3	1.3
Stearyl alcohol	3.2	3.2	3.2	3.2
Soy Oligomer3	1.0	1.0	-	-
Soy Oligomer Blend4	-	-	-	-

Aminosilicone ⁵	-	-	1.0	1.0
Perfume	0.5	0.5	0.5	0.5
Disodium EDTA	0.1	0.1	0.1	0.1
Panthenol	-	-	-	-
Panthenyl ethyl ether	-	-	-	-
MG1 Aptamer	0.01	0.001	0.1	0.01
Benzyl Alcohol	0.4	0.4	0.4	0.4
Preservatives	0.03	0.03	0.03	0.03
Deposition Aid polymer ⁶	0.5	-	0.5	-

1 Behenyltrimethylammonium methylsulfate, from Feixiang

2 Behenyltrimethylammonium chloride, Genamin KDMP, from Clariant

3 HY-3050, from Dow Corning

4 HY-3051, from Dow Corning

5 Y-14945; 10,000 cps aminodimethicone, from Momentive

6ABC1459 from Mitsubishi Chemical

EXAMPLES OF LEAVE-ON TREATMENT (LOT) COMPOSITIONS

Components	LOT Ex. 1	LOT Ex. 2	LOT Ex. 3
Dipropyleneglycol Monomethylether	0.500	0.500	0.500
Disodium Ethylene diamine diacetic acid	0.141	0.141	0.141
PEG-40 Hydrogenated Castor Oil	0.500	0.500	0.500
Polysorbate 801	0.120	0.120	-
Amodimethicone and Cetrimonium Chloride	1.810	1.810	1.928
Polyquaternium 112	1.335	1.335	1.335
Citric Acid Anhydrous	0.080	0.080	0.20
2-Amino-2-methyl-1-propanol	0.100	0.100	0.100
DMDM Hydantoin (55%) ³	0.370	-	-
Benzyl Alcohol	-	0.400	0.4
Neolone 950 Preservative ⁴	-	0.053	0.053

Perfume	0.200	0.200	0.10
MG1 Aptamer	0.01	0.001	0.1
Water-USP Purified & Minors	QS to 100%	QS to 100%	QS to 100%

1 Nonionic surfactant and emulsifier derived from polyethoxylated sorbitan and oleic acid

2 Copolymer of vinylpyrrolidone and quaternized dimethylaminoethyl methacrylate

3 1,3-Bis(hydroxymethyl)-5,5-dimethylimidazolidine-2,4-dione

4 Preservative containing Methylisothiazolinone

V. EXAMPLES

EXAMPLE 1. Aptamers Design.

5 A. Growth of Fungus

A.1. Growth Conditions

Malassezia globosa ATCC® MYA-4612 are grown as a cell suspension in 50 mL of Modified Dixon Broth at 30-35 °C with constant shaking (250-300 rpm) in 250 mL autoclaved glass flasks. The broth is prepared by mixing the following materials: 36 g Bacto malt extract (VWR, catalog # 90001-014), 20 g Difco Oxgall dehydrated fresh bile (VWR, catalog # 90000-728), 10 mL tween 40 (Sigma, catalog # P1504), 36 g BBL polypeptone (BD, catalog # 211677), 2 mL oleic acid (Sigma, catalog # O1383), 2 mL glycerol (Sigma, catalog # G5516), and 1 L distilled water. The broth is autoclaved prior to use. After autoclaving, 0.5 mg of chloramphenicol (Sigma, catalog # C0378) is added.

15 A.2. Initial Inoculum

Cultures are initiated following ATCC recommendations. In summary, frozen ampoules are placed in a 25 °C water bath. Immediately after thawing, the surface of the ampoule is sterilized with 70% ethanol and the contents are aseptically transferred into an aliquot of the broth. An aliquot of the cultures is transferred to fresh broth every two weeks.

20

B. Aptamer Selection

B.1. Preparation of the Immobilization Field for FRELEX

An immobilization field is prepared by synthesizing a random library of eight nucleotide oligonucleotides with a disulfide group on the 5'-end (immobilization field library) (IDT DNA).

25 The library is dissolved at a concentration of 10 μM in 1X PBS buffer. The surface of a gold coated

glass slide with dimensions of 7 mm x 10 mm x 0.3 mm is used. This surface is treated with five sequential 10 μ L drops of the immobilization field library. The slide is then allowed to incubate for 1 hour in the dark and in the presence of humidity in order to facilitate conjugation of the immobilization field library onto the gold surface.

5 After this incubation period, the immobilization field library is considered to have been conjugated onto the gold surface. The remaining solution is removed, and the surface is allowed to dry at room temperature.

10 The remaining surface is then blocked with short PEG molecules having the following general structure: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{SH}$ and an average molecular weight of 550 daltons. The PEG molecules are applied at a concentration of 286 μM in 1X PBS buffer and allowed to incubate overnight prior to removal. This process is repeated in a second blocking step with an incubation period of 30 minutes at room temperature.

Following blocking the chip is washed in 1X HEPES buffer (10 mM HEPES, pH 7.4, 120 mM NaCl, 5 mM KCl, 5 mM MgCl_2) for 5 minutes with shaking at room temperature.

15

B.2. Library Preparation

A DNA library of about 1015 different sequences (10 nmoles), containing a random region of 40 nucleotides flanked by two conserved regions, i.e. a 5' forward primer recognition sequence (5'-TAGGGAAGAGAAGGACATATGAT-3') and a 3' reverse primer recognition sequence (5'-TTGACTAGTACATGACCACTTGA-3'), is solubilized in 100 μL of H_2O and split into aliquots of 16.6 μL (about 1.66 nmoles of DNA). An equimolar amount of blockers that bind the primer regions sequences (5'-ATCATATGTCCTTCTCTCCCTA-3' and 5'-TCAAGTGGTCATGTACTAGTCAA-3'), selection buffer (final concentration: 10 mM HEPES; pH 7.3), and water are incubated with the selection library in a total volume of 50 μL . The library solution with the blockers is denatured for 5 minutes at 95 $^\circ\text{C}$ to heat-denature the DNA. After this step, the temperature is decreased by one degree per minute to allow the blockers to anneal. When needed, 5 μL of a commercial antidandruff shampoo with zinc pyrithione is substituted for water in the 50 μL library solution.

30 B.3. Negative Selection with FRELEX

Aptamer selection is performed in two sequential steps. In the first step (negative selection), the library is enriched for aptamers that did not bind to shampoo formulation components using

the FRELEX protocol. In the second step (positive selection), the library is enriched for sequences that bound to *Malassezia globosa* ATCC® MYA-4612.

FRELEX is an aptamer selection platform (Lecocq S. et al., “Aptamers as biomarkers for neurological disorders. Proof of concept in transgenic mice” Plos One 19326201, January 5, 2018, Vol. 13, Issue 1) that enables partitioning of aptamers into bound and unbound states. During the negative selection, this approach is only used to select aptamer sequences that did not bind to undesirable target molecules.

First, the immobilization field described in section B.1. is placed inside a Petri dish. An aliquot of 50 µl of selection library solution (prepared as described in section B.2.) is added slowly to the top surface of the gold chip and incubated for 30 minutes at room temperature with gentle shaking (50 rpm). The supernatant solution is then removed from the immobilization field and discarded. It is presumed that the removed DNA sequences are either those that had too much secondary structure to facilitate hybridization to the immobilized 8-mers or those that are bound to compounds that are present in the negative selection library. Starting in selection round 2 and continuing for all subsequent selection rounds, 5 µL of a commercial antidandruff shampoo with zinc pyrithione is substituted for water in the 50 µL selection library solution. Thus, aptamers that bound to any compound within this formulation are discarded.

The immobilization field is then washed twice with 50 µL of 10X TE buffer (pH 7.3) and each wash solution is also discarded. Finally, the chip is placed inside a 2 mL plastic tube in the presence of 0.6 mL of selection buffer and heated to 95°C for 15 minutes to denature the hybridized aptamers from the 8-mers and to release them into the solution. The solution is transferred to a fresh 1.5 mL Eppendorf tube. The recovered aptamer library is purified with a Genejet PCR cleanup kit (ThermoFisher Scientific, Catalog # K0702) according to manufacturer’s instructions.

B.4. Positive Selection

During each selection round, negative selection as described in section B.3. is applied first. Then, the aptamers remaining from this process are used for positive selection. The completion of a negative selection process and a positive selection process constituted a single selection round.

For each positive selection, between 1.5×10^5 and 3.0×10^6 cells are collected from the broth suspension. The required broth volume is determined by counting cells in a defined volume with a Haemocytometer. The cells are pelleted gently (800 g) to remove the growth broth and washed twice with 1 mL of selection buffer followed by gentle centrifugation. The DNA library from the

negative selection (described in section B.3.) is applied to the pellet (total volume of 250 μ L). Then, the cells are resuspended and incubated with the aptamer library for 30 minutes at 35 °C with gentle rotation, followed by centrifugation (800 g) and removal of the supernatant. With this step, aptamers that did not bind to the fungal cells are discarded. Finally, the cell pellet is washed
5 twice with 500 μ L of selection buffer by pipetting the solution up and down and the cells are recovered by gentle centrifugation (800 g).

Aptamers bound to the cells are then recovered by resuspending the pellet in 500 μ L of lysis solution (1 N NaOH) followed by incubation for 10 minutes at 95 °C with gently mixing. The suspension is pelleted again by centrifugation and the supernatant containing the bound aptamers
10 are recovered. The pellet is resuspended one more time in 500 μ L of lysis buffer, incubated, and centrifuged, and the supernatant is recovered. The two separate aliquots of recovered aptamers are combined and purified using a GeneJET PCR Purification Kit (ThermoFisher Scientific, Catalog # K0702), following manufacturer's instructions.

The recovered library is PCR amplified in two stages. First, the purified library is subjected
15 to test PCR reactions using several aliquots of 5 μ L of recovered library and increasing number cycles. The products of these test PCR reactions are analyzed by polyacrylamide electrophoresis and the optimum number of cycles is determined. Then, a larger portion of the recovered library is amplified using this number of cycles. PCR amplification is carried out with Taq buffer (5 μ L; New England BioLabs, Catalog # B9014S), Taq DNA polymerase (0.25 μ L; New England
20 BioLabs, Catalog # M0273X), dNTPs mixture solution (10 mM each, 1 μ L; New England BioLabs, Catalog # N0447L), forward primer (10 μ M, 1 μ L), reverse primer (10 μ M, 1 μ L), water (36.75 μ L) and library template (5 μ L). PCR reactions are performed with an annealing temperature of 55 °C for the first two selection rounds and an annealing temperature of 60 °C for subsequent selection rounds.

