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(54) **Title**: TOPICAL SKIN COMPOSITIONS HAVING PROTEINS AND METHODS OF USE

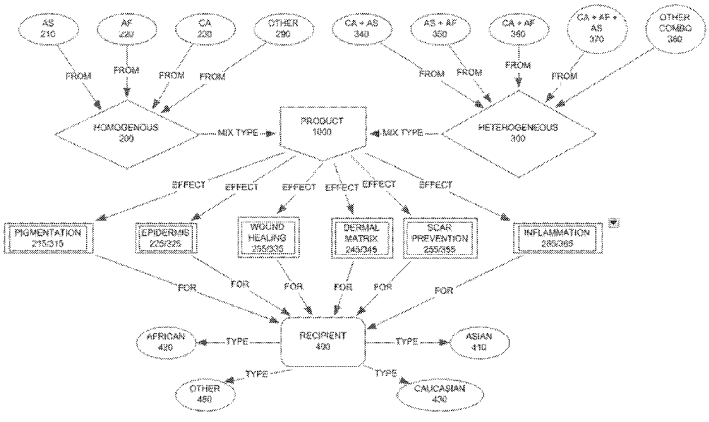

FIG. 1

(57) **Abstract**: There is provided a topical skin composition directed to one or more desired benefits. The composition includes one or more proteins selected based on the desired skin benefit to be derived by application of the topical skin composition. In one embodiment, each protein is from one donor group having two or more individuals. In another embodiment, the protein is from two or more donor group.

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TOPICAL SKIN COMPOSITIONS HAVING PROTEINS AND METHODS OF USE

BACKGROUND OF THE DISCLOSURE

1. Field of the Disclosure

[0001] The present disclosure relates to a determination of protein production levels in cultured fibroblast from human dermal tissue samples. The present disclosure also relates to a determination of protein production levels in cultured fibroblast supernatant from human dermal tissue samples from different ethnic populations through protein microarray performance. The present disclosure further relates to analyzing protein microarray performance to understand protein production levels that are present and unique in each ethnic group. Proteins can be blended together in a product that imparts one or more desired characteristics to the skin of a recipient who is not a source of the mixture and any individual fibroblasts, hereinafter a non-autologous product.

2. Description of the Related Art

[0002] The growth of eukaryotic cells is modulated by various influences, of which growth factors are among the most important. Factors which inhibit growth also exist. Growth factors have mitogenic effects on a range of cells. These mitogens stimulate the growth and activation of various cell types, including fibroblasts (which produce collagen and elastin precursors, and ground substance) and epithelial cells (e.g. skin cells or keratinocytes).

[0003] One primary function of a fibroblast is to maintain the structural integrity of connective tissues by continuously secreting precursors of the extracellular matrix. A fibroblast secretes precursors of all components of the extracellular matrix, primarily the ground substance and a variety of fibers or structural proteins. The fibroblasts also secrete small molecular weight diffusible factors that influence and coordinate the function

and product of neighboring cells to enhance tissue response. The composition of the extracellular matrix significantly determines the physical properties of connective tissues.

[0004] Known in the art are methods of treatment using autologous fibroblasts (i.e. fibroblast obtained from a donor who will also be the recipient of cultured fibroblasts). Among the known uses of such fibroblasts are a method of promoting healing of wounds, such as an epithelial wound or fistula, by administering cultured fibroblasts; a method of corrective surgery by the augmentation of tissue sub-adjacent to a vocal cord defect; and a method of treatment of vocal fold scarring and repair of skin and soft tissue defects.

[0005] Also known in the art are dosage units consisting of autologous fibroblasts grown for an individual who is also the donor. Further, there are known methods of growing fibroblasts for use in autologous applications.

[0006] Applicants of the present application have filed an earlier patent application directed to a non-autologous product that is a homogeneous or heterogeneous mixture of two or more fibroblasts cultures, extracts derived therefrom, and/or diffusible elements recovered from the culture media from the same sex. It was believed that each mixture of homogeneous and/or heterogeneous fibroblasts cultures or extracts therefrom, from the same sex, can have "weighted" factors based on the characteristics desired to be obtained by the mixture and, thus, the resultant product could be tailored for certain objectives. The resultant product based on weighted factors and/or tailoring could be a product for one ethnic group, or could combine factors from two or more ethnic groups for a resultant product that would have product benefits that are universal. The mechanism to achieve these products were based on a belief that certain proteins or enzymes are more prevalent or unique or inherent from people of certain ethnic groups and thus a blending of factors in an ethnic group or a blend of factors from two or more ethnic groups would achieve the optimum product. Heretofore, there was a need to better understand what proteins and levels thereof are clearly different in each ethic group and, if so, how different.

SUMMARY OF THE DISCLOSURE

[0007] The present disclosure provides a determination of protein production levels in cultured fibroblast supernatant from human dermal tissue samples from different ethnic populations using a protein microarray.

[0008] The present disclosure also provides for protein microarray analysis to understand differences in protein production levels in an ethnic group and/or between or amongst two or more ethnic groups.

[0009] The present disclosure further provides analysis of relative measurements of protein production levels, interactions, and/or functions, to determine what proteins or cells or factors, can be blended together, from a single ethnic group, or two or more ethnic groups, to formulate a product that imparts desired characteristics or benefits to the skin of a recipient who is not a source of the mixture or any individual fibroblasts, so that the product is defined as a non-autologous product.

[0010] The present disclosure still further provides that based on the knowledge of the measurement of the relationship of protein levels, interactions, and/or functions in an ethnic group, as well as between or amongst two or more ethnic groups, methods of optimizing the potency or potential of the proteins in a mixture to impart the desired characteristics to the recipient's skin can be achieved.

[0011] The present disclosure also provides that such measured proteins can lead to the derivation of a homogeneous and/or heterogeneous mixture that is based on the characteristics desired to be obtained to produce the desired characteristics in a resultant product.

[0012] The present disclosure further provides that different resultant products can be made with each resultant product directed to enhance, modulate, or treat one or more desired characteristics of the user of the composition of the present disclosure.

[0013] The present disclosure also provides that Biological Significance demonstrated a majority of proteins met the criteria in at least one ethnic group.

[0014] The present disclosure further provides that there are uniquely altered proteins, which is Biologically Significant proteins.

[0015] The present disclosure shows that there are average production level changes relative to control in all three groups.

[0016] The present disclosure provides a topical composition to treat a targeted skin disorder based on a desired benefit or treatment.

[0017] The present disclosure also shows that according to statistical significance, the Asian skin demonstrated the largest number or amount of protein production levels altered/dysregulated/varied relative to African skin, and the second largest amount of protein production levels altered/dysregulated/varied relative to Caucasian skin, while the least amount of protein production levels altered/dysregulated/varied was African skin relative to Caucasian skin.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] FIG. 1 is a concept map describing various embodiments of the present disclosure.

[0019] FIG. 2 shows an exemplary process for producing the embodiments of the present disclosure.

[0020] FIG. 3 shows an overall protein network expressed for the African and Asian groups.

[0021] FIG. 4 shows an overall protein network expressed for the Caucasian and Asian groups.

[0022] FIG. 5 shows an overall protein network expressed for the Caucasian and African groups.

[0023] FIG. 6 is a pie chart of a Caucasian to African interpretation of top-50 biological processes.

[0024] FIG. 7 is a pie chart of an African to Asian interpretation of top-50 biological processes.

[0025] FIG. 8 is a pie chart of a Caucasian to Asian interpretation of top-50 biological processes.

[0026] FIG. 9 shows an overall protein network expressed for the African to Asian groups relating to a wound healing process.

[0027] FIG. 10 shows an overall protein network expressed for the Caucasian to Asian groups relating to an immune system process.

[0028] FIG. 11 shows an overall protein network expressed for the Caucasian to African groups relating to an immune system process.

[0029] FIG. 12 shows several Venn Diagrams comparing the differential gene expression among the Caucasian, African, and Asian ethnic groups.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0030] As used herein, the term “homogeneous” means the use of fibroblast cultures obtained from donors (of the same-sex) who constitute a group whose bloodlines are 80% or greater of a single race or ethnicity, preferably 90% or greater, more preferably 95 % or greater, and most preferably essentially 100%. Thus, a fibroblast culture obtained from a homogeneous set of donors (of the same-sex), such as a group of: Asian women, African

women, Caucasian women, Asian men, African men, or Caucasian men, are from a single source or ethnic group or ethnic subgroup. Mixed-sex combinations are also envisioned.

[0031] The term "heterogeneous" as used herein means the use of non-ethnic homogeneity fibroblasts, such as fibroblasts obtained from same-sex, but a combination of two from different groups or sources, such as, for example, a group of: African women and Asian women, African women and Caucasian women, or Asian women and Caucasian women, Asian women and Caucasian women and African women, African men and Asian men, African men and Caucasian men, Asian men and Caucasian men, or Asian men and Caucasian men and African men. Although discussed with respect to three ethnic groups, the present disclosure provides for many more ethnic groups and subgroups so that the heterogenous mixtures can be a blend or combination of four or more ethnic groups or subgroups. Mixed-sex combinations are also envisioned.

[0032] Biological Significance or Biologically Significant means greater than a twofold increase/decrease relative to a comparator sample or a Control.

[0033] Unique is defined herein as Biologically Significant in only one group relative to a comparator sample or a Control.

[0034] A donor, as used herein, is an individual from whom cells are obtained for culturing to derive the product of the present disclosure. The donors are either male or female, or both. A donor is selected for having a desired benefit or characteristic or combination of skin characteristics.

[0035] A Caucasian donor is defined as an individual of northern European descent, whose grandparents and great-grand parents are known to have genetic roots from the area. It is envisioned that a Caucasian donor group can be further subdivided into, for example, Latin European, Hispanic European, Anglo-Saxon European, and Slavic.

[0036] An African donor is defined as an individual of sub-Saharan descent, whose grandparents and great-grandparents are known to have genetic roots from the area. It is

envisioned that an African donor group can be further subdivided, including, but not limited to, West African, and East African.

[0037] An Asian donor is defined as an individual of Asian descent, or subgroups thereof including, for example: northern and southern Asia. Moreover, Asian donor group can be subdivided into; China, Japan, and Korea subgroups. An Asian donor is one whose grandparents and great-grandparents are known to have genetic roots from the area.

[0038] A donor is preferably screened for disease. Also, premature aging due to environmental conditions, such as free radical generating, namely sun and higher neoplasms, as well as premature aging due to smoking, should be eliminated from the donor "pool".

[0039] A donor preferably has a bloodline that is 80% or greater of a single race or ethnicity, preferably 90% or greater, more preferably 95 % or greater, and most preferably essentially 100%.

[0040] A donor is preferably of a young age since their skin and fibroblasts are at an optimal state of life. Such an age range can vary based on ethnicity. It is believed that the preferred age range is from 18 to 35, more preferably 18 to 30 years of age. However, it is envisioned that the age range can have a lower limit, as low as permitted by applicable law where the donor resides and where the biopsy occurs.

[0041] In contrast, a recipient is an individual having skin onto which the product of the present disclosure is applied or administered, and preferably skin with one or more of the skin conditions discussed herein. A recipient is not a source of the product, mixture, or any individual fibroblasts, and thus is not subject the same scrutiny discussed above for a donor. A recipient derives the benefit or characteristic or combination of skin characteristics as discussed herein.

[0042] A Caucasian recipient is defined as an individual who self-identifies as being genetically most identified as having European genetic background and typically present with Fitzpatrick skin types I-IV.

[0043] An African recipient is defined as an individual who self-identifies as being genetically most identified as having sub-Saharan genetic background and typically present with Fitzpatrick skin types IV-VI.

[0044] An Asian recipient is defined as an individual self-identifies as being genetically identified as having Asian genetic background and typically present with Fitzpatrick skin types III-V.

[0045] The following terms used in this application ("as used herein") are defined as follows. Skin pigmentation means skin color imparted by the deposition of various melanin pigments in the skin. Skin pigmentation includes hyper-pigmentation, hypo-pigmentation, de-pigmentation, and uneven pigmentation. Hyper-pigmentation means areas of uneven pigmentation where portions of the skin appear darker or more pigmented than the common or background color. Hypo-pigmentation means areas of uneven pigmentation where portions of the skin appear lighter or less pigmented than the common or background. De-pigmentation means skin devoid of melanin pigment. Uneven pigmentation means areas of the skin with mixed or mottled pigmentation, and a random or non-contiguous pattern of normal and hypo and hyper pigmentation.

[0046] As used herein, wound healing means the ability of the skin to self-direct and regulate its own repair under the influence of locally produced and disseminated proteins, cells that comprise the dermal matrix, and other biological or cellular molecules. Cells that comprise the dermal matrix include fibroblast, blood vessel endothelial cells, blood cells (neutrophils and lymphocytes), lymphatic cells, macrophages, and mast cells. A wound can be acute or chronic. Acute means that the wound heals quickly on its own. Chronic means that the wound heals slowly and often requiring treatment.

[0047] As used herein, inflammation means the response of skin to an internal or external stimulus that may or may not cause explicit visual injury. Once initiated, the response to the stimulus is inflammation. It is controlled or regulated by locally produced proteins.

[0048] Inflammation includes reduction and prevention. As used herein, reduction means the limiting the cascade of proteins that are pro-inflammatory. This also includes the process of reversing the effects of inflammation. As used herein, prevention means the use of biologic molecules to reverse, without visual effect on the surface of the skin, the effects of internal or external (environmental) insults that may induce pro-inflammatory cascades of biological proteins and other cellular products.

[0049] As used herein, dermal matrix means the mix of one or more collagen, elastin, hyaluronic acid, proteoglycans, and other macromolecules that creates the reticular or basement layer of the dermis. Dermal matrix includes wrinkles, aging, scarring and thinning.

[0050] These following terms used in this application are defined as. Wrinkles means the uneven surface of the skin caused by sub-sufficient levels of moisture in the epidermis or damage to the reticular dermis often caused by internal or external inflammatory stimulus. Pre-mature aging means the appearance of the surface of skin marked by wrinkles, sagging, uneven pigmentation and/or superficial blood vessel damage, making the appearance of age to appear older than the chronological age of the individual. Scarring means the response to severe injury of the skin in which the deposition of collagen and other dermal macromolecules produce an uneven surface that makes it distinctly differentiated from the surrounding skin. Thinning means the reduced capacity of the skin to fully repair and regenerate resulting in a reduced depth and density of the dermal and epidermal layers of the skin.

[0051] As used herein, scar prevention means reduction of the healing process that allows abnormal amounts of collagen to be deposited in a random, not basket weave, pattern that typifies the surrounding or undamaged skin. Scar prevention includes

prevention of a keloid scar, a hypertrophic scar, an atrophic scar, a contracting scar, a hyper-pigmented scar, and a hypo-pigmented scar. As used herein, keloid scar is a form of hypertrophic scarring in which the excessive production of collagen continues to grow indefinitely into large raised lesions that extend outside the area of the initial wound. As used herein, a hypertrophic scar is a scar resulting from the overproduction and deposition of collagen during the healing of a serious wound that results in the resulting scar to be raised over the surface of the surrounding skin. As used herein, atrophic scar is a scar that has an appearance that is depressed below the surface of the surrounding skin. Atrophic scar is typically caused by an inflammatory process that damages the surrounding support tissue. As used herein, hyper-pigmented scar is a scar with a degree of pigmentation that is higher or darker than the surrounding skin. As used herein, hypo-pigmented scar is a scar with a degree of pigmentation that is less or lighter than the surrounding skin.

[0052] As used herein, epidermis means the layer of the skin that covers the body and forms a protective membrane, layer, or covering over the body. The epidermis includes a layer known as the stratum corneum. The epidermis has significant role in immunity, and contains the melanin pigment that determines skin color. Epidermis includes pores, skin texture and barrier function. As used herein, a pore is an anatomical structure of the skin created by the sebaceous follicle, and serves as a duct for passage of sweat and/or sebum. A pore appears as an unfilled or filled opening in the surface of the skin. As used herein, skin texture means the normal topography and glyphic pattern apparent on the surface of the skin. Skin texture is influenced by the perceived moisture level, softness, resilience, and elasticity of the skin. As used herein, barrier function means the ability of the skin to regulate: the degree of moisture permeability, the protection from external (environmental) insults, and the immune functions protecting the skin and underlying tissues and structure.

[0053] As used herein, up regulated means increase in normalized gene expression, and/or protein production in a given cell line/type or individual relative to a control sample

or a cell line/type standard, or a baseline value of an individual from an earlier time point or prior to treatment.

[0054] As used herein, down regulated means decrease in normalized gene expression, and/or protein production in a given cell line/type or individual relative to a control sample or a cell line/type standard, or a baseline value of an individual from an earlier time point or prior to treatment.

[0055] The use of fibroblast cell cultures, coculture of cells, extracts from cells or cultures, diffusible elements that form the cell culture, or culture media, either alone or with environmental conditions, are used to grow cells and induce the cells to produce their array of biologically active elements. These elements are produced by and secreted by or extracted from the cells. These cells, cultures, coculture of cells, diffusible elements form the cell culture and culture media.

[0056] Referring to FIG. 1, the present disclosure provides a product generally represented by reference numeral 1000 that modifies cellular communication at a skin site to stimulate the production of new tissues. Specifically, the present disclosure provides a composition having proteins obtained from one or more donors, and formulating a topical product to stimulate gene expression. Specifically, the proteins can be derived from fibroblasts, cells, cocultures, cultures, diffusible elements that form the cell culture, and culture media and/or elements. For example, fibroblasts can grow and form a new, provisional extracellular matrix (ECM) by excreting collagen and fibronectin (collectively hereinafter called tissue cultures). The proteins derived from any of the above are the subject of the present disclosure. Proteins from cell signaling pathways can modulate the 'behavior' of fibroblasts including proliferation and migration, and this aspect is also the subject of the present disclosure.

[0057] For each embodiment of the present disclosure, recipient 400 of product 1000 is not a source or donor of the cell mixture or any individual fibroblast. Thus, recipient 400 of the proteins is not the same person whose cells were used to produce the proteins so that application to recipient 400 of the derived product 1000 is "non-autologous".

[0058] In the present disclosure, product 400 is directed to treat a condition or provide a benefit that recipient 400 desires.

[0059] In product 1000, the proteins are blended together. However, each product 1000 is intended for a specific sex, namely women or men, so that only proteins from one sex are blended together.

[0060] The present disclosure provides a topical composition to treat a targeted skin disorder based on a desired benefit or desired characteristic. Some desired benefits or characteristics that have been found by the studies of the present disclosure are to prevent, reduce, and/or reverse visual signs of aged or prematurely aged skin (hereinafter collectively called "skin and related benefits"). Such skin and related benefits include, but are not limited to, improve or normalize pigmentation; improved barrier function; improve dermal matrix; improve the epidermis or skin quality; facilitate wound healing; minimize or prevent scarring; reduce or eliminate inflammation; treat wrinkles, stretch marks, sagging skin, scars such as surgical, traumatic, acne or chickenpox scars.

[0061] The derived products are a blend of proteins derived from certain donors, and will result in a product composition that achieves desired benefits including those benefits set forth above. The present disclosure has now proven by the studies of the present disclosure that demonstrate that certain ethnic donors have certain genes that are up-regulated gene expressions, and others that are down-regulated gene expression, and yet others that are neither.

[0062] The present disclosure contemplates that product 1000 can be either a homogenous product 200 or a heterogenous product 300.

[0063] Homogenous products 200 will first be described.

[0064] In one embodiment, homogenous product 200 is a product that has proteins derived from tissue cultures solely from a single ethnic group, such as, for example, female Asian donors 210. Analogously, in another embodiment, homogenous product

200 is derived from tissue cultures obtained solely from a group of male Asian donors 210. Likewise, homogenous product 200 is derived from tissue cultures obtained from a mixed group of male and female Asian donors 210.

[0065] In still another embodiment, homogenous product 200 is derived from tissue cultures obtained solely from a group of female African donors 220. In yet another embodiment, homogenous product 200 is derived from tissue cultures obtained solely from a group of male African donors 220. Analogously, homogenous product 200 is derived from tissue cultures obtained from a mixed group of male and female African donors 220.

[0066] In a further embodiment, homogenous product 200 is derived from tissue cultures obtained solely from a group of female Caucasian donors 230. In yet further embodiment, homogenous product 200 is derived from tissue cultures obtained solely from a group of male Caucasian donors 230. In a still yet further embodiment, homogenous product 200 is derived from tissue cultures obtained solely from a mixed group of male and female Caucasian donors 230.

[0067] Other donors 290 could also form the basis of homogenous product 200, consistent with this disclosure.

[0068] Also, it should be understood that recipient 400 can be from the same ethnic group as the donor ethnic group in homogenous product 200 or from another ethnic group, yet the product is still considered a homogenous product.

[0069] Heterogenous products 300 will now be described.

[0070] In one embodiment, heterogenous product 300 is derived from tissue cultures obtained from two or more ethnic groups. For example, one heterogenous product 300 is derived from a group 340 of female Asian and female Caucasian donors. In another embodiment, heterogenous product 300 is derived from tissue cultures obtained from a group 340 of male Asian and male Caucasian donors. Additionally, heterogenous product

300 is derived from tissue cultures obtained from a group 340 of male Asian and female Caucasian donors, or a group 340 of female Asian and male Caucasian donors, or a mixed group 340 of male and female Asian and male and female Caucasian donors.

[0071] In another embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 350 of female Asian and female African donors. In yet another embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 350 of male Asian and male African donors. Still further, heterogenous product 300 is derived from tissue cultures obtained solely from a group 350 of male Asian and female African donors, or heterogenous product 300 is derived from tissue cultures obtained solely from a group 350 of female Asian and male African donors, or heterogenous product 300 is derived from tissue cultures obtained from a mixed group 350 of male or female Asian and male or female African donors.

[0072] In a further embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 360 of female Caucasian and female African donors. In yet another embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 360 of male Caucasian and male African donors. In a still further embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 360 of male Caucasian and female African donors, a group 360 of female Caucasian and male African donors, or a mixed group 360 of male and female Caucasian and male and female African donors.

[0073] In a still yet further embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 370 of female Caucasian and female African and female Asian donors. In another embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 370 of male Caucasian and male African and male Asian donors. In another embodiment, heterogenous product 300 is derived from tissue cultures obtained solely from a group 370 of male Caucasian and male African and male Asian donors.

[0074] Other groups 380 of donors could also form the basis of heterogenous product 300, consistent with this disclosure.

[0075] The homogenous and heterogenous embodiments discussed above and further herein are exemplary and non-limiting, and the scope of the present disclosure will be apparent to a person having ordinary skill in the art upon understanding the present disclosure.

[0076] Homogenous product 200 and heterogenous product 300 are products that are targeted to have a desired effect imparted to the skin of recipient 400.

[0077] These targeted products are shown in FIG. 1 (as species of product 1000), with targeted homogenous products represented by a 200-series numeral and targeted heterogenous products represented by a 300-series numeral. Thus, the targeted products contemplated by the present disclosure include, at least, pigmentation 215, 315, epidermis 225, 325, wound healing 235, 335, dermal matrix 245, 345, scar prevention 255, 355, and inflammation 265, 365. Further, the proof of concept and details for the composition of such targeted products are established by the studies discussed herein.

[0078] As discussed, targeted products 215, 315, 225, 335, 245, 345, 255, 355, 265, and 365 are for an intended recipient, such as recipient 400. Recipient 400 is a female or male Asian 410, a female or male African 420, a female or male Caucasian 430, or a female or male of another ethnic origin, other 480.

[0079] As discussed in the present disclosure, the selection and weighting of cell culture proteins for product 1000 can be predicated on the particular property or pigment or other characteristic desired to be improved or imparted to the skin of recipient 400. Thus, a selection of donors of a single ethnic group, or groups of donors of different ethnic groups, and a “weighted” composition to achieve a resultant product that delivers at least one property, preferably to the skin, is possible. Moreover, one property can be improved on any person (of any ethnic background) that uses product 1000.

[0080] Thus, the data set forth herein concerning the differences in certain protein expression levels and their Biological Significance makes it clear that mixtures of homogeneous and/or heterogeneous tissue or fibroblast cultures can also be "tailored" to provide a specific desirable skin benefit or characteristic or combination of skin characteristics. Thus, “tailoring” can include a larger percentage of fibroblast cultures or derived proteins from one homogeneous group or amongst donors of the heterogeneous group. The “tailoring” can include more of one ethnic group than another ethnic group. Further, the “tailoring” can include consideration of factors based on the characteristics (noted above) desired to be obtained by the mixture. The factors include, but are not limited to, age, DNA testing, ethnic homogeneity, health, and physical beauty. For example, physical beauty could be determined by adherence to classic beauty as described by the golden ratio of physical or physiological proportions, or other similar derivations or approximations using a Fibonacci series.

[0081] What the data clearly shows is the ability to determine what fibroblasts or cells (and as stated above) of different donors in an ethnic group or different donors in different ethnic groups can be mixed to obtain the desired characteristics. This can be done at the protein level. Accordingly, the discussion herein is directed to the benefits or characteristics or combination of skin characteristics derived from proteins, and preferably derived from fibroblast cells or cell cultures of a donor to a recipient by means of a product.

[0082] FIG. 2 is exemplary, and is by no means exhaustive, of the present disclosure. In practice, a master cell bank will be created for each individual donor in donor groups 210, 220, 230, 340, 350, 360, 370, 380, and 290.

[0083] In one example of a homogenous product 200, master cell banks 510 and 520 are created for individual donors 212 and 214 of donor group 210, respectively. A working cell bank is 610 is derived therefrom by mixing the cells produced from master cell banks 510 and 520. Homogenous product 200 of Asian donors 210 is formulated from working cell bank 610. A targeted product, such as pigmentation 215, is then derived from homogenous product 200 for a recipient 400.

[0084] In another example for a heterogeneous product 300, a master cell bank 520 is created for an individual donor 214 of donor group 210, and master cell banks 530 and 540 are created for each of individual donor 232 and 234 of donor group 230, respectively. Cells produced from master cell banks 520, 530 and 540 are blended together in a working cell bank 630. Since donor 214 is Asian, and donors 232 and 234 are Caucasian, heterogenous product 300 is created. A targeted product, such as pigmentation or pigmentation enhancing product 315 can then derived from heterogenous product 300 for recipient 400.

[0085] Product 1000 is a topical composition. The preferred topical composition is a cream, serum, or lotion. The composition can include delivery vehicles, such as liposomes and micelles. The composition can also include transport molecules, such as a protein or a macromolecule that promotes or provides molecular sledding. The use of such transport molecules enables delivery of the elements to the epidermis or dermis of a recipient. However, the composition can be parental (e.g. injectable, intravenous, or the like), delivered by device (e.g. laser, micron needle, inhaler, or the like), or an oral periodontal including a mouthwash.

[0086] The compositions comprise, in some embodiments, a pharmaceutically and/or topically acceptable vehicle to provide bulk and physical form. In other embodiments, the vehicle is hypoallergenic, as allergens and other irritating agents exacerbate pigmentation. Suitable vehicles for these benefits include, but are not limited to, cetyl alcohol, ethanol, glycerin, myristyl palmitate, polyvinyl alcohol, propylene glycol, propanol, and water, and mixtures thereof.

[0087] The topical composition can be easily prepared in any method known in the art, using the proteins herein together with at least one carrier and additives, which are commonly used in the field of preparing topical compositions. Examples of topical agents include emollients, humectants, colorants, pigments, fragrances, moisturizers, viscosity modifiers and any other topical forming agent. One or more topical agents can be included in the topical composition. The form of the topical composition can be a powder, lotion, gel, spray, stick cream, ointment, liquid, emulsion, or foam. Additional active

ingredients as known in the art may also be used. Examples of the carriers may include, but are not limited to, a skin softener, a skin permeation enhancer, a colorant, an aromatic, an emulsifier, a thickener, and a solvent. Also, the topical composition may further comprise a perfumery, a pigment, a bactericidal agent, an antioxidant, a preservative and a moisturizer, and also a thickener, inorganic salts and synthetic polymer substances, for the purpose of improving physical properties.

[0088] Lists of such materials, and formulations for the creation of particular types of lotions, creams, and other such forms are widely available in the patent literature and in commercial handbooks and can be used by those skilled in the preparation of such formulations to incorporate the composition herein.

[0089] In one example, the cream or Product 1000 can be prepared by adding the composition to a general oil-in-water (O/W) cream base. The cream may further comprise a perfumery, a chelating agent, a pigment, an antioxidant, and a preservative, and also synthetic or natural materials, minerals, and vitamins, for the purpose of improving physical properties.

[0090] Product 1000 can have other biologically compatible constituents in addition to the proteins discussed above. These constituents can include one or more antioxidants, polypeptides, vitamins, plant extracts, materials derived from plant stem cells, oils, preservatives, thickening agents, ceramides, skin lighteners, exfoliants, anti-aging and anti-wrinkle agents, sunscreens, skin barrier repair agents, moisturizing ingredients, essential fatty acids, humectants, emollients, solvents, surfactants, emulsifiers, fillers, polymers, buffers, temperature regulating agents, and the like, and combinations thereof.

[0091] These constituents can comprise the delivery vehicle in the topical product. It is envisioned that the vehicle can include water. Further, the vehicle will be up to 99 wt.% of the resultant product.

[0092] It is envisioned that all the cells in the epidermis and dermis (including sub dermis) can be impacted by a topical formulation. Certain delivery vehicles can have an impact even deeper than the sub dermis.

[0093] The present disclosure has proven that proteins derived from working cell bank 610 or 630 applied in a composition to the skin of recipient 400 can have one or more of the specific effects discussed below.

[0094] In one mechanism of the embodiments of the present disclosure, the protein itself can be absorbed and utilized directly. For example, collagen can be deposited through the skin to be used as matrix structural glycoprotein or other macromolecular ground substance. Alternately MMP-1 can be absorbed to degrade collagen.

[0095] In another mechanism of the embodiments of the present disclosure, the protein can stimulate future gene expression changes. For example, cells detecting excessive amounts of deposited/delivered pro-inflammatory proteins may stimulate anti-inflammatory gene responses. It may also create a positive feedback loop that can 'supercharge' more pro-inflammatory protein production. Alternatively, it can bind a specific membrane site and initiate a second messenger response by activating gene or protein synthesis.

[0096] In yet another mechanism of the embodiments of the present disclosure, a protein can bind to active sites or cellular receptors. This can either halt a process by tying up all available cellular machinery or cause conformational changes in the cells and/or cellular network.

[0097] In still another mechanism of the embodiments of the present disclosure, tProtein can be broken down and subsequent components can be utilized to fuel skin/cellular process.

[0098] In yet still another mechanism of the embodiments of the present disclosure, tProtein can be used to replace "non-functional" or "mutated" proteins and restore proper

cellular function/processes. Yet further, tProtein can also replace "functional" with "mutated/nonfunctional" or variant proteins.

[0099] The present disclosure contemplated different combinations and applications of the embodiments discussed herein.