25 C. Aptamers Sequencing

After 8 selection rounds, the aptamer libraries are sequenced. In summary, the selected libraries 3 to 8 are prepared for next generation sequencing (NGS) through a two-step PCR process. In the first step, a different hex code (6 base sequence) and a portion of a universal sequencing
30 primer is added to the 5' end of each aptamer library. In the second step, complete universal sequencing primers are added to both ends. After the second PCR step, the libraries are purified through acrylamide electrophoresis and balanced for relative quantity. These libraries are then

pooled and sent to the Hospital for Sick Children in Toronto for NGS with an Illumina HiSeq 2500 instrument.

The sequencing data is tabulated and analyzed. A total of 25,895,781 sequences are analyzed and each library contained more than 300,000 sequences (see Figure 1). The sequences from selection round 8 are sorted by copy number and named in descending order with the highest copy number sequence being named Mg-1. These top sequences are listed in Table 1.

The copy numbers of the top sequences of selection round 8 (Table 1) are determined on the libraries obtained from the other selection rounds. Finally, the frequency is computed for each sequence by dividing observed copy number by the total number of sequences observed in the particular library. Enrichment trajectories of the top 20 sequences in terms of frequency across different selection rounds are plotted (see Figure 2). During the selection, these sequences are enriching at a similar rate.

EXAMPLE 2. Aptamers Binding.

Quantitative polymerase chain reaction (qPCR) is used to determine the amount of aptamer bound to the target. In brief, a 5 μ L aliquot of the eluted aptamer and an aliquot of SYBR green are mixed and the DNA is PCR amplified. As the concentration of double stranded DNA increases, the fluorescent signal also increases, providing an indication on the relative amounts of eluted aptamer (see Figure 3). The results indicate that aptamers Mg-1 and Mg-2 bound to the fungal cells significantly better than aptamer Mg-4.

The Ct value is the number of PCR cycles at which the sample crosses a threshold detection value. In the figure 4, the Ct values are adjusted for the amplification efficiency for each of the aptamers. The selected aptamers have significant secondary structure and thus amplify less efficiently than the negative sequence.

EXAMPLE 3. Motif Analysis.

The frequency of motifs of six nucleotides from the random regions of the top two aptamers (Mg-1 and Mg-2) within all the sequences of selection round 8 library is determined. Then, the average motif frequency is subtracted from the frequency of each motif and this value is divided by the standard deviation of all the motifs frequencies in that selection round, resulting in a Z value for every motif (see Figures 5 and 7). It stands to reason that sequences containing high frequency motifs also bind to *M. globosa* may be part of the present invention.

The prediction of the secondary structures of the aptamers is performed with DINAmelt (<http://unafold.rna.albany.edu/?q=DINAmelt/Quickfold>; from RNA Institute of College of Arts and Sciences of the State University of New York at Albany) and the motifs are highlighted within these structures (see Figures 6 and 8).

5

A. Analysis of random region of aptamer Mg-1:

The motifs:

SEQ ID NO 101: 5'-GGTATGAAG-3'

SEQ ID NO 102: 5'-AAAATG-3'

10

SEQ ID NO 103: 5'-GGTATGAAGNNNNNNNANNAATG-3'

from the variable region of sequence Mg-1 (SEQ ID NO 1):

5'-TTGAGACGGTATGAAGGCTTTTGAGAAAATGCGCCACGAA-3'

where N stands for any nucleotide, are found at a significantly higher frequency than would be expected randomly. This means that these particular motifs are positively selected for within this

15

M. globosa based aptamer selection process. Any sequences containing this motif are also expected to bind to M. globosa may be part of the present invention.

B. Analysis of random region of aptamer Mg-2:

The analysis of the variable region of Mg-2 (SEQ ID NO 2):

20

5'-TGGCAAGTATTTGTACATATACTGACGTTTGCCTTACTGC-3'

suggests that the entire sequence has been selected for.

EXAMPLE 4. Analysis of Sequences Similarity.

25

Alignment of SEQ ID NO 1 to SEQ ID NO 100 is performed using the software Align X, a component of Vector NTI Advanced 11.5.4 by Invitrogen. Several groups of sequences have at least 90%, at least 70%, or at least 50% nucleotide sequence identity as illustrated in the alignments of Figures 9, 10, and 11. In these alignments, only the central variable region of the aptamers is included for simplicity. Thus, oligonucleotides with at least 50%, at least 70%, or at least 90%

30 nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100 are included and may be part of the current invention.

EXAMPLE 5. Delivery of Personal Care Active Ingredients with Aptamers.

Aptamers of the current invention are chemically synthesized. A solution of a personal care active ingredient containing a free amine group (0.25 M) and imidazole (0.1 M) in water (pH 6) is prepared. Then, EDC (1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride) is weighed in a reaction vial and mixed with an aliquot of an aptamer solution. An aliquot of the amine/imidazole solution is added immediately to the reaction vial and vortexed until all the components are dissolved. An additional aliquot of imidazole solution (0.1 M, pH 6) is added to the reaction vial and the reaction mixture is incubated at room temperature for at least 2 hours. Following incubation, the unreacted EDC and its by-products and imidazole are separated from the modified aptamer by dialysis or by using a spin desalting column and a suitable buffer (e.g. 10 mM sodium phosphate, 0.15 M NaCl, 10 mM EDTA, pH 7.2). Additional details about the conjugation protocols are described in Hermanson G. T., "Bioconjugate Techniques", pp. 969-1002, 2nd Edition, Academic Press, San Diego, 2008, the content of which is incorporated herein by reference.

The produced modified aptamer conjugated with a personal care active ingredient can be formulated in a hair care composition (e.g. shampoo or conditioner) to provide benefits when contacted with hair.

TABLE 1. List of top sequences from selection experiment.

SEQ ID NO	Name	Sequence
1	Mg-1	TAGGGAAGAGAAGGACATATGATTTGAGACGGTATGAAG GCTTTTGAGAAAATGCGCCACGAATTGACTAGTACATGAC CACTTGA
2	Mg-2	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
3	Mg-3	TAGGGAAGAGAAGGACATATGATGACCGAGGTTCCGGCG ACAGAGCAAATTTGTAATTTGGAGTTGACTAGTACATGAC CACTTGA

4	Mg-4	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACACCTGTTTCCCTGTTGACTAGTACATGACC ACTTGA
5	Mg-5	TAGGGAAGAGAAGGACATATGATTAAAGAACAGGATGAT CAGGGTTGATGGATTTTGACGATGTTGACTAGTACATGAC CACTTGA
6	Mg-6	TAGGGAAGAGAAGGACATATGATTCCTCTGCTGGTGAGA GGCGTCCAATGAATCATATTACCGTTGACTAGTACATGAC CACTTGA
7	Mg-7	TAGGGAAGAGAAGGACATATGATAGTCAAATAAAATTTT GTGTGAATCGAGTGTGCTATTGCTTTGACTAGTACATGAC CACTTGA
8	Mg-8	TAGGGAAGAGAAGGACATATGATGGTGTGAAAGTTATG TAATTATTTAGGGAACGTATGGACTTGACTAGTACATGAC CACTTGA
9	Mg-9	TAGGGAAGAGAAGGACATATGATGGGGAAGAGTGATAAT CTAAAGGTACTACAATGTACTACATTGACTAGTACATGAC CACTTGA
10	Mg-10	TAGGGAAGAGAAGGACATATGATTAGCAAGTATTTGTAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
11	Mg-11	TAGGGAAGAGAAGGACATATGATACCCTCGATACGTATAT TCGATATGAGGGAGTATTCCGTGTTGACTAGTACATGACC ACTTGA
12	Mg-12	TAGGGAAGAGAAGGACATATGATGAGTAACAGTTCAACC TTGTTATTACACTAACTCCGTGACTTGACTAGTACATGACC ACTTGA
13	Mg-13	TAGGGAAGAGAAGGACATATGATGATGTTGATAAATTTGC AATGACTAGATCCATCCGCTTTATTGACTAGTACATGACC ACTTGA
14	Mg-14	TAGGGAAGAGAAGGACATATGATGAACGGATCCGATACG AACGTTAACAAATGAGGGTTTAAGTTGACTAGTACATGAC CACTTGA

15	Mg-15	TAGGGAAGAGAAGGACATATGATAATTGATATGCAGCAA TTACCAGTATAAGGCATCTACTACTTGACTAGTACATGAC CACTTGA
16	Mg-16	TAGGGAAGAGAAGGACATATGATCCATTTTCTCGACTTTG CCATTGCTATAAATAGCTTCACATTGACTAGTACATGACC ACTTGA
17	Mg-17	TAGGGAAGAGAAGGACATATGATTGGCAAATATTTGTAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
18	Mg-18	TAGGGAAGAGAAGGACATATGATATATTCACGCTAGTGG GAGCGCTGTTGATCATAACGGCTGCTTGACTAGTACATGAC CACTTGA
19	Mg-19	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGTCTTACTGCTTGACTAGTACATGACC ACTTGA
20	Mg-20	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACACCTGTTTCTCTGTTGACTAGTACATGACC ACTTGA
21	Mg-21	TAGGGAAGAGAAGGACATATGATATTAAGTTAGGTCCGT AATGACACTTAAACGGATCCATACTTGACTAGTACATGAC CACTTGA
22	Mg-22	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGCCTTACTACTTGACTAGTACATGACC ACTTGA
23	Mg-23	TAGGGAAGAGAAGGACATATGATTAAAGAACAGGATGAT CAGGGTTGATGGATTTTGATGATGTTGACTAGTACATGAC CACTTGA
24	Mg-24	TAGGGAAGAGAAGGACATATGATTAGGCTAACTGTTTCAG GGATTTGATATGCATGAGGAGCACTTGACTAGTACATGAC CACTTGA
25	Mg-25	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTAACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA

26	Mg-26	TAGGGAAGAGAAGGACATATGATTGACAAGTATTTGTAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
27	Mg-27	TAGGGAAGAGAAGGACATATGATTCTCGAGTGCAAAAAC GTTGAGCCAAGAATTAACTATCTTGACTAGTACATGAC CACTTGA
28	Mg-28	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGCCTTACTGTTTGACTAGTACATGACC ACTTGA
29	Mg-29	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGATGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
30	Mg-30	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGCCTTATTGCTTGACTAGTACATGACC ACTTGA
31	Mg-31	TAGGGAAGAGAAGGACATATGATTGGTAAGTATTTGTACA TATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACCA CTTGA
32	Mg-32	TAGGGAAGAGAAGGACATATGATGTCAATCTATCACAAA CGCGAGGTAAGGCCACGCGATTATTGACTAGTACATGAC CACTTGA
33	Mg-33	TAGGGAAGAGAAGGACATATGATCGCTCTAATTGGCGTG GAGGGAGTGTTCTCCAACGGTAATTGACTAGTACATGAC CACTTGA
34	Mg-34	TAGGGAAGAGAAGGACATATGATGCATGCACGTCTGAAG AAATCCTTGAATTGTACCGGAAGATTGACTAGTACATGAC CACTTGA
35	Mg-35	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTACCTTACTGCTTGACTAGTACATGACC ACTTGA
36	Mg-36	TAGGGAAGAGAAGGACATATGATCTAAACAGTACTTCAA CCTAAAGAGTCACGTACGCAGTAATTGACTAGTACATGAC CACTTGA

37	Mg-37	TAGGGAAGAGAAGGACATATGATTGCCATCGTATAAAATCT CAAAAGGGATCATTGTAAAATCCTTGACTAGTACATGACC ACTTGA
38	Mg-38	TAGGGAAGAGAAGGACATATGATCTGGGGGCTTCCCGGA GTTCCGTAAAGTAGTGAGATCTTGTTGACTAGTACATGAC CACTTGA
39	Mg-39	TAGGGAAGAGAAGGACATATGATTTGTGATCAAGAAAAT GGAACCCACATAACTATTCCGAGTTTGACTAGTACATGAC CACTTGA
40	Mg-40	TAGGGAAGAGAAGGACATATGATGAGCCTAGATCATTTTG ATCTTGCAATCTATGGCAGAATCTTGACTAGTACATGACC ACTTGA
41	Mg-41	TAGGGAAGAGAAGGACATATGATACAATTTGGATAGTAC CGCGATCAGGTACAAAGAATATTCTTGACTAGTACATGAC CACTTGA
42	Mg-42	TAGGGAAGAGAAGGACATATGATGCATTACAGTAGCAA TTGTATTTCCCTTGATAGGAATGAATTGACTAGTACATGAC CACTTGA
43	Mg-43	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACACCTATTTCCCTGTTGACTAGTACATGACC ACTTGA
44	Mg-44	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATATTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
45	Mg-45	TAGGGAAGAGAAGGACATATGATTGTGGAAACCAAATAG AAGATATAACACTCTTATCTACAGTTGACTAGTACATGAC CACTTGA
46	Mg-46	TAGGGAAGAGAAGGACATATGATTGAAGTGGAGACCGTA GAGGAGATTACAATATGAATCCGGTTGACTAGTACATGAC CACTTGA
47	Mg-47	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACATTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA

48	Mg-48	TAGGGAAGAGAAGGACATATGATCTCAGTACTGCAAGGA TTTAAGATACAGCGCATTGCAGAATTGACTAGTACATGAC CACTTGA
49	Mg-49	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTATAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
50	Mg-50	TAGGGAAGAGAAGGACATATGATTTAAACAGGATCCGCA CGAATACAGTGTACACAATTCAGGTTGACTAGTACATGAC CACTTGA
51	Mg-51	TAGGGAAGAGAAGGACATATGATCTATGGATCGACTAGT AATCAAGCCTTCGGACTCTTATGATTGACTAGTACATGAC CACTTGA
52	Mg-52	TAGGGAAGAGAAGGACATATGATTGGGGACGTAACAGTA TGAAC TTGAAGACTTATCATTGTATTGACTAGTACATGAC CACTTGA
53	Mg-53	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTATA TATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACCA CTTGA
54	Mg-54	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGTTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
55	Mg-55	TAGGGAAGAGAAGGACATATGATCAGGAATGCTTCAATT CCTTG TAGCATTCACTTGTAGACATTGACTAGTACATGAC CACTTGA
56	Mg-56	TAGGGAAGAGAAGGACATATGATTACGGGGATAAGGAGC AACATATTAAGCAAAGTACTAAAATTGACTAGTACATGAC CACTTGA
57	Mg-57	TAGGGAAGAGAAGGACATATGATAAAACATGAAGCTGAA CGCGTAACTCCCGGCTGGCGAATATTGACTAGTACATGAC CACTTGA
58	Mg-58	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATATACCTGTTTCCCTGTTGACTAGTACATGACC ACTTGA

59	Mg-59	TAGGGAAGAGAAGGACATATGATCTGACGGGAGTCAGAA CCCTTGTTAAGGGACCACCTGTTTTTGACTAGTACATGACC ACTTGA
60	Mg-60	TAGGGAAGAGAAGGACATATGATGTAAGACTTGTACTAT GAAATGTTATGGAGGATGTAGATTTTGACTAGTACATGAC CACTTGA
61	Mg-61	TAGGGAAGAGAAGGACATATGATGCCGTAAGAAACCTCC TGGTGTTCGAAATATGGAAAGTCTTTGACTAGTACATGAC CACTTGA
62	Mg-62	TAGGGAAGAGAAGGACATATGATGAGTTTTAAAAGGCAA TATGTCTTGAGAGACAAGGTTAGATTGACTAGTACATGAC CACTTGA
63	Mg-63	TAGGGAAGAGAAGGACATATGATATTGACATTCTAAGCTA ATGAAAGTGTAATAACGACTAGCTTGACTAGTACATGACC ACTTGA
64	Mg-64	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACACCTGTTTCCCTATTGACTAGTACATGACC ACTTGA
65	Mg-65	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTA TGTCAGAATACACCTGTTTCCCTGTTGACTAGTACATGACC ACTTGA
66	Mg-66	TAGGGAAGAGAAGGACATATGATTCCTCTGCTGGTGAGA GGTGTCCAATGAATCATATTACCGTTGACTAGTACATGAC CACTTGA
67	Mg-67	TAGGGAAGAGAAGGACATATGATAGAGTAAGAATCCATA ATTTGGCAAGTAGACATTCGCATATTGACTAGTACATGAC CACTTGA
68	Mg-68	TAGGGAAGAGAAGGACATATGATGTTTAGGACGTATCTTA GAGCTGGCCCTCAATGAAAGGTTTTGACTAGTACATGACC ACTTGA
69	Mg-69	TAGGGAAGAGAAGGACATATGATGAGAGGCAGTAGGTCT AATGAAGAATCTCTAGGTTGCAAATTGACTAGTACATGAC CACTTGA

70	Mg-70	TAGGGAAGAGAAGGACATATGATGGCCTATACTTGGTTGC TTCTATAGCTTAGTGCGGGGGATTGACTAGTACATGACC ACTTGA
71	Mg-71	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACACTTGTTTCCCTGTTGACTAGTACATGACC ACTTGA
72	Mg-72	TAGGGAAGAGAAGGACATATGATCACGAAACATAAATTG TGTCAGAATACACCTGTTTCCCTGTTGACTAGTACATGACC ACTTGA
73	Mg-73	TAGGGAAGAGAAGGACATATGATCTGACGGGAGTCAGAA CCCTTGTTAAGGGATCACCTGTTTTTGACTAGTACATGACC ACTTGA
74	Mg-74	TAGGGAAGAGAAGGACATATGATTCCTCTGTTGGTGAGAG GCGTCCAATGAATCATATTACCGTTGACTAGTACATGACC ACTTGA
75	Mg-75	TAGGGAAGAGAAGGACATATGATCACAACGTAATTTTCG GGTGAATGATGCAGCCAAGAGAAATTGACTAGTACATGA CCACTTGA
76	Mg-76	TAGGGAAGAGAAGGACATATGATTAAGTTGGAAAGTGGT AGAATGCTTAGACAGGCGGGGACTTGACTAGTACATGA CCACTTGA
77	Mg-77	TAGGGAAGAGAAGGACATATGATGTTATAATGGTGCAAA CTATAGCTAATAAGATGCCACTGATTGACTAGTACATGAC CACTTGA
78	Mg-78	TAGGGAAGAGAAGGACATATGATGTGAATTCGCATGACTT GGAAGAGGTAAACAAAAGTAGCTTTGACTAGTACATGAC CACTTGA
79	Mg-79	TAGGGAAGAGAAGGACATATGATAAGGTTTACTCAACTC GGATTCAAAGAACATGTACTTAACTTGACTAGTACATGAC CACTTGA
80	Mg-80	TAGGGAAGAGAAGGACATATGATCACGAAACATAAGTTG TGTCAGAATACATCTGTTTCCCTGTTGACTAGTACATGACC ACTTGA

81	Mg-81	TAGGGAAGAGAAGGACATATGATGCTCGTTTATTCGGACC TCAGGGGCTGTCAGCATTTGAATTTGACTAGTACATGACC ACTTGA
82	Mg-82	TAGGGAAGAGAAGGACATATGATTGCGGCTATAAGTTTAT GTGTGAATATTGGTATGATATAATTGACTAGTACATGACC ACTTGA
83	Mg-83	TAGGGAAGAGAAGGACATATGATGACGCACAGTATGCGT GCTATCAATTTTGAGTATAGTGTATTGACTAGTACATGAC CACTTGA
84	Mg-84	TAGGGAAGAGAAGGACATATGATTGGCAAGTATTTGTAC ATATACTGACGCTTGCCTTACTGCTTGACTAGTACATGACC ACTTGA
85	Mg-85	TAGGGAAGAGAAGGACATATGATTCCTCTGCTGGTGAGA GGCGTTCAATGAATCATATTACCGTTGACTAGTACATGAC CACTTGA
86	Mg-86	TAGGGAAGAGAAGGACATATGATTCCTTTGCTGGTGAGAG GCGTCCAATGAATCATATTACCGTTGACTAGTACATGACC ACTTGA
87	Mg-87	TAGGGAAGAGAAGGACATATGATCTGACACCATTTTACAA ATTGAAATAATACAGCTTATACGTTGACTAGTACATGACC ACTTGA
88	Mg-88	TAGGGAAGAGAAGGACATATGATCCGCCTGACGAACACA AGGAACCGGAATTAAGCGAATGCCTTGACTAGTACATGAC CACTTGA
89	Mg-89	TAGGGAAGAGAAGGACATATGATTGACTAGTACATGACC ACTTGAGATCGGAAGAGCACACGTTTGACTAGTACATGAC CACTTGA
90	Mg-90	TAGGGAAGAGAAGGACATATGATCTTATACCAATCAATA ACGCGCATTTTTAGCAAGACAAGATTGACTAGTACATGAC CACTTGA
91	Mg-91	TAGGGAAGAGAAGGACATATGATTAAAGAACAAGATGAT CAGGGTTGATGGATTTTGACGATGTTGACTAGTACATGAC CACTTGA