[0100] TYK2 directly regulates IL-22 dependent inflammation and epidermal hyperplasia. TYK2 deficiency has multiple effects leading to reduced immune response and increased infection (viral and mycobacterial). The Asian population has reduced levels of TYK2. Thus, supplementation of TYK2 protein from African cells (who produce greater amounts of TYK2 than the other groups) could boost immune response and/or lower infection rates. Such a formulation or composition can include proteins derived from African donor group 220 in a homogenous product, or proteins derived from Caucasian and African donor group 360.

[0101] Asian skin has lower amounts of GDF3 that is a negative regulator of TGFB, which is pro-fibrotic. Application of African and/or Caucasian GDF3 can assist to decrease the rate/amount of scarring or keloid formation. Such a formulation or composition would thus include cells derived from donors of African donors 220 and Caucasian donors 230 in a homogenous product 200, or Caucasian and African donors 360, in a heterogeneous product 300.

[0102] Asian skin demonstrates a lower concentration of Visfatin enzyme, which is anti-fibrotic. Supplementation of this enzyme could decrease scarring, keloid formation and/or psoriasis. Thus, a targeted product or composition would include cells derived from donors of African donors 220 and Caucasian donors 230 in a homogenous product 200, or Caucasian and African donors 360, in a heterogeneous product 300.

[0103] Asian skin has lower levels of VitaminK1 which when applied topically can suppress pigmentation and improve wound healing. Addition of Caucasian VITK1 could function as a pigment lightener. A targeted product or composition 300 would have cells

derived from donors of donors 230 in a homogenous product 200 and cells derived from donors of Caucasian and African donors 360.

[0104] In one embodiment, to treat an Asian recipient for the epidermis, a product 1000 has TSH. A homogeneous product 200 is derived from African donors 220. A heterogeneous product 300 is derived from Caucasian and African donors 360. Heterogeneous product 300 has a ratio of African Donors to Caucasian donors that is about 50% African Donors to 50% Caucasian donors, 60% African Donors to 40 % Caucasian donors, 70% African Donors to 30% Caucasian donors, 80% African Donors to 20% Caucasian donors or 90% African Donors to 10% Caucasian donors. About in this paragraph means plus or minus 8%, preferably plus or minus 5%, and most preferably, plus or minus 3%, the total not exceeding 100%.

[0105] In another embodiment, to treat an Asian recipient for skin pigmentation, a product 1000 has Vitamin K1. A homogeneous product 200 is derived from Caucasian donors 230.

[0106] Caucasian skin produces more EDAR protein, which contributes to dryness and eczema through sebaceous gland interaction. Application of EDAR might be a potential treatment for oily skin. A targeted product or composition would have cells derived from donors of donors 230 in a homogenous product 200. Another targeted product or composition 300 would have cells derived from donors of Caucasian and Asian donors 340, or Caucasian and Asian and African donors 370.

[0107] Other formulation components and considerations for product 1000 are contemplated. For anti-Scarring, Follistatin, MMP7, MMP1, GDF3, Visfatin, TPA, Vasopressin, MMP10, and Pro-MMP13 are the potential proteins that when applied directly in some combination(s) have been shown to be direct components in scar and/or keloid formation. Thus, a target product would have proteins from a particular ethnic group in which these proteins are expressed, either up-regulated or down regulated based on the desired effect.

[0108] Likewise, for wound healing, the proteins TYR10, RBP4, uPA, bFGF, MMP7, IL24, Latent TGFB1, TPA, TPM1, Thrombin, IL-19, MMP8, MBL, NM23-H1/H2, NOV/CCN3, IL6, PYK2, Pro-MMP13 are considered important. Accordingly, a target product would have proteins from a particular ethnic group or groups in which these proteins are expressed, based on the desired effects.

[0109] Thus, a target product would have proteins from a particular ethnic group in which these proteins are expressed as set forth below.

[0110] For skin pigmentation, the proteins SHBG, DTK, GDNF, and Vitamin K dependent protein have been found to have a positive remedial effect.

[0111] For anti-Inflammatory effects, IL28A, Follistatin, MMP8, FIH, SERPINA12, and SSTR2 are useful.

[0112] For anti-aging effects, the effective proteins are NRG2, Kallikrein 6, RBP4, bFGF, Kallikrein 14, Kallikrein 8, Latent TGFB1, VDUP1, INSL3, Thrombin, Trappin-2/Elafin, GRP75, PARK7, Mammaglobin A, TMEFF1/Tomoregulin1.

[0113] Anti-Oxidant Enzymes include A1M and GPX3.

[0114] An anti-aging/wrinkles formulation has one or more of: RBP4, bFGF, Latent TGFB1, INSL3, Trappin-2, GRP75, PARK7, Mammaglobin A, TMEFF1/Tomoregulin1, A1M, and GPX3.

[0115] These proteins have certain benefits. For example, RBP4 is the main carrier of retinol. bFGF stimulates the growth of fibroblasts. Latent TGFB1 stimulates elastic fiber production. INSL3 reduces skin wrinkling, enhance skin appearance and improve barrier function. Trappin-2 facilitates inhibition of elastin breakdown. GRP75 prevents wrinkles and supports collagen production. PARK7 stimulates Glycation repair. Mammaglobin is a boosts barrier function. TMEFF1/Tomoregulin1 inhibit BMP signaling and generally

exhibit anti-aging properties. A1M is a radical scavenger and heme binder. GPX3 is an anti-oxidant.

[0116] An anti-scarring formulation could have Follistatin. Follistatin is an activin antagonist that is anti-fibrotic and anti-inflammatory. Alternatively, or in combination, such an anti-scarring formulation could have Visfatin, which is an anti-fibrotic via enhancing inflammatory response. MMP1, MMP7, MMP10, and MMP13 assist extracellular matrix remodeling and degradation of structural components of skin. TPA has a role in wound healing and is anti-fibrotic.

[0117] A pigment lightening formulation could include SHBG. With age and decreased estrogen levels, SHBG decreases. This can lead to higher testosterone levels and pigment dyschromia as well as unwanted facial hair.

[0118] A pigment lightening formulation could also have Vitamin K dependent protein S for suppression of pigmentation.

[0119] A wound healing formulation could include: TYRO10, RBP4, uPA, bFGF, MMP1, MMP7, MMP8, Latent TGFB1, TPA, TPM1, Thrombin, IL19, NM23-H1/H2, NOV/CCN3, IL6, and PYK2.

[0120] TYRO10 mediates fibroblast migration and contributes to cutaneous wound healing. RBP4 is a main carrier of Retinol. uPA is a plasminogen activator that is a key regulator of wound healing processes. bFGF stimulates growth of fibroblasts. MMP1, MMP7, MMP8 facilitate the matrix remodeling, which is a phase of wound healing. Latent TGFB1 stimulates elastic fiber production. TPA is a plasminogen activator, has a role in wound healing, and is anti-fibrotic. TPM1 facilitates cell migration during the wound healing process. Thrombin mediates fibroblast proliferation. IL19 promotes wound healing by increasing other growth factor expression (KGF). NM23-H1/H2 is implicated in wound healing. NOV/CCN3 effects NOTCH1 mediated signaling that helps wound healing process. IL6 is required for normal wound healing. PYK2 promotes re-epithelialization.

[0121] It is envisioned that product 1000 will be proportioned based on ratios of differential protein expressions. In some embodiments, formulation methods involve a 2 to 1 to 1 ratio of a first protein to second protein to a third protein C. Further, product 1000 has a concentration or an amount of 0.0001 weight percent (wt%) to 10.0 wt% of the actives (or proteins), preferably 0.001 wt.% to 5.0 wt.%, and most preferably, 0.001 wt.% to1.0 wt.%, based on the total weight of the product composition.

[0122] The method of application of the product to the skin will be by any topical application method known in the art. It is envisioned that the application will be administered once daily. However, it is also envisioned that the application can be twice daily if the desired benefit, such as scar healing, will tolerate repeated applications in a day. Also, the recommend number of applications per day and the period of time of application will vary based on the desired benefits of the product that will be imparted to the recipient.

[0123] Further, it is envisioned that the application of the product can continue for prolong periods of time.

[0124] Different embodiments of product 1000 can be used sequentially, mirroring the phases of wound healing. For example, a first embodiment of product 1000 that is anti-inflammatory is administered at a first time. At a second time, a second embodiment of product 1000 that is anti-hyperpigmentation is administered. At a third time, a third embodiment of product 1000 that is anti-scarring is administered.

[0125] For acute injuries, it is desirable to begin treatment as quickly as possible after the injury occurs. For example, to treat an acute injury such as a sunburn, an thermal burn, an abrasion, a traumatic injury or an elective procedure such as a laser treatment or surgical incision for Asian skin, Asian 410, at the first time, product 1000 is formulated to have IL28A, at the second time, product 1000 is formulated to have Vitamin K, and at the third time, product 1000 is formulated to have GDF3.

[0126] More specifically, frequent treatment for an initial healing phase (typically 1-10 days), up to 3 or more times per day, is desirable for the formulations of product 1000 that accelerate wound healing.

[0127] After the initial healing phase or re-epithelialization occurs treatment with product 1000 can change to 1-2 times per day using a formulation of product 1000 that reduce inflammations, reduce abnormal pigmentations, reduces risk of hypertrophic or atrophic scarring. For this second phase, administering to the skin can be in a single two or three in one combination of the product 1000 or alternating in the AM and PM with single or two in one combinations of product 1000. This second phase could continue typically for one to four (or more) weeks. In some cases, to prevent hyperpigmentation or prevent scarring, this second phase can continue for months or longer. Preferably, an anti-inflammatory product 1000 would cease to be administered after four weeks.

[0128] It is also envisioned that recipient 400 can be treated with a product 1000 before an elective procedure to minimize the risk of abnormal pigmentation. Treatment can be one to four weeks prior to the elective procedures. Specifically, a product 1000 formulated for wound healing will prepare the skin to heal faster. Such a product 1000 would include tretinoin and application would be daily for one to two weeks prior to the elective procedure.

[0129] Besides the targeted products discussed herein, additional products can focus or have properties that derive the following desired particular property or characteristics that include, but is not limited to, accelerating wound healing, improving, reducing or improving stretch marks, reducing bruising, improving sebum production, hair growth, enhancing or modulating skin firmness or smoothness, the appearance of skin, the beauty of skin, more fullness of the skin, skin tone, skin elasticity, reduced scarring, reduced wrinkles, reduced pore size, response to inflammatory stimulus, minimizing bruising, ability to retain moisture, propensity to produce new vasculature and deliver nutrients and skin thickness or density, improve response to injury or free-radical damage, reduced scarring, improved wound healing, skin disease prevention, or combination of positive skin characteristics that will be apparent to those of skill in the art. Also, the present disclosure

can be used to treat 'damaged' skin from environmental damage, aging or disease. Further, the present disclosure can be used in veterinary applications. The present disclosure can be used as adjunctive care for treatment of skin diseases including but not limited to acne, atopic dermatitis, rosacea and psoriasis.

[0130] It is envisioned that although discussed with respect to skin, the present disclosure applies to nails, and hair. For example, the nail plate, the hard part of the nail, made of translucent keratin protein, undergoes bio-processes analogous to the skin. Likewise, hair is a protein filament that grows from follicles in the skin, and is primarily comprised of protein, and notably keratin.

[0131] The present disclosure also applies to a commercial production of an artificial gene that can be tailored to specific needs. An envisioned exemplary technique follows. Techniques include sequencing of proteins or DNA from desirable genes or gene products or complete synthetic construction of de novo gene sequences. Once a desired double stranded DNA sequence has been identified, combination into plasmid vectors with appropriate coding and non-coding sectors, as well as promotor sequences, can occur. For example, the DNA sequence can be inserted into compatible bacteria and used as factories for replication of RNA or protein product. Sequence optimization and oligo design occurs first, followed by oligo synthesis, gene assembly, sequence verification and error correction, and finally preparation of synthetic DNA for application.

[0132] As stated above, the present disclosure describes testing and analysis to determine protein production levels in cultured fibroblast supernatant from human dermal tissue samples from three (3) different ethnic populations through protein microarray performance.

Example 1

[0133] An assay was performed in which six (6) samples of cell culture supernatant from healthy volunteers that satisfied the ethnic ancestry requirements from each of the three (3) ethnic skin groups (Asian, African, Caucasian/European) and one concentrated

media control were examined for differing protein production levels (for 1,000 human proteins) as measured by protein microarrays (AAH-BLM-1000, RayBiotech, Norcross; GA). The volunteers were female and ranged in age from 18 to 30 years. Although females were selected, it is believed similar results would be obtained if males were selected as volunteers, or combinations thereof. The following is an explanation of the microarray process performed by RayBiotech. The first step in using the Human L-1000 arrays is to biotinylate the primary amine of the proteins in the sample. The membrane arrays are then blocked in a fashion similar to standard Western blot, and the biotin-labeled sample is added onto the pre-printed array. The array is pre-printed with capture antibodies specific to a target protein and the proteins in the sample bind with the antibodies on the array during the incubation period. After incubation using an HRP-Conjugated Streptavidin, the signal can be visualized by chemiluminescent methods and quantified. Images of the arrays are generated and analyzed for strength of signal.

[0134] The following is an analysis of the results.

[0135] The samples were accounted for as follows. Nineteen (19) samples arrived, de-identified and coded to the testing facility. All samples performed within manufacturer's limitations and data tables and array images were generated.

[0136] Data was derived including array Images. Individual images of each sample array following completion by coded identification number (sample groups are designated by prefix: As= Asian, Af=African, and Ca=Caucasian). The amount of produced protein can be visualized through the size and density of the spot generated on the array. Each array has the same proteins in the same locations for ease of visual reference.

[0137] The following are Data Tables.

[0138] Table 1 is a list of average production levels for each sample ethnic group for all proteins on the protein microarray (AAH-BLM-1000). An Asterisk ("*") marks protein levels indicating Biological Significance (greater than a twofold increase/decrease relative

to comparator sample; in this case, the Control= conditioned media). The three sample groups were As=Asian, Af=African, and Ca=Caucasian.

TABLE 1

	CONTROL	AS Average	AF Average	CA Average
Positive Control	68,183.33	68,097.33	68,097.33	68,183.33
Neg	924.62	718.07	600.39	837.75
6Ckine	129.67	1.04*	87.80	156.30
Activin A	162.69	1.04*	26.95*	252.29
Activin B	184.35	1.04*	134.33	387.17*
Activin C	319.16	41.87*	275.53	982.78*
Activin RIA / ALK-2	301.83	78.60*	370.14	898.16*
Activin RIB / ALK-4	177.85	55.59*	328.09	814.56*
Activin RII A/B	318.07	132.49*	613.17	962.78*
Activin RIIA	390.62	51.76*	582.13	997.10*
Adiponectin / Acrp30	746.32	166.10*	892.57	1,626.73*
AgRP	448.55	157.54*	590.86	941.67*
ALCAM	501.07	138.10*	523.27	778.31
Angiogenin	397.66	262.88	492.45	815.27*
Angiopoietin-1	1,187.56	635.44	889.09	1,739.25
Angiopoietin-2	709.50	378.18	472.85	1,406.26
Angiopoietin-4	685.14	249.09*	400.68	1,302.65
Angiopoietin-like 1	842.69	259.31*	477.29	1,500.64
Angiopoietin-like 2	710.59	590.06*	711.49	1,438.05
Angiopoietin-like Factor	627.21	116.81*	361.17	996.98
Angiostatin	1,071.70	216.87*	711.23	1,343.92
APJ	536.26	11.82*	184.92*	403.49
AR (Amphiregulin)	661.86	37.18*	223.18*	441.40
APRIL	823.74	116.65*	326.49*	812.58
Artemin	557.37	199.55*	66.39*	393.26
Axl	628.84	272.47*	85.71*	400.63
B7-1 /CD80	801.54	228.52*	16.48*	449.74
BAFF R / TNFRSF13C	648.33	107.81*	1.01*	617.99
BCMA / TNFRSF17	1.08	67.49*	208.10*	194.35*
BD-1	129.12	65.17	382.42*	402.77*
BDNF	339.73	75.17*	613.54	834.53*
beta-Catenin	158.36	56.20*	273.78	391.54*
BAX	90.68	552.02*	357.12*	759.17*
beta-NGF	199.51	358.85*	478.62*	897.43*

BIK	5,551.78	7,225.66	9,648.28	14,321.51*
BLC / BCA-1 / CXCL13	330.52	557.36	909.49*	1,321.99*
BMP-2	331.61	244.58	621.09	1,045.93*
BMP-3	612.05	409.46	862.35	1,394.85*
BMP-3b / GDF-10	450.17	304.92	575.64	916.69*
BMP-4	492.40	466.21	819.89	1,234.96*
BMP-5	352.72	442.04	607.76	911.57*
BMP-6	699.76	767.21	1,230.53	1,785.35*
BMP-7	500.52	425.00	642.05	925.88
BMP-8	522.18	269.31	594.91	975.93
BMP-15	609.35	89.63*	531.69	768.08
BMPR-IA / ALK-3	803.71	201.22*	685.58	865.25
BMPR-IB / ALK-6	812.91	126.71*	614.33	753.41
BMPR-II	679.19	122.46*	506.20	587.06
BTC	643.99	99.02*	385.47	319.45*
Cardiotrophin-1 / CT-1	679.19	52.57*	330.43*	721.03
CCL14 / HCC-1 / HCC-3	482.66	74.14*	187.07*	236.13*
CCL28 / VIC	491.86	23.82*	1,115.09*	743.42
CCR1	642.91	38.55*	369.10	357.10
CCR2	560.62	43.11*	297.77	324.95
CCR3	245.52	21.27*	275.09	319.12
CCR4	181.10	221.30	159.21	306.58
CCR5	71.19	143.29*	192.98*	313.52*
CCR6	111.26	122.49	321.72*	660.49*
CCR7	437.72	452.52	841.57	1,092.91*
CCR8	1,018.10	598.45	1,257.90	1,677.89
CCR9	352.72	211.93	720.76*	746.79*
CD14	175.14	181.90	426.88*	590.71*
CD27 / TNFRSF7	119.92	239.53	468.66*	828.46*
CD30 / TNFRSF8	111.26	272.19*	446.20*	489.25*
CD30 Ligand / TNFSF8	438.80	597.57	908.21*	1,295.22*
CD40 / TNFRSF5	262.85	484.17	672.82*	904.00*
CD40 Ligand / TNFSF5 /CD154	659.15	710.35	1,131.54	1,455.18*
CD 163	944.47	1,775.95	2,269.77*	3,457.06*
Cerberus 1	551.42	844.48	784.21	1,473.97*
Chem R23	457.75	689.12	680.21	1,006.74*
Chordin-Like 1	755.52	760.62	918.92	1,233.52
Chordin-Like 2	609.35	683.02	931.67	1,299.52*
Csk	2,524.28	3,252.64	5,507.31*	5,510.66*
CLC	497.82	539.58	763.91	990.60
CNTF	719.25	653.90	1,577.91*	1,661.29*
CNTF R alpha	1,247.11	897.87	1,679.58	2,264.41

Coagulation Factor III / Tissue Factor	538.96	435.74	693.02	747.54
CRIM 1	815.08	527.66	766.91	819.49
Cripto-1	581.73	291.49	497.48	510.38
CRTH-2	658.07	175.22*	475.55	488.39
Cryptic	584.98	161.00*	470.95	550.17
CTACK / CCL27	871.38	440.23	903.29	1,020.30
CTGF / CCN2	433.93	178.17*	445.48	270.78
CTLA-4 /CD152	419.31	165.58*	588.91	228.33
CV-2 / Crossveinless-2	108.01	18.99*	450.71*	45.32*
CXCL14 / BRAK	687.85	730.98	662.88	799.70
CXCL16	44.67	293.17*	389.68*	380.72*
CXCR1 / IL-8 RA	353.26	382.73	735.14*	658.46
CXCR2 / IL-8 RB	328.90	485.84	763.62*	696.30*
CXCR3	300.21	318.38	588.38	438.89
CXCR4 (fusin)	353.26	393.13	1,955.26*	615.73
CXCR5 /BLR-1	465.33	310.15	650.04	650.99
CXCR6	438.26	431.89	748.94	1,253.17*
D6	216.83	435.25*	652.24*	453.43*
DAN	686.77	1,597.31*	2,464.56*	2,888.04*
DANCE	454.51	511.09	737.37	709.65
DcR3 / TNFRSF6B	622.34	927.20	1,286.49*	1,462.71*
Decorin	461.00	1,900.72*	4,089.23*	3,161.92*
Dkk-1	609.89	2,836.46*	3,118.77*	3,029.36*
Dkk-3	863.26	6,466.27*	5,277.86*	6,745.95*
Dkk-4	754.44	853.57	1,099.56	1,228.59
DR3 / TNFRSF25	620.17	520.59	812.51	874.13
DR6 / TNFRSF21	617.47	587.92	1,141.45	1,039.20
Dtk	732.24	1,115.96	2,856.32*	3,481.06*
EDA-A2	813.45	45,352.87*	86,934.18*	102,337.42*
EDAR	578.49	1,715.75*	2,752.31*	3,558.44*
EDG-1	753.36	517.24	1,101.42	980.91
EGF	1,057.08	804.21	1,455.25	1,379.46
EGF R / ErbB1	596.89	572.81	829.08	668.71
EG-VEGF / PK1	967.75	477.34*	889.30	782.98
EMAP-II	595.81	282.08	724.99	537.13
ENA-78	559.54	334.91	801.05	403.78
Endocan	671.61	1,233.80	1,919.73*	1,631.78*
Endoglin / CD105	511.35	348.01	878.27	333.41
Endostatin	1,248.20	2,031.72	3,492.62*	2,175.26
EN-RAGE	515.14	635.45	620.78	729.35
Eotaxin / CCL11	1,498.32	559.22*	563.75*	583.23*
Eotaxin-2 / MPIF-2	397.66	545.51	578.71	525.92

Eotaxin-3 / CCL26	272.05	475.03	437.37	499.31
Epiregulin	510.81	956.19	710.28	1,017.19
ErbB2	516.22	687.68	643.10	779.11
ErbB3	568.20	505.73	557.91	902.36
ErbB4	710.59	929.88	961.35	1,377.37
Erythropoietin	1,011.61	1,328.05	1,363.61	1,787.40
E-Selectin	434.47	621.02	822.96	766.18
Endothelin	4,035.32	3,698.55	3,500.99	6,526.71
FADD	471.83	861.06	1,015.13*	1,006.16*
FAM3B	1,191.89	2,408.77*	2,220.45	2,201.66
Fas / TNFRSF6	659.15	963.98	1,126.12	1,045.59
Fas Ligand	869.22	1,041.61	1,047.34	1,297.45
FGF Basic	892.50	913.25	1,070.88	1,014.87
FGF-BP	812.91	743.57	822.53	862.25
FGF R3	837.82	896.54	921.54	922.49
FGF R4	717.63	823.16	1,041.09	1,105.28
FGF R5	674.85	1,554.38*	2,334.15*	2,276.60*
FGF-4	742.53	693.36	992.91	945.37
FGF-5	795.05	569.83	1,207.66	857.43
FGF-6	690.01	533.12	1,219.22	783.20
FGF-7 / KGF	698.68	419.83	974.20	663.87
FGF-8	684.06	268.04*	928.30	562.73
FGF-9	688.93	356.72	1,032.44	707.72
FGF-10 / KGF-2	664.03	364.21	928.11	859.52
FGF-11	858.93	452.56	1,027.67	590.53
FGF-12	568.20	313.15	918.76	531.95
FGF-13 1B	713.84	333.88	1,055.18	604.71
FGF-16	760.94	1,063.44	628.74	929.24
FGF-17	792.88	881.75	898.80	1,133.31
FGF-18	327.28	542.26	452.27	506.29
FGF-19	409.57	560.82	496.34	503.71
FGF-20	482.66	624.20	715.54	588.27
FGF-21	559.54	687.95	780.45	752.21
FGF-23	1,106.89	1,228.41	1,178.19	1,927.55
FLRG	654.82	470.54	657.76	907.18
Flt-3 Ligand	561.70	580.12	786.25	588.98
Follistatin	1,096.61	1,517.05	1,970.24	2,259.23*
Follistatin-like 1	3,372.11	2,632.57	3,143.13	5,471.44
Fractalkine	601.77	725.25	970.37	855.59
Frizzled-1	634.79	1,193.13	1,234.68	1,294.11
Frizzled-3	702.47	927.29	1,281.45	1,096.65
Frizzled-4	813.45	936.57	1,105.16	1,098.27
Frizzled-5	1,000.24	976.11	1,221.93	1,295.82

Frizzled-6	814.54	752.23	923.13	857.59
Frizzled-7	875.71	726.64	837.95	704.22
Galectin-3	935.27	1,214.96	1,576.53	1,065.51
GASP-1 / WFIKKNRP	863.26	774.45	1,194.13	1,008.42
GASP-2 / WFIKKN	949.89	588.74	1,026.76	728.60
GCP-2 / CXCL6	791.26	438.11	1,088.36	624.91
GCSF	828.61	332.82*	921.43	491.36
G-CSF R / CD 114	1,033.26	354.90*	1,141.81	590.72
GDF1	1,111.76	483.82*	1,610.55	823.26
GDF3	3,578.92	4,531.00	11,028.23*	8,524.73*
GDF5	1,168.07	1,085.02	2,955.55*	1,591.81
GDF8	709.50	438.75	1,003.97	528.23
GDF9	1,021.89	550.33	1,530.81	969.54
GDF11	782.05	326.46*	1,788.77*	916.98
GDF-15	1,169.15	1,695.58	1,474.42	1,852.05
GDNF	852.43	1,048.30	855.87	1,229.68
GFR alpha-1	706.26	806.45	782.02	893.06
GFR alpha-2	486.99	791.81	890.19	984.65*
GFR alpha-3	773.93	1,090.87	1,645.07*	1,332.54
GFR alpha-4	600.14	717.99	873.03	1,197.73
GITR / TNFRF18	579.57	672.36	834.29	1,503.39*
GITR Ligand / TNFSF18	684.60	830.03	1,169.62	2,155.31*
Glucagon	750.11	668.12	861.19	889.11
Glut1	734.95	669.05	831.57	841.10
Glut2	963.42	1,011.25	1,528.02	1,533.56
Glut3	718.71	841.86	1,552.83*	1,146.30
Glut5	823.74	1,037.65	1,527.07	1,228.58
Glypican 3	5,638.95	8,992.11	15,523.37*	15,039.53*
Glypican 5	1,064.12	1,177.50	2,206.01*	1,877.10
GM-CSF	942.31	776.65	1,291.47	1,212.68
GM-CSF R alpha	1,122.05	807.13	1,555.05	1,316.34
Granzyme A	950.43	798.26	1,362.27	1,141.08
GREMLIN	3,976.85	3,596.94	6,204.15	6,163.27
GRO	874.63	756.08	1,429.54	932.18
GRO-a	842.15	427.97	1,064.41	683.69
Growth Hormone (GH)	1,610.39	818.75	1,920.17	1,539.95
Growth Hormone R (GHR)	1,234.12	875.68	1,958.46	1,421.15
HB-EGF	933.64	496.70	1,334.73	851.17
HCC-4 / CCL16	1,837.24	938.99	1,451.66	1,266.74
HCR / CRAM-A/B	1,137.75	611.82	1,456.60	963.83
Hepassocin	1,105.81	527.18*	1,257.02	939.06
GLO-1	948.80	377.68*	954.76	689.95
HGF	768.52	307.61*	987.65	536.86

HGFR	860.01	257.00*	1,025.92	280.02
HRG-alpha / NRG1-alpha	878.42	1,668.37	675.14	1,100.20
HRG-beta 1 / NRG1-beta 1	992.66	1,820.68	1,078.54	1,636.71
HVEM / TNFRSF14	814.54	1,446.50	954.58	1,290.55
I-309	751.19	1,100.69	905.79	1,023.92
ICAM-1	858.39	1,142.13	1,189.69	1,381.08
ICAM-2	1,928.19	3,678.69	3,997.86*	4,048.00*
ICAM-3 (CD50)	597.43	815.45	847.23	3,273.74*
ICAM-5	680.81	853.84	996.91	3,453.60*
IFN-alpha / beta R1	760.94	822.80	980.25	1,248.04
IFN-alpha / beta R2	743.07	943.90	1,274.51	1,106.74
IFN-beta	767.43	946.59	1,351.76	985.88
IFN-gamma	784.22	938.59	1,450.03	1,107.31
IFN-gamma R1	1,054.38	1,213.84	1,667.96	1,360.48
IGFBP-1	1,446.89	1,990.44	2,757.24	2,804.42
IGFBP-2	1,230.33	11,164.80*	22,591.35*	23,988.15*
IGFBP-3	1,211.38	4,239.29*	5,899.29*	7,880.22*
IGFBP-4	1,045.17	1,306.00	2,071.58	1,725.43
IGFBP-6	1,520.52	2,899.78	4,019.98*	4,500.41*
IGFBP-rp1 / IGFBP-7	11,808.74	76,254.45*	90,204.78*	94,029.81*
IGF-I	1,396.00	2,727.98	3,375.51*	3,317.66*
IGF-I SR	1,114.47	698.60	1,327.13	1,320.74
IGF-II	1,063.04	691.36	1,447.24	1,306.61
IGF-II R	1,063.04	761.02	1,690.45	1,400.97
IL-1 alpha	851.89	470.82	892.28	962.01
IL-1 beta	998.61	483.09*	915.40	780.48
IL-1 F5 / FIL1delta	998.61	538.11	1,032.52	908.99
IL-1 F6 / FIL1 epsilon	1,609.85	1,150.85	2,492.58	2,461.83
IL-1 F7 / FIL1 zeta	1,202.18	598.54*	1,232.35	1,262.28
IL-1 F8 / FIL1 eta	1,098.23	599.85	1,113.49	931.43
IL-1 F9 / IL-1 H1	1,138.83	483.57*	1,141.34	719.34
IL-1 F10 / IL-1HY2	871.38	1,635.97	1,270.14	1,312.48
IL-1 R3 / IL-1 R AcP	823.20	1,955.99	865.40	995.25
IL-1 R4 /ST2	1,274.73	2,118.88	1,817.45	1,822.67
IL-1 R6 / IL-1 Rrp2	898.45	1,525.80	978.33	1,154.15
IL-1 R8	1,002.94	1,332.27	1,107.02	1,556.52
IL-1 R9	1,022.43	1,167.67	1,206.69	2,452.64*
IL-1 ra	1,111.22	1,200.55	1,430.59	3,565.28*
IL-1 sRI	821.03	1,025.90	1,353.87	4,205.60*
IL-1 sRII	874.63	1,253.81	1,732.58	1,719.92
IL-2	887.08	1,210.26	1,539.61	1,469.06
IL-2 R alpha	859.47	1,427.19	2,055.22*	2,053.81*
IL-2 R beta /CD122	772.85	1,432.81	1,731.74*	1,822.64*