92	Mg-92	TAGGGAAGAGAAGGACATATGATTAAAGAATAGGATGAT CAGGGTTGATGGATTTTGACGATGTTGACTAGTACATGAC CACTTGA
93	Mg-93	TAGGGAAGAGAAGGACATATGATTTCGCAGAATTCTAATA GACCTGGAGAAGACAGGGGGTTATTTGACTAGTACATGAC CACTTGA
94	Mg-94	TAGGGAAGAGAAGGACATATGATATTACGAGTTTATAAG ATTTGGCGCTGCCTACTCATCATCTTGACTAGTACATGACC ACTTGA
95	Mg-95	TAGGGAAGAGAAGGACATATGATTAAAGAACAAGATAAT CAGGGTTGATGGATTTTGACGATGTTGACTAGTACATGAC CACTTGA
96	Mg-96	TAGGGAAGAGAAGGACATATGATACATAAAATTTCCAGA TCTACCTGATGTGTGCCGTCTATATTGACTAGTACATGACC ACTTGA
97	Mg-97	TAGGGAAGAGAAGGACATATGATCGGATGAATAAACAAT GCTGGGTACTGATCAGTATGACCTTTGACTAGTACATGAC CACTTGA
98	Mg-98	TAGGGAAGAGAAGGACATATGATGAAGGGCAAGCCTTAT AAATTCGTACTGTATCTTATTGAATTGACTAGTACATGACC ACTTGA
99	Mg-99	TAGGGAAGAGAAGGACATATGATCGGTGTCGGTAGAAAC AAAGAGAGGTTATGCATATCTATGTTGACTAGTACATGAC CACTTGA
100	Mg-100	TAGGGAAGAGAAGGACATATGATCAAGGATGTCATGGAA CTGGTGAACGTCTAAAATCACCATTGACTAGTACATGAC CACTTGA

Additional Combinations/Examples

- A. An aptamer composition comprising at least one oligonucleotide consisting of:
deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of

ribonucleotides, and mixtures thereof; wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*.

- B. The aptamer composition according to Paragraph A, wherein said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof.
- C. The aptamer composition according to Paragraph A-B, wherein said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.
- D. The aptamer composition according to Paragraph A-C, comprising at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 50% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100.
- E. The aptamer composition according to Paragraph A-D, comprising at least one oligonucleotide selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100.
- F. The aptamer composition according to Paragraph A-E, comprising at least one oligonucleotide selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4.
- G. The aptamer composition according to Paragraph A-F, wherein said at least one oligonucleotide comprises one or more motifs selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103.
- H. The aptamer composition according to Paragraph A-G, wherein said at least one oligonucleotide comprises natural or non-natural nucleobases.
- I. The aptamer composition according to Paragraph A-H, wherein said non-natural nucleobases are selected from the group comprising hypoxanthine, xanthine, 7-methylguanine, 5,6-dihydrouracil, 5-methylcytosine, 5-hydroxymethylcytosine, thiouracil, 1-methylhypoxanthine, 6-methylisoquinoline-1-thione-2-yl, 3-methoxy-2-naphthyl, 5-propynyluracil-1-yl, 5-methylcytosin-1-yl, 2-aminoadenin-9-yl, 7-deaza-7-iodoadenin-9-yl, 7-deaza-7-propynyl-2-aminoadenin-9-yl, phenoxazinyl, phenoxazinyl-G-clam, and mixtures thereof.
- J. The aptamer composition according to Paragraph A-I, wherein the nucleosides of said at least one oligonucleotide are linked by a chemical motif selected from the group comprising natural phosphate diester, chiral phosphorothionate, chiral methyl phosphonate, chiral

phosphoramidate, chiral phosphate chiral triester, chiral boranophosphate, chiral phosphoroselenoate, phosphorodithioate, phosphorothionate amidate, methylenemethylimino, 3'-amide, 3' achiral phosphoramidate, 3' achiral methylene phosphonates, thioformacetal, thioethyl ether, and mixtures thereof.

- K. The aptamer composition according to Paragraph A-J, where said derivatives of ribonucleotides or said derivatives of deoxyribonucleotides are selected from the group comprising locked oligonucleotides, peptide oligonucleotides, glycol oligonucleotides, threose oligonucleotides, hexitol oligonucleotides, altritol oligonucleotides, butyl oligonucleotides, L-ribonucleotides, arabino oligonucleotides, 2'-fluoroarabino oligonucleotides, cyclohexene oligonucleotides, phosphorodiamidate morpholino oligonucleotides, and mixtures thereof.
- L. The aptamer composition according to Paragraph A-K, further comprising at least one polymeric material, wherein said at least one polymeric material is covalently linked to said at least one oligonucleotide.
- M. The aptamer composition according to Paragraph A-L, wherein said at least one polymeric material is polyethylene glycol.
- N. The aptamer composition according to Paragraph A-M, wherein the nucleotides at the 5'- and 3'- ends of said at least one oligonucleotide are inverted.
- O. The aptamer composition according to Paragraph A-N, wherein at least one nucleotide of said at least one oligonucleotide is fluorinated at the 2' position of the pentose group.
- P. The aptamer composition according to Paragraph A-O, wherein the pyrimidine nucleotides of said at least one oligonucleotide are fluorinated at the 2' position of the pentose group.
- Q. The aptamer composition according to Paragraph A-P, wherein said at least one oligonucleotide is covalently or non-covalently attached to one or more personal care benefit agents, wherein said one or more personal care benefit agents are selected from the group comprising: anti-fungal agents, cooling agents, natural extracts, peptides, enzymes, conditioning agents, scalp health agents, anti-frizz agents, gloss improving agents, hair strengthening agents, hair growth actives, artificial color preserving agents, perfumes, malodor absorbing agents, styling agents, chelants, hair coloring dyes, sebum absorbing agents, sebum modification agents, and mixtures thereof.
- R. The aptamer composition according to Paragraph A-Q, wherein said one or more personal care active ingredients are selected from the group consisting of antifungal agents.

- S. The aptamer composition according to Paragraph A-R, wherein said one or more personal care active ingredients are selected from the group consisting of zinc pyrithione, piroctone olamine, ketoconazole, and selenium disulfide.
- T. The aptamer composition according to Paragraph A-R, wherein said at least one oligonucleotide is covalently or non-covalently attached to one or more nanomaterials.
- U. A personal care composition according to Paragraph A-T, comprising at least one nucleic acid aptamer; wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*.
- V. The personal care composition according to Paragraph A-U, wherein said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof.
- W. The personal care composition according to Paragraph A-U, wherein said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.
- X. The personal care composition according to Paragraph A-W, wherein said composition comprises at least two different nucleic acid aptamers; and wherein said at least two different nucleic acid aptamers have binding affinities for different epitopes of said one or more fungi species from the genus *Malassezia*.
- Y. A method for delivering one or more personal care active ingredients to the scalp or the skin according to Paragraph A-X, comprising administering a personal care composition comprising at least one nucleic acid aptamer and one or more personal care active ingredients; wherein said at least one nucleic acid aptamer and said one or more personal care active ingredients are covalently or non-covalently attached; and wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*.
- Z. The method according to Paragraph A-Y, wherein said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.
- AA. The method according to Paragraph A-Z, where said one or more personal care active ingredients are selected from the group comprising antifungal agents.
- BB. A method for delivering one or more personal care active ingredients to the scalp or the skin according to Paragraph A-AA, comprising administering a personal care composition

comprising: at least one nucleic acid aptamer and one or more nanomaterials; wherein said at least one nucleic acid aptamer and said one or more nanomaterials are covalently or non-covalently attached; wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*; and wherein said one or more nanomaterials comprise one or more personal care active ingredients.

- CC. A diagnostic method for detecting a fungus on a surface or a liquid according to Paragraph A-BB wherein said diagnostic method comprises:
- a. mixing the liquid with, or contacting the surface a diagnostic composition comprising:
 - (1) an aptamer composition comprising at least one oligonucleotide consisting of deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof; wherein said aptamer composition has a binding affinity for one or more fungi species
 - (2) a detection agent composition which enables the detection of the complex of the fungi species and the aptamer;
 - b. Detecting the presence of the complex of the fungi species and the aptamer.
- DD. The diagnostic method according to Paragraph A-CC, wherein the surface is scalp, skin, foot, other body parts, surfaces of articles which come into contact with human hands or other parts of human body or pet body and cause contamination.
- EE. The diagnostic method according to Paragraph A-DD, wherein the liquid is blood, other body fluids, intravenous drugs, other drugs, food sources, food preparation, drinking water, or other water supply.
- FF. The diagnostic method according to Paragraph A-EE, wherein the fungus is *malassezia*.
- GG. The diagnostic method according to Paragraph A-FF, wherein the contacting of the diagnostic composition with surface is performed by rubbing (a) a swab or (b) a woven substrate or (c) or nonwoven substrate or (d) comb, which comprise a region having an absorbing element comprising the aptamer composition and a detection agent composition.
- HH. The diagnostic method according to Paragraph A-GG, wherein the detecting step is observed by a color change developed by the creation of the complex of the fungi species and the aptamer composition in the presence of the detection agent composition.
- II. The diagnostic method according to Paragraph A-HH, wherein the detecting step comprises an analytical determination using x ray, other spectroscopic techniques, MRI, radionuclide techniques which can quantitatively determine the creation of the complex of the fungi species and the aptamer composition in the presence of the detection agent composition.

The dimensions and values disclosed herein are not to be understood as being strictly limited to the exact numerical values recited. Instead, unless otherwise specified, each such dimension is intended to mean both the recited value and a functionally equivalent range surrounding that value. For example, a dimension disclosed as "40 mm" is intended to mean "about 40 mm."

All documents cited in the Detailed Description of the Invention are, in relevant part, incorporated herein by reference; the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention. To the extent that any meaning or definition of a term in this document conflicts with any meaning or definition of the same term in a document incorporated by reference, the meaning or definition assigned to that term in this document shall govern.