IL-2 R gamma	979.66	1,440.19	1,602.61	1,821.47
IL-3	1,118.26	1,818.82	1,971.30	2,369.44*
IL-3 R alpha	982.37	1,837.07	2,077.86*	2,169.15*
IL-4	1,123.68	1,557.32	1,772.86	1,757.93
IL-4 R	3,284.40	2,700.92	3,384.74	4,704.27
IL-5	1,240.08	1,682.21	2,004.37	2,070.95
IL-5 R alpha	1,489.12	3,137.10*	3,075.82*	3,982.92*
IL-6	978.04	1,502.19	1,930.21	2,591.63*
IL-6 R	1,025.68	866.20	1,630.12	1,619.06
IL-7	1,214.63	942.45	1,551.42	1,707.75
IL-7 R alpha	1,212.46	1,221.60	1,899.36	1,908.75
IL-8	1,300.71	836.08	1,193.16	1,494.92
IL-9	995.90	708.33	1,137.45	1,018.95
IL-10	1,135.04	677.63	1,044.99	1,018.25
IL-10 R alpha	1,062.50	710.57	1,132.07	1,058.13
IL-10 R beta	1,111.76	605.73	986.08	886.46
IL-11	1,251.99	699.67	1,003.71	959.33
IL-12 p40	1,555.17	859.87	1,676.54	1,090.19
IL-12 p70	1,191.89	1,424.88	1,556.92	1,681.00
IL-12 R beta 1	1,076.57	1,411.21	1,352.07	1,740.12
IL-12 R beta 2	2,022.94	4,457.84*	6,617.74*	7,987.21*
IL-13	2,448.48	2,611.50	2,626.23	4,435.29
IL-13 R alpha 1	930.40	1,270.79	1,345.81	1,593.24
IL-13 R alpha 2	892.50	1,314.15	1,352.48	1,931.95*
IL-15	921.73	1,288.79	1,317.45	1,713.47
IL-15 R alpha	1,080.90	1,586.74	1,575.32	2,851.23*
IL-16	1,167.53	1,581.88	1,486.05	1,967.21
IL-17	1,481.54	1,530.49	1,458.11	2,146.07
IL-17B	1,593.61	1,771.99	1,664.38	2,534.18
IL-17B R	1,605.52	1,572.19	1,524.19	2,281.38
IL-17C	1,988.83	1,797.99	1,902.92	2,841.57
IL-17D	1,481.54	1,287.88	1,303.66	1,806.32
IL-17E	1,305.04	1,355.70	1,397.57	1,925.20
IL-17F	1,136.67	986.78	1,134.73	1,391.13
IL-17R	1,126.92	1,097.36	1,530.86	1,771.58
IL-17RC	2,280.65	2,719.20	4,631.07*	5,247.83*
IL-17RD	1,538.93	2,293.43	2,337.81	3,481.11*
IL-18 BPa	1,312.08	996.32	1,569.63	1,678.07
IL-18 R alpha /IL-1 R5	1,191.35	879.37	1,461.92	1,427.80
IL-18 R beta /AcPL	1,242.78	917.24	1,163.68	1,338.43
IL-19	1,488.58	1,048.58	1,678.47	1,749.11
IL-20	1,178.36	744.74	1,053.19	1,074.57
IL-20 R alpha	1,506.99	906.17	1,358.78	1,365.94

IL-20 R beta	1,235.20	863.38	1,775.17	1,189.55
IL-21	991.57	1,359.62	1,013.24	1,326.37
IL-21 R	845.94	1,251.77	1,101.00	1,313.91
IL-22	873.55	1,188.37	1,224.95	1,631.76
IL-22 BP	823.74	1,009.44	1,078.76	1,465.05
IL-22 R	783.13	994.00	917.09	1,365.21
IL-23	1,063.58	1,488.63	1,315.07	2,084.62
IL-23 R	876.80	1,333.15	1,135.22	1,674.62
IL-24	1,015.40	1,464.60	1,190.86	1,896.41
IL-26	1,270.94	1,529.58	1,263.03	2,256.14
IL-27	1,355.94	1,651.98	1,476.52	2,472.08
IL-28A	1,259.57	1,388.22	1,146.49	1,986.92
IL-29	1,473.42	1,478.44	1,255.22	2,577.44
IL-31	1,153.45	960.07	925.66	1,633.63
IL-31 RA	1,146.41	1,002.13	909.86	1,459.91
BACE-1	1,196.22	1,108.51	1,040.26	1,572.98
FACX	1,047.88	996.02	1,014.70	1,394.57
Insulin	1,070.08	857.52	1,081.85	1,131.61
Insulin R	1,126.92	930.01	1,277.26	1,439.58
Insulysin / IDE	1,817.21	1,685.20	2,563.70	3,264.46
IP-10	1,358.10	910.12	1,517.16	1,720.63
I-TAC / CXCL11	1,892.46	1,099.39	2,026.82	2,420.30
Kininostatin / kininogen	2,319.63	1,645.60	2,622.11	3,234.01
Kremen-1	980.75	851.20	1,145.99	1,321.05
Kremen-2	1,010.52	1,194.89	1,865.48	1,931.15
Lck	1,020.81	864.75	1,387.45	1,542.06
Latent TGF-beta bp1	922.82	4,029.66*	7,681.24*	6,544.87*
LBP	739.82	1,164.35	1,527.46	1,327.60
LECT2	936.89	1,051.80	1,210.37	1,191.53
Lefty - A	864.89	950.60	1,267.29	1,277.01
Leptin R	988.33	1,196.73	1,412.49	1,880.36
Leptin (OB)	722.50	1,616.88	1,276.53	1,720.56*
LFA-1 alpha	611.51	1,354.79*	1,250.51*	1,524.15*
LIF	624.50	1,169.36	1,020.34	1,561.29*
LIF R alpha	932.02	1,288.14	1,185.20	1,951.66*
LIGHT / TNFSF14	1,070.62	1,452.53	1,412.29	2,078.84
Lipocalin-1	1,293.67	1,330.40	1,165.17	2,006.71
LRP-1	2,188.61	2,890.83	3,069.30	4,717.33*
LRP-6	1,394.92	2,364.58	2,607.56	4,087.56*
L-Selectin (CD62L)	1,267.69	1,382.26	1,261.10	1,929.25
Lipocalin-2	2,476.63	1,714.70	1,896.41	3,278.27
Lymphotactin / XCL1	1,098.77	1,312.00	1,330.06	2,054.79

Lymphotoxin beta / TNFSF3	1,365.14	994.38	1,087.69	1,611.76
Lymphotoxin beta R / TNFRSF3	1,200.01	977.19	1,166.55	1,623.79
MAC-1	1,048.42	862.67	1,163.06	1,504.15
MCP-1	1,129.63	1,265.71	2,430.37*	2,927.03*
MCP-2	1,419.82	928.78	1,394.29	1,690.51
MCP-3	1,783.64	715.44*	1,247.71	1,365.85
MCP-4 / CCL13	1,465.30	727.71*	1,057.67	1,252.35
M-CSF	1,502.11	1,201.53	1,923.83	2,237.99
M-CSF R	1,508.07	826.40	1,295.48	1,580.06
MDC	1,169.69	846.17	1,091.48	1,415.72
MFG-E8	1,131.80	872.70	1,128.30	1,462.37
MFRP	1,345.65	1,467.26	822.38	1,120.95
MIF	1,268.77	1,505.63	1,009.50	1,418.99
MIG	919.03	1,182.19	1,157.38	1,197.39
MIP-1a	1,062.50	1,603.22	1,442.09	2,240.14*
MIP-1b	1,432.81	1,780.78	1,923.16	2,801.09
MIP-1d	720.33	957.50	1,033.11	1,025.64
MIP 2	812.91	1,202.63	1,345.46	1,554.83
MIP-3 alpha	752.27	1,098.79	1,299.21	2,124.54*
MIP-3 beta	1,536.22	3,864.34*	4,525.98*	5,350.64*
MMP-1	974.25	46,620.53*	53,622.33*	38,420.38*
MMP-2	890.87	2,317.71*	2,954.82*	2,737.83*
MMP-3	871.92	6,219.51*	7,061.18*	8,496.31*
MMP-7	1,365.68	1,847.91	2,036.66	2,255.43
MMP-8	1,148.58	1,599.00	1,500.34	1,771.33
MMP-9	1,063.58	1,463.73	1,136.51	1,667.24
MMP-10	1,000.24	1,414.52	1,193.34	1,726.21
MMP-11 /Stromelysin-3	1,012.69	1,254.77	1,157.85	1,693.37
MMP-12	994.82	1,143.14	979.01	1,512.12
MMP-13	1,191.35	1,078.47	1,011.75	1,495.32
MMP-14	1,486.95	916.70	907.97	1,338.15
MMP-15	884.92	917.37	866.83	1,260.41
MMP-16 / MT3-MMP	1,966.63	2,112.37	2,387.14	3,465.00
MMP-19	1,672.65	1,421.14	1,371.97	1,941.23
MMP-20	3,688.29	2,978.21	3,537.24	5,325.25
MMP-24 / MT5-MMP	2,324.50	811.10*	1,058.40*	1,195.20
MMP-25 / MT6-MMP	1,484.25	1,220.55	1,056.60	1,111.16
Musk	1,294.76	1,250.11	2,918.24*	2,445.54
MSP alpha Chain	1,335.90	967.98	1,256.59	1,535.42
MICA	1,621.22	946.70	1,401.84	1,595.52
NAP-2	1,169.69	806.53	1,202.42	1,087.58

NCAM-1 / CD56	1,980.71	1,778.31	1,443.41	2,299.71
Neuritin	1,378.67	1,336.50	972.64	1,591.44
NeuroD1	909.82	1,149.84	994.24	1,234.65
Neuropilin-2	789.09	1,196.15	1,099.20	1,328.89
Neurturin	1,096.61	1,375.09	1,208.00	1,520.63
NGF R	750.65	1,103.03	941.67	1,170.63
NOV / CCN3	620.71	1,086.36	1,005.70	1,320.93*
NRG1 Isoform GGF2	736.03	1,192.45	1,237.58	1,436.60
Nidogen-1	1,167.53	3,590.00*	4,048.72*	4,497.40*
NrCam	1,193.52	2,442.48*	3,271.70*	3,210.07*
NRG2	1,441.48	1,749.67	2,059.84	2,382.91
NRG3	1,374.34	1,736.13	1,891.69	2,313.99
NT-3	1,120.43	1,392.99	1,202.29	1,353.57
NT-4	942.31	1,557.07	1,357.60	1,357.37
Orexin A	1,120.43	1,809.08	1,600.93	1,877.55
Orexin B	771.22	1,572.81*	1,347.76	1,699.51*
OSM	1,122.05	1,536.35	1,426.09	1,918.03
Osteoactivin / GPNMB	839.98	1,279.25	1,262.17	1,559.33
Osteocrin	822.66	1,153.43	1,176.48	1,445.54
Osteoprotegerin / TNFRSF11B	974.25	2,120.02*	2,149.40*	3,157.01*
OX40 Ligand / TNFSF4	1,029.47	1,051.41	1,275.32	1,572.17
PARC / CCL18	1,117.72	1,029.19	1,384.60	1,576.61
PD-ECGF	1,084.15	1,043.40	1,267.25	1,343.42
PDGF R alpha	1,214.09	986.83	1,122.81	1,231.32
PDGF R beta	2,061.38	1,254.24	2,032.44	1,900.76
PDGF-AA	1,408.45	1,310.35	1,532.25	1,467.41
PDGF-AB	1,268.23	924.10	2,110.42	1,431.92
PDGF-BB	1,284.47	953.54	2,303.68	1,426.55
PDGF-C	1,236.29	1,084.41	2,432.17	1,591.44
PDGF-D	1,211.38	933.24	2,300.94	1,362.53
PECAM-1 /CD31	2,262.24	1,106.12*	844.02*	1,558.11
Pentraxin3 / TSG-14	1,721.92	1,381.56	1,620.95	1,868.87
Persephin	1,104.73	911.80	1,150.43	1,114.11
PF4 / CXCL4	1,026.22	1,244.27	1,435.22	1,387.35
PlGF	796.13	956.91	1,122.33	1,188.07
PLUNC	662.40	896.18	1,058.82	1,080.51
Pref-1	859.47	1,358.95	1,536.54	1,644.12
Progranulin	653.74	1,963.25*	2,328.68*	1,521.58*
Prolactin	880.05	1,536.04	1,752.35*	1,937.09*
P-selectin	1,210.84	1,728.37	2,182.05	2,064.46
RAGE	1,138.29	1,214.77	1,404.05	1,597.04
RANK / TNFRSF11A	1,444.73	1,779.27	1,990.66	2,221.48

RANTES	975.87	1,489.53	1,341.73	1,519.37
RELM beta	852.43	1,569.27	1,380.69	1,447.78
RELT / TNFRSF19L	1,193.52	2,109.96	1,898.43	2,192.58
ROBO4	927.69	1,908.04*	1,408.25	1,820.76
S100 A8/A9	1,204.88	2,363.44	2,269.53	2,659.45*
S100A10	6,838.69	10,077.83	10,485.84	10,679.37
SAA	1,109.06	1,550.81	1,548.44	1,894.56
SCF	3,868.03	4,734.89	5,077.24	6,759.07
SCF R /CD117	1,331.57	1,372.95	1,607.01	1,790.92
SDF-1 / CXCL12	1,002.40	1,153.57	1,404.86	1,486.05
sFRP-1	835.65	993.15	1,428.34	1,157.91
sFRP-3	1,607.69	1,452.67	1,932.14	2,041.60
sFRP-4	18,001.81	24,248.20	32,713.49	41,545.55*
sgp130	2,145.30	2,375.82	2,949.22	3,282.83
SIGIRR	3,403.51	2,541.45	3,038.71	3,827.48
Siglec-5/CD170	1,778.23	1,727.81	1,953.84	2,069.61
Siglec-9	1,628.80	1,493.06	2,025.24	2,542.46
SLPI	1,126.92	1,139.11	1,708.26	2,184.82
Smad 1	2,072.75	1,431.28	1,354.99	2,104.24
Smad 4	2,805.26	2,835.98	8,232.29*	4,904.66
Smad 5	1,359.73	1,243.34	5,963.74*	1,906.20
Smad 7	791.26	1,267.67	2,347.11*	1,278.30
Smad 8	862.18	1,451.05	1,283.31	1,418.07
Prdx	533.01	1,162.32*	1,306.85*	1,280.77*
Soggy-1	966.13	2,179.15*	1,993.02*	2,347.68*
Sonic Hedgehog (Shh N-terminal)	704.63	1,508.09*	1,550.51*	1,747.30*
SPARC	956.92	8,863.21*	8,852.43*	14,857.38*
Spinesin	743.61	1,736.29*	2,210.92*	2,700.87*
TACI / TNFRSF13B	1,051.13	1,835.72	2,038.77	2,507.01*
Tarc	873.01	1,469.03	1,386.36	2,127.31*
TCCR / WSX-1	1,014.85	1,512.51	1,455.58	1,956.80
TECK / CCL25	1,024.06	1,636.63	1,511.86	1,868.04
TFPI	1,264.98	2,263.32	2,041.19	2,294.98
TGF-alpha	727.91	1,742.60*	1,428.26	1,881.89*
TGF-beta 1	876.26	1,795.74*	1,418.00	1,906.18*
TGF-beta 2	1,190.27	1,874.23	1,888.48	2,330.21
TGF-beta 3	1,098.77	1,771.08	1,947.87	2,354.60*
TGF-beta 5	5,353.09	7,576.21	9,248.68	7,894.59
TGF-beta RI / ALK-5	1,720.84	2,988.49	3,184.01	3,341.05
TGF-beta RII	1,030.55	1,407.11	1,687.88	1,817.73
Grb2	943.39	1,110.77	1,390.05	1,438.76
TGF-beta RIII	1,486.41	1,385.01	1,861.39	1,824.49

Thrombopoietin (TPO)	2,431.70	2,241.07	3,233.90	2,987.64
TPX	4,423.51	3,688.17	3,254.43	4,908.28
Thrombospondin-1	64,279.03	65,678.75	49,684.26	82,706.21
Thrombospondin-2	5,093.76	5,089.23	4,487.73	9,647.94
Thrombospondin-4	1,697.02	1,385.86	1,678.72	2,814.18
Thymopoietin	1,039.22	998.68	1,456.02	2,411.46*
Tie-1	1,588.20	1,547.54	2,148.41	2,450.29
Tie-2	1,206.51	2,185.01	2,345.60	3,182.89*
TIMP-1	1,295.84	14,201.02*	16,620.57*	25,661.55*
TIMP-2	820.49	28,405.89*	22,696.06*	26,642.47*
TIMP-3	559.00	1,753.62*	2,267.47*	2,468.84*
TIMP-4	1,091.73	1,806.14	2,138.00	2,983.50*
TL1A / TNFSF15	1,014.31	1,508.55	1,601.68	2,125.42*
TLR1	943.93	1,607.92	1,872.94	2,282.20*
TLR2	932.56	1,872.01*	2,033.23*	2,700.80*
TLR3	1,183.23	2,016.94	1,977.37	2,862.29*
TLR4	1,130.71	1,801.69	1,803.61	2,677.74*
TMEFF1 / Tomoregulin-1	1,668.32	2,141.06	2,194.53	3,544.15*
TMEFF2	1,064.12	1,974.74	2,133.12*	2,626.45*
TNF-alpha	1,092.27	1,822.24	1,569.82	2,494.98*
TNF-beta	1,312.62	2,217.41	2,084.36	3,590.22*
TNF RI / TNFRSF1A	1,078.20	1,586.44	1,452.81	2,172.68*
TNF RII / TNFRSF1B	2,177.78	1,927.28	2,208.75	3,175.53
TRADD	1,475.04	1,476.87	1,520.04	2,104.60
TRAIL / TNFSF10	1,321.29	1,307.47	1,593.30	2,226.75
TRAIL R1 / DR4 / TNFRSF10A	1,504.82	1,329.39	1,531.22	1,924.02
TRAIL R2 / DR5 / TNFRSF10B	1,995.87	1,518.44	1,932.76	2,443.97
TRAIL R3 / TNFRSF10C	2,222.17	2,274.87	3,171.18	2,904.21
TRAIL R4 / TNFRSF10D	2,354.28	1,965.74	2,118.98	2,338.33
TRANCE	5,532.83	4,363.26	4,194.06	6,347.90
TREM-1	1,413.87	1,333.65	1,923.92	2,503.24
TROY / TNFRSF19	1,098.23	1,546.46	1,980.55	2,656.45*
TSG-6	1,122.59	1,787.06	2,297.39*	2,782.84*
TSLP R	1,051.67	1,285.14	1,500.27	1,813.06
TWEAK / TNFSF12	1,177.27	1,341.84	1,620.97	2,050.17
TWEAK R / TNFRSF12	1,171.32	1,830.00	1,680.44	2,274.93
Ubiquitin+1	1,439.85	1,723.28	1,994.16	2,801.97
uPA	1,427.94	1,843.28	2,078.28	3,230.23*
uPAR	1,265.52	1,973.16	1,990.85	2,855.24*
Vasorin	1,321.29	2,213.59	2,146.23	3,898.00*
VCAM-1 (CD106)	1,267.15	1,843.52	1,499.51	2,820.62*

VE-Cadherin	1,219.50	1,974.43	1,530.16	3,071.04*
VEGF	1,548.67	2,275.91	2,431.67	4,687.78*
VEGF R2 (KDR)	1,195.68	1,733.34	1,367.12	3,178.56*
VEGF R3	1,259.57	1,733.65	1,522.55	2,852.67*
VEGF-B	1,093.36	1,309.05	1,272.29	2,274.69*
VEGF-C	1,454.47	1,460.05	1,724.70	2,508.73
VEGF-D	2,017.53	1,857.74	2,348.98	3,409.78
VEGI / TNFSF15	1,150.20	961.24	1,234.62	1,727.08
WIF-1	1,257.40	1,211.39	1,556.77	1,921.83
WISP-1 / CCN4	1,195.68	1,347.81	1,584.64	1,646.05
XEDAR	1,414.95	1,592.80	1,822.48	2,751.63*

Table 1

	CONTROL	**AS Average**	**AF Average**	**CA Average**
Positive Control	19,613.33	19,613.33	19,613.33	19,613.33
Neg	1.16	153.65*	411.23*	130.50*
11b-HSD1	1.16	9.43*	1.03	69.25*
2B4	1.16	36.20*	9.28*	73.02*
4-1BB	1.16	44.55*	19.13*	67.57*
A1BG	1.16	114.05*	42.87*	115.12*
A2M	211.47	1,600.89*	1,136.95*	2,328.91*
ABL1	477.41	502.67	359.45	791.51
ACE	78.80	193.80*	68.06	270.68*
ACE-2	194.09	326.54	237.09	405.17*
ACK1	477.41	647.94	512.69	686.25
ACPP	313.45	481.05	486.23	820.72*
ACTH	414.84	595.44	800.49	1,444.69*
ADAM-9	446.70	472.90	706.03	1,062.23*
ADAMTS-1	717.85	367.14	851.87	985.02
ADAMTS-10	1,469.89	3,168.98*	3,839.53*	5,165.18*
ADAMTS-13	719.59	247.44*	601.62	574.50
ADAMTS-15	555.63	121.77*	558.53	438.44
ADAMTS-17	300.12	96.17*	345.21	295.50
ADAMTS-18	63.73	83.59	448.50*	505.98*
ADAMTS-19	1.16	50.06*	361.51*	207.95*
ADAMTS-4	1.16	58.51*	313.92*	161.25*
ADAMTS-5	1.16	11.18*	286.18*	218.20*
ADAMTS-L2	1.16	69.63*	559.99*	726.19*

Adipsin	1.16	1,233.42*	5,756.54*	1,943.35*
Afamin	1,208.59	141.80*	753.15	2,936.23*
AFP	2,181.37	65.56*	684.57*	1,530.48
ALBUMIN	4,443.86	604.61*	1,541.23*	2,317.00
Aldolase A	1.16	110.96*	150.78*	104.91*
Aldolase B	1.16	33.13*	50.87*	26.21*
Aldolase C	1.16	141.93*	81.12*	79.57*
ALK	1.16	105.42*	66.77*	96.93*
Alpha 1 AG	1.16	162.29*	170.43*	284.78*
Alpha 1 Microglobulin	1.16	306.58*	234.13*	591.28*
Alpha Lactalbumin	280.42	381.04	263.45	493.19
ALPP	183.08	513.50*	455.35*	786.07*
AMICA	315.18	451.98	536.48	908.83*
AMPKa1	177.87	268.69	323.94	447.34*
Amylin	358.64	523.14	649.22	836.06*
ANGPTL3	405.57	451.96	675.38	616.26
ANGPTL4	541.14	344.80	784.43	884.98
Annexin A7	603.14	264.54*	743.79	753.06
APC	732.92	335.35*	863.68	954.10
APCS	460.61	243.76	577.74	592.61
Apelin	651.80	383.81	700.36	730.64
Apex1	823.88	304.48*	516.56	508.56
APN	130.94	103.98	331.28*	281.25*
ApoA1	145.42	91.21	347.19*	317.18*
ApoA2	176.13	92.10*	327.31	313.48
ApoA4	175.55	115.46	507.64*	554.46*
ApoB	1.16	22.98*	389.11*	401.33*
ApoB100	303.60	27.93*	401.06	543.36
ApoC1	2,526.11	43.49*	517.26*	764.06*
ApoC2	6,480.97	1,667.31*	3,446.03	3,573.17
ApoC3	98,174.53	99,021.84	118,299.42	145,523.00
ApoD	1.16	270.70*	422.17*	411.17*
ApoE	1.16	98.24*	439.38*	15.84*
ApoE3	1.16	119.91*	195.12*	22.22*
ApoH	1.16	185.87*	170.33*	65.28*
ApoM	1.16	178.23*	219.26*	187.02*
APP	1.16	2,545.55*	2,551.79*	2,560.93*
ASPH	1.16	204.00*	204.89*	174.64*
Attractin	1.16	127.47*	150.90*	118.11*
B3GNT1	1.16	173.58*	221.68*	198.86*
BAF57	1.16	198.59*	218.13*	216.41*
BAFF	1.16	201.77*	264.89*	252.07*
BAI-1	254.93	324.81	445.54	481.31

BCAM	325.61	498.10	671.55*	627.02
Beta 2M	412.52	2,635.25*	3,669.88*	3,451.24*
Beta Defensin 4	1,734.09	1,059.32	1,511.85	2,061.92
Beta IG-H3	643.69	7,717.55*	7,511.18*	18,306.78*
Biglycan	554.47	624.68	819.28	1,006.07
BLAME	695.84	383.35	677.00	644.94
BMP-9	600.82	258.65*	527.62	578.95
BMX	432.80	247.72	588.89	520.72
BNIP2	854.01	708.38	1,044.63	722.72
BNP	108.34	229.07*	393.92*	406.62*
Btk	230.01	342.75	617.12*	667.78*
C2	151.80	175.42	412.82*	314.57*
C3a	301.28	69.16*	333.27	259.56
C5/C5a	1.16	48.23*	291.43*	211.11*
C7	527.24	140.86*	447.49	755.93
C8B	2,329.69	18.40*	329.57*	450.97*
C9	3,010.47	359.91*	768.15*	1,482.85*
CA9	2,275.23	2,029.32	2,016.56	4,700.01*
CA15-3	1.16	255.70*	223.13*	369.19*
CA19-9	1.16	301.47*	335.34*	153.30*
CA125	1.16	313.04*	298.27*	166.63*
Cadherin-13	1.16	314.86*	458.31*	413.20*
Calbindin	2,618.81	2,167.38	2,064.99	3,732.71
Calbindin D	190.04	266.92	349.99	487.43*
Calcitonin	191.78	230.39	223.17	353.91
Calreticulin	39.98	175.45*	256.30*	252.87*
Calsyntenin-1	1.16	137.85*	305.11*	182.14*
CART	17.96	199.66*	269.76*	316.66*
Caspase-3	263.62	298.03	374.00	508.82
Caspase-8	338.94	427.22	471.59	1,154.52*
Cathepsin B	382.39	392.09	570.98	1,830.89*
Cathepsin D	628.05	320.66	643.39	2,269.65*
Cathepsin L	914.84	427.39*	818.41	1,754.78
Cathepsin S	837.21	403.24*	807.82	1,271.07
CBP	1,471.05	1,130.35	1,914.18	2,290.66
CCK	2,319.27	877.40*	1,551.89	2,288.94
CD23	964.67	200.71*	592.20	713.19
CD24	392.24	124.37*	479.67	517.42
CD36	355.74	72.25*	452.72	422.25
CD38	509.86	109.68*	420.48	423.82
CD44	336.04	29.20*	269.98	315.01
CD45	481.47	97.96*	352.40	375.07
CD46	390.50	91.75*	328.05	335.17

CD47	366.17	69.10*	454.75	1,125.47*
CD55	343.57	45.41*	339.31	392.46
CD59	989.58	31.08*	291.57*	391.36*
CD61	751.46	108.98*	510.44	820.02
CD71	734.66	1,336.56	524.85	957.47
CD74	1.16	478.12*	577.33*	721.31*
CD79 alpha	85.75	386.11*	594.13*	603.35*
CD90	1.16	193.34*	326.88*	245.74*
CD97	161.07	169.18	402.60*	337.07*
CD200	171.50	152.30	364.80*	382.47*
CEA	48.09	107.86*	271.54*	324.26*
CEACAM-1	1.16	118.58*	272.14*	350.90*
Ceruloplasmin	1.16	62.42*	210.45*	231.17*
CFHR2	1.16	118.91*	248.80*	305.94*
Chemerin	1.16	211.16*	499.05*	560.39*
CHI3L1	97.34	386.78*	668.44*	1,240.82*
Chromogranin A	296.64	309.79	626.30*	1,196.58*
Chymase	474.51	259.06	553.40	1,080.93*
cIAP-2	652.96	278.39*	688.69	1,306.68*
Ck beta 8-1	877.18	236.89*	705.17	1,245.08
CK-MB	784.48	302.21*	722.15	962.44
Claudin-3	747.40	187.58*	757.04	700.43
Claudin-4	766.52	190.35*	638.20	675.76
CLEC3B	443.81	168.00*	645.21	824.09
Clusterin	447.28	35.90*	695.19	641.26
CNDP1	801.29	128.46*	768.47	1,031.40
COCO	115.88	42.75*	434.58*	442.03*
Complement factor H	1.16	29.70*	358.92*	357.02*
Contactin-1	924.11	970.29	2,078.23*	1,491.32
Contactin-2	124.57	389.77*	323.82*	292.41*
Corticosteroid-binding globulin	346.47	258.77	1,509.12*	1,007.06*
COX-2	125.73	106.79	367.71*	509.07*
C-peptide	566.64	253.52*	783.19	1,310.38*
CPN2	974.52	436.21	1,540.54	1,731.99
Creatinine	24,459.77	27,733.72	36,863.11	42,606.45
CRP	1.16	274.28*	622.99*	499.57*
CRTAM	56.78	126.63*	402.34*	252.36*
CSH1	315.76	163.67	601.50	379.19
cTnT	321.56	76.83*	472.14	362.64
CutA	89.22	13.30*	291.89*	237.14*
Cyclin D1	52.72	19.48*	338.28*	281.74*
Cystatin A	31.87	41.28	335.28*	382.80*

Cystatin B	143.11	168.01	399.29*	434.29*
Cystatin C	13.33	156.76*	371.89*	435.83*
Cytochrome C	1.16	147.29*	447.82*	533.46*
Cytokeratin 8	1.74	186.03*	461.25*	570.57*
Cytokeratin18	308.81	247.58	646.00*	687.05*
Cytokeratin19	286.21	198.38	603.87*	553.21
DBI	440.33	173.25*	599.73	482.00
DCBLD2	570.11	149.49*	655.67	591.06
D-Dimer	954.24	1,388.15	1,984.01*	2,992.84*
DEFA1/3	742.77	110.47*	630.23	630.80
Defensin	410.78	97.17*	569.32	583.18
Desmin	646.01	265.86*	914.42	1,195.33
DLL1	713.22	152.91*	800.76	836.42
DLL4	464.66	103.12*	743.53	626.97
DMP-1	504.64	364.45	1,205.64*	1,160.89*
DPPIV	183.66	150.61	708.51*	646.68*
E-Cadherin	413.68	119.15*	470.11	536.61
Endorphin Beta	204.52	86.27*	380.05	288.02
Endothelin Receptor A	195.25	125.60	406.49*	304.60
Enolase 2	200.47	134.83	474.45*	402.37*
ENPP2	285.06	126.10	607.26*	727.38*
EpCAM	438.01	81.50*	559.59	919.72*
EphA1	1,309.98	450.72*	1,095.72	1,924.97
EphA2	1.16	148.42*	465.87*	299.77*
EphA3	384.13	381.58	1,053.80*	1,085.43*
EphA4	505.80	169.49*	675.22	494.89
EphA5	1,052.74	356.71*	1,068.15	1,090.24
EphA6	168.02	124.64	549.03*	462.61*
EphA7	372.54	152.44*	466.49	578.01
EphA8	895.72	401.57*	895.55	1,156.06
EphB1	902.10	426.40*	811.55	1,108.08
EphB2	931.07	389.46*	727.95	1,009.72
EphB3	851.69	567.00	905.66	1,217.81
EphB4	1.16	170.38*	488.75*	535.43*
EphB6	144.85	222.27	563.62*	638.01*
ERRa	544.62	256.42*	905.78	1,132.77*
Erythropoietin R	628.63	325.89	727.64	731.78
ESAM	672.66	260.47*	677.34	639.52
EV15L	848.22	245.00*	670.71	652.17
EXTL2	738.13	375.10	934.56	963.63
FABP1	669.77	212.31*	810.51	1,015.16
FABP2	367.91	162.11*	565.40	748.39
FABP3	250.29	140.27	501.71*	614.11*