While the present invention has been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be made without departing from the spirit and scope of the invention. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

CLAIMS

What is claimed is:

1. An aptamer composition comprising at least one oligonucleotide consisting of: deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof; wherein said aptamer composition has a binding affinity for one or more fungi species from the genus *Malassezia*, preferably wherein the one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof, preferably wherein the one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.
2. The aptamer composition according to any preceding claims, comprising at least one oligonucleotide selected from the group consisting of oligonucleotides with at least 50% nucleotide sequence identity to sequences selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100.
3. The aptamer composition according to any preceding claims, comprising at least one oligonucleotide selected from the group consisting of SEQ ID NO 1 to SEQ ID NO 100, preferably at least one oligonucleotide selected from the group consisting of SEQ ID NO 1, SEQ ID NO 2, and SEQ ID NO 4.
4. The aptamer composition according to any preceding claims, wherein said at least one oligonucleotide comprises one or more motifs selected from the group consisting of SEQ ID NO 101, SEQ ID NO 102, and SEQ ID NO 103.
5. The aptamer composition according to any preceding claims, wherein said at least one oligonucleotide comprises natural or non-natural nucleobases, preferably wherein the non-natural nucleobases are selected from the group comprising hypoxanthine, xanthine, 7-methylguanine, 5,6-dihydrouracil, 5-methylcytosine, 5-hydroxymethylcytosine, thiouracil, 1-methylhypoxanthine, 6-methylisoquinoline-1-thione-2-yl, 3-methoxy-2-naphthyl, 5-propynyluracil-1-yl, 5-methylcytosin-1-yl, 2-aminoadenin-9-yl, 7-deaza-7-

iodoadenin-9-yl, 7-deaza-7-propynyl-2-aminoadenin-9-yl, phenoxazinyl, phenoxazinyl-G-clam, and mixtures thereof.

6. The aptamer composition according to any preceding claims, wherein the nucleosides of said at least one oligonucleotide are linked by a chemical motif selected from the group comprising natural phosphate diester, chiral phosphorothionate, chiral methyl phosphonate, chiral phosphoramidate, chiral phosphate chiral triester, chiral boranophosphate, chiral phosphoroselenoate, phosphorodithioate, phosphorothionate amidate, methylenemethylimino, 3'-amide, 3' achiral phosphoramidate, 3' achiral methylene phosphonates, thioformacetal, thioethyl ether, and mixtures thereof.
7. The aptamer composition according to any preceding claims, where said derivatives of ribonucleotides or said derivatives of deoxyribonucleotides are selected from the group comprising locked oligonucleotides, peptide oligonucleotides, glycol oligonucleotides, threose oligonucleotides, hexitol oligonucleotides, altritol oligonucleotides, butyl oligonucleotides, L-ribonucleotides, arabino oligonucleotides, 2'-fluoroarabino oligonucleotides, cyclohexene oligonucleotides, phosphorodiamidate morpholino oligonucleotides, and mixtures thereof.
8. The aptamer composition according to any preceding claims, further comprising at least one polymeric material, wherein said at least one polymeric material is covalently linked to said at least one oligonucleotide, preferably wherein the at least one polymeric material is polyethylene glycol.
9. The aptamer composition according to any preceding claims, wherein the nucleotides at the 5'- and 3'- ends of said at least one oligonucleotide are inverted.
10. The aptamer composition according to any preceding claims, wherein at least one nucleotide of said at least one oligonucleotide is fluorinated at the 2' position of the pentose group, preferably wherein the pyrimidine nucleotides of said at least one oligonucleotide are fluorinated at the 2' position of the pentose group.

11. The aptamer composition according to any preceding claims, wherein said at least one oligonucleotide is covalently or non-covalently attached to one or more personal care benefit agents, wherein said one or more personal care benefit agents are selected from the group comprising: anti-fungal agents, cooling agents, natural extracts, peptides, enzymes, conditioning agents, scalp health agents, anti-frizz agents, gloss improving agents, hair strengthening agents, hair growth actives, artificial color preserving agents, perfumes, malodor absorbing agents, styling agents, chelants, hair coloring dyes, sebum absorbing agents, sebum modification agents, and mixtures thereof, preferably wherein the one or more personal care active ingredients are selected from the group consisting of antifungal agents, preferably wherein the one or more personal care active ingredients are selected from the group consisting of zinc pyrithione, piroctone olamine, ketoconazole, and selenium disulfide.
12. A personal care composition according to any preceding claims, comprising at least one nucleic acid aptamer; wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*, preferably wherein the one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, *M. caprae*, *M. cuniculi*, *M. dermatis*, *M. equine*, *M. japonica*, *M. nana*, *M. obtuse*, *M. pachydermatis*, *M. slooffiae*, *M. sympodialis*, *M. yamatoensis*, and mixtures thereof, preferably wherein the said one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof.
13. A method for delivering one or more personal care active ingredients to the scalp or the skin according to any preceding claims comprising administering a personal care composition comprising at least one nucleic acid aptamer and one or more personal care active ingredients; wherein said at least one nucleic acid aptamer and said one or more personal care active ingredients are covalently or non-covalently attached; and wherein said at least one nucleic acid aptamer has a binding affinity for one or more fungi species from the genus *Malassezia*, preferably wherein the one or more fungi species are selected from the group consisting of: *M. globosa*, *M. furfur*, *M. restricta*, and mixtures thereof, preferably wherein the one or more personal care active ingredients are selected from the group comprising antifungal agents.

14. A diagnostic method for detecting a fungus on a surface or a liquid according to any preceding claims wherein said diagnostic method comprises:
- a. mixing the liquid with, or contacting the surface a diagnostic composition comprising:
 - 1) an aptamer composition comprising at least one oligonucleotide consisting of deoxyribonucleotides, ribonucleotides, derivatives of deoxyribonucleotides, derivatives of ribonucleotides, and mixtures thereof; wherein said aptamer composition has a binding affinity for one or more fungi species
 - 2) a detection agent composition which enables the detection of the complex of the fungi species and the aptamer;
 - b. Detecting the presence of the complex of the fungi species and the aptamer, preferably wherein the surface is scalp, skin, foot, other body parts, surfaces of articles which come into contact with human hands or other parts of human body or pet body and cause contamination, preferably wherein the liquid is blood, other body fluids, intravenous drugs, other drugs, food sources, food preparation, drinking water, or other water supply, preferably wherein the fungus is malassezia, preferably wherein the detecting step is observed by a color change developed by the creation of the complex of the fungi species and the aptamer composition in the presence of the detection agent composition, preferably wherein the detecting step comprises an analytical determination using x ray, other spectroscopic techniques, MRI, radionuclide techniques which can quantitatively determine the creation of the complex of the fungi species and the aptamer composition in the presence of the detection agent composition.
15. A diagnostic method for detecting a fungus on a surface or a liquid according to any preceding claims wherein the contacting of the diagnostic composition with surface is performed by rubbing (a) a swab or (b) a woven substrate or (c) or nonwoven substrate or (d) comb, which comprise a region having an absorbing element comprising the aptamer composition and a detection agent composition.

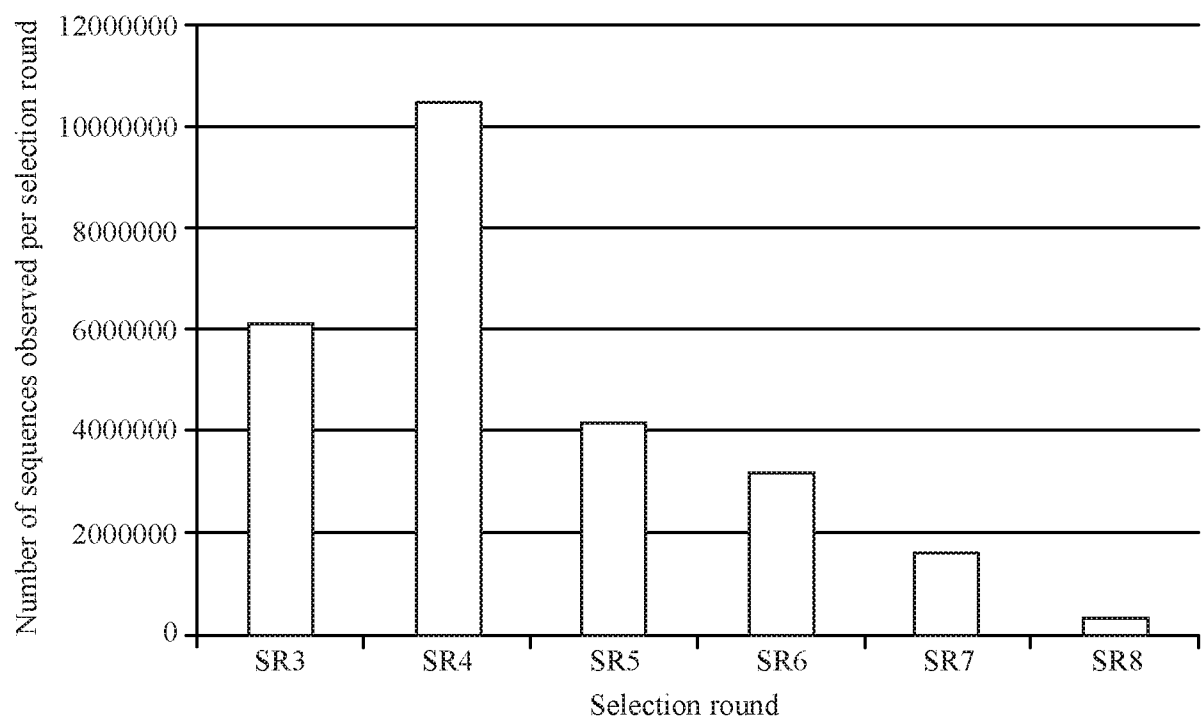


Figure 1

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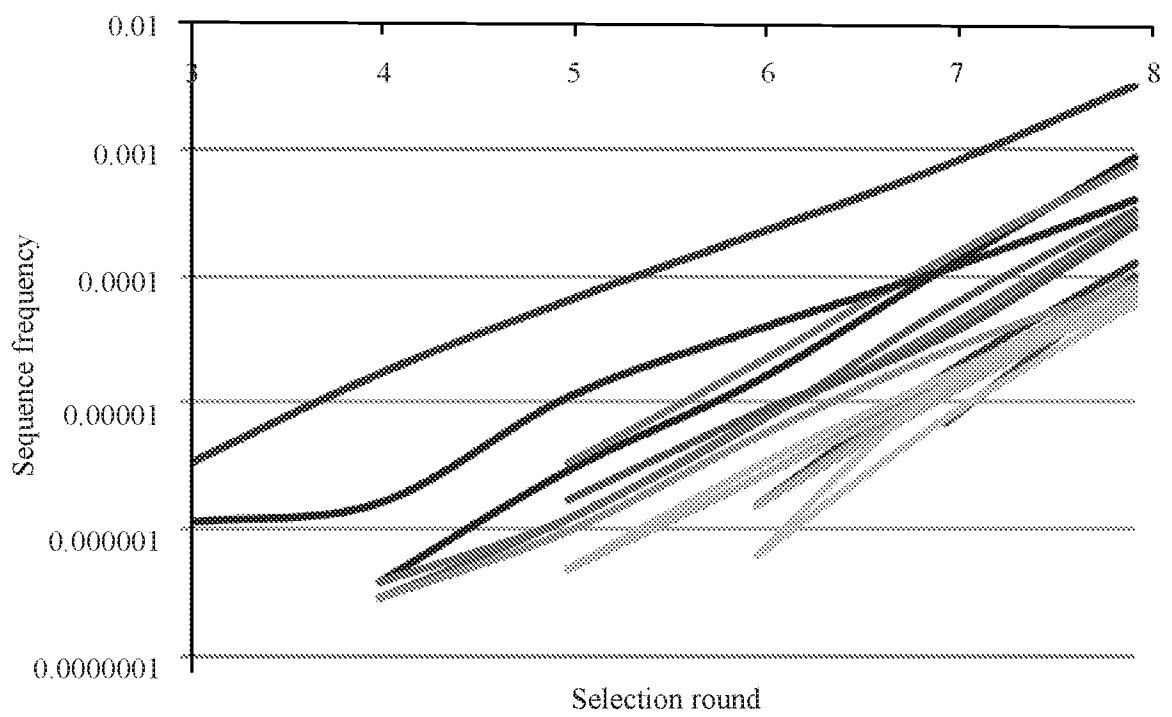