FABP4	529.56	828.56	1,852.88*	2,616.67*
Factor XIII A	18,130.02	48,560.06*	59,351.02*	79,043.79*
Factor XIII B	690.04	1,868.35*	2,488.59*	3,152.99*
FAK	505.80	102.03*	489.58	511.57
FAP	1,625.17	129.78*	490.19*	468.82*
Fc RIIB/C	820.98	124.61*	444.18	507.94
Fen 1	45.19	136.69*	484.46*	581.16*
FER	396.88	185.63*	685.08	1,029.11*
Ferritin	626.89	58.44*	517.85	768.93
Fetuin A	409.62	47.09*	504.40	729.06
Fetuin B	1.16	200.35*	768.38*	569.76*
FGFR1	209.74	254.36	1,122.23*	1,353.40*
FGFR1 alpha	136.73	134.14	736.12*	446.89*
FGFR2	694.68	508.85	1,270.68	1,459.78*
Fibrinogen	530.13	9,202.76*	13,333.01*	21,925.77*
Fibrinopeptide A	276.94	692.98*	1,348.75*	2,031.59*
Fibronectin	550.41	18,570.43*	28,116.82*	41,847.45*
Ficolin-3	59.10	626.64*	1,014.16*	1,362.72*
FIH	107.77	187.69	314.49*	478.26*
FOLR1	266.52	371.75	648.03*	804.23*
FOXN3	7,686.66	9,269.48	13,035.73	10,005.07
FoxO1	578.22	619.85	947.14	1,115.03
FoxP3	451.34	226.39*	612.67	704.19
FRK	1,754.37	1,547.28	2,738.80	3,489.41
FSH	618.78	351.97	788.29	675.01
Furin	770.00	405.58	765.36	716.12
Fyn	771.74	312.23*	672.14	621.95
GADD45A	711.48	407.14	742.24	889.34
Galanin	334.88	327.20	586.71	830.90*
Galectin-1	128.62	199.38	543.07*	686.95*
Galectin-3BP	243.92	330.51	732.15*	947.58*
Galectin-7	513.91	1,083.84*	1,486.76*	2,699.46*
gamma-Thrombin	47.51	233.70*	586.83*	667.71*
Gas1	320.98	185.42	593.10	547.42
Gastrin	312.29	67.87*	489.67	412.76
GATA-3	387.61	86.58*	549.91	571.94
GATA-4	2.32	54.24*	469.00*	453.90*
Gelsolin	224.22	89.75*	544.17*	607.43*
Ghrelin	615.88	94.58*	748.09	878.58
GLP-1	832.57	53.28*	959.43	1,323.73
GMNN	1.16	245.25*	695.85*	527.85*
GPBB	1.16	147.93*	713.46*	545.19*
GPI	1.16	111.65*	607.64*	405.04*

GPR-39	284.48	232.12	581.32*	506.37
GPX1	281.58	592.73*	829.28*	926.51*
GPX3	245.66	296.84	540.85*	943.51*
GRP	298.38	938.00*	1,120.75*	1,747.49*
GRP75	1.16	346.33*	406.21*	766.37*
GRP78	190.62	299.02	366.03	698.84*
GSR	237.55	375.76	468.69	780.06*
GST	573.59	615.94	761.21	1,141.42
HADHA	345.31	319.92	485.54	691.57*
HAI-1	751.46	477.71	732.34	831.14
HAI-2	596.18	411.40	630.86	735.68
Haptoglobin	798.97	520.79	835.12	882.58
hCG alpha	482.63	449.92	701.08	653.19
hCGb	599.08	404.72	705.61	698.29
Hck	661.07	696.80	970.65	1,456.76*
HE4	765.94	500.66	665.10	1,371.54
Hemopexin	99.65	246.91*	522.14*	645.26*
Hepcidin	2,332.59	1,878.39	2,468.08	3,035.34
HOXA10	418.89	250.02	733.49	969.12*
HSP10	233.49	201.92	573.54*	612.09*
HSP20	81.11	168.70*	524.19*	631.09*
HSP27	265.94	954.61*	1,434.63*	1,441.15*
HSP32	378.92	121.52*	622.81	924.98*
HSP40	214.95	104.23*	557.77*	696.00*
HSP60	213.79	83.41*	553.85*	708.74*
HSP70	2.90	16.42*	567.39*	716.37*
HSP90	145.42	20.96*	615.34*	588.50*
HSPA8	227.70	175.45	497.30*	574.46*
HTRA2	466.40	304.41	741.02	1,110.21*
IBSP	16,123.62	14,446.85	20,211.41	29,611.81
IGF2BP1	912.53	598.70	993.81	1,447.17
IGFBP-5	170.92	257.12	350.61*	605.88*
IL-23p19	246.82	356.98	459.70	701.96*
IL-33	238.13	271.70	418.56	702.02*
IL-34	413.68	306.40	464.44	699.77
IL36RN	429.90	332.20	541.50	652.26
INSL3	493.05	450.70	617.57	634.07
INSRR	684.25	428.69	572.56	642.92
Integrin alpha V	1,019.71	936.88	1,081.80	1,401.20
Itk	1,013.34	928.22	1,737.00	1,736.11
ITM2B	390.50	445.20	1,130.71*	897.85*
Kallikrein 2	176.71	346.85	656.22*	892.67*
Kallikrein 5	269.99	357.07	950.22	1,267.60

Kallikrein 6	112.98	200.30	625.79*	669.91*
Kallikrein 7	178.45	314.16	663.73*	899.42*
Kallikrein 8	1.16	228.78*	520.51*	526.08*
Kallikrein 10	23.18	244.84*	551.24*	672.79*
Kallikrein 11	1.16	169.94*	448.90*	517.98*
Kallikrein 14	1.16	218.18*	482.29*	582.76*
KCC3	1.16	140.90*	534.97*	476.73*
KCTD10	1.16	156.82*	573.66*	604.07*
KIF3B	1.16	196.27*	701.09*	894.29*
KLF4	67.21	184.46*	773.71*	1,038.51*
LAG-3	440.91	87.13*	475.77	523.69
Layilin	456.55	105.13*	421.32	648.24
LDL R	969.89	436.83*	792.51	1,051.27
Legumain	382.97	186.84*	394.32	582.36
LH	148.32	154.21	275.06	499.92*
LIMPII	324.45	126.23*	293.81	655.25*
LIN41	333.14	195.59	286.60	640.24
Livin	402.67	208.20	365.33	532.68
LOX-1	579.96	330.34	459.19	704.74
LPS	1,444.98	936.70	1,516.72	3,377.81*
LRG1	984.95	445.33*	744.38	1,021.03
LTF	910.79	732.79	1,276.51	1,319.82
LTK	1,148.33	770.68	1,050.21	1,139.59
Lumican	386.45	224.88	532.11	665.56
Lyn	557.94	703.58	1,178.34*	1,462.97*
LYRIC	265.94	258.97	552.31	1,155.46*
LYVE-1	1.16	227.30*	497.99*	532.83*
LZTS1	101.97	221.95*	548.54*	757.35*
Mammaglobin A	1.16	217.39*	428.96*	742.71*
Marapsin	64.31	234.40*	378.03*	602.72*
MATK	39.40	323.89*	628.50*	759.82*
MBL	45.77	332.55*	576.16*	784.43*
MBL-2	151.80	421.26*	753.06*	1,394.77*
Mer	236.39	217.85	623.56	680.69
Mesothelin	42.87	202.92*	629.06*	619.08*
MICB	258.40	229.81	732.37*	721.71*
Midkine	337.20	115.15*	434.42	486.19
MINA	680.19	173.09*	590.88	743.97
MSHa	329.09	42.74*	280.93	486.59
MTUS1	669.19	116.72*	381.78	993.23
Myoglobin	436.85	127.78*	256.00	483.10
NAIP	346.47	103.11*	217.91	469.72
Nanog	454.24	137.26*	231.49	491.24

NELL2	368.49	198.31	320.67	460.11
NEP	590.39	293.14	413.02	666.76
Nesfatin	1,358.65	772.73	1,075.13	1,637.44
Nestin	659.92	324.28*	555.09	600.03
NET1	705.69	330.06*	493.78	577.33
Netrin G2	455.97	227.86	534.65	527.96
Netrin-4	433.38	156.80*	452.15	487.89
Neurokinin-A	278.10	284.81	535.09	594.02
Neuropeptide Y	85.75	220.99*	680.95*	540.43*
NF1	1.16	175.96*	445.36*	457.17*
NM23-H1/H2	180.19	119.58	410.80*	403.92*
Notch-1	1.16	205.31*	429.90*	455.91*
NPTX1	1.16	261.23*	430.64*	465.00*
NPTXR	1.16	215.70*	355.49*	514.51*
NR3C3	1.16	757.02*	402.10*	431.06*
Ntn1	814.03	632.94	1,663.06*	1,882.51*
OCT3/4	61.99	297.65*	514.87*	566.50*
Omentin	2,597.95	2,435.18	3,536.67	4,293.12
Osteocalcin	257.82	201.88	610.42*	435.75
Osteopontin	336.62	364.06	868.17*	381.26
OX40	438.01	288.30	776.16	328.95
p21	420.05	240.09	700.30*	408.30
p27	502.90	190.55*	542.61	342.82
p53	347.05	130.49*	455.78	338.62
PAI-1	20.86	701.04*	1,662.47*	2,454.59*
PAK7	198.15	197.43	336.99	480.83*
Pancreastatin	545.20	173.38*	463.08	502.72
Pancreatic Polypeptide	329.67	57.79*	299.19	419.26
Pappalysin-1	373.12	119.07*	270.21	445.54
PARK7	130.94	145.20	335.55*	439.50*
P-Cadherin	466.40	271.86	489.41	580.17
PCAF	298.38	246.49	445.97	482.03
PD-1	384.71	325.49	543.54	617.89
PDX-1	512.75	277.83	481.55	433.81
PEDF	380.65	214.19	542.23	550.61
PEPSINOGEN I	256.09	179.04	465.05	449.14
PEPSINOGEN II	112.98	157.87	515.22*	548.96*
PGRP-S	23.75	286.05*	626.66*	877.90*
PI 16	1.16	154.88*	632.80*	830.47*
PI 3Kinase p85 beta	37.66	129.52*	536.89*	590.47*
PIM2	1.16	50.27*	360.55*	363.27*
PKM2	1.16	146.93*	398.24*	551.75*
Plasminogen	1.16	1,137.55*	3,677.66*	3,358.75*

Podocalyxin	1.16	189.31*	509.40*	505.68*
POMC	223.06	407.33	702.04*	1,022.91*
PON1	1.16	304.75*	492.62*	452.95*
PON2	1.16	110.61*	499.41*	690.37*
PPARg2	53.30	214.39*	683.36*	575.00*
PPP2R5C	133.26	295.86*	929.31*	915.39*
Presenilin 1	444.97	355.83	974.47*	387.80
Presenilin 2	290.27	294.29	766.72*	277.90
Pro-BDNF	445.54	261.57	550.60	295.81
Procalcitonin	187.14	195.88	600.62*	377.33*
Pro-Cathepsin B	68.95	299.96*	745.63*	529.31*
Progesterone	1.16	68.74*	446.96*	353.70*
pro-Glucagon	314.60	131.63*	689.57*	1,104.88*
Prohibitin	1.16	84.54*	303.03*	379.16*
Pro-MMP-7	1.16	110.58*	328.87*	359.80*
Pro-MMP-9	79.95	98.30	298.81*	393.38*
Pro-MMP-13	249.71	171.72	423.65	480.26
ProSAAS	121.09	306.45*	617.31*	523.80*
Prostasin	186.56	289.62	664.56*	618.30*
Protein p65	170.92	215.02	511.90*	404.87*
PSA-Free	144.85	223.69	524.95*	501.94*
PSA-total	220.74	179.48	594.41*	545.79*
PSP	1.16	125.16*	455.47*	589.44*
PTH	1.16	533.71*	845.09*	2,143.04*
PTHLP	7,014.00	30,003.94*	25,623.63*	43,869.68*
PTN	1.16	815.10*	1,204.22*	1,688.76*
PTPRD	314.60	323.72	857.87*	1,229.51*
PYK2	1.16	122.90*	485.82*	801.01*
PYY	165.12	386.93*	1,005.10*	1,993.06*
Ras	66.63	3,697.36*	8,124.49*	14,353.17*
RBP4	1.16	195.55*	747.93*	748.67*
RECK	1.16	240.27*	647.48*	692.97*
RELM alpha	181.93	303.27	858.80*	672.35*
Resistin	1.16	125.17*	600.75*	581.38*
RET	1.16	232.98*	735.07*	651.36*
RIP1	1.16	115.00*	672.18*	355.42*
ROCK1	1,150.07	447.56*	1,261.36	1,108.93
ROCK2	625.15	358.61	935.14	669.09
ROR1	311.71	356.60	682.71*	378.45
ROR2	51.56	250.44*	510.09*	265.49*
ROS	34.18	272.58*	805.13*	692.06*
RYK	670.34	349.57	854.57	910.82
S100A4	25.49	106.27*	548.25*	557.05*

S100A6	1.16	167.09*	655.29*	755.59*
S100A8	1.16	63.15*	530.90*	625.94*
S-100b	19.70	66.68*	358.95*	481.14*
SART1	60.26	91.06	405.98*	400.59*
SART3	67.79	91.22	522.90*	445.85*
SCG3	35.92	135.93*	542.17*	474.98*
Selenoprotein P	1,366.18	1,031.64	1,830.32	2,211.78
SEMA3A	234.65	170.55	791.12*	529.39*
Serotonin	144.27	76.71	658.75*	589.15*
Serping 1	506.96	467.61	1,220.29*	1,300.01*
Serpin A1	210.90	190.35	726.38*	937.22*
Serpin A3	310.55	932.66*	1,181.20*	1,906.23*
Serpin A4	1.16	119.99*	622.57*	642.78*
Serpin A5	1.16	55.56*	559.85*	669.43*
Serpin A8	1,717.87	1,718.74	2,992.20	4,339.85*
Serpin A9	1.16	19.85*	496.21*	526.73*
Serpin A12	1.16	125.63*	589.49*	761.49*
Serpin B5	1.16	66.45*	466.03*	420.79*
Serpin D1	1.16	11.46*	434.52*	239.48*
Serpin I1	1.16	6.19*	510.88*	365.53*
SERTAD2	1.16	85.84*	597.65*	580.78*
SHBG	1.16	128.57*	859.98*	562.89*
SMAC	1.16	20.76*	700.13*	268.20*
SNCG	7,622.35	4,667.80	5,455.71	9,088.43
Somatotropin	1,280.43	430.37*	1,081.35	500.02*
SOST	725.39	336.02*	801.78	438.27
SOX17	296.06	224.82	610.50*	390.03
SOX2	307.07	179.94	660.12*	472.10
SPARCL1	1,124.00	602.01	1,391.83	1,676.50
SPINK1	1.16	60.57*	476.02*	478.31*
SRMS	381.23	560.22	1,276.04*	1,579.85*
SSEA-1	1.16	125.19*	629.99*	603.41*
SSEA-4	97.34	347.22*	543.72*	617.26*
SSTR2	270.57	383.46	807.43*	918.23*
SSTR5	1.16	238.95*	761.82*	622.90*
Survivin	191.20	238.95	833.72*	588.45*
SYK	425.85	250.15	984.88*	684.07
Syndecan-1	234.07	283.81	890.53*	650.29*
Syndecan-3	39.98	90.24*	807.73*	969.06*
TACE	161.65	99.81	819.77*	629.18*
TAF4	1.16	32.94*	647.13*	518.04*
Tec	274.05	234.99	1,106.33*	1,179.67*
TFF1	553.31	427.03	1,170.02*	1,457.40*

TFF3	1.16	117.74*	548.67*	788.19*
Thrombin	1.16	131.45*	560.74*	492.24*
Thrombomodulin	1.16	108.75*	488.74*	359.09*
Thymidine Kinase-1	1.16	84.36*	529.55*	418.31*
Thyroglobulin	1.16	629.61*	570.80*	376.26*
TIM-1	1.16	134.86*	564.46*	450.91*
TNK1	847.64	1,215.16	1,890.56*	2,189.62*
TOPORS	1.16	156.34*	667.07*	423.96*
TPA	1.16	158.32*	707.80*	364.07*
TPM1	1.16	167.65*	783.88*	407.91*
TRA-1-60	272.31	195.13	782.50*	406.75
TRA-1-81	146.58	188.10	666.38*	409.63
Transferrin	292.59	258.05	701.47*	504.41
Trappin-2	48.67	120.79*	542.44*	524.63*
TRKB	250.87	275.42	765.39*	681.24*
Troponin I	189.46	238.62	635.42*	518.48*
Troponin C	441.49	377.57	884.41*	904.31*
TRPC1	3,001.20	2,611.70	3,843.63	3,197.62
TRPC6	216.69	268.23	885.02*	552.92*
TRPM7	264.20	322.11	954.04*	1,038.30*
Trypsin 1	377.18	324.59	1,028.25*	634.40
TSH	180.19	250.15	1,077.27*	586.90*
TSLP	127.46	294.62*	1,419.29*	678.46*
TXK	1,507.55	1,977.02	3,083.03*	3,098.88*
Tyk2	58.52	176.40*	951.65*	589.09*
TYRO10	45.19	226.37*	849.45*	756.23*
Uromodulin	1,234.08	87.29*	711.55	428.77*
Vasopressin	1.16	141.88*	670.52*	460.77*
VDUP-1	16.80	163.28*	906.36*	600.84*
VEGF R1	1.16	144.03*	609.10*	429.33*
VGF	1.16	71.98*	563.05*	315.72*
VIP Receptor 2	1.16	127.08*	609.75*	265.00*
Visfatin	1.16	175.82*	825.67*	463.03*
Vitamin D Receptor	3,224.84	3,079.79	3,742.43	5,376.98
Vitamin D-BP	88.07	201.02*	629.39*	212.06*
Vitamin K-dependent protein S	1.16	188.38*	488.99*	279.33*
Vitronectin	163.97	300.66	503.70*	692.94*
VWF	4,164.60	4,004.52	4,065.54	5,997.39
Wilms Tumor 1	400.93	544.67	755.06	683.51
XIAP	461.19	534.02	620.92	645.07
ZAG	461.77	605.23	756.15	739.26
ZAP70	482.63	665.08	799.14	620.49

[0139] Table 1 shows that a total of 661/1000 (66.1%) of the tested proteins demonstrated Biological Significance as described in the testing protocol (≥2 fold increase/decrease relative to control/comparator sample) in at least one of the averaged sample groups.

[0140] Table 2 is a listing of average production levels for each sample ethnic group (As=Asian, Af=African, Ca=Caucasian) that demonstrated Biological Significance across all three (3) groups. These shared proteins became the basis for the initial assessment that follows.

Table 2

	Control	AS Average	AF Average	CA Average
BCMA / TNFRSF17	1.08	67.49	208.10	194.35
BAX	90.68	552.02	357.12	759.17
beta-NGF	199.51	358.85	478.62	897.43
CCL14 / HCC-1 / HCC-3	482.66	74.14	187.07	236.13
CCR5	71.19	143.29	192.98	313.52
CD30 / TNFRSF8	111.26	272.19	446.20	489.25
CV-2 / Crossveinless-2	108.01	18.99	450.71	45.32
CXCL16	44.67	293.17	389.68	380.72
D6	216.83	435.25	652.24	453.43
DAN	686.77	1,597.31	2,464.56	2,888.04
Decorin	461.00	1,900.72	4,089.23	3,161.92
Dkk-1	609.89	2,836.46	3,118.77	3,029.36
Dkk-3	863.26	6,466.27	5,277.86	6,745.95
EDA-A2	813.45	45,352.87	86,934.18	102,337.42
EDAR	578.49	1,715.75	2,752.31	3,558.44
Eotaxin / CCL11	1,498.32	559.22	563.75	583.23
FGF R5	674.85	1,554.38	2,334.15	2,276.60
IGFBP-2	1,230.33	11,164.80	22,591.35	23,988.15
IGFBP-3	1,211.38	4,239.29	5,899.29	7,880.22

IGFBP-rp1 / IGFBP-7	11,808.74	76,254.45	90,204.78	94,029.81
IL-5 R alpha	1,489.12	3,137.10	3,075.82	3,982.92
IL-12 R beta 2	2,022.94	4,457.84	6,617.74	7,987.21
Latent TGF-beta bp1	922.82	4,029.66	7,681.24	6,544.87
LFA-1 alpha	611.51	1,354.79	1,250.51	1,524.15
MIP-3 beta	1,536.22	3,864.34	4,525.98	5,350.64
MMP-1	974.25	46,620.53	53,622.33	38,420.38
MMP-2	890.87	2,317.71	2,954.82	2,737.83
MMP-3	871.92	6,219.51	7,061.18	8,496.31
Nidogen-1	1,167.53	3,590.00	4,048.72	4,497.40
NrCam	1,193.52	2,442.48	3,271.70	3,210.07
Osteoprotegerin / TNFRSF11B	974.25	2,120.02	2,149.40	3,157.01
Progranulin	653.74	1,963.25	2,328.68	1,521.58
Prdx	533.01	1,162.32	1,306.85	1,280.77
Soggy-1	966.13	2,179.15	1,993.02	2,347.68
Sonic Hedgehog (Shh N-terminal)	704.63	1,508.09	1,550.51	1,747.30
SPARC	956.92	8,863.21	8,852.43	14,857.38
Spinesin	743.61	1,736.29	2,210.92	2,700.87
TIMP-1	1,295.84	14,201.02	16,620.57	25,661.55
TIMP-2	820.49	28,405.89	22,696.06	26,642.47
TIMP-3	559.00	1,753.62	2,267.47	2,468.84
TLR2	932.56	1,872.01	2,033.23	2,700.80
2B4	1.16	36.20	9.28	73.02
4-1BB	1.16	44.55	19.13	67.57
A1BG	1.16	114.05	42.87	115.12
A2M	211.47	1,600.89	1,136.95	2,328.91
ADAMTS-10	1,469.89	3,168.98	3,839.53	5,165.18
ADAMTS-19	1.16	50.06	361.51	207.95
ADAMTS-4	1.16	58.51	313.92	161.25
ADAMTS-5	1.16	11.18	286.18	218.20
ADAMTS-L2	1.16	69.63	559.99	726.19
Adipsin	1.16	1,233.42	5,756.54	1,943.35
Aldolase A	1.16	110.96	150.78	104.91
Aldolase B	1.16	33.13	50.87	26.21
Aldolase C	1.16	141.93	81.12	79.57
ALK	1.16	105.42	66.77	96.93
Alpha 1 AG	1.16	162.29	170.43	284.78
Alpha 1 Microglobulin	1.16	306.58	234.13	591.28
ALPP	183.08	513.50	455.35	786.07
ApoB	1.16	22.98	389.11	401.33
ApoD	1.16	270.70	422.17	411.17

ApoE	1.16	98.24	439.38	15.84
ApoE3	1.16	119.91	195.12	22.22
ApoH	1.16	185.87	170.33	65.28
ApoM	1.16	178.23	219.26	187.02
APP	1.16	2,545.55	2,551.79	2,560.93
ASPH	1.16	204.00	204.89	174.64
Attractin	1.16	127.47	150.90	118.11
B3GNT1	1.16	173.58	221.68	198.86
BAF57	1.16	198.59	218.13	216.41
BAFF	1.16	201.77	264.89	252.07
Beta 2M	412.52	2,635.25	3,669.88	3,451.24
Beta IG-H3	643.69	7,717.55	7,511.18	18,306.78
BNP	108.34	229.07	393.92	406.62
C5/C5a	1.16	48.23	291.43	211.11
C8B	2,329.69	18.40	329.57	450.97
C9	3,010.47	359.91	768.15	1,482.85
CA15-3	1.16	255.70	223.13	369.19
CA19-9	1.16	301.47	335.34	153.30
CA125	1.16	313.04	298.27	166.63
Cadherin-13	1.16	314.86	458.31	413.20
Calreticulin	39.98	175.45	256.30	252.87
Calsyntenin-1	1.16	137.85	305.11	182.14
CART	17.96	199.66	269.76	316.66
CD59	989.58	31.08	291.57	391.36
CD74	1.16	478.12	577.33	721.31
CD79 alpha	85.75	386.11	594.13	603.35
CD90	1.16	193.34	326.88	245.74
CEA	48.09	107.86	271.54	324.26
CEACAM-1	1.16	118.58	272.14	350.90
Ceruloplasmin	1.16	62.42	210.45	231.17
CFHR2	1.16	118.91	248.80	305.94
Chemerin	1.16	211.16	499.05	560.39
CHI3L1	97.34	386.78	668.44	1,240.82
COCO	115.88	42.75	434.58	442.03
Complement factor H	1.16	29.70	358.92	357.02
Contactin-2	124.57	389.77	323.82	292.41
CRP	1.16	274.28	622.99	499.57
CRTAM	56.78	126.63	402.34	252.36
CutA	89.22	13.30	291.89	237.14
Cyclin D1	52.72	19.48	338.28	281.74
Cystatin C	13.33	156.76	371.89	435.83
Cytochrome C	1.16	147.29	447.82	533.46
Cytokeratin 8	1.74	186.03	461.25	570.57

EphA2	1.16	148.42	465.87	299.77
EphB4	1.16	170.38	488.75	535.43
Factor XIII A	18,130.02	48,560.06	59,351.02	79,043.79
Factor XIII B	690.04	1,868.35	2,488.59	3,152.99
FAP	1,625.17	129.78	490.19	468.82
Fen 1	45.19	136.69	484.46	581.16
Fetuin B	1.16	200.35	768.38	569.76
Fibrinogen	530.13	9,202.76	13,333.01	21,925.77
Fibrinopeptide A	276.94	692.98	1,348.75	2,031.59
Fibronectin	550.41	18,570.43	28,116.82	41,847.45
Ficolin-3	59.10	626.64	1,014.16	1,362.72
Galectin-7	513.91	1,083.84	1,486.76	2,699.46
gamma-Thrombin	47.51	233.70	586.83	667.71
GATA-4	2.32	54.24	469.00	453.90
Gelsolin	224.22	89.75	544.17	607.43
GMNN	1.16	245.25	695.85	527.85
GPBB	1.16	147.93	713.46	545.19
GPI	1.16	111.65	607.64	405.04
GPX1	281.58	592.73	829.28	926.51
GRP	298.38	938.00	1,120.75	1,747.49
GRP75	1.16	346.33	406.21	766.37
Hemopexin	99.65	246.91	522.14	645.26
HSP20	81.11	168.70	524.19	631.09
HSP27	265.94	954.61	1,434.63	1,441.15
HSP40	214.95	104.23	557.77	696.00
HSP60	213.79	83.41	553.85	708.74
HSP70	2.90	16.42	567.39	716.37
HSP90	145.42	20.96	615.34	588.50
Kallikrein 8	1.16	228.78	520.51	526.08
Kallikrein 10	23.18	244.84	551.24	672.79
Kallikrein 11	1.16	169.94	448.90	517.98
Kallikrein 14	1.16	218.18	482.29	582.76
KCC3	1.16	140.90	534.97	476.73
KCTD10	1.16	156.82	573.66	604.07
KIF3B	1.16	196.27	701.09	894.29
KLF4	67.21	184.46	773.71	1,038.51
LYVE-1	1.16	227.30	497.99	532.83
LZTS1	101.97	221.95	548.54	757.35
Mammaglobin A	1.16	217.39	428.96	742.71
Marapsin	64.31	234.40	378.03	602.72
MATK	39.40	323.89	628.50	759.82
MBL	45.77	332.55	576.16	784.43
MBL-2	151.80	421.26	753.06	1,394.77

Mesothelin	42.87	202.92	629.06	619.08
Neuropeptide Y	85.75	220.99	680.95	540.43
NF1	1.16	175.96	445.36	457.17
Notch-1	1.16	205.31	429.90	455.91
NPTX1	1.16	261.23	430.64	465.00
NPTXR	1.16	215.70	355.49	514.51
NR3C3	1.16	757.02	402.10	431.06
OCT3/4	61.99	297.65	514.87	566.50
PAI-1	20.86	701.04	1,662.47	2,454.59
PGRP-S	23.75	286.05	626.66	877.90
PI 16	1.16	154.88	632.80	830.47
PI 3Kinase p85 beta	37.66	129.52	536.89	590.47
PIM2	1.16	50.27	360.55	363.27
PKM2	1.16	146.93	398.24	551.75
Plasminogen	1.16	1,137.55	3,677.66	3,358.75
Podocalyxin	1.16	189.31	509.40	505.68
PON1	1.16	304.75	492.62	452.95
PON2	1.16	110.61	499.41	690.37
PPARg2	53.30	214.39	683.36	575.00
PPP2R5C	133.26	295.86	929.31	915.39
Pro-Cathepsin B	68.95	299.96	745.63	529.31
Progesterone	1.16	68.74	446.96	353.70
pro-Glucagon	314.60	131.63	689.57	1,104.88
Prohibitin	1.16	84.54	303.03	379.16
Pro-MMP-7	1.16	110.58	328.87	359.80
ProSAAS	121.09	306.45	617.31	523.80
PSP	1.16	125.16	455.47	589.44
PTH	1.16	533.71	845.09	2,143.04
PTHLP	7,014.00	30,003.94	25,623.63	43,869.68
PTN	1.16	815.10	1,204.22	1,688.76
PYK2	1.16	122.90	485.82	801.01
PYY	165.12	386.93	1,005.10	1,993.06
Ras	66.63	3,697.36	8,124.49	14,353.17
RBP4	1.16	195.55	747.93	748.67
RECK	1.16	240.27	647.48	692.97
Resistin	1.16	125.17	600.75	581.38
RET	1.16	232.98	735.07	651.36
RIP1	1.16	115.00	672.18	355.42
ROR2	51.56	250.44	510.09	265.49
ROS	34.18	272.58	805.13	692.06
S100A4	25.49	106.27	548.25	557.05
S100A6	1.16	167.09	655.29	755.59
S100A8	1.16	63.15	530.90	625.94

S-100b	19.70	66.68	358.95	481.14
SCG3	35.92	135.93	542.17	474.98
Serpin A3	310.55	932.66	1,181.20	1,906.23
Serpin A4	1.16	119.99	622.57	642.78
Serpin A5	1.16	55.56	559.85	669.43
Serpin A9	1.16	19.85	496.21	526.73
Serpin A12	1.16	125.63	589.49	761.49
Serpin B5	1.16	66.45	466.03	420.79
Serpin D1	1.16	11.46	434.52	239.48
Serpin I1	1.16	6.19	510.88	365.53
SERTAD2	1.16	85.84	597.65	580.78
SHBG	1.16	128.57	859.98	562.89
SMAC	1.16	20.76	700.13	268.20
SPINK1	1.16	60.57	476.02	478.31
SSEA-1	1.16	125.19	629.99	603.41
SSEA-4	97.34	347.22	543.72	617.26
SSTR5	1.16	238.95	761.82	622.90
Syndecan-3	39.98	90.24	807.73	969.06
TAF4	1.16	32.94	647.13	518.04
TFF3	1.16	117.74	548.67	788.19
Thrombin	1.16	131.45	560.74	492.24
Thrombomodulin	1.16	108.75	488.74	359.09
Thymidine Kinase-1	1.16	84.36	529.55	418.31
Thyroglobulin	1.16	629.61	570.80	376.26
TIM-1	1.16	134.86	564.46	450.91
TOPORS	1.16	156.34	667.07	423.96
TPA	1.16	158.32	707.80	364.07
TPM1	1.16	167.65	783.88	407.91
Trappin-2	48.67	120.79	542.44	524.63
TSLP	127.46	294.62	1,419.29	678.46
Tyk2	58.52	176.40	951.65	589.09
TYRO10	45.19	226.37	849.45	756.23
Vasopressin	1.16	141.88	670.52	460.77
VDUP-1	16.80	163.28	906.36	600.84
VEGF R1	1.16	144.03	609.10	429.33
VGF	1.16	71.98	563.05	315.72
VIP Receptor 2	1.16	127.08	609.75	265.00
Visfatin	1.16	175.82	825.67	463.03
Vitamin D-BP	88.07	201.02	629.39	212.06
Vitamin K-dependent protein S	1.16	188.38	488.99	279.33

[0141] Table 2 shows that a total of 231/616 (37.5%) of the proteins identified as Biologically Significant relative to Control were shared across all three (3) ethnic groups. The remaining 385/616 (62.5%) proteins demonstrated Biologically Significance in 2 or fewer of the sample groups.