Figure 2

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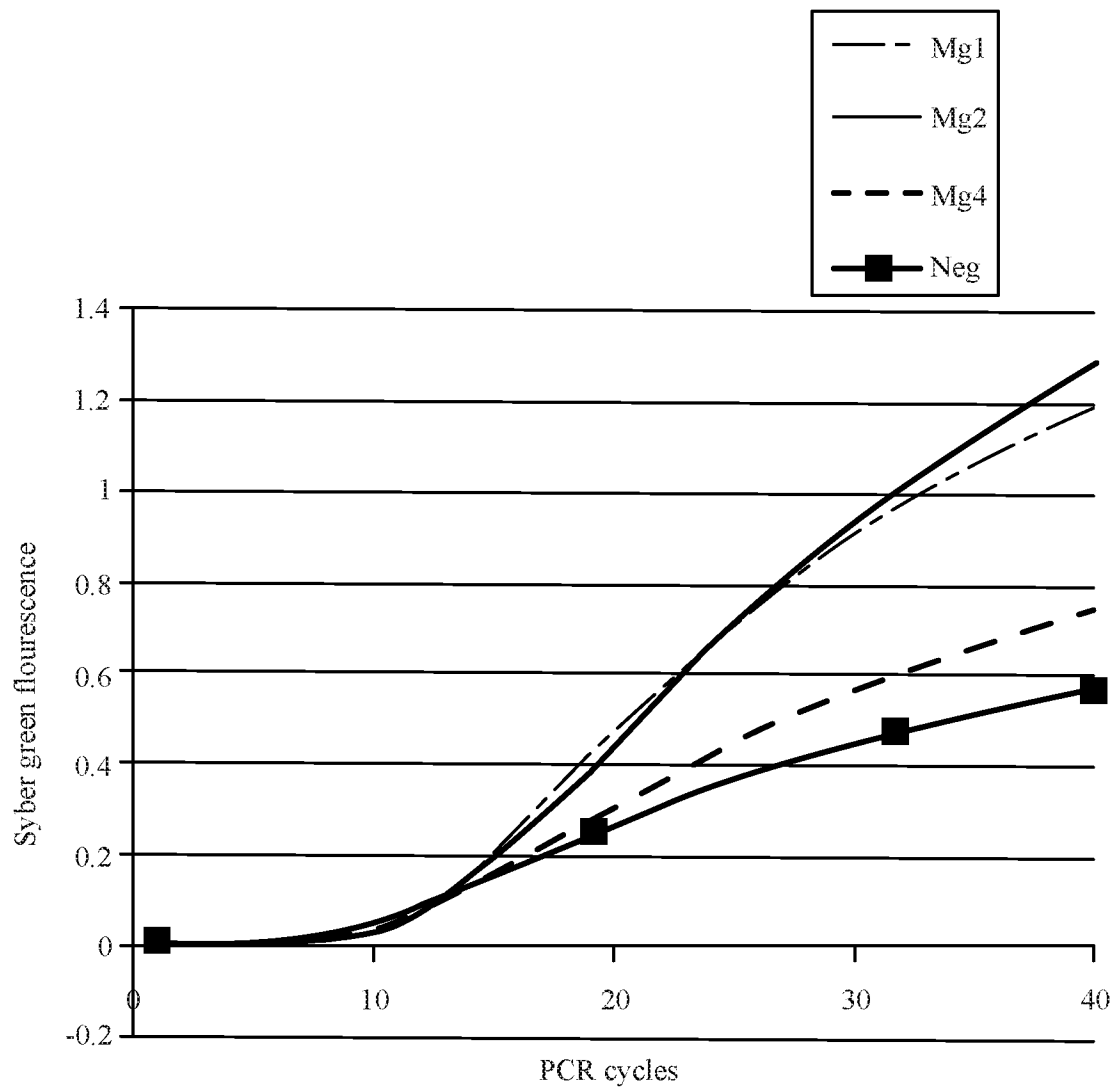


Figure 3

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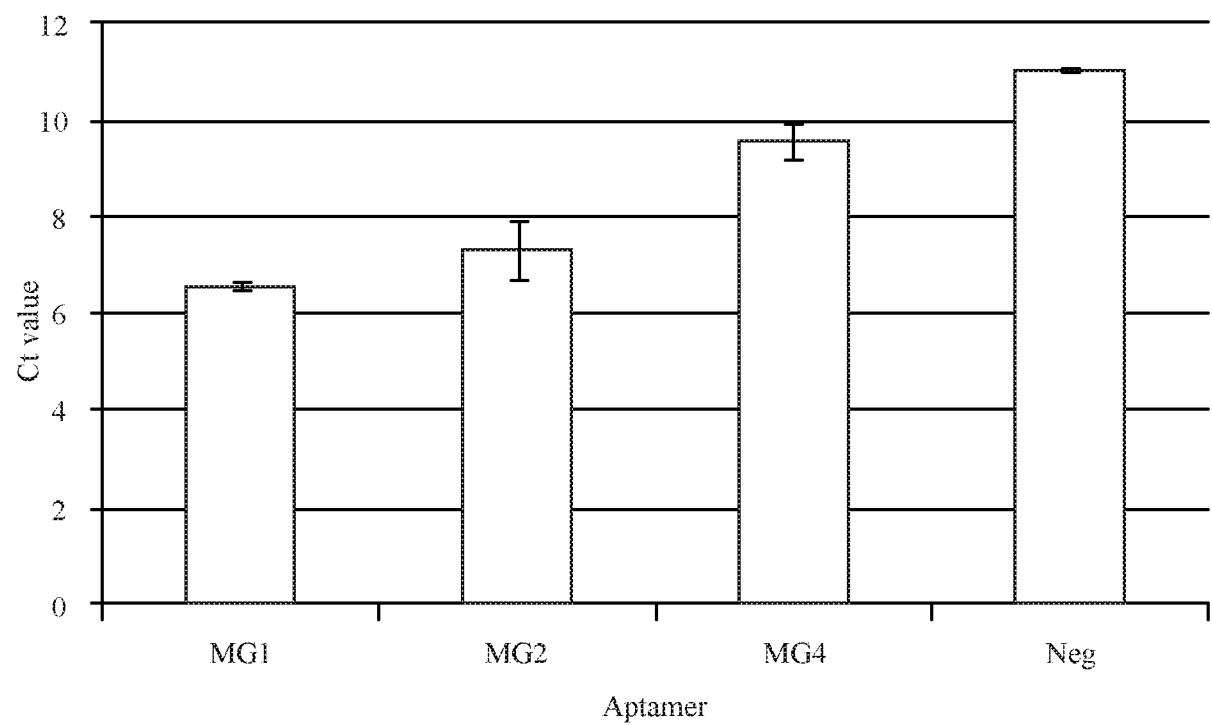


Figure 4

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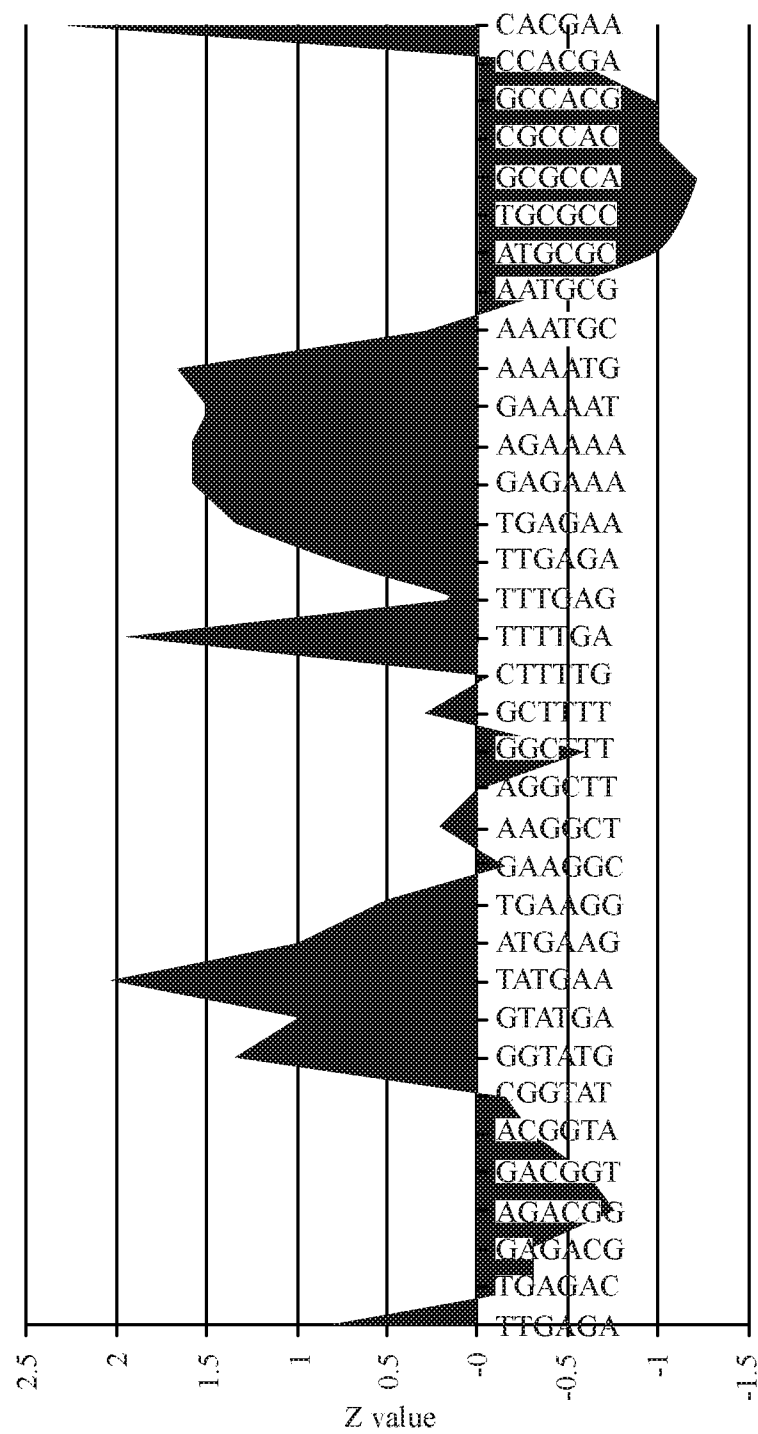