[0142] Table 3 is a comparison of average production levels of the Asian (As) samples compared to African (Af) samples in the 231 shared, biologically significant proteins. Using the criteria of ≥ 25% increase/decrease in relative production levels as described in the protocol, Asian sample proteins were assessed as increased (one asterisk, "*") or decreased production (three asterisks, "***") than African samples.

TABLE 3

	CONTROL	AS Average	AF Average
BCMA / TNFRSF17	1.08	67.49***	208.10***
BAX	90.68	552.02*	357.12*
beta-NGF	199.51	358.85***	478.62***
CCL14 / HCC-1 / HCC-3	482.66	74.14***	187.07***
CCR5	71.19	143.29***	192.98***
CD30 / TNFRSF8	111.26	272.19***	446.20***
CV-2 / Crossveinless-2	108.01	18.99***	450.71***
CXCL16	44.67	293.17	389.68
D6	216.83	435.25***	652.24***
DAN	686.77	1,597.31***	2,464.56***
Decorin	461.00	1,900.72***	4,089.23***
Dkk-1	609.89	2,836.46	3,118.77
Dkk-3	863.26	6,466.27	5,277.86
EDA-A2	813.45	45,352.87***	86,934.18***
EDAR	578.49	1,715.75***	2,752.31***
Eotaxin / CCL11	1,498.32	559.22	563.75
FGF R5	674.85	1,554.38***	2,334.15***
IGFBP-2	1,230.33	11,164.80***	22,591.35***
IGFBP-3	1,211.38	4,239.29***	5,899.29***
IGFBP-rp1 / IGFBP-7	11,808.74	76,254.45	90,204.78
IL-5 R alpha	1,489.12	3,137.10	3,075.82
IL-12 R beta 2	2,022.94	4,457.84***	6,617.74***

Latent TGF-beta bp1	922.82	4,029.66***	7,681.24***
LFA-1 alpha	611.51	1,354.79	1,250.51
MIP-3 beta	1,536.22	3,864.34	4,525.98
MMP-1	974.25	46,620.53	53,622.33
MMP-2	890.87	2,317.71	2,954.82
MMP-3	871.92	6,219.51	7,061.18
Nidogen-1	1,167.53	3,590.00	4,048.72
NrCam	1,193.52	2,442.48***	3,271.70***
Osteoprotegerin / TNFRSF11B	974.25	2,120.02	2,149.40
Progranulin	653.74	1,963.25	2,328.68
Prdx	533.01	1,162.32	1,306.85
Soggy-1	966.13	2,179.15	1,993.02
Sonic Hedgehog (Shh N-terminal)	704.63	1,508.09	1,550.51
SPARC	956.92	8,863.21	8,852.43
Spinesin	743.61	1,736.29	2,210.92
TIMP-1	1,295.84	14,201.02	16,620.57
TIMP-2	820.49	28,405.89*	22,696.06*
TIMP-3	559.00	1,753.62	2,267.47
TLR2	932.56	1,872.01	2,033.23
2B4	1.16	36.20*	9.28*
4-1BB	1.16	44.55*	19.13*
A1BG	1.16	114.05*	42.87*
A2M	211.47	1,600.89*	1,136.95*
ADAMTS-10	1,469.89	3,168.98	3,839.53
ADAMTS-19	1.16	50.06***	361.51***
ADAMTS-4	1.16	58.51***	313.92***
ADAMTS-5	1.16	11.18***	286.18***
ADAMTS-L2	1.16	69.63***	559.99***
Adipsin	1.16	1,233.42***	5,756.54***
Aldolase A	1.16	110.96	150.78
Aldolase B	1.16	33.13***	50.87***
Aldolase C	1.16	141.93*	81.12*
ALK	1.16	105.42*	66.77*
Alpha 1 AG	1.16	162.29	170.43
Alpha 1 Microglobulin	1.16	306.58*	234.13*
ALPP	183.08	513.50	455.35
ApoB	1.16	22.98***	389.11***
ApoD	1.16	270.70***	422.17***
ApoE	1.16	98.24***	439.38***
ApoE3	1.16	119.91***	195.12***
ApoH	1.16	185.87	170.33

ApoM	1.16	178.23	219.26
APP	1.16	2,545.55	2,551.79
ASPH	1.16	204.00	204.89
Attractin	1.16	127.47	150.90
B3GNT1	1.16	173.58	221.68
BAF57	1.16	198.59	218.13
BAFF	1.16	201.77	264.89
Beta 2M	412.52	2,635.25***	3,669.88***
Beta IG-H3	643.69	7,717.55	7,511.18
BNP	108.34	229.07***	393.92***
C5/C5a	1.16	48.23***	291.43***
C8B	2,329.69	18.40***	329.57***
C9	3,010.47	359.91***	768.15***
CA15-3	1.16	255.70	223.13
CA19-9	1.16	301.47	335.34
CA125	1.16	313.04	298.27
Cadherin-13	1.16	314.86***	458.31***
Calreticulin	39.98	175.45***	256.30***
Calsyntenin-1	1.16	137.85***	305.11***
CART	17.96	199.66***	269.76***
CD59	989.58	31.08***	291.57***
CD74	1.16	478.12	577.33
CD79 alpha	85.75	386.11***	594.13***
CD90	1.16	193.34***	326.88***
CEA	48.09	107.86***	271.54***
CEACAM-1	1.16	118.58***	272.14***
Ceruloplasmin	1.16	62.42***	210.45***
CFHR2	1.16	118.91***	248.80***
Chemerin	1.16	211.16***	499.05***
CHI3L1	97.34	386.78***	668.44***
COCO	115.88	42.75***	434.58***
Complement factor H	1.16	29.70***	358.92***
Contactin-2	124.57	389.77	323.82
CRP	1.16	274.28***	622.99***
CRTAM	56.78	126.63***	402.34***
CutA	89.22	13.30***	291.89***
Cyclin D1	52.72	19.48***	338.28***
Cystatin C	13.33	156.76***	371.89***
Cytochrome C	1.16	147.29***	447.82***
Cytokeratin 8	1.74	186.03***	461.25***
EphA2	1.16	148.42***	465.87***
EphB4	1.16	170.38***	488.75***
Factor XIII A	18,130.02	48,560.06	59,351.02

Factor XIII B	690.04	1,868.35	2,488.59
FAP	1,625.17	129.78***	490.19***
Fen 1	45.19	136.69***	484.46***
Fetuin B	1.16	200.35***	768.38***
Fibrinogen	530.13	9,202.76***	13,333.01***
Fibrinopeptide A	276.94	692.98***	1,348.75***
Fibronectin	550.41	18,570.43***	28,116.82***
Ficolin-3	59.10	626.64***	1,014.16***
Galectin-7	513.91	1,083.84***	1,486.76***
gamma-Thrombin	47.51	233.70***	586.83***
GATA-4	2.32	54.24***	469.00***
Gelsolin	224.22	89.75***	544.17***
GMNN	1.16	245.25***	695.85***
GPBB	1.16	147.93***	713.46***
GPI	1.16	111.65***	607.64***
GPX1	281.58	592.73***	829.28***
GRP	298.38	938.00	1,120.75
GRP75	1.16	346.33	406.21
Hemopexin	99.65	246.91***	522.14***
HSP20	81.11	168.70***	524.19***
HSP27	265.94	954.61***	1,434.63***
HSP40	214.95	104.23***	557.77***
HSP60	213.79	83.41***	553.85***
HSP70	2.90	16.42***	567.39***
HSP90	145.42	20.96***	615.34***
Kallikrein 8	1.16	228.78***	520.51***
Kallikrein 10	23.18	244.84***	551.24***
Kallikrein 11	1.16	169.94***	448.90***
Kallikrein 14	1.16	218.18***	482.29***
KCC3	1.16	140.90***	534.97***
KCTD10	1.16	156.82***	573.66***
KIF3B	1.16	196.27***	701.09***
KLF4	67.21	184.46***	773.71***
LYVE-1	1.16	227.30***	497.99***
LZTS1	101.97	221.95***	548.54***
Mammaglobin A	1.16	217.39***	428.96***
Marapsin	64.31	234.40***	378.03***
MATK	39.40	323.89***	628.50***
MBL	45.77	332.55***	576.16***
MBL-2	151.80	421.26***	753.06***
Mesothelin	42.87	202.92***	629.06***
Neuropeptide Y	85.75	220.99***	680.95***
NF1	1.16	175.96***	445.36***

Notch-1	1.16	205.31***	429.90***
NPTX1	1.16	261.23***	430.64***
NPTXR	1.16	215.70***	355.49***
NR3C3	1.16	757.02*	402.10*
OCT3/4	61.99	297.65***	514.87***
PAI-1	20.86	701.04***	1,662.47***
PGRP-S	23.75	286.05***	626.66***
PI 16	1.16	154.88***	632.80***
PI 3Kinase p85 beta	37.66	129.52***	536.89***
PIM2	1.16	50.27***	360.55***
PKM2	1.16	146.93***	398.24***
Plasminogen	1.16	1,137.55***	3,677.66***
Podocalyxin	1.16	189.31***	509.40***
PON1	1.16	304.75***	492.62***
PON2	1.16	110.61***	499.41***
PPARg2	53.30	214.39***	683.36***
PPP2R5C	133.26	295.86***	929.31***
Pro-Cathepsin B	68.95	299.96***	745.63***
Progesterone	1.16	68.74***	446.96***
pro-Glucagon	314.60	131.63***	689.57***
Prohibitin	1.16	84.54***	303.03***
Pro-MMP-7	1.16	110.58***	328.87***
ProSAAS	121.09	306.45***	617.31***
PSP	1.16	125.16***	455.47***
PTH	1.16	533.71***	845.09***
PTHLP	7,014.00	30,003.94	25,623.63
PTN	1.16	815.10***	1,204.22***
PYK2	1.16	122.90***	485.82***
PYY	165.12	386.93***	1,005.10***
Ras	66.63	3,697.36***	8,124.49***
RBP4	1.16	195.55***	747.93***
RECK	1.16	240.27***	647.48***
Resistin	1.16	125.17***	600.75***
RET	1.16	232.98***	735.07***
RIP1	1.16	115.00***	672.18***
ROR2	51.56	250.44***	510.09***
ROS	34.18	272.58***	805.13***
S100A4	25.49	106.27***	548.25***
S100A6	1.16	167.09***	655.29***
S100A8	1.16	63.15***	530.90***
S-100b	19.70	66.68***	358.95***
SCG3	35.92	135.93***	542.17***
Serpin A3	310.55	932.66	1,181.20

Serpin A4	1.16	119.99***	622.57***
Serpin A5	1.16	55.56***	559.85***
Serpin A9	1.16	19.85***	496.21***
Serpin A12	1.16	125.63***	589.49***
Serpin B5	1.16	66.45***	466.03***
Serpin D1	1.16	11.46***	434.52***
Serpin I1	1.16	6.19***	510.88***
SERTAD2	1.16	85.84***	597.65***
SHBG	1.16	128.57***	859.98***
SMAC	1.16	20.76***	700.13***
SPINK1	1.16	60.57***	476.02***
SSEA-1	1.16	125.19***	629.99***
SSEA-4	97.34	347.22***	543.72***
SSTR5	1.16	238.95***	761.82***
Syndecan-3	39.98	90.24***	807.73***
TAF4	1.16	32.94***	647.13***
TFF3	1.16	117.74***	548.67***
Thrombin	1.16	131.45***	560.74***
Thrombomodulin	1.16	108.75***	488.74***
Thymidine Kinase-1	1.16	84.36***	529.55***
Thyroglobulin	1.16	629.61	570.80
TIM-1	1.16	134.86***	564.46***
TOPORS	1.16	156.34***	667.07***
TPA	1.16	158.32***	707.80***
TPM1	1.16	167.65***	783.88***
Trappin-2	48.67	120.79***	542.44***
TSLP	127.46	294.62***	1,419.29***
Tyk2	58.52	176.40***	951.65***
TYRO10	45.19	226.37***	849.45***
Vasopressin	1.16	141.88***	670.52***
VDUP-1	16.80	163.28***	906.36***
VEGF R1	1.16	144.03***	609.10***
VGF	1.16	71.98***	563.05***
VIP Receptor 2	1.16	127.08***	609.75***
Visfatin	1.16	175.82***	825.67***
Vitamin D-BP	88.07	201.02***	629.39***
Vitamin K-dependent protein S	1.16	188.38***	488.99***

[0143] Table 3 shows that Asian samples relative to African samples demonstrated 25% difference in production levels in 183/231 (78%) of the compared proteins. Of those,

only 10/182 (5%) demonstrated increase production levels relative to African samples. The remaining 172/182 (95%) demonstrated decreased production levels relative to African samples.

[0144] Table 4 is a comparison of average production levels of the Caucasian (Ca) samples compared to African (Af) samples in the 231 shared, biologically significant proteins. Using the criteria of ≥ 25% increase/decrease in relative production levels as described in the protocol, Caucasian (Ca) sample proteins were assessed as increased (one asterisk, "*") or decreased production (three asterisks, "***") than African samples.

TABLE 4

	CONTROL	AF Average	CA Average
BCMA / TNFRSF17	1.08	208.10	194.35
BAX	90.68	357.12*	759.17*
beta-NGF	199.51	478.62*	897.43*
CCL14 / HCC-1 / HCC-3	482.66	187.07*	236.13*
CCR5	71.19	192.98*	313.52*
CD30 / TNFRSF8	111.26	446.20	489.25
CV-2 / Crossveinless-2	108.01	450.71***	45.32***
CXCL16	44.67	389.68	380.72
D6	216.83	652.24***	453.43***
DAN	686.77	2,464.56	2,888.04
Decorin	461.00	4,089.23	3,161.92
Dkk-1	609.89	3,118.77	3,029.36
Dkk-3	863.26	5,277.86*	6,745.95*
EDA-A2	813.45	86,934.18	102,337.42
EDAR	578.49	2,752.31*	3,558.44*
Eotaxin / CCL11	1,498.32	563.75	583.23
FGF R5	674.85	2,334.15	2,276.60
IGFBP-2	1,230.33	22,591.35	23,988.15
IGFBP-3	1,211.38	5,899.29*	7,880.22*
IGFBP-rp1 / IGFBP-7	11,808.74	90,204.78	94,029.81
IL-5 R alpha	1,489.12	3,075.82*	3,982.92*
IL-12 R beta 2	2,022.94	6,617.74	7,987.21
Latent TGF-beta bp1	922.82	7,681.24	6,544.87

LFA-1 alpha	611.51	1,250.51	1,524.15
MIP-3 beta	1,536.22	4,525.98	5,350.64
MMP-1	974.25	53,622.33***	38,420.38***
MMP-2	890.87	2,954.82	2,737.83
MMP-3	871.92	7,061.18	8,496.31
Nidogen-1	1,167.53	4,048.72	4,497.40
NrCam	1,193.52	3,271.70	3,210.07
Osteoprotegerin / TNFRSF11B	974.25	2,149.40*	3,157.01*
Progranulin	653.74	2,328.68***	1,521.58***
Prdx	533.01	1,306.85	1,280.77
Soggy-1	966.13	1,993.02	2,347.68
Sonic Hedgehog (Shh N-terminal)	704.63	1,550.51	1,747.30
SPARC	956.92	8,852.43*	14,857.38*
Spinesin	743.61	2,210.92	2,700.87
TIMP-1	1,295.84	16,620.57*	25,661.55*
TIMP-2	820.49	22,696.06	26,642.47
TIMP-3	559.00	2,267.47	2,468.84
TLR2	932.56	2,033.23*	2,700.80*
2B4	1.16	9.28*	73.02*
4-1BB	1.16	19.13*	67.57*
A1BG	1.16	42.87*	115.12*
A2M	211.47	1,136.95*	2,328.91*
ADAMTS-10	1,469.89	3,839.53*	5,165.18*
ADAMTS-19	1.16	361.51***	207.95***
ADAMTS-4	1.16	313.92***	161.25***
ADAMTS-5	1.16	286.18	218.20
ADAMTS-L2	1.16	559.99*	726.19*
Adipsin	1.16	5,756.54***	1,943.35***
Aldolase A	1.16	150.78	104.91
Aldolase B	1.16	50.87***	26.21***
Aldolase C	1.16	81.12	79.57
ALK	1.16	66.77*	96.93*
Alpha 1 AG	1.16	170.43*	284.78*
Alpha 1 Microglobulin	1.16	234.13*	591.28*
ALPP	183.08	455.35*	786.07*
ApoB	1.16	389.11	401.33
ApoD	1.16	422.17	411.17
ApoE	1.16	439.38***	15.84***
ApoE3	1.16	195.12***	22.22***
ApoH	1.16	170.33***	65.28***

ApoM	1.16	219.26	187.02
APP	1.16	2,551.79	2,560.93
ASPH	1.16	204.89	174.64
Attractin	1.16	150.90	118.11
B3GNT1	1.16	221.68	198.86
BAF57	1.16	218.13	216.41
BAFF	1.16	264.89	252.07
Beta 2M	412.52	3,669.88	3,451.24
Beta IG-H3	643.69	7,511.18*	18,306.78*
BNP	108.34	393.92	406.62
C5/C5a	1.16	291.43	211.11
C8B	2,329.69	329.57*	450.97*
C9	3,010.47	768.15*	1,482.85*
CA15-3	1.16	223.13*	369.19*
CA19-9	1.16	335.34***	153.30***
CA125	1.16	298.27***	166.63***
Cadherin-13	1.16	458.31	413.20
Calreticulin	39.98	256.30	252.87
Calsyntenin-1	1.16	305.11***	182.14***
CART	17.96	269.76	316.66
CD59	989.58	291.57*	391.36*
CD74	1.16	577.33	721.31
CD79 alpha	85.75	594.13	603.35
CD90	1.16	326.88	245.74
CEA	48.09	271.54	324.26
CEACAM-1	1.16	272.14*	350.90*
Ceruloplasmin	1.16	210.45	231.17
CFHR2	1.16	248.80	305.94
Chemerin	1.16	499.05	560.39
CHI3L1	97.34	668.44*	1,240.82*
COCO	115.88	434.58	442.03
Complement factor H	1.16	358.92	357.02
Contactin-2	124.57	323.82	292.41
CRP	1.16	622.99	499.57
CRTAM	56.78	402.34***	252.36***
CutA	89.22	291.89	237.14
Cyclin D1	52.72	338.28	281.74
Cystatin C	13.33	371.89	435.83
Cytochrome C	1.16	447.82	533.46
Cytokeratin 8	1.74	461.25	570.57
EphA2	1.16	465.87***	299.77***
EphB4	1.16	488.75	535.43

Factor XIII A	18,130.02	59,351.02*	79,043.79*
Factor XIII B	690.04	2,488.59*	3,152.99*
FAP	1,625.17	490.19	468.82
Fen 1	45.19	484.46	581.16
Fetuin B	1.16	768.38***	569.76***
Fibrinogen	530.13	13,333.01*	21,925.77*
Fibrinopeptide A	276.94	1,348.75*	2,031.59*
Fibronectin	550.41	28,116.82*	41,847.45*
Ficolin-3	59.10	1,014.16*	1,362.72*
Galectin-7	513.91	1,486.76*	2,699.46*
gamma-Thrombin	47.51	586.83	667.71
GATA-4	2.32	469.00	453.90
Gelsolin	224.22	544.17	607.43
GMNN	1.16	695.85	527.85
GPBB	1.16	713.46	545.19
GPI	1.16	607.64***	405.04***
GPX1	281.58	829.28	926.51
GRP	298.38	1,120.75*	1,747.49*
GRP75	1.16	406.21*	766.37*
Hemopexin	99.65	522.14	645.26
HSP20	81.11	524.19	631.09
HSP27	265.94	1,434.63	1,441.15
HSP40	214.95	557.77	696.00
HSP60	213.79	553.85*	708.74*
HSP70	2.90	567.39*	716.37*
HSP90	145.42	615.34	588.50
Kallikrein 8	1.16	520.51	526.08
Kallikrein 10	23.18	551.24	672.79
Kallikrein 11	1.16	448.90	517.98
Kallikrein 14	1.16	482.29	582.76
KCC3	1.16	534.97	476.73
KCTD10	1.16	573.66	604.07
KIF3B	1.16	701.09*	894.29*
KLF4	67.21	773.71*	1,038.51*
LYVE-1	1.16	497.99	532.83
LZTS1	101.97	548.54*	757.35*
Mammaglobin A	1.16	428.96*	742.71*
Marapsin	64.31	378.03*	602.72*
MATK	39.40	628.50	759.82
MBL	45.77	576.16*	784.43*
MBL-2	151.80	753.06*	1,394.77*
Mesothelin	42.87	629.06	619.08
Neuropeptide Y	85.75	680.95	540.43

NF1	1.16	445.36	457.17
Notch-1	1.16	429.90	455.91
NPTX1	1.16	430.64	465.00
NPTXR	1.16	355.49*	514.51*
NR3C3	1.16	402.10	431.06
OCT3/4	61.99	514.87	566.50
PAI-1	20.86	1,662.47*	2,454.59*
PGRP-S	23.75	626.66*	877.90*
PI 16	1.16	632.80*	830.47*
PI 3Kinase p85 beta	37.66	536.89	590.47
PIM2	1.16	360.55	363.27
PKM2	1.16	398.24*	551.75*
Plasminogen	1.16	3,677.66	3,358.75
Podocalyxin	1.16	509.40	505.68
PON1	1.16	492.62	452.95
PON2	1.16	499.41*	690.37*
PPARg2	53.30	683.36	575.00
PPP2R5C	133.26	929.31	915.39
Pro-Cathepsin B	68.95	745.63***	529.31***
Progesterone	1.16	446.96	353.70
pro-Glucagon	314.60	689.57*	1,104.88*
Prohibitin	1.16	303.03	379.16
Pro-MMP-7	1.16	328.87	359.80
ProSAAS	121.09	617.31	523.80
PSP	1.16	455.47*	589.44*
PTH	1.16	845.09*	2,143.04*
PTHLP	7,014.00	25,623.63*	43,869.68*
PTN	1.16	1,204.22*	1,688.76*
PYK2	1.16	485.82*	801.01*
PYY	165.12	1,005.10*	1,993.06*
Ras	66.63	8,124.49*	14,353.17*
RBP4	1.16	747.93	748.67
RECK	1.16	647.48	692.97
Resistin	1.16	600.75	581.38
RET	1.16	735.07	651.36
RIP1	1.16	672.18***	355.42***
ROR2	51.56	510.09***	265.49***
ROS	34.18	805.13	692.06
S100A4	25.49	548.25	557.05
S100A6	1.16	655.29	755.59
S100A8	1.16	530.90	625.94
S-100b	19.70	358.95	481.14
SCG3	35.92	542.17	474.98

Serpin A3	310.55	1,181.20*	1,906.23*
Serpin A4	1.16	622.57	642.78
Serpin A5	1.16	559.85	669.43
Serpin A9	1.16	496.21	526.73
Serpin A12	1.16	589.49*	761.49*
Serpin B5	1.16	466.03	420.79
Serpin D1	1.16	434.52***	239.48***
Serpin I1	1.16	510.88***	365.53***
SERTAD2	1.16	597.65	580.78
SHBG	1.16	859.98***	562.89***
SMAC	1.16	700.13***	268.20***
SPINK1	1.16	476.02	478.31
SSEA-1	1.16	629.99	603.41
SSEA-4	97.34	543.72	617.26
SSTR5	1.16	761.82	622.90
Syndecan-3	39.98	807.73	969.06
TAF4	1.16	647.13	518.04
TFF3	1.16	548.67*	788.19*
Thrombin	1.16	560.74	492.24
Thrombomodulin	1.16	488.74***	359.09***
Thymidine Kinase-1	1.16	529.55	418.31
Thyroglobulin	1.16	570.80***	376.26***
TIM-1	1.16	564.46	450.91
TOPORS	1.16	667.07***	423.96***
TPA	1.16	707.80***	364.07***
TPM1	1.16	783.88***	407.91***
Trappin-2	48.67	542.44	524.63
TSLP	127.46	1,419.29***	678.46***
Tyk2	58.52	951.65***	589.09***
TYRO10	45.19	849.45	756.23
Vasopressin	1.16	670.52***	460.77***
VDUP-1	16.80	906.36***	600.84***
VEGF R1	1.16	609.10***	429.33***
VGF	1.16	563.05***	315.72***
VIP Receptor 2	1.16	609.75***	265.00***
Visfatin	1.16	825.67***	463.03***
Vitamin D-BP	88.07	629.39***	212.06***
Vitamin K-dependent protein S	1.16	488.99***	279.33***

[0145] Table 4 shows that Caucasian samples relative to African samples demonstrated 25% difference in production levels in 104/231 (45%) of the compared

proteins. Of those, only 64/104 (62%) demonstrated increase production levels relative to African samples. The remaining 40/104 (38%) demonstrated decreased production levels relative to African samples.

[0146] Table 5 is a comparison of average production levels of the Caucasian (Ca) samples compared to Asian (As) samples in the 231 shared, biologically significant proteins. Using the criteria of ≥ 25% increase/decrease in relative production levels as described in the protocol, Caucasian (Ca) sample proteins were assessed as increased (one asterisk, "*") or decreased production (three asterisks, "***") than African samples.

TABLE 5

	CONTROL	AS Average	CA Average
BCMA / TNFRSF17	1.08	67.49*	194.35*
BAX	90.68	552.02*	759.17*
beta-NGF	199.51	358.85*	897.43*
CCL14 / HCC-1 / HCC-3	482.66	74.14*	236.13*
CCR5	71.19	143.29*	313.52*
CD30 / TNFRSF8	111.26	272.19*	489.25*
CV-2 / Crossveinless-2	108.01	18.99*	45.32*
CXCL16	44.67	293.17*	380.72*
D6	216.83	435.25	453.43
DAN	686.77	1,597.31*	2,888.04*
Decorin	461.00	1,900.72*	3,161.92*
Dkk-1	609.89	2,836.46	3,029.36
Dkk-3	863.26	6,466.27	6,745.95
EDA-A2	813.45	45,352.87*	102,337.42*
EDAR	578.49	1,715.75*	3,558.44*
Eotaxin / CCL11	1,498.32	559.22	583.23
FGF R5	674.85	1,554.38*	2,276.60*
IGFBP-2	1,230.33	11,164.80*	23,988.15*
IGFBP-3	1,211.38	4,239.29*	7,880.22*
IGFBP-rp1 / IGFBP-7	11,808.74	76,254.45	94,029.81
IL-5 R alpha	1,489.12	3,137.10*	3,982.92*
IL-12 R beta 2	2,022.94	4,457.84*	7,987.21*
Latent TGF-beta bp1	922.82	4,029.66*	6,544.87*

LFA-1 alpha	611.51	1,354.79	1,524.15
MIP-3 beta	1,536.22	3,864.34*	5,350.64*
MMP-1	974.25	46,620.53	38,420.38
MMP-2	890.87	2,317.71	2,737.83
MMP-3	871.92	6,219.51*	8,496.31*
Nidogen-1	1,167.53	3,590.00*	4,497.40*
NrCam	1,193.52	2,442.48*	3,210.07*
Osteoprotegerin / TNFRSF11B	974.25	2,120.02*	3,157.01*
Progranulin	653.74	1,963.25	1,521.58
Prdx	533.01	1,162.32	1,280.77
Soggy-1	966.13	2,179.15	2,347.68
Sonic Hedgehog (Shh N-terminal)	704.63	1,508.09	1,747.30
SPARC	956.92	8,863.21*	14,857.38*
Spinesin	743.61	1,736.29*	2,700.87*
TIMP-1	1,295.84	14,201.02*	25,661.55*
TIMP-2	820.49	28,405.89	26,642.47
TIMP-3	559.00	1,753.62*	2,468.84*
TLR2	932.56	1,872.01*	2,700.80*
2B4	1.16	36.20*	73.02*
4-1BB	1.16	44.55*	67.57*
A1BG	1.16	114.05	115.12
A2M	211.47	1,600.89*	2,328.91*
ADAMTS-10	1,469.89	3,168.98*	5,165.18*
ADAMTS-19	1.16	50.06*	207.95*
ADAMTS-4	1.16	58.51*	161.25*
ADAMTS-5	1.16	11.18*	218.20*
ADAMTS-L2	1.16	69.63*	726.19*
Adipsin	1.16	1,233.42*	1,943.35*
Aldolase A	1.16	110.96	104.91
Aldolase B	1.16	33.13	26.21
Aldolase C	1.16	141.93***	79.57***
ALK	1.16	105.42	96.93
Alpha 1 AG	1.16	162.29*	284.78*
Alpha 1 Microglobulin	1.16	306.58*	591.28*
ALPP	183.08	513.50*	786.07*
ApoB	1.16	22.98*	401.33*
ApoD	1.16	270.70*	411.17*
ApoE	1.16	98.24***	15.84***
ApoE3	1.16	119.91***	22.22***
ApoH	1.16	185.87***	65.28***

ApoM	1.16	178.23	187.02
APP	1.16	2,545.55	2,560.93
ASPH	1.16	204.00	174.64
Attractin	1.16	127.47	118.11
B3GNT1	1.16	173.58	198.86
BAF57	1.16	198.59	216.41
BAFF	1.16	201.77	252.07
Beta 2M	412.52	2,635.25*	3,451.24*
Beta IG-H3	643.69	7,717.55*	18,306.78*
BNP	108.34	229.07*	406.62*
C5/C5a	1.16	48.23*	211.11*
C8B	2,329.69	18.40*	450.97*
C9	3,010.47	359.91*	1,482.85*
CA15-3	1.16	255.70*	369.19*
CA19-9	1.16	301.47***	153.30***
CA125	1.16	313.04***	166.63***
Cadherin-13	1.16	314.86*	413.20*
Calreticulin	39.98	175.45*	252.87*
Calsyntenin-1	1.16	137.85*	182.14*
CART	17.96	199.66*	316.66*
CD59	989.58	31.08*	391.36*
CD74	1.16	478.12*	721.31*
CD79 alpha	85.75	386.11*	603.35*
CD90	1.16	193.34*	245.74*
CEA	48.09	107.86*	324.26*
CEACAM-1	1.16	118.58*	350.90*
Ceruloplasmin	1.16	62.42*	231.17*
CFHR2	1.16	118.91*	305.94*
Chemerin	1.16	211.16*	560.39*
CHI3L1	97.34	386.78*	1,240.82*
COCO	115.88	42.75*	442.03*
Complement factor H	1.16	29.70*	357.02*
Contactin-2	124.57	389.77	292.41
CRP	1.16	274.28*	499.57*
CRTAM	56.78	126.63*	252.36*
CutA	89.22	13.30*	237.14*
Cyclin D1	52.72	19.48*	281.74*
Cystatin C	13.33	156.76*	435.83*
Cytochrome C	1.16	147.29*	533.46*
Cytokeratin 8	1.74	186.03*	570.57*
EphA2	1.16	148.42*	299.77*
EphB4	1.16	170.38*	535.43*
Factor XIII A	18,130.02	48,560.06*	79,043.79*

Factor XIII B	690.04	1,868.35*	3,152.99*
FAP	1,625.17	129.78*	468.82*
Fen 1	45.19	136.69*	581.16*
Fetuin B	1.16	200.35*	569.76*
Fibrinogen	530.13	9,202.76*	21,925.77*
Fibrinopeptide A	276.94	692.98*	2,031.59*
Fibronectin	550.41	18,570.43*	41,847.45*
Ficolin-3	59.10	626.64*	1,362.72*
Galectin-7	513.91	1,083.84*	2,699.46*
gamma-Thrombin	47.51	233.70*	667.71*
GATA-4	2.32	54.24*	453.90*
Gelsolin	224.22	89.75*	607.43*
GMNN	1.16	245.25*	527.85*
GPBB	1.16	147.93*	545.19*
GPI	1.16	111.65*	405.04*
GPX1	281.58	592.73*	926.51*
GRP	298.38	938.00*	1,747.49*
GRP75	1.16	346.33*	766.37*
Hemopexin	99.65	246.91*	645.26*
HSP20	81.11	168.70*	631.09*
HSP27	265.94	954.61*	1,441.15*
HSP40	214.95	104.23*	696.00*
HSP60	213.79	83.41*	708.74*
HSP70	2.90	16.42*	716.37*
HSP90	145.42	20.96*	588.50*
Kallikrein 8	1.16	228.78*	526.08*
Kallikrein 10	23.18	244.84*	672.79*
Kallikrein 11	1.16	169.94*	517.98*
Kallikrein 14	1.16	218.18*	582.76*
KCC3	1.16	140.90*	476.73*
KCTD10	1.16	156.82*	604.07*
KIF3B	1.16	196.27*	894.29*
KLF4	67.21	184.46*	1,038.51*
LYVE-1	1.16	227.30*	532.83*
LZTS1	101.97	221.95*	757.35*
Mammaglobin A	1.16	217.39*	742.71*
Marapsin	64.31	234.40*	602.72*
MATK	39.40	323.89*	759.82*
MBL	45.77	332.55*	784.43*
MBL-2	151.80	421.26*	1,394.77*
Mesothelin	42.87	202.92*	619.08*
Neuropeptide Y	85.75	220.99*	540.43*
NF1	1.16	175.96*	457.17*

Notch-1	1.16	205.31*	455.91*
NPTX1	1.16	261.23*	465.00*
NPTXR	1.16	215.70*	514.51*
NR3C3	1.16	757.02***	431.06***
OCT3/4	61.99	297.65*	566.50*
PAI-1	20.86	701.04*	2,454.59*
PGRP-S	23.75	286.05*	877.90*
PI 16	1.16	154.88*	830.47*
PI 3Kinase p85 beta	37.66	129.52*	590.47*
PIM2	1.16	50.27*	363.27*
PKM2	1.16	146.93*	551.75*
Plasminogen	1.16	1,137.55*	3,358.75*
Podocalyxin	1.16	189.31*	505.68*
PON1	1.16	304.75*	452.95*
PON2	1.16	110.61*	690.37*
PPARg2	53.30	214.39*	575.00*
PPP2R5C	133.26	295.86*	915.39*
Pro-Cathepsin B	68.95	299.96*	529.31*
Progesterone	1.16	68.74*	353.70*
pro-Glucagon	314.60	131.63*	1,104.88*
Prohibitin	1.16	84.54*	379.16*
Pro-MMP-7	1.16	110.58*	359.80*
ProSAAS	121.09	306.45*	523.80*
PSP	1.16	125.16*	589.44*
PTH	1.16	533.71*	2,143.04*
PTHLP	7,014.00	30,003.94*	43,869.68*
PTN	1.16	815.10*	1,688.76*
PYK2	1.16	122.90*	801.01*
PYY	165.12	386.93*	1,993.06*
Ras	66.63	3,697.36*	14,353.17*
RBP4	1.16	195.55*	748.67*
RECK	1.16	240.27*	692.97*
Resistin	1.16	125.17*	581.38*
RET	1.16	232.98*	651.36*
RIP1	1.16	115.00*	355.42*
ROR2	51.56	250.44	265.49
ROS	34.18	272.58*	692.06*
S100A4	25.49	106.27*	557.05*
S100A6	1.16	167.09*	755.59*
S100A8	1.16	63.15*	625.94*
S-100b	19.70	66.68*	481.14*
SCG3	35.92	135.93*	474.98*
Serpin A3	310.55	932.66*	1,906.23*

Serpin A4	1.16	119.99*	642.78*
Serpin A5	1.16	55.56*	669.43*
Serpin A9	1.16	19.85*	526.73*
Serpin A12	1.16	125.63*	761.49*
Serpin B5	1.16	66.45*	420.79*
Serpin D1	1.16	11.46*	239.48*
Serpin I1	1.16	6.19*	365.53*
SERTAD2	1.16	85.84*	580.78*
SHBG	1.16	128.57*	562.89*
SMAC	1.16	20.76*	268.20*
SPINK1	1.16	60.57*	478.31*
SSEA-1	1.16	125.19*	603.41*
SSEA-4	97.34	347.22*	617.26*
SSTR5	1.16	238.95*	622.90*
Syndecan-3	39.98	90.24*	969.06*
TAF4	1.16	32.94*	518.04*
TFF3	1.16	117.74*	788.19*
Thrombin	1.16	131.45*	492.24*
Thrombomodulin	1.16	108.75*	359.09*
Thymidine Kinase-1	1.16	84.36*	418.31*
Thyroglobulin	1.16	629.61***	376.26***
TIM-1	1.16	134.86*	450.91*
TOPORS	1.16	156.34*	423.96*
TPA	1.16	158.32*	364.07*
TPM1	1.16	167.65*	407.91*
Trappin-2	48.67	120.79*	524.63*
TSLP	127.46	294.62*	678.46*
Tyk2	58.52	176.40*	589.09*
TYRO10	45.19	226.37*	756.23*
Vasopressin	1.16	141.88*	460.77*
VDUP-1	16.80	163.28*	600.84*
VEGF R1	1.16	144.03*	429.33*
VGF	1.16	71.98*	315.72*
VIP Receptor 2	1.16	127.08*	265.00*
Visfatin	1.16	175.82*	463.03*
Vitamin D-BP	88.07	201.02	212.06
Vitamin K-dependent protein S	1.16	188.38*	279.33*

[0147] Table 5 shows that Caucasian samples relative to Asian samples demonstrated 25% difference in production levels in 204/231 (88%) of the compared proteins. Of those, 196/204 (96%) demonstrated increase production levels relative to Asian samples. The

remaining 8/204 (4%) demonstrated decreased production levels relative to Asian samples.

[0148] Table 6 is a list (and directional indication relative to Control) of Biologically Significant (≥2-fold dysregulation) proteins unique to each sample group.

TABLE 6

Biologically Significant Proteins With Values Uniquely Dysregulated Relative to Control In Asian Group	Biologically Significant Proteins With Values Uniquely Dysregulated Relative to Control In African Group	Biologically Significant Proteins With Values Uniquely Dysregulated Relative to Control In Caucasian Group
6Ckine ↓	CXCR1 ↑	Angiogenin ↑
Angiopoietin 4 ↓	CXCR4 ↑	BIK ↑
Angiopoietin Like 1 ↓	Endostatin ↑	BMP2 ↑
Angiopoietin like 2 ↓	GDF5 ↑	BMP3 ↑
Angiopoietin like Factor↓	GFR Alpha3 ↑	BMP3b ↑
Angiostatin ↓	GLUT3 ↑	BMP4 ↑
BMP 15 ↓	Glypican 5 ↑	BMP5 ↑
BMPR-1A/ALK3 ↓	Musk ↑	BMP6 ↑
BMPR-1B/ALK 6 ↓	SMAD 4 ↑	CCR7 ↑
CCR1 ↓	SMAD 5 ↑	CD40 Ligand ↑
CCR2 ↓	SMAD 7 ↑	Cerberus 1 ↑
CCR3 ↓	BCAM ↑	Chem R23 ↑
CRTH-2 ↓	Contactin ↑	Chordin Like 2 ↑
Cryptic ↓	Cytokeratin 19 ↑	CXCR6 ↑
CTGF ↓	Endothelin RA ↑	Follistatin ↑
CTLA-4 ↓	GPR 39 ↑	GFR-Alpha 2 ↑
EG-VEGF ↓	Osteocalcin ↑	GITR ↑
FAM 3B ↑	P21 ↑	GITR Ligand ↑
FGF8 ↓	Presenilin 1↑	ICAM 3 ↑
GCSF ↓	Presenilin 2 ↑	ICAM 5 ↑
CD114 ↓	ROR1 ↑	IL1 R9 ↑
Hepassocin ↓	SOX17 ↑	IL1 RA ↑
GLO-1 ↓	SOX2 ↑	IL1 sRI ↑
HGF ↓	SYK ↑	IL3 ↑
HGF-R ↓	TRA-1-60 ↑	IL6 ↑
IL1-Beta ↓	TRA-1-81 ↑	IL13 Alpha 2 ↑
IL1-F7 ↓	Transferrin ↑	IL15R Alpha ↑
IL1-F9 ↓	Trypsin 1 ↑	IL17 RD ↑
MCP3 ↓		Leptin ↑
MCP4 ↓		LIF ↑
		LIF R Alpha ↑

ROBO4 ↑		LRP1 ↑
ADAMTS-13 ↓		MIP 1A ↑
ADAMTS-15 ↓		MIP 3 Alpha ↑
ADAMTS-17 ↓		NOV ↑
Annexin A7 ↓		S100A8 ↑
APC ↓		sFRP 4 ↑
Apex1 ↓		TACI ↑
ApoA2 ↓		Tarc ↑
APoB100 ↓		TGF beta 3↑
Apo C2 ↓		Thymopoeitin ↑
BMP 9 ↓		TIE 2 ↑
C3A ↓		TIMP 4 ↑
C7 ↓		TL1A ↑
Cathepsin L ↓		TLR1 ↑
Cathepsin S ↓		TLR3 ↑
CCK ↓		TLR4 ↑
CD23 ↓		TMEFF1 ↑
CD24 ↓		TNF Alpha ↑
CD36 ↓		TNF Beta ↑
CD38 ↓		TNF RI ↑
CD44 ↓		TROY ↑
CD45 ↓		uPA ↑
CD46 ↓		uPAR ↑
CD55 ↓		Vasorin ↑
CD61 ↓		VCAM-1 ↑
CK Beta 8-1 ↓		VE-Cadherin ↑
CK-MB ↓		VEGF ↑
Claudin 3 ↓		VEGF R2 ↑
Claudin 4 ↓		VEGF R3 ↑
CLEC3B ↓		VEGF B↑
Clusterin ↓		XEDAR ↑
CNDP1 ↓		ACE-2 ↑
CPN2 ↓		ACPP ↑
cTnT ↓		ACTH ↑
DBI ↓		ADAM 9 ↑
DCBLD2 ↓		AMICA ↑
DEFA 1/3 ↓		AMPKa1 ↑
Defensin ↓		CA9 ↑
Desmin ↓		Calbindin D ↑
DLL1 ↓		Caspase 8 ↑
DLL4 ↓		Cathepsin B ↑
E-Cadherin ↓		Cathepsin D ↑
Endorphin Beta ↓		Chymase ↑
EphA4 ↓		FGFR ↑
EphA5 ↓		Galanin ↑
AphA7 ↓		GRP78 ↑

EphA8 ↓ EphB1 ↓ EphB2 ↓ ESAM ↓ EV15L ↓ FABP1 ↓ FABP2 ↓ FAK ↓ FcRIIB/C ↓ Ferritin ↓ Fetuin A ↓ FoxP3 ↓ Fyn ↓ Gastrin ↓ GATA3 ↓ Ghrelin ↓ GLP-1 ↓ LAG-3 ↓ Layilin ↓ LDL R ↓ Legumain ↓ LRG ↓ Midkine ↓ MINA↓ MSHa ↓ MTUS1 ↓ Myoglobin ↓ NAIP ↓ Nanog ↓ Nestin ↓ NET1 ↓ Netrin-4 ↓ P27 ↓ P53 ↓ Pancreastatin ↓ Pancreatic Polypeptide ↓ Pappalysin-1 ↓ ROCK1 ↓ SOST ↓		GSR ↑ HADHA ↑ Hck ↑ HOXA10 ↑ HTRA2 ↑ IL-23p19 ↑ IL-33 ↑ LH ↑ LPS ↑ LYRIC ↑ PAK7 ↑ Serpin A8 ↑

[0149] Table 6 shows that Asian samples demonstrated unique dysregulation (primarily less production than Control in all but two (2) instances) in 114/1000 {11.4%} proteins. African samples demonstrated unique dysregulation (all demonstrated greater production than Control) in 30/1000 {3%} proteins. Caucasian samples demonstrated unique dysregulation (all demonstrated greater production than Control) in 88/1000 {8.8%} proteins.

[0150] Table 7 is a list (with directional indication relative to comparator) of Statistically Significant (≥0.05) proteins for African relative to Asian.

TABLE 7

African Relative to Asian	Fold Change	Mann-Whitney U test
		p<0.05, significant difference
Contactin-1	4.785894	0.002
RBP4	3.833005	0.002
S100A8	8.433062	0.002
Selenoprotein P	464.1391	0.002
SOX2	19.86845	0.002
SRMS	4.999207	0.002
SSEA-1	5.044852	0.002
TRA-1-60	14.72112	0.002
Trappin-2	5.165469	0.002
TSLP	6.735374	0.002
VDUP-1	5.84716	0.002
GDF3	6.088395	0.004
FGFR1 alpha	8.376882	0.004
PAI-1	2.413475	0.004
pro-Glucagon	20.06152	0.004
RELM alpha	4.326569	0.004
Serpin A12	4.718214	0.004
SPINK1	7.882159	0.004
Tec	27.83664	0.004
Transferrin	8.263479	0.004
TRKB	6.809241	0.004
TXK	3.26606	0.004

Smad 4	14.28682	0.009
FGFR1	6.441568	0.009
Kallikrein 5	3.86346	0.009
NM23-H1/H2	5.984695	0.009
Plasminogen	3.235235	0.009
ROS	3.08605	0.009
S100A4	5.34344	0.009
Serping 1	8.999197	0.009
Serpin A8	8.339236	0.009
SYK	13.80922	0.009
TRA-1-81	5.74969	0.009
Trypsin 1	12.7068	0.009
GDF11	59.09495	0.015
Clusterin	322.4728	0.015
cTnT	184.3612	0.015
CutA	217.5524	0.015
Cyclin D1	27.38391	0.015
Cystatin A	9.459818	0.015
Defensin	227.0208	0.015
Desmin	348.2456	0.015
DLL4	356.3274	0.015
FGFR2	13.38653	0.015
Fibrinogen	1.47624	0.015
Fibrinopeptide A	2.450378	0.015
Gas1	7.062109	0.015
Gastrin	229.4557	0.015
GATA-3	226.9231	0.015
Gelsolin	19.97257	0.015
Ghrelin	222.7011	0.015
GLP-1	230.2016	0.015
HSP32	131.6209	0.015
HSP60	31.54389	0.015
HSP90	494.1763	0.015
Omentin	7.116758	0.015
PIM2	7.22723	0.015
S100A6	3.931869	0.015
SCG3	4.290052	0.015
Serotonin	19.47403	0.015
Serpin I1	90.50669	0.015
SMAC	34.58259	0.015
TACE	16.5547	0.015
TAF4	19.69919	0.015
Vitamin D-BP	3.8112	0.015

EDA-A2	1.933584	0.026
GREMLIN	7.798717	0.026
ADAMTS-5	26.30608	0.026
ADAMTS-L2	8.092354	0.026
Adipsin	4.670584	0.026
COCO	80.78475	0.026
Complement factor H	12.27403	0.026
Creatinine	3.381759	0.026
CSH1	19.40335	0.026
Cystatin B	4.660797	0.026
DPPIV	8.806647	0.026
Endorphin Beta	12.18614	0.026
EphA3	4.353228	0.026
ERRa	8.560323	0.026
EXTL2	9.640182	0.026
FABP2	15.48814	0.026
FoxP3	11.10388	0.026
FRK	6.539991	0.026
GATA-4	8.792889	0.026
GPBB	4.819533	0.026
GPI	5.458149	0.026
Hepcidin	8.654806	0.026
HSP40	24.74462	0.026
HSP70	36.41347	0.026
Midkine	7.50768	0.026
PD-1	4.574154	0.026
PI 16	4.103296	0.026
Pro-MMP-9	4.890788	0.026
Pro-MMP-13	6.168079	0.026
Prostasin	3.562363	0.026
PTPRD	5.714606	0.026
Ras	2.219349	0.026
RECK	2.698033	0.026
RYK	14.21574	0.026
SART1	4.866865	0.026
SART3	7.807252	0.026
SEMA3A	21.36675	0.026
Serpin A1	10.82167	0.026
Serpin A5	10.12044	0.026
Serpin A9	25.61264	0.026
Serpin D1	39.69157	0.026
SOX17	6.136459	0.026
Survivin	5.51442	0.026

Syndecan-3	11.02041	0.026
TFF1	13.13231	0.026
TFF3	4.672818	0.026
Thymidine Kinase-1	6.306063	0.026
TPA	4.485392	0.026
TPM1	4.696349	0.026
Troponin I	3.969662	0.026
TRPC6	6.015505	0.026
TRPM7	5.534693	0.026
TSH	6.897905	0.026
VEGF R1	4.237943	0.026
Vitamin K-dependent protein S	2.602491	0.026
Csk	3.714331	0.041
GDF5	7.403583	0.041
GDF9	7.627866	0.041
Latent TGF-beta bp1	2.175335	0.041
CRP	2.274928	0.041
DBI	8.18511	0.041
FABP3	6.118762	0.041
Fetuin B	3.836071	0.041
HSP20	3.982229	0.041
Itk	5.91214	0.041
ITM2B	4.979435	0.041
Kallikrein 6	4.252369	0.041
Kallikrein 11	2.647301	0.041
KCTD10	3.669272	0.041
KLF4	5.015021	0.041
PEPSINOGEN II	4.863297	0.041
PI 3Kinase p85 beta	4.839435	0.041
PPARg2	3.64854	0.041
Pro-Cathepsin B	2.548219	0.041
Progesterone	6.519625	0.041
ProSAAS	2.417423	0.041
Protein p65	4.260583	0.041
PSA-total	8.690313	0.041
PYK2	3.968538	0.041
PYY	3.097189	0.041
Resistin	4.827942	0.041
RET	3.163772	0.041
RIP1	5.863169	0.041
Serpin A4	5.20463	0.041
Serpin B5	7.07585	0.041

SHBG	6.730152	0.041
SSTR5	3.193597	0.041
Syndecan-1	5.401464	0.041
Thrombin	4.282239	0.041
TIM-1	4.201384	0.041
TOPORS	4.280719	0.041
TRPC1	10.01976	0.041
Tyk2	6.504028	0.041
TYRO10	4.131835	0.041
Vasopressin	4.743533	0.041
VGF	7.867878	0.041
Visfatin	4.710721	0.041

[0151] Table 7 shows that African samples demonstrated a minimum of a two fold increases over Asian samples in all 161 statistically significant proteins (determined by the Mann-Whitney U Test). This was the largest collection of statistically significant proteins in all three (3) relative comparisons.

[0152] Table 8 is a list (and directional indication relative to comparator) of Statistically Significant (≥0.05) proteins for Caucasian relative to Asian.

TABLE 8

Caucasian Relative to Asian	Fold Change	Mann-Whitney U test
		p<0.05, significant difference
Activin B	233.5384	0.015
Activin C	710.1567	0.015
Activin RIB / ALK-4	41.81165	0.015
Activin RIIA	652.6	0.015
HSP60	44.54578	0.015
HSP90	467.3104	0.015
Activin RIA / ALK-2	30.44423	0.026
BMP-3	11.79482	0.026
CCR8	26.44067	0.026
EDA-A2	2.279418	0.026

ApoC3	13.22354	0.026
Fen 1	4.761872	0.026
GATA-4	8.507966	0.026
HSP70	46.01337	0.026
TRPM7	6.563931	0.026
Activin RII A/B	14.30805	0.041
beta-Catenin	8.715446	0.041
MCP-1	4.242993	0.041
ADAMTS-L2	10.49804	0.041
FER	43.20704	0.041
FGFR1	8.320166	0.041
HSP40	33.77603	0.041
TAF4	15.76296	0.041
Tec	31.81704	0.041

[0153] Table 8 shows that Caucasian samples demonstrated a minimum of a twofold increases over Asian samples in all 24 statistically significant proteins (determined by the Mann-Whitney U Test). This was the second largest collection of statistically significant proteins in all three (3) relative comparisons.

[0154] Table 9 is a list (and directional indication relative to comparator) of Statistically Significant (≥0.05) proteins for Caucasian relative to African.

TABLE 9

Caucasian Relative to African	**Fold Change**		**Mann-Whitney U test**
			$p<0.05$, significant difference
Presenilin 1	0.17695	(-5.65131)	0.026
Presenilin 2	0.201391	(-4.96546)	0.026
TSLP	0.442966	(-2.25750)	0.026
Vitamin D-BP	0.28323	(-3.53069)	0.026
Osteopontin	0.262119	(-3.81506)	0.041

[0155] Table 9 shows that Caucasian samples demonstrated a minimum of a twofold decreases compared to African samples in all 5 statistically significant proteins

(determined by the Mann-Whitney U Test). This was the smallest collection of statistically significant proteins in all three (3) relative comparisons.

[0156] The above data supports at least the following conclusions.

[0157] Biological Significance means greater than a 2-fold increase or decrease relative to comparator sample as written in the protocol definition. Biological Significance demonstrated 616/1000 proteins that met the criteria in at least one group. Also, 231/616 were common across all groups.

[0158] The data further showed that uniquely altered proteins (biologically significant in only one group):

Asian: 114/1000
African: 30/1000
Caucasian: 88/1000

[0159] A change in average production level is defined as greater than 25% increased/decreased relative to comparator per protocol definition. The data shows that the average production level changes demonstrated variations in all three groups in the shared 231 biologically significant proteins. In general, Asian sample or skin, relative to African and Caucasian samples or skin, showed decreased protein production levels, while Caucasian skin showed the most increase in production levels.

[0160] The statistical significance of the data using the Mann Whitney test further showed that the Asian skin demonstrated the largest number or amount of proteins, in the 95% confidence interval, relative to African skin. The second largest amount of proteins was Asian skin relative to Caucasian skin. The least amount of proteins was African skin relative to Caucasian skin.

[0161] The data supports the belief that a further analysis of the proteins and their pathways will improve the understanding of the differences in the structure, function, health and beauty of the skin amongst these ethnic groups.

[0162] The data confirms, as noted in the further studies below, that the mixture of two or more tissue cultures whether homogeneous or heterogeneous from the same sex is possible to achieve desired effect on a recipient. In other words, the blending of tissue cultures of one ethnic group, or amongst two or more ethnic groups, in a product, based on characteristics of the proteins in each ethnic group and desired characteristic(s) to be imparted to the skin of the recipient, is possible.

Example II

[0163] Global gene expression (i.e. protein levels) by dermal fibroblasts between 3 ethnic groups, Caucasians (CA), African (AF) and Asian (AS) were compared. 6 patients from each ethnicity were recruited for this study. Dermal fibroblasts were isolated from each biopsy and grown under similar tissue culture conditions. Protein was extracted and samples underwent protein assay, testing and analysis according to in-house protocols. Data was further corrected and interpreted by BioFast Consultant Group as specified herein.

[0164] To evaluate protein expression in all samples, RayBio® Human Biotin Label Based Antibody Arrays -- Human L-507 Array was utilized. This array is designed to evaluate 1000 proteins in duplicates. Two normalization steps were done to account for differences between the different arrays (intra array) or within each array (inter array). This includes normalization to the positive control and then background value is subtracted (negative control). Duplicates values were then averaged (this gives one final intensity value that is used for the final analysis and statistics).

[0165] From a biological perspective, it is expected that following data normalization, the average gene expression intensity will not differ between the different test groups (i.e. AS, AF and CA). Therefore, in order to test this, global intensity average of each sample (i.e. total of 18 samples) and ethnic group were calculated. Results of this initial analysis are shown in Table 10 below, shown as Table 10A 10B and 10C for pagination purposes.

[0166] Table 10A

Prior to Data Correction	AS1	AS2	AS3	AS4	AS5	AS6
average intensity	413.2	597.1	343.8	893.2	718.5	736.2
average per group	617.0					
SEM	93.25					

[0167] Table 10B

Prior to Data Correction	AF1	AF2	AF3	AF4	AF5	AF6
average intensity	984.2	1171.7	455.4	556.8	1060.4	1968.1
average per group	1032.8					
SEM	241.4					

[0168] Table 10C

Prior to Data Correction	CA1	CA2	CA3	CA4	CA5	CA6
average intensity	1506.5	2324.8	380.3	358.6	3146.8	821.6
average per group	1423.1					
SEM	504.9					

[0169] Using the original normalized data values, fold changes for each gene was calculated among the different groups by performing 3 independent comparisons: AF/AS, CA/AS, CA/AF. Summarized results showing the overall number of statistically significant (ttest) up-regulated and down-regulated genes are shown in Table 11 below.

[0170] Table 11

Result Summary Prior to Data Correction					
	AF/AS		CA/AS		CA/AF
Total significantly upregulated	259.0		94.0		7.0
Total significantly downregulated	1.0		0.0		13.0

[0171] It has been noted that many of the intensity (i.e. gene expression) values equaled “1”. This means that either the expression level of a given protein was below the lower detection limit of the assay (or lower than the negative control) or that an undetermined technical reason(s) caused the detection to fail for that particular protein. When all these "1's" are included in the analysis, they might provide false positive results. For example, if the average intensity of geneX for the Asian group is 1 and the average intensity of the same gene in African group is 300, data analysis will suggest a 300 fold up-regulation in the African group, where in fact the expression of geneX in the Asian group simply could not be determined (for unknown reasons).

[0172] From comparing the averages of the global intensity, it was noted that there were obvious differences in overall detection signal between the ethnic groups, with the lowest values observed in the Asian group and the highest in Caucasians. This means that on average “more protein” was detected in the Caucasian group compared with the other groups. This phenomenon is unexpected and is most likely a result of an artifact due to an unequal protein loading, non-consistent washing of the membranes, or other technical issues that evidently could not be corrected by the intra and inter array normalization steps.

[0173] Without wishing to be bound by a single theory, a series of issues were identified that could explain, at least partly, the unequal intensity detection levels between

groups, as well as the abundance of undetermined detections. Protein loading in the arrays was not equal, some samples had very low to no detection, there is a saturation issue such that the intensity was very high to exceed the normal detection range of the scanner or to the point where it overlapped with another spot in the array, there is a background issue such that in some membranes it was noted that certain areas were darker ("dirty areas") compared with the rest of the membrane.

[0174] In order to address the above issues and avoid drawing conclusions based on potentially false positive and negative results, the following steps were undertaken:

[0175] Data points that were deemed as artifacts were filtered out. Only intensity values that are larger than 100 but smaller than 50000 are considered valid. Therefore, all values smaller than 101 and higher than 49999 were filtered out/excluded. A summary of how many data points were "lost" due to this action is specified in the Table 12 shown below.

[0176] Table 12

	AS 1	**AS 2**	**AS 3**	**AS 4**	**AS 5**	**AS 6**
Total removed samples following data correction	668	675	916	420	504	553
Average of removed data point per group*	623					
	AF 1	**AF 2**	**AF 3**	**AF 4**	**AF 5**	**AF 6**
Total removed samples following data correction	266	374	865	542	246	190
Average of removed data point per group*	414					
	CA 1	**CA 2**	**CA 3**	**CA 4**	**CA 5**	**CA 6**
Total removed samples following data correction	114	186	826	688	59	794
Average of removed data point per group*	344					

[0177] To ensure that this change was sufficient in correcting the data, averages of global protein expression was compared between the groups. It was noted that filtering "bad" data points overall improved the data set, as the changes in global protein expression between the ethnic groups were mostly abolished. This is shown in the Table 13 below, shown as Tables 13A, 13B, and 13C for pagination purposes.

[0178] Table 13A

Post Data Correction	AS1	AS2	AS3	AS4	AS5	AS6
average intensity	1027.7	1386.4	3400.3	1292.1	1215.8	1115.4
average per group	1572.9					
SEM	404.3					

[0179] Table 13B

Post Data Correction	AF1	AF2	AF3	AF4	AF5	AF6
average intensity	1082.6	1324.2	2193.5	922.0	1063.4	2039.5
average per group	1437.5					
SEM	243.2					

[0180] Table 13C

Post Data Correction	CA1	CA2	CA3	CA4	CA5	CA6
average intensity	1487.2	2245.1	1744.0	785.5	2371.5	2,390
average per group	1837.3					
SEM	282.5					

[0181] After DATA filtering (above), the intensity values of any given protein for any given group (AS, AF and CA) were further analyzed only if at least 3 of these values were

available (n >= 3 in a given group). For the entries/proteins respecting this parameter (n >= 3), fold changes/ratios between the groups were calculated.

[0182] A summary of significantly up- and down-regulated genes after data correction is also shown in the Table 14 below.