Figure 5

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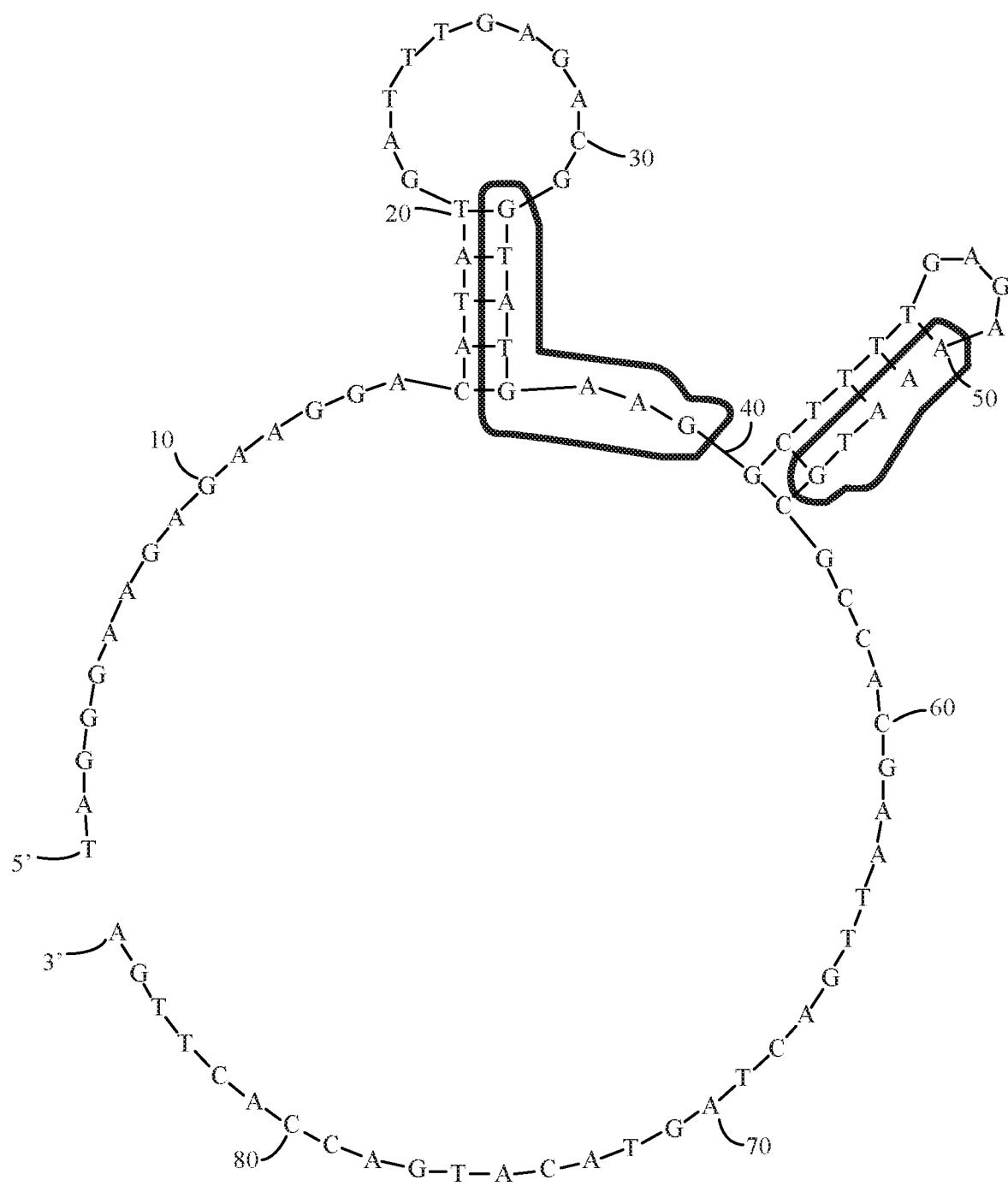
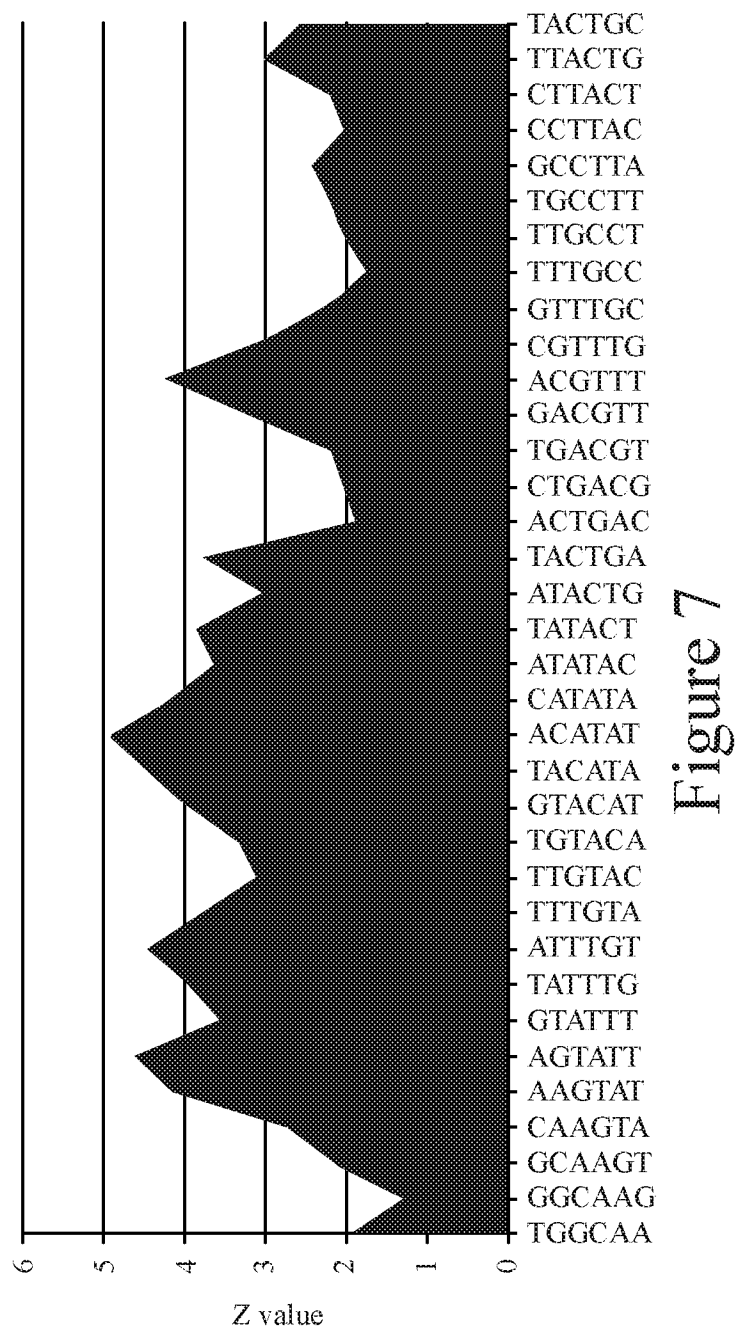


Figure 6



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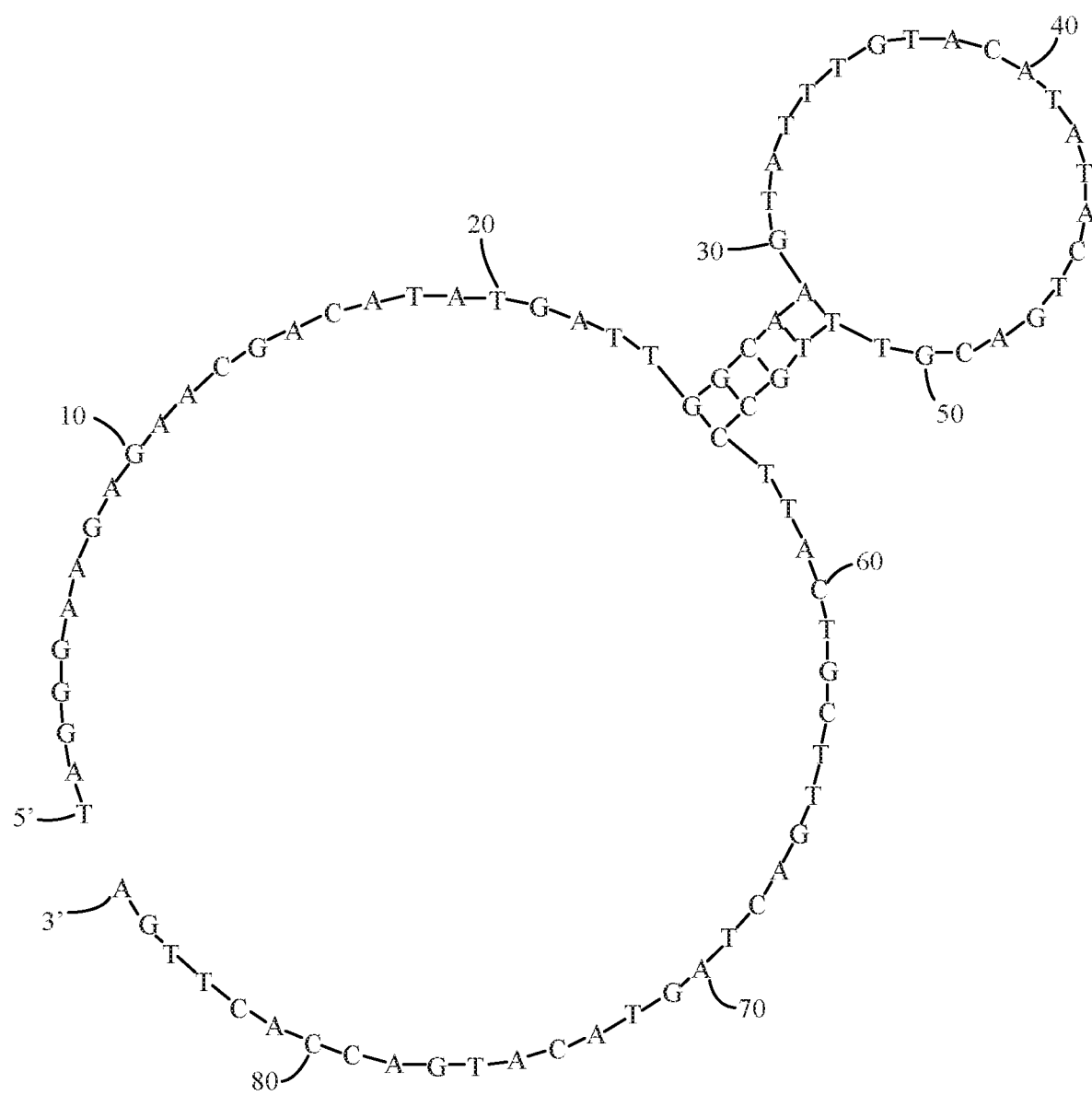