[0183] Table 14

	Results Summary After Data Correction		
RATIO - ETHNICITY	**AF/AS**	**CA/AS**	**CA/AF**
TOTAL	60	108	49
Down	0	1	6
Up	60	107	43

[0184] The significantly changed proteins were subsequently utilized for the study of protein network interactions, described below.

[0185] In order to identify the major Biological processes and cell signaling pathways that were differentially modulated from one ethnic group to another, data was subjected to a string network analysis. As input for the software, 3 separate lists of entries were used (as mentioned above), which included only the proteins that presented significant differences ($p < 0.05$ by one tailed T-TEST) in expression levels between the groups (AF/AS; CA/AS; CA/AF. The overall protein networks for each of these 3 lists are shown in FIGS. 3 to 5.

[0186] FIGS. 3 to 5 show protein network AF/AS, CA/AS and CA/AF. The line thickness is proportional to the strength of data in support of functional interactions between protein

[0187] Out of the string network analysis, the first 50 (Top-50 ranked for statistical significance/ false discovery rate) Biological processes were categorized/ interpreted. Of note, processes that were considered generic/ potentially pertinent to any biological process (e.g. "Cell Signaling") were ignored.

[0188] FIGS 6 to 8 describe the main biological processes that are differentially modulated from one group to another are reported herein.

[0189] In addition, significant examples on how the top or best scoring biological processes fit within the overall protein networks are shown FIGS 9 to 11.

[0190] In FIG 9, it is apparent that most of the genes identified for wound healing processes (in red) do appear to be at the core of the strongest functional interactions of the network.

[0191] In FIG 10, it is apparent that that most of the genes identified for immune response (in red) do appear to be functionally linked in the overall network.

[0192] In FIG 11 however, only 50% of the identified genes for immune response (in red) appear to be functionally linked in the overall network.

[0193] The most significant pathways fitting within the overall protein network for each of the 3 list of differentially modulated proteins, AF/AS, CA/AS and CA/AS, were "Complement and Coagulation Cascade", "Cytokine – Cytokine Receptor interaction" and again "Cytokine – Cytokine Receptor interaction", respectively.

[0194] Several conclusions can be drawn from the protein network analysis.

[0195] For AF/AS, the wound healing process, as well as the regulation of extracellular matrix, are the main biological processes that can distinguish AF from AS at molecular level. These processes are mostly up-regulated in AF compared to AS (as the majority of

the proteins were up-regulated for that ratio). Notably, the "complement and coagulation pathway" seems to be at the core of the wound healing process.

[0196] For CA/AS, the immune system response / Inflammation is the main biological process at play, mostly up-regulated in CA, compared to AS (as the majority of the proteins were up-regulated for that ratio). Moreover, "cytokine-cytokine receptor pathway" and "JAK-STAT pathway" are likely involved in such differential basal modulation of the immune system between CA and AS.

[0197] For CA/AF, the immune response was again the top-scoring biological process, up-regulated in CA, compared to AF (as the majority of the proteins were up-regulated for that ratio). However, the same process did not strongly cover the core of the functional interactions of the overall STRING network (of differentially expressed proteins). Perhaps, in this case (CA/AF) there is a balance of several different processes at play, which we cannot clearly infer from the protein list and subsequent Network analysis. At any rate, a mixture of "cytokine-cytokine receptor pathway" and "complement and coagulation cascade" seem to cover the main differences between CA and AF.

[0198] Next, skin-relevant genes in each ethnic group were identified as follows. When values from at least 3 subjects (n =>3) of a given ethnicity/group were available, these values were averaged. The averages were compared to the value averages of the rest of the ethnicities, contingently that there was also availability of at least 3 values from the rest of the ethnicities. Significant differences between groups were tested by T-TEST ($p < 0.05$ is considered statistically significant).

[0199] From the above, several conclusions are possible. CA presents mostly up-regulated genes, compared to the other ethnicities. AS presents mostly down-regulated genes, compared to the other ethnicities. AF presents equally UP- and DOWN-regulations, compared to other ethnicities. See Table 15.

[0200] TABLE 15

	p < 0.05	*p < 0.05*	*p < 0.05*
RATIO	**AS / (AF + CA)**	**AF / (AS + CA)**	**CA / (AS + AF)**
TOTAL	79	23	141
Down	78	11	3
Up	1	12	138

[0201] In order to select/shortlist target genes that are differentially expressed/modulated in a specific group, while, at the same time, reducing the chance of selecting false positive, an approach was taken that favors the identification of genes that are differentially regulated in a particular group no matter what the control population is. Seventeen (17) genes were identified for the AS, fourteen (14) for the CA and four (4) for the AF group, as shown in the Venn diagrams of FIG 12.

[0202] The following Tables 16, 17 and 18 summarize the findings discussed in the preceding paragraph.

[0203] Table 16

AS					
Gene name	**Fold change**	**p-Value**	**Mass (kDa)**	**Function**	**Relevance to Skin**
SRMS	0.169108	0.04084	54.5	Non-receptor tyrosine-kinase	n/a
GDF3	0.216263	0.00761	41.4	Negative regulator of TGFb/BMP signaling	TGFb is a major pro-fibrotic pathway in skin. Reduced expression of this protein may contribute to hypertrophic scars or keloids in the Asian population
SHBG	0.238325	0.00815	43.8	Complexes with sex hormones	Sex hormones affect various aspects of skin biology and pathology. may have a role in skin pigmentation and androgen actions in skin of Asians
Tyk2	0.239025	0.00402	133.6	Tyrosine kinase enzyme	Tyk2 is a therapeutic target for psoriasis-like skin inflammation. TYK2 deficiency is associated with skin bacterial infections which may suggest a role in barrier function

Creatinine	0.262378	0.02641	n/a	Byproduct of muscle cell metabolism	n/a
TSH	0.271665	0.01403	28	Thyroid stimulating hormone	TSH and the TSH receptor involved in skin keratinocyte and fibroblast growth; Reduced TSH levels associated with hair loss and dry rough pale skin.
TXK	0.287523	0.03243	61.2	Tyrosine kinase enzyme	Overexpression is observed in Behcet's disease
TIM-1	0.297133	0.00795	38.7	membrane receptor	May be involved in modulation of allergic diseases such as asthma, allergic rhinitis and atopic dermatitis.
RET	0.303647	0.00297	124.3	Cell surface receptor tyrosine kinase	Overexpression was found to induce melanoma; mutations leading to hyperactivation is associated with cutaneous lichen amyloidosis.
Visfatin	0.30562	0.00908	55.5	Enzyme	Contribute to resolution of skin sclerosis; has direct anti-fibrotic effects; May be relevant to hypertrophic scars/keloids in Asians. May be also involved in inflammatory responses in psoriasis.
TYRO10	0.320326	0.00904	96.7	Tyrosine kinase receptor for collagen	Regulate remodelling of the extracellular matrix and promote fibroblast migration during wound healing.
RELM alpha	0.322593	0.00424	11.4	Also known as FIZZ- 1	Small secreted molecule associated with dermal fibrosis via its role in the induction of dermal adipocytes to myfibroblasts.
PSA-Free	0.36243	0.03103	34	Prostate specific antigen; klk3	n/a
SCG3	0.369737	0.01215	53	Secretogranin III	n/a
KCTD10	0.378113	0.02082	35.4	Potassium Channel Tetramerization Domain Containing 10	n/a
Vitamin K-dependent protein S	0.447402	0.01595	75.1	Anticoagulant function	Topical of Vitamin K1 suppresses pigmentation and improves wound healing

[0204] Table 17

CA					
Gene name	**Fold change**	**p-Value**	**Mass (kDa)**	**Function**	**Relevance to Skin**
EDAR	1.797218	0.01252	48.6	TNFR superfamily member	EDAR agonists may improve skin dryness and eczema
Pro-MMP-7	2.130663	0.00299	29.7	Matrix metallo Protease	Degrades ECM components. May play a role in skin aging. May be added to products designed to treat HS/keloids. It may contribute to remodelling of elastotic areas in sundamaged skin
SSEA-4	2.280554	0.01109	n/a	Stage-specific embryonic antigen	n/a
MMP-10	2.3408	0.004	54.1	Matrix metallo Protease	It might have a role in controlling scar formation during wound repair. Thus, it might be useful to control fibrosis and scan formation.
Vitronectin	2.423404	0.00089	54.3	Glycoprotein promoting cell adhesion via integrins	Regulate extra cellular matrix proteolysis and cell migration via stabilization of PAI1.
TWEAK R / TNFRSF12	2.65139	0.0026	45.4	TNFR superfamily member	The expression is altered in eczema skin, thus providing an antagonist might be beneficial in eczema.
uPA	2.924766	0.00111	48.5	Urokinase/ serine protease	The absence of uPA signaling might be associated with the progression of dermal fibrosis has been shown to increase fibroblast proliferation and stimulate fibronectin secretion. May reduce wrinkles in Asians.
uPAR	2.969332	0.00025	37	Urokinase receptor	The absence of uPAR might be associated with the progression of dermal fibrosis
GDNF	3.011637	0.00189	23.7	Signaling molecule (promotes cell survival in neurons)	It decreases with age. Thus providing it (at least in CA) might prevent aging marks, including wrinkles
IL-17B	3.071995	0.00327	20.4	Pro-inflammatory cytokine	It might enhance skin inflammatory response

VCAM-1 (CD106)	3.145728	0.00103	81.3	Adhesion molecule	It might increase susceptibility to atopic dermitisis
Lymphotactin / XCL1	3.313039	0.00104	12.5	Chemokine	Proinflammatory mediator that could be involved in skin inflammation.
SRMS	4.053276	0.00219	54.5	Non-receptor tyrosine-kinase	n/a

[0205] Table 18

AF					
Gene name	**Fold change**	**p-Value**	**Mass (kDa)**	**Function**	**Relevance to skin**
TPM1	2.203069	0.01017	32.7	Tropomyosin 1	Regulate skin migration during wound healing
Tyk2	2.374957	0.00377	133.6	Tyrosine kinase enzyme	Tyk2 is a therapeutic target for psoriasis-like skin inflammation. TYK2 deficiency is associated with skin bacterial infections which may suggest a role in barrier function
TSLP	2.537861	0.00297	18.1	Thymic Stromal Lymphopoietin	Upregulated in skin of systemic sclerosis and promote fibrosis, may explain why individuals of African descent are more susceptible to keloids.
Adipsin	3.027837	0.00189	27	Serine peptidase (enzyme)	n/a

[0206] The analysis described above revealed that the number of genes that were differentially modulated in AS, AF and CA when compared to the rest of the groups (combined) were 79, 23 and 141, respectively. Further comparative analysis identified various genes that were found to be differentially regulated in each one of the tested group independently of the control group (as shown in the Venn diagram). Seventeen (17) genes were identified for the AS, fourteen (14) for the CA and four (4) for the AF group. Based on this data, it can be concluded that various genes (expressed by dermal

fibroblasts) that control different aspects of skin function and pathology are differentially regulated in African, Asian and Caucasian skin. Thus, this data supports the proposition that differential gene regulation plays a role in racial differences of skin properties, appearance or pathology.

[0207] Furthermore, the data of the present disclosure proves and enables the rational for developing cosmetic and therapeutic products specifically suited for Asian, African or Caucasian (or other ethnic group or subgroup) skin based on proteins derived from the gene cells. Moreover, this data proves that the proteins can be selected from an ethnic group (or subgroup) in order to derive the benefit or characteristic desired of the product that can be used by any recipient.

[0208] Thus, the present disclosure has unexpectedly found that each ethnic group (and/or subgroup) has genes that are differentially regulated so that formulation of a targeted product that achieves maximimization of a desired benefit or characteristic is now possible. Further, the targeted product can also be formulated with a higher proportionality of proteins in the overall product composition based on the desired benefits or characteristics of the product. This “tailoring” can be achieved by a single donor in a single ethnic group (or subgroup), as well as two or more donors in a single ethnic group or subgroup, and also in two or more donors in two or more groups and/or subgroups.

[0209] Table 19 that follows is a full list of non-redundant genes determined by the present disclosure.

FULL LIST OF NON-REDUNDANT GENES			
SRMS	Follistatin	SPINK1	Neurokinin-A
IL-13	Kremen-2	EDAR	Beta IG-H3
Musk	MMP-7	NPTXR	CNTF
SHBG	IL-24	SART3	Troponin C
IL-27	IL-23	IL-7	Mammaglobin A
Lipocalin-1	PPARg2	S-100b	Serpin A1
CCR5	IL-1 R8	CFHR2	LRP-1
Creatinine	Pro-MMP-7	XIAP	L-Selectin (CD62L)

NRG2	TOPORS	Wilms Tumor 1	PYK2
IL-29	BNIP2	Troponin I	TWEAK R / TNFRSF12
Dkk-4	Vitamin K-dependent protein S	MMP-8	IL-26
Resistin	MIP 2	SART1	IL-15 R alpha
TXK	Kallikrein 14	GFR alpha-2	VE-Cadherin
Dtk	IL-12 R beta 2	PTN	TMEFF1 / Tomoregulin-1
IL-28A	ProSAAS	CD 163	Itk
XEDAR	TIMP-4	Orexin B	S100A8
Plasminogen	Kallikrein 8	MBL	NRG3
TIM-1	Latent TGF-beta bp1	sFRP-4	GFR alpha-4
RET	MMP-1	FIH	VEGF R2 (KDR)
CLC	GDF3	MMP-11 /Stromelysin-3	Pro-MMP-13
KCC3	Tyk2	TECK / CCL25	IL-31
TYRO10	TSH	Insulysin / IDE	uPAR
RELM alpha	TSLP	S100A6	Livin
Cytokeratin 8	Visfatin	OSM	VCAM-1 (CD106)
Csk	Adipsin	NRG1 Isoform GGF2	D-Dimer
Kallikrein 6	VDUP-1	VEGF R3	IL-17B R
RBP4	TPA	MMP-9	IL-17C
Frizzled-5	HADHA	NM23-H1/H2	IL-17D
LIGHT / TNFSF14	IL-8	Pro-MMP-9	Hck
Frizzled-3	IGFBP-5	NOV / CCN3	Galanin
LIF R alpha	IL-33	IL-17R	Lymphotactin / XCL1
IL-22 BP	IL-23p19	Trappin-2	HTRA2
RANK / TNFRSF11A	IL36RN	A2M	SSTR2
GDNF	LH	Kallikrein 7	FRK
Frizzled-4	IL-11	SSEA-4	PTPRD
IL-17B	PCAF	Kininostatin / kininogen	MMP-20
PSA-Free	IL-18 R beta /AcPL	VEGF-C	MIP-3 alpha
MIG	INSL3	GRP75	Alpha 1 Microglobulin
HSP20	VEGF R1	TRKB	IL-31 RA
uPA	Vasopressin	ADAMTS-10	GPX3
SCG3	VIP Receptor 2	Tarc	IBSP
MIP-1d	TPM1	MMP-10	IL-1 R9
IL-5	IL-1 F9 / IL-1 H1	PARK7	Endothelin
Prostasin	Presenilin 2	GDF-15	pro-Glucagon
KCTD10	Transferrin	Vitronectin	GADD45A

FGF R4	Thrombin	IL-6	Omentin
IL-12 p70	Kallikrein 11	HSPA8	
Fen 1	IL-19	Serpin A12	
NeuroD1	Prohibitin	IL-17RC	
FGF Basic	TIMP-1	PAI-1	
Cerberus 1	SPARC	TCCR / WSX-1	
NGF R	TMEFF2	BMP-5	

[0210] Table 20 below contains information on each gene/protein that found to be differentially regulated in any group as compared with the average of the other two groups.

Table 20

#	Protein symbol	Accession Number	Full Name	Mass (kDa)	Function
1	SRMS	Q9H3Y6	Src-Related Kinase Lacking C-Terminal Regulatory Tyrosine And N-Terminal	54.5	Non-receptor tyrosine-kinase
2	IL-13	P35225	Interleukin 13	12.6	Secreted cytokine
3	Musk	O15146	Muscle Associated Receptor Tyrosine Kinase	97	gene encodes a muscle-specific tyrosine kinase receptor
4	SHBG	P04278	Sex Hormone Binding Globulin	43.8	a steroid binding protein
5	IL-27	Q8NEV9	Interleukin 27	27.4	heterodimeric cytokine which functions in innate immunity
6	Lipocalin-1	P31025	Lipocalin-1	19.2	Small secretory extracellular transport protein that bind hydrophobic ligands
7	CCR5	P51681	C-C Motif Chemokine Receptor 5	40.5	a member of the beta chemokine receptor family, which is predicted to be a seven transmembrane protein similar to G protein-coupled receptors
8	Creatinine	N/A			Byproduct of muscle cell metabolism
9	NRG2	O14511	Neuregulin 2	91.6	member of the neuregulin family of growth and differentiation factors
10	IL-29	Q8IU54	Interferon, Lambda 1; Interleukin-29	21.8	Cytokine with antiviral, antitumour and immunomodulatory activities.
11	Dkk-4	Q9UBT3	Dickkopf WNT Signaling Pathway Inhibitor 4	24.8	secreted protein; is involved in embryonic development through its interactions with the Wnt signaling pathway.
12	Resistin	Q9HD89	Resistin; FIZZ3	11.4	Secreted protein
13	TXK	P42681	TXK Tyrosine Kinase; PTK4	61.2	Enzyme with a tyrosine kinase activity
14	Dtk	Q06418	TYRO3 Protein Tyrosine Kinase	96.9	transmembrane receptor kinase receptor

15	IL-28A	Q8IZJ0	Interleukin-28A; Interferon, Lambda 2; INFL2	22.2	Cytokine with antiviral, antitumour &immunomodulatory activities. Plays a critical role in the antiviral defense, predominantly in epithelial tissues
16	XEDAR	Q9HAV5	Ectodysplasin A2 Receptor; EDA-A2 Receptor	32.7	type III transmembrane protein of the TNFR (tumor necrosis factor receptor) superfamily
17	Plasminogen	P00747	Plasminogen, PLG gene	90	Protein encoded by this gene is a secreted blood zymogen that is activated by proteolysis and converted to plasmin and angiostatin.
18	TIM-1	Q96D42	Hepatitis A Virus Cellular Receptor 1	38.7	Membrane receptor
19	RET	P07949	Ret Proto-oncogene	124.3	Receptor tyrosine kinase
20	CLC	Q05315	Charcot-Leyden Crystal Galectin	164.5	Enzyme that regulates immune responses
21	KCC3	Q9UHW9	Solute Carrier Family 12 Member 6	127.6	Member of the K-Cl cotransporter (KCC) family.
22	TYRO10	Q16832	Discoidin Domain Receptor Tyrosine Kinase 2	96.7	Tyrosine kinase that functions as cell surface receptor for fibrillar collagen and regulates cell differentiation, remodeling of the extracellular matrix, cell migration and cell proliferation.
23	RELM alpha	Q9EP95	Resistin-like molecule (Relm) alpha	11.9	Secreted protein and a hallmark signature gene for alternatively activated macrophages
24	Cytokeratin 8	P05787	Cytokeratin 8	53.7	Member of the type II keratin family
25	Csk	P41240	C-Src Tyrosine Kinase	50.7	Enzyme
26	Kallikrein 6	Q92876	Kallikrein Related Peptidase 6	26.8	kallikrein subfamily of the peptidase S1 family of serine proteases (enzyme)
27	RBP4	P02753	Retinol Binding Protein 4	23	Belongs to the lipocalin family and is the specific carrier for retinol (vitamin A alcohol) in the blood
28	Frizzled-5	Q13467	Frizzled Class Receptor 5	64.5	Transmembrane receptor involved in Wnt signaling
29	LIGHT / TNFSF14	O43557	Tumor Necrosis Factor Superfamily Member 14	26.35	ligand for TNFRSF14, which is a member of the tumor necrosis factor receptor superfamily
30	Frizzled-3	Q9NPG1	Frizzled Class Receptor 3	76	Transmembrane protein receptor for the wingless type MMTV integration site family of signaling proteins.
31	LIF R alpha	P15018	Leukemia Inhibitory Factor	22	involved in the induction of hematopoietic differentiation in normal and myeloid leukemia cells
32	IL-22 BP	Q9GZX6	Interleukin 22	20	Cytokine that contributes to the inflammatory response in vivo.
33	RANK / TNFRSF11A	Q9Y6Q6	Tumor Necrosis Factor Receptor Superfamily Member	66	Receptor for TNFSF11/RANKL/TRANCE/OPGL
34	GDNF	P39905	Glial Cell Derived Neurotrophic Factor	24	Neurotrophic factor that enhances survival and morphological

					differentiation of dopaminergic neurons
35	Frizzled-4	Q9ULV1	Frizzled Class Receptor 4	60	Transmembrane receptor coupled to the beta-catenin (CTNNB1) canonical signalling pathway.
36	IL-17B	Q9UHF5	Interleukn 17B	20	Stimulates the release of the proinflammatory cytokines tumor necrosis factor alpha and IL-1-beta from the monocytic cell line THP-1.
37	PSA-Free	P07288	Kallikrein Related Peptidase 3	28	Hydrolyzes semenogelin-1 thus leading to the liquefaction of the seminal coagulum.
38	MIG	Q07325	Chemokine (C-X-C Motif) Ligand 9	14	Cytokine that affects the growth, movement, or activation state of cells that participate in immune and inflammatory response. Chemotactic for activated T-cells.
39	HSP20	O14558	Heat Shock Protein Family	17	Encodes a heat shock protein
40	uPA	P00749	Plasminogen Activator, Urokinase	48.5	Specifically cleaves the zymogen plasminogen to form the active enzyme plasmin.
41	SCG3	Q8WXD2	Secretogranin III	53	A member of the chromogranin/secretogranin family of neuroendocrine secretory proteins.
42	MIP-1d	Q16663	Macrophage Inflammatory Protein 5	12	Chemotactic factor that attracts T-cells and monocytes.
43	IL-5	P05113	Interleukin 5	15	Signaling compounds that are mediators of the immune response. They control many different cellular functions including proliferation, differentiation and cell survival/apoptosis
44	Prostasin	Q16651	Serine Protease 8	36	Enzyme
45	KCTD10	Q9H3F6	Potassium Channel Tetramerization Domain Containing 10	35	May be involved in cell proliferation
46	FGF R4	P22455	Fibroblast Growth Factor Receptor 4	87.9	mediate angiogenesis, wound healing, cell migration, neural outgrowth and embryonic development.
47	IL-12 p70	P29459	Interleukin 12A	24.8	Cytokine that can act as a growth factor for activated T and natural killer cells and enhance the lytic activity of NK/lymphokine-activated Killer cells
48	Fen 1	P39748	Flap Structure-Specific Endonuclease 1	42.5	The enzyme removes 5' overhanging flaps in DNA repair and processes the 5' ends of Okazaki fragments in lagging strand DNA synthesis.
49	NeuroD1	Q13562	Neuronal Differentiation 1	40	This gene encodes a member of the NeuroD family of basic helix-loop-helix (bHLH) transcription

					factors.
50	FGF Basic	P09038	Basic Fibroblast Growth Factor	30	Growth factor that stimulate cell growth of fibroblasts
51	Cerberus 1	O95813	Cerberus 1, DAN Family BMP Antagonist	30	belongs to a group of bone morphogenetic protein (BMP) antagonists.
52	NGF R	P08138	Nerve Growth Factor receptor	45	Membrane-bound receptor for nerve growth factor
53	Follistatin	P19883	Follistatin	38	single-chain gonadal protein that specifically inhibits follicle-stimulating hormone release.
54	Kremen-2	Q8NCW0	Kringle Containing Transmembrane Protein 2	49	Receptor for Dickkopf protein. Cooperates with Dickkopf to block Wnt/beta-catenin signaling.
55	MMP-7	P09237	Matrix Metallopeptidase 7	29.6	Enzyme that breaks down extracellular matrix
56	IL-24	Q13007	Interleukin 24	23.8	Cytokine
57	IL-23	Q9NPF7	Interleukin 23	20.7	heterodimeric cytokine which functions in innate and adaptive immunity.
58	PPARg2	P37231	Peroxisome Proliferator Activated Receptor Gamma	57.6	Nuclear receptor
59	IL-1 R8	Q9NZN1	Interleukin 1 Receptor Accessory Protein Like 1	79.9	IL-1 receptor.
60	Pro-MMP-7				
61	TOPORS	Q9NS56	TOP1 Binding Arginine/Serine Rich Protein	119	ubiquitin-protein E3 ligase (enzyme) .
62	BNIP2	Q12982	BCL2/Adenovirus E1B 19kDa Interacting Protein 2	36	Intracellular protein
63	Vitamin K-dependent protein S	P07225	Protein S (Alpha)	75	Anticoagulant plasma protein; It helps to prevent coagulation and stimulating fibrinolysis.
64	MIP 2	P19875	C-X-C Motif Chemokine Ligand 2	11	Produced by activated monocytes and neutrophils and expressed at sites of inflammation.
65	Kallikrein 14	Q9P0G3	Kallikrein Related Peptidase 14	29	enzyme
66	IL-12 R beta 2	Q99665	Interleukin 12 Receptor Subunit Beta 2	89	Receptor for interleukin-12.
67	ProSAAS	Q9UHG2	Proprotein Convertase Subtilisin/Kexin Type 1 Inhibitor	27	Has an endopeptidase inhibitor activity; inhibitor of prohormone convertase 1
68	TIMP-4	Q99727	TIMP Metallopeptidase Inhibitor 4	25	Inhibitors of the matrix metalloproteinases,
69	Kallikrein 8	O60259	Kallikrein Related Peptidase 8	28	Serine protease (enzyme)
70	Latent TGF-beta bp1	Q14766	Latent Transforming Growth Factor Beta Binding Protein 1	186.7	Involved in the assembly, secretion and targeting of TGFB1 to action sites
71	MMP-1	P03956	Matrix Metallopeptidase 1	54	Enzyme envolves in degradation of extracellular matrix
72	GDF3	Q9NR23	Growth Differentiation Factor 3	41.3	Growth factor
73	Tyk2	P29597	Tyrosine Kinase 2	133.6	Tyrosine kinase enzyme
74	TSH	P01222	Thyroid Stimulating Hormone Beta	15.6	Hormone
75	TSLP	Q969D9	Thymic Stromal Lymphopoietin	18.1	Cytokine

76	Visfatin	P43490	Nicotinamide Phosphoribosyltransferase	55.5	Enzyme
77	Adipsin	P00746	Complement Factor D (Adipsin)	27	Serine peptidase (enzyme)
78	VDUP-1	Q9H3M7	Thioredoxin Interacting Protein	43.6	Enzyme
79	TPA	P00750	Plasminogen Activator, Tissue Type	62.9	Enzyme
80	HADHA	P40939	Hydroxyacyl-CoA Dehydrogenase/3-Ketoacyl-CoA Thiolase/Enoyl-CoA Hydratase (Trifunctional Protein), Alpha Subunit	83	An enzyme involved in Lipid metabolism.
81	IL-8	P10145	Chemokine (C-X-C Motif) Ligand 8	11.1	This chemokine is one of the major mediators of the inflammatory response
82	IGFBP-5	P24593	Insulin Like Growth Factor Binding Protein 5	30.5	IGF-binding proteins prolong the half-life of the IGFs and mediate the growth promoting effects of IGFs.
83	IL-33	O95760	Interleukin 33	30.7	Cytokine that binds to and signals through the IL1RL1/ST2 receptor which in turn activates NF-kappa-B and MAPK signaling pathways in target cells
84	IL-23p19	Q9NPF7	Interleukin 23 Subunit Alpha	20.7	Associates with IL12B to form the IL-23 interleukin, a heterodimeric cytokine which functions in innate and adaptive immunity.
85	IL36RN	Q9UBH0	Interleukin 36 Receptor Antagonist	16.9	member of the interleukin 1 cytokine family with specific anti-inflammatory properties
86	LH	P22888	Luteinizing Hormone/Choriogonadotropin Receptor	78.6	G protein coupled receptor type 1
87	IL-11	P20809	Interleukin 11	21.4	Cytokine that stimulates the proliferation of various cells
88	PCAF	Q92831	Lysine Acetyltransferase 2B	93	This enzyme associates with other factors to regulate gene transcription.
89	IL-18 R beta /AcPL	O95256	Interleukin 18 Receptor Accessory Protein	68.3	The protein encoded by this gene is an accessory subunit of the heterodimeric receptor for interleukin 18 (IL18), a proinflammatory cytokine involved in inducing cell-mediated immunity.
90	INSL3	P51460	Insulin Like 3	14.5	member of the insulin-like hormone superfamily
91	VEGF R1	P17948	Vascular Permeability Factor Receptor;	150.7	Tyrosine-protein kinase receptor

			Tyrosine-Protein Kinase Receptor FLT; Fms Related Tyrosine Kinase 1		
92	Vasopressin	P01185	Arginine Vasopressin; Prepro-Arginine-Vasopressin-Neurophysin II; Antidiuretic Hormone	17.3	Arginine vasopressin is a posterior pituitary hormone that is synthesized in the supraoptic nucleus and paraventricular nucleus of the hypothalamus.
93	VIP Receptor 2	P41587	Vasoactive Intestinal Peptide Receptor 2; Pituitary Adenylate Cyclase-Activating Polypeptide Type III Receptor	49.4	Vasoactive intestinal peptide is involved in smooth muscle relaxation
94	TPM1	P09493	Tropomyosin 1 (Alpha); Cardiomyopathy, Hypertrophic 3	32.7	actin-binding proteins involved in the contractile system of striated and smooth muscles and the cytoskeleton of non-muscle cells.
95	IL-1 F9 / IL-1 H1	Q9NZH8	Interleukin 36, Gamma; Interleukin-1 Homolog 1; Interleukin-1 Epsilon	18.7	Belongs to IL1 cytokine family
96	Presenilin 2	P49810	Presenilin 2; Alzheimer Disease 4	50.1	Presenilins are postulated to regulate ameloid precursor protein processing through their effects on gamma-secretase, an enzyme that cleaves APP.
97	Transferrin	P02787	Transferrin; Beta-1 Metal-Binding Globulin; Siderophilin	77	transport iron from the intestine, reticuloendothelial system, and liver parenchymal cells to all proliferating cells in the body
98	Thrombin	P00734	Coagulation Factor II (Thrombin); Prepro-Coagulation Factor II	70	Coagulation factor II is proteolytically cleaved to form thrombin in the first step of the coagulation cascade which ultimately results in the stemming of blood loss. have antimicrobial activity against E. coli and P. aeruginosa.
99	Kallikrein 11	Q9UBX7	Kallikrein Related Peptidase 11; Trypsin-Like Protease; Serine Protease 20; Hippostasin	31	Kallikreins are a subgroup of serine proteases having diverse physiological functions. Growing evidence suggests that many kallikreins are implicated in carcinogenesis and some have potential as novel cancer and other disease biomarkers.
100	IL-19	Q9UHD0	Interleukin 19	20.4	cytokine that belongs to the IL10 cytokine subfamily found to be preferentially expressed in monocytes. It can lead to the activation of the signal transducer and activator of transcription 3 (STAT3).
101	Prohibitin	P35232	Prohobitin	29.8	play a role in human cellular senescence and tumor suppression. localized in the inner membrane of mitochondria.
102	TIMP-1	P01033	Metalloproteinase inhibitor 1	23.2	Irreversibly inactivates collagenases
103	SPARC	P09486	Basement-membrane protein 40 /	34.6	regulates cell growth through