Figure 8

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	(1)	1	10	20	30	40					
Mg-59	(1)	CTGACGGGAGTCAGAACCCTTGTTAAGGGGACACCTGTTT									
Mg-73	(1)	CTGACGGGAGTCAGAACCCTTGTTAAGGGGACACCTGTTT									

	(1)	1	10	20	30	40					
Mg-6	(1)	TCCTCTGCTGGTGAGAGGCGTCCAATGAATCATATTACCG									
Mg-66	(1)	TCCTCTGCTGGTGAGAGGCGTCCAATGAATCATATTACCG									
Mg-74	(1)	TCCTCTGCTGGTGAGAGGCGTCCAATGAATCATATTACCG									
Mg-85	(1)	TCCTCTGCTGGTGAGAGGCGTCCAATGAATCATATTACCG									
Mg-86	(1)	TCCTCTGCTGGTGAGAGGCGTCCAATGAATCATATTACCG									

	(1)	1	10	20	30	40					
Mg-20	(1)	TAAAGAACAGGATGATCAGCAGGGTTGATTTTGATGATG									
Mg-4	(1)	TAAAGAACAGGATGATCAGCAGGGTTGATTTTGACGATG									
Mg-43	(1)	TAAAGAACAGGATGATCAGCAGGGTTGATTTTGACGATG									
Mg-58	(1)	TAAAGAACAGGATGATCAGCAGGGTTGATTTTGACGATG									
Mg-64	(1)	TAAAGAAACAGGATGATCAGCAGGGTTGATTTTGACGATG									

Figure 9

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	(1)	1	10	20	30	40
Mg-20	(1)	CACGAAACATAAGTTGTGTCAGAAATACACCTGTTTCTCTG				
Mg-4	(1)	CACGAAACATAAGTTGTGTCAGAAATACACCTGTTTCCCTG				
Mg-43	(1)	CACGAAACATAAGTTGTGTCAGAAATACACCTATTTCCTG				
Mg-58	(1)	CACGAAACATAAGTTGTGTCAGAAATATACCTGTTTCCCTG				
Mg-64	(1)	CACGAAACATAAGTTGTGTCAGAAATACACCTGTTTCCCTA				
Mg-65	(1)	CACGAAACATAAGTTATGTCAGAAATACACCTGTTTCCCTG				
Mg-71	(1)	CACGAAACATAAGTTGTGTCAGAAATACACTTGTTTCCCTG				
Mg-72	(1)	CACGAAACATAAATTGTGTCAGAAATACACCTGTTTCCCTG				
Mg-80	(1)	CACGAAACATAAGTTGTGTCAGAAATACATCTGTTTCCCTG				

Figure 10

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	(1)	1	10	20	30	40																																				
Mg-10	(1)	T	A	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-17	(1)	T	G	G	C	A	A	A	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-19	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	T	T	A	C	T	G	C					
Mg-2	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-22	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	A	C	T	G	C
Mg-25	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	A	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-26	(1)	T	G	A	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-28	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-29	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	T	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-30	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-31	(1)	T	G	G	T	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-35	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	A	C	C	T	T	A	C	T	G	C			
Mg-44	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	T	A	T	G	A	C	G	T	T	A	C	C	T	T	A	C	T	G	C			
Mg-47	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	A	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-49	(1)	T	G	G	C	A	A	G	T	A	T	T	T	A	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-53	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			
Mg-54	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	T	T	A	C	T	G	C				
Mg-84	(1)	T	G	G	C	A	A	G	T	A	T	T	T	G	T	A	C	A	T	A	C	T	G	A	C	G	T	T	T	G	C	C	T	T	A	C	T	G	C			

Figure 11

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/115 A61K31/7088 A61Q5/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12N A61K A61Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2016/176203 A1 (DOTS TECH CORP [US]) 3 November 2016 (2016-11-03) paragraph [0020] - paragraph [0043] paragraph [0067]	1,5-15
Y	WO 02/083737 A1 (COTDE INC [KR]; LEE & JOE BIOTECH CO [KR] ET AL.) 24 October 2002 (2002-10-24) claims 1-6	1,5-15
	----- -/-	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

5 June 2019

Date of mailing of the international search report

14/06/2019

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Bucka, Alexander

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/017154

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LOW S Y ET AL: "DNA aptamers bind specifically and selectively to (1-3)-beta-d-glucans", BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ELSEVIER, AMSTERDAM, NL, vol. 378, no. 4, 4 December 2008 (2008-12-04), pages 701-705, XP025841481, ISSN: 0006-291X, DOI: 10.1016/J.BBRC.2008.11.087 [retrieved on 2008-12-04] abstract; figures 1,3 -----	1,5-15
Y	GAO SHUNXIANG ET AL: "Post-SELEX optimization of aptamers", ANALYTICAL AND BIOANALYTICAL CHEMISTRY, SPRINGER, DE, vol. 408, no. 17, 12 May 2016 (2016-05-12), pages 4567-4573, XP035982368, ISSN: 1618-2642, DOI: 10.1007/S00216-016-9556-2 [retrieved on 2016-05-12]	5-11
A	page 4568, right-hand column - page 4570, right-hand column; figure 1 -----	1,12-15
Y	US 10 001 496 B2 (JUNG EDWARD K Y [US]; LEUTHARDT ERIC C [US] ET AL.) 19 June 2018 (2018-06-19) column 10 - column 11 column 28 - column 29; claim 1 -----	1,5-15
A	EP 2 881 466 A1 (UNIV HIROSHIMA [JP]) 10 June 2015 (2015-06-10) page 8 - page 9; examples 7,8 -----	1,5-15
A	WO 2017/035666 A1 (NEOVENTURES BIOTECHNOLOGY INC [CA]) 9 March 2017 (2017-03-09) the whole document -----	1,5-15
A	TANG X-L ET AL: "Improved detection of deeply invasive candidiasis with DNA aptamers specific binding to (1->3)-[beta]-D-glucans fromCandida albicans", EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES, SPRINGER, WIESBADEN, DE, vol. 35, no. 4, 25 January 2016 (2016-01-25), pages 587-595, XP035893069, ISSN: 0934-9723, DOI: 10.1007/S10096-015-2574-8 [retrieved on 2016-01-25] figures 2,3 -----	1,5-15
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International application No
PCT/US2019/017154

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	N. SHIBATA ET AL: "The cell wall galactomannan antigen from <i>Malassezia furfur</i> and <i>Malassezia pachydermatis</i> contains -1,6-linked linear galactofuranosyl residues and its detection has diagnostic potential", JOURNAL OF GENERAL MICROBIOLOGY, vol. 155, no. 10, 1 October 2009 (2009-10-01), pages 3420-3429, XP55593805, ISSN: 1350-0872, DOI: 10.1099/mic.0.029967-0 figure 1 -----	1,5-15
A	ARISTEA VELEGRAKI ET AL: "Malassezia Infections in Humans and Animals: Pathophysiology, Detection, and Treatment", PLOS PATHOGENS, vol. 11, no. 1, 8 January 2015 (2015-01-08), page e1004523, XP55593798, DOI: 10.1371/journal.ppat.1004523 the whole document -----	1,5-15

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International application No.
PCT/US2019/017154

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 2-4
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 2-4

The specific sequences of claims 2 to 4 have, according to PCT Rule 13ter.1.d, not been searched, since the sequence listing as present in the description does not comply with WIPO standard ST 25 prescribed in the administrative instructions under Rule 5.2. The sequence listing has been furnished neither in paper form nor in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the time limit fixed in the invitation pursuant to PCT Rule 13ter.1.a.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/017154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2016176203	A1	03-11-2016	
		AU 2016256391 A1	26-10-2017
		CA 2983307 A1	03-11-2016
		CN 108064264 A	22-05-2018
		EP 3289064 A1	07-03-2018
		JP 2018519796 A	26-07-2018
		US 2018128835 A1	10-05-2018
		WO 2016176203 A1	03-11-2016
WO 02083737	A1	24-10-2002	
		AT 348842 T	15-01-2007
		CN 1524091 A	25-08-2004
		DE 60216906 T2	26-07-2007
		EP 1379556 A1	14-01-2004
		ES 2274966 T3	01-06-2007
		JP 4002187 B2	31-10-2007
		JP 2005502594 A	27-01-2005
		KR 20020079238 A	19-10-2002
		WO 02083737 A1	24-10-2002
US 10001496	B2	19-06-2018	NONE
EP 2881466	A1	10-06-2015	
		EP 2881466 A1	10-06-2015
		JP 6232618 B2	22-11-2017
		JP WO2014003008 A1	02-06-2016
		US 2015238581 A1	27-08-2015
		US 2016363598 A1	15-12-2016
		WO 2014003008 A1	03-01-2014
WO 2017035666	A1	09-03-2017	
		EP 3344805 A1	11-07-2018
		JP 2018526030 A	13-09-2018
		US 2019112593 A1	18-04-2019
		WO 2017035666 A1	09-03-2017