			Osteonectin		interactions with the extracellular matrix and cytokines
104	TMEFF2	Q9UIK5	Transmembrane Protein With EGF-Like And Two Follistatin-Like Domains 2	41.4	Transmembrane protein
105	SPINK1	P00995	Serine protease inhibitor Kazal-type 1	8.5	Serine protease inhibitor which exhibits anti-trypsin activity
106	EDAR	Q9UNE0	Tumor necrosis factor receptor superfamily member EDAR	48.6	TNF Receptor superfamily member
107	NPTXR	O95502	Neuronal pentraxin receptor	52.8	Receptor
108	SART3	Q15020	Squamous cell carcinoma antigen recognized by T-cells 3	109.9	functions as a recycling factor of the splicing machinery
109	IL-7	P13232	Interleukin-7	20.2	Cytokine
110	S-100b	P04271	Protein S100-B	10.7	Small protein that binds ions
111	CFHR2	P36980	Complement factor H-related protein 2	30.6	Involved in complement regulation
112	XIAP	P98170	E3 ubiquitin-protein ligase XIAP	56.7	Enzyme
113	Wilms Tumor 1	P19544	Wilms tumor protein	49.2	Transcription factor that plays an important role in cellular development and cell survival
114	Troponin I	P19237	Troponin I, cardiac muscle	24	Troponin I is the inhibitory subunit of troponin, the thin filament regulatory complex which confers calcium-sensitivity to striated muscle actomyosin ATPase activity
115	MMP-8	P22894	Neutrophil collagenase	53.4	Enzyme; Can degrade fibrillary type I, II, and III collagens
116	SART1	O43290	Squamous Cell Carcinoma Antigen Recognized By T-Cells 1	90.2	Plays a role in mRNA splicing as a component of the U4/U6-U5 tri-snRNP
117	GFR alpha-2	O00451	GDNF family receptor alpha-2	51.5	Receptor for neurturin, canonically
118	PTN	P21246	Pleiotrophin	18.9	growth factor that induces neurite outgrowth and which is mitogenic for fibroblasts, epithelial, and endothelial cells
119	CD 163	Q86VB7	Scavenger receptor cysteine-rich type 1 protein M130	125.4	Receptor that may protect from oxidative damage
120	Orexin B	O43612	Orexin (Hypocretin)	13.4	Neuropeptide
121	MBL	P11226	mannose-binding lectin 2 / Mannose-binding protein C	26.1	Calcium-dependent lectin involved in innate immune defense.
122	sFRP-4	Q6FHJ7	Secreted frizzled-related protein 4	39.8	Soluble frizzled-related proteins
123	FIH	Q9NWT6	Hypoxia-inducible factor 1-alpha inhibitor	40.3	Inhibitor of HIF1-alpha
124	MMP-11 /Stromelysin-3	P24347	Stromelysin-3 / Matrix metalloproteinase-11	54.6	Matrix metallo proteinase
125	TECK / CCL25	O15444	C-C motif chemokine 25	16.6	Signalling chemokine, ligand of receptor CCR9
126	Insulysin / IDE	P14735	Insulin-degrading enzyme	118	Plays a role in the cellular breakdown of insulin, IAPP, glucagon, bradykinin, kallidin and other peptides
127	S100A6	P06703	Protein S100-A6	10.2	May function as calcium sensor and modulator, contributing to cellular calcium signaling
128	OSM	P13725	Oncostatin-M	28.5	Growth regulator. Inhibits the proliferation of a number of tumor cell lines

129	NRG1 Isoform GGF2	Q02297	Neuregulin 1	70.4	Direct ligand for ERBB3 and ERBB4 tyrosine kinase receptors. Concomitantly recruits ERBB1 and ERBB2 coreceptors
130	VEGF R3	P35916	Vascular endothelial growth factor receptor 3	152.7	Tyrosine-protein kinase receptor
131	MMP-9	P14780	Matrix metalloproteinase-9	78.4	May play a role in proteolysis of the extracellular matrix (Collagen type III degradation)
132	NM23-H1/H2	P15531	Nucleoside diphosphate kinase A	17.1	Major role in the synthesis of nucleoside triphosphates other than ATP
133	Pro-MMP-9	P14780	Pro-Matrix metalloproteinase-9	78.4	May play a role in proteolysis of the extracellular matrix (Collagen type III degradation)
134	NOV / CCN3	P48745	Protein NOV homolog	39.1	playing a role in various cellular processes including proliferation, adhesion, migration, differentiation and survival. It binds to integrins and membrane receptors such as NOTCH1
135	IL-17R	Q96F46	Interleukin-17 receptor A	96.1	Pro-inflammatory cytokine receptor
136	Trappin-2	P19957	Elafin (Elastase-specific inhibitor)	12.3	Neutrophil and pancreatic elastase-specific inhibitor of skin. It may prevent elastase-mediated tissue proteolysis
137	A2M	P01023	Alpha-2-macroglobulin	163.3	It Is able to inhibit all four classes of proteinases by a unique 'trapping' mechanism
138	Kallikrein 7	P49862	Kallikrein-7	27.5	May catalyze the degradation of intercellular cohesive structures in the cornified layer of the skin in the continuous shedding of cells from the skin surface
139	SSEA-4	n/a	Stage-specific embryonic antigen 4 /	n/a	n/a
140	Kininostatin / kininogen	P01042	Kininogen-1	72	Kininogens are inhibitors of thiol proteases
141	VEGF-C	P49767	Vascular endothelial growth factor C	46.9	Growth factor active in angiogenesis, and endothelial cell growth (ligand of VEGFR3)
142	GRP75	P38646	Heat Shock Protein Family A (Hsp70) Member 9	73.7	Implicated in the control of cell proliferation and cellular aging. May also act as a chaperone for protein folding
143	TRKB	Q16288	Neurotrophic Tyrosine Kinase, Receptor, Type 3	92	Receptor tyrosine kinase
144	ADAMTS-10	Q9H324	ADAM Metallopeptidase With Thrombospondin Type 1 Motif 10	120.9	Metalloprotease that participate in microfibrils assembly.
145	Tarc	Q92583	C-C motif chemokine 17	10.5	Signalling chemokine. Chemotactic factor for T-lymphocytes but not monocytes or granulocytes. May play a role in T-cell development in thymus and in trafficking and activation of mature

					T-cells
146	MMP-10	P09238	Stromelysin-2 (matrix metallo proteinase 10)	54.1	Matrix metallo Proteinase
147	PARK7	Q99497	Protein deglycase DJ-1	19.9	Protein deglycase that repairs methylglyoxal- and glyoxal-glycated amino acids and proteins
148	GDF-15	Q99988	Growth/differentiation factor 15	34.1	belonging to the transforming growth factor beta superfamily that has a role in regulating inflammatory and apoptotic pathways in injured tissues and during disease processes
149	Vitronectin	P04004	Vitronectin (VN) (S-protein) (Serum-spreading factor)	54.3	Glycoprotein promoting cell adhesion via integrins
150	IL-6	P05231	Interleukin-6	23.7	Pro-inflammatory cytokine
151	HSPA8	P11142	Heat shock cognate 71 kDa protein	70.9	Acts as a repressor of transcriptional activation and a chaperone
152	Serpin A12	Q8IW75	Serpin A12	47.2	Adipokine that modulates insulin action by specifically inhibiting its target protease KLK7 in white adipose tissues
153	IL-17RC	Q8NAC3	Interleukin-17 receptor C	86.2	Pro-inflammatory cytokine receptor
154	PAI-1	P05121	Plasminogen activator inhibitor 1	45	Serine protease inhibitor. This inhibitor acts as 'bait' for tissue plasminogen activator, urokinase
155	TCCR / WSX-1	Q6UWB1	Interleukin-27 receptor subunit alpha	69.5	Receptor for IL27. This signaling system acts through STAT3 and STAT1 and it is Involved in the regulation of Th1-type immune responses
156	BMP-5	P22003	Bone morphogenetic protein 5	51.7	Induces cartilage and bone formation
157	Neurokinin-A	P20366	Tachykinin Precursor 1	15	Tachykinins are active peptides which excite neurons, evoke behavioral responses, are potent vasodilators and secretagogues, and contract (directly or indirectly) many smooth muscles
158	Beta IG-H3	Q15582	Transforming Growth Factor Beta Induced	74.7	May play a role in cell-collagen interactions
159	CNTF	P26441	Ciliary neurotrophic factor	22.9	CNTF is a survival factor for various neuronal cell types.
160	Troponin C	P63316	Troponin C, slow skeletal and cardiac muscles	18.4	Central regulatory protein of striated muscle contraction
161	Mammaglobin A	Q13296	Mammaglobin-A	10.5	Expressed mainly in mucosa, secretoglobins seem to be involved in cell signalling, immune response, and chemotaxis, and may also serve as transporters for steroid hormones in humans
162	Serpin A1	P01009	Alpha-1-antitrypsin	46.7	Inhibitor of serine proteases
163	LRP-1	Q07954	Prolow-density lipoprotein receptor-related protein 1	504.6	Endocytic receptor involved in endocytosis and in phagocytosis

					of apoptotic cells
164	L-Selectin (CD62L)	P14151	L-selectin	42.2	Cell surface adhesion protein. Mediates the adherence of lymphocytes to endothelial cells
165	PYK2	Q14289	Protein-tyrosine kinase 2-beta	115.9	Non-receptor protein-tyrosine kinase that regulates reorganization of the actin cytoskeleton
166	TWEAK R / TNFRSF12	Q93038	Tumor necrosis factor receptor superfamily member 25	45.4	TNFR superfamily member
167	IL-26	Q9NPH9	Interleukin-26	19.8	Pro-inflammatory Signalling cytokine
168	IL-15 R alpha	Q13261	Interleukin-15 receptor subunit alpha	28.2	Cytokine receptor
169	VE-Cadherin	P33151	Cadherin-5	87.5	calcium-dependent cell adhesion proteins
170	TMEFF1 / Tomoregulin-1	Q8IYR6	Tomoregulin-1	40.9	Transmembrane protein
171	Itk	Q08881	Tyrosine-protein kinase ITK/TSK	71.8	Tyrosine kinase that plays an essential role in regulation of the adaptive immune response
172	S100A8	P05109	Protein S100-A8	10.8	Calcium- and zinc-binding protein which plays a prominent role in the regulation of inflammatory processes and immune response
173	NRG3	P56975	Pro-neuregulin-3	77.9	Direct activator of the ERBB4 tyrosine kinase receptor.
174	GFR alpha-4	Q9GZZ7	GDNF family receptor alpha-4	31.7	Receptor for persephin
175	VEGF R2 (KDR)	P35968	Vascular endothelial growth factor receptor 2	151.5	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFC and VEGFD. Plays an essential role in the regulation of angiogenesis
176	Pro-MMP-13	P45452	Matrix Metallopeptidase 13	53.8	Matrix metallo proteinase (collagenase 3)
177	IL-31	Q6EBC2	Interleukin-31	82.9	Signalling cytokine
178	uPAR	Q03405	Plasminogen Activator, Urokinase Receptor	37	Urokinase receptor
179	Livin	Q96CA5	Baculoviral IAP repeat-containing protein 7	32.8	Apoptotic regulator (mostly anti-apoptotic)
180	VCAM-1 (CD106)	P19320	Vascular cell adhesion protein 1	81.3	Adhesion molecule
181	D-Dimer	n/a	D dimer (a fibrin degradation product)	200	A fibrin degradation product
182	IL-17B R	Q9NRM6	Interleukin-17 receptor B	55.9	Interleukin-17 receptor B
183	IL-17C	Q9P0M4	Interleukin-17C	21.7	Interleukin 17 family member
184	IL-17D	Q8TAD2	Interleukin-17D	21.8	Interleukin 17 family member
185	Hck	P08631	HCK Proto-Oncogene, Src Family Tyrosine Kinase	59.6	Tyrosine-protein kinase HCK
186	Galanin	P22466	Galanin peptides	13.3	Endocrine hormone
187	Lymphotactin / XCL1	P47992	Lymphotactin (ATAC) (C motif chemokine 1)	12.5	Pro-inflammatory Chemokine
188	HTRA2	O43464	Serine protease HTRA2, mitochondrial	48.8	Serine protease (enzyme)
189	SSTR2	P30874	Somatostatin receptor type 2	41.3	Receptor for somatostatin-14 and -28
190	FRK	P42685	Tyrosine-protein kinase FRK	58.2	Non-receptor tyrosine-protein kinase that negatively regulates

					cell proliferation
191	PTPRD	P23468	Receptor-type tyrosine-protein phosphatase delta	214.8	Receptor-type tyrosine-protein phosphatase delta
192	MMP-20	O60882	Matrix metalloproteinase-20	54.4	Matrix metallo proteinase
193	MIP-3 alpha	P78556	C-C Motif Chemokine Ligand 20	13.4	Chemokine for monocytes
194	Alpha 1 Microglobulin	P02760	Alpha 1 Microglobulin	27	A1M binds and degrades heme, is a radical scavenger as well as a reductase
195	IL-31 RA	Q8NI17	Interleukin-31 receptor subunit alpha	82.9	Interleukin-31 receptor subunit alpha
196	GPX3	P22352	Glutathione peroxidase 3	25.6	Anti-oxidant enzyme
197	IBSP	P21815	Bone sialoprotein 2	35.1	Binds tightly to hydroxyapatite. Appears to form an integral part of the mineralized bone matrix. Probably important to cell-matrix interaction.
198	IL-1 R9	Q9NP60	X-linked interleukin-1 receptor accessory protein-like 2	78.7	Member of the interleukin 1 receptor family
199	Endothelin	P05305	Endothelin	24.4	It is a potent vasoconstrictor and is produced by vascular endothelial cells
200	pro-Glucagon	P01275	Glucagon preprotein	20.9	Regulates blood glucose by increasing gluconeogenesis and decreasing glycolysis
201	GADD45A	P24522	Growth Arrest And DNA Damage Inducible Alpha	18.3	It stimulates DNA excision repair and inhibits entry of cells into S phase
202	Omentin	Q8WWA0	Omentin	34.9	It enhances insulin-stimulated glucose uptake in adipocytes

[0211] The present disclosure has been described with reference to one or more exemplary data embodiments. However, it will be understood by those skilled in the art that various changes can be made, and equivalents can be substituted, without departing from the scope of the present disclosure. In addition, modifications can be made to adapt a particular material to the teachings of the present disclosure without departing from the scope thereof. Therefore, the present disclosure is not intended to be limited to the particular material or embodiment disclosed, but includes all materials and embodiments falling within the scope hereof.

WHAT IS CLAIMED IS:

1. A topical skin composition formulated to achieve a desired skin benefit, the composition comprising:

a blend of proteins that have been selected based on the desired skin benefit to be derived by application of the topical skin composition,

wherein each one of the blend of proteins are from a homogenous donor group having two or more individuals;

a delivery vehicle for the proteins,

wherein the blend of proteins is present in an amount from 0.0001 wt.% to 10 wt.% based on the total weight of the topical skin composition.

2.The topical skin composition of claim 1, wherein the amount is 0.001 wt.% to 5.0 wt.%.

3.The topical skin composition of claim 1, wherein the amount is 0.001 wt.% to 1.0 wt.%.

4. The topical skin composition of claim 1, wherein the homogenous donor group is selected from the group consisting of: Asian, African, and Caucasian.

5. The topical skin composition of claim 4, wherein the homogenous donor group comprises donors who constitute a group whose bloodlines are 80% or greater of a single race or ethnicity.

6. The topical skin composition of claim 1, wherein the proteins are synthetically derived.

7. The topical skin composition of claim 1, wherein the desired skin effect is at least one skin effect selected from the group consisting of: pigmentation, wound healing, inflammation, dermal matrix, wrinkles, scar prevention, and epidermis.

8. The topical skin composition of claim 1, wherein the topical skin composition is an emulsion.

9. The topical skin composition of claim 8, wherein the emulsion is an oil in water emulsion.

10. The topical skin composition of claim 1, wherein the vehicle includes at least one ingredient selected from the group consisting of one or more antioxidants, polypeptides, vitamins, plant extracts, materials derived from plant stem cells, oils, preservatives, thickening agents, ceramides, skin lighteners, exfoliants, anti-aging and anti-wrinkle agents, sunscreens, skin barrier repair agents, moisturizing ingredients, essential fatty acids, humectants, emollients, solvents, surfactants, emulsifiers, fillers, polymers, buffers, temperature regulating agents, and the like, and combinations thereof.

11. The topical skin composition of claim 10, wherein the vehicle can include water.

12. The topical skin composition of claim 11, wherein the vehicle is up to 99 wt.% based on the total weight of the topical skin composition.

13. A topical skin composition formulated to achieve a desired skin benefit, the composition comprising:

a blend of proteins that have been selected based on the desired skin benefit to be derived by application of the topical skin composition,

wherein the blend of proteins is from one or more donors from at least two or more donor groups;

a delivery vehicle for the proteins,

wherein the blend of proteins is present in an amount from 0.0001 wt.% to 10 wt.% based on the total weight of the topical skin composition.

14. The topical skin composition of claim 13, wherein the donor group is heterogenous and is selected from the group consisting of: Asian and African; Asian and Caucasian; African and Caucasian; and Asia, African, and Caucasian.

15. The topical skin composition of claim 13, wherein the amount is 0.001 wt.% to 5.0 wt.%.

16. The topical skin composition of claim 13, wherein the amount is 0.001 wt.% to 1.0 wt.%.

17. The topical skin composition of claim 13, wherein the proteins are synthetically derived.

18. The topical skin composition of claim 13, wherein the desired skin effect is at least one skin effect selected from the group consisting of: pigmentation, wound healing, inflammation, dermal matrix, wrinkles, scar prevention, and epidermis.

19. The topical skin composition of claim 13, wherein the topical skin composition is an emulsion.

20. The topical skin composition of claim 13, wherein the vehicle includes at least one ingredient selected from the group consisting of one or more antioxidants, polypeptides, vitamins, plant extracts, materials derived from plant stem cells, oils, preservatives, thickening agents, ceramides, skin lighteners, exfoliants, anti-aging and anti-wrinkle agents, sunscreens, skin barrier repair agents, moisturizing ingredients, essential fatty acids, humectants, emollients, solvents, surfactants, emulsifiers, fillers, polymers, buffers, temperature regulating agents, and the like, and combinations thereof.

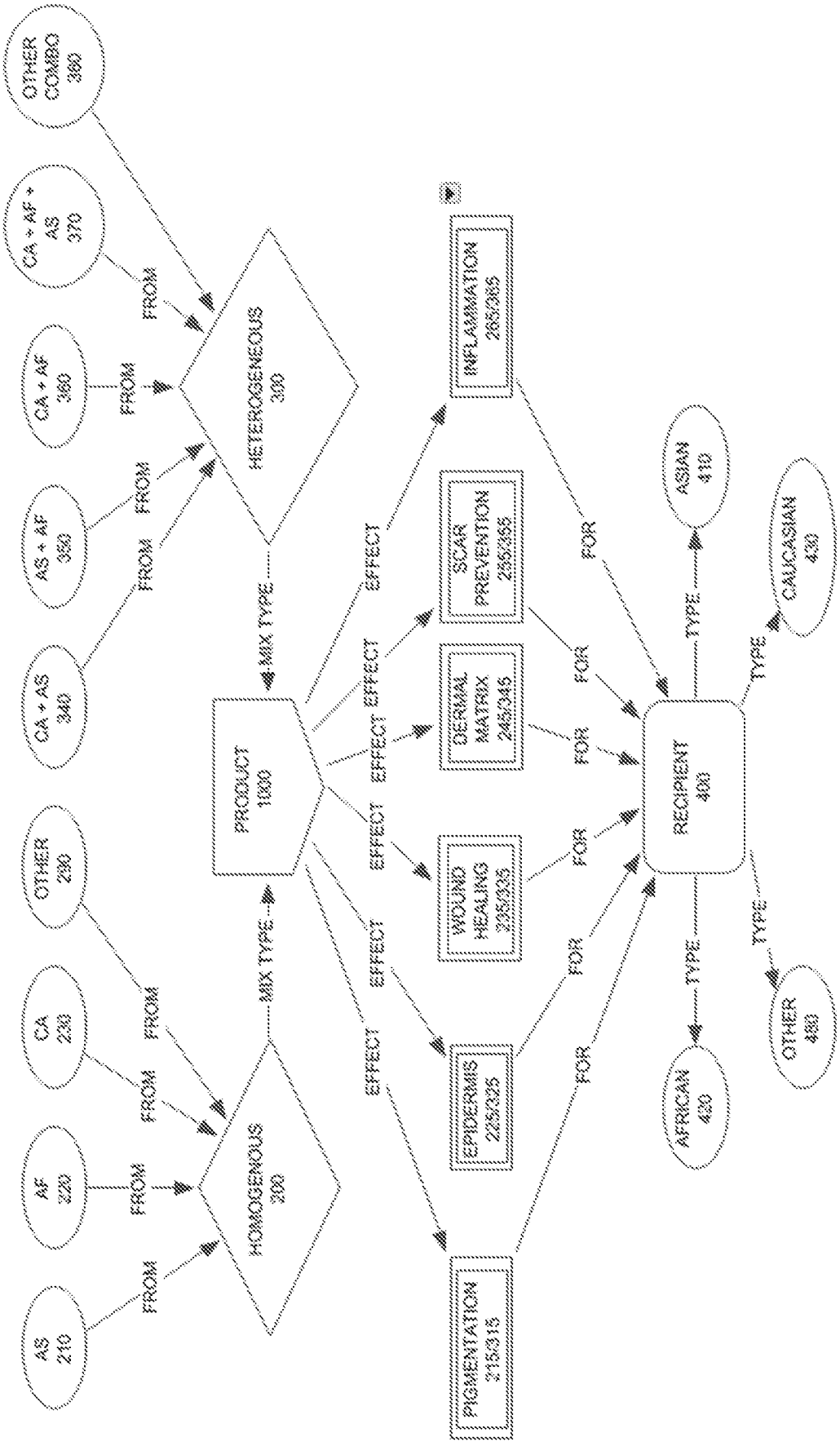

PRODUCT
1000
HOMOGENEOUS
200
HETEROGENEOUS
300
MIX TYPE
MIX TYPE
FROM
AS
210
AF
220
CA
230
OTHER
290
CA + AS
340
AS + AF
350
CA + AF
360
CA + AF + AS
370
OTHER COMBO
380
EFFECT
PIGMENTATION
215/315
EPIDERMIS
225/325
WOUND HEALING
235/335
DERMAL MATRIX
245/345
SCAR PREVENTION
255/355
INFLAMMATION
265/365
FOR
RECIPIENT
400
TYPE
AFRICAN
420
ASIAN
410
CAUCASIAN
430
OTHER
490

FIG. 1

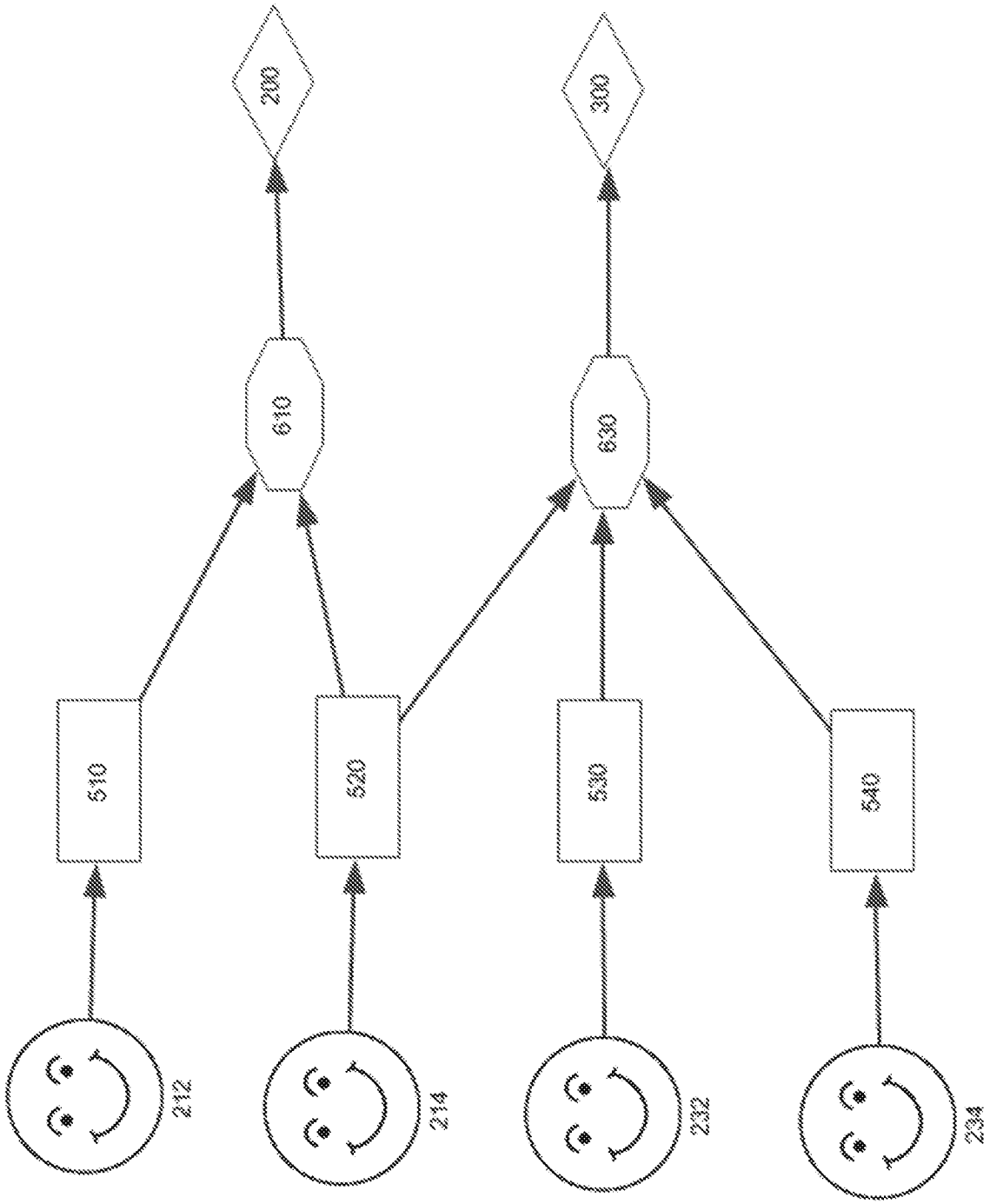
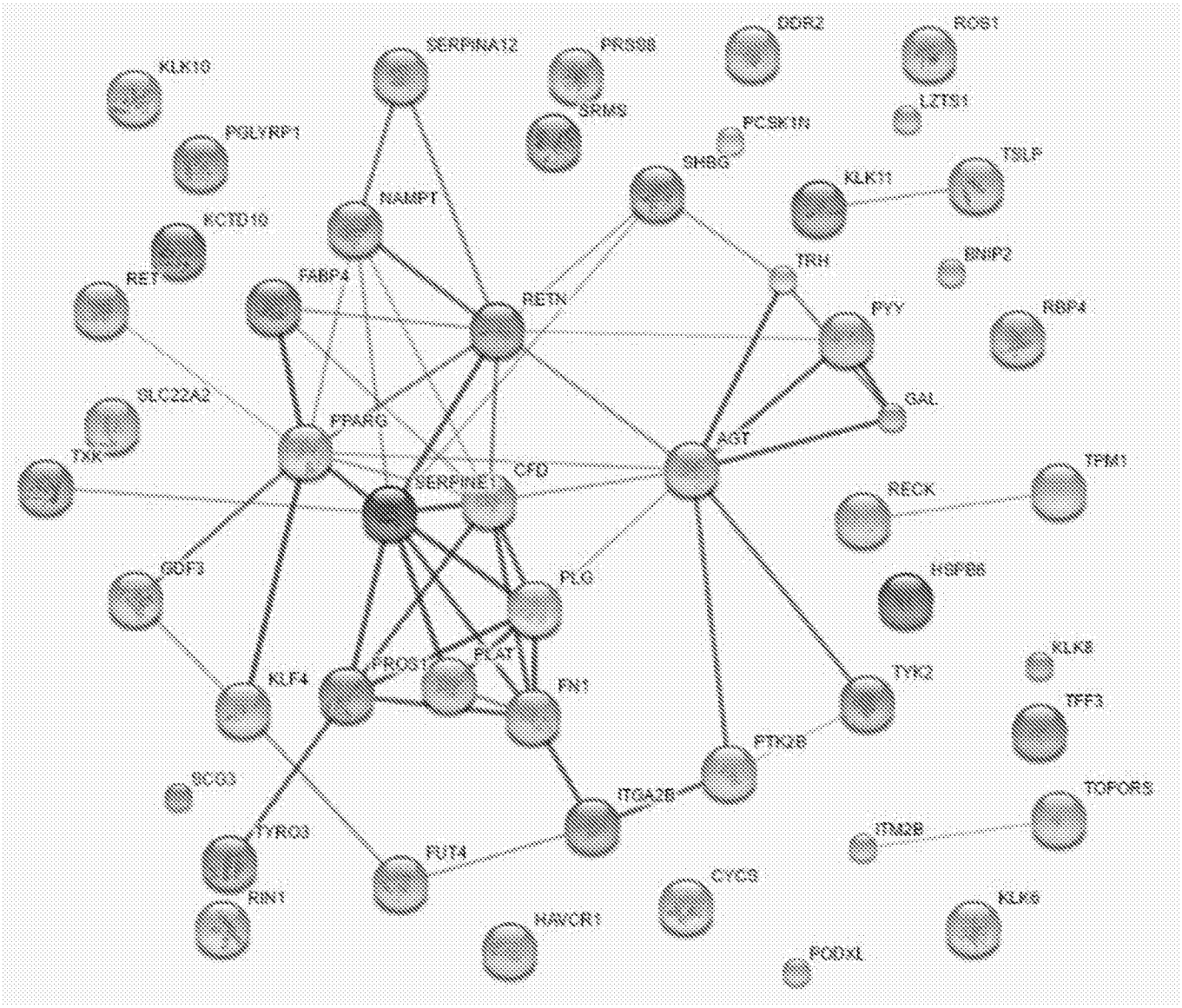


FIG. 2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PSLYRP1
KCTD10
RET
FABP4
SERPINA12
PRSS8
SPMS
NAMPT
RETN
DDR2
ROS1
LZTS1
PCSK1N
SNRG
KLK11
TSLP
TRH
BNIP3
PYY
RBP4
GAL
SLC22A2
TXR
PPARG
SERPINE1
CFD
AGT
TPM1
RECK
HSPB8
GDF3
PLG
KLF4
PROS1
PLAT
FN1
TYK2
KLK8
TFF3
FTR2B
SCG3
ITGA2B
TOPORS
TYRO3
FUT4
ITM2B
RIN1
CYCS
KLK6
HAVCR1
PODXL

FIG. 3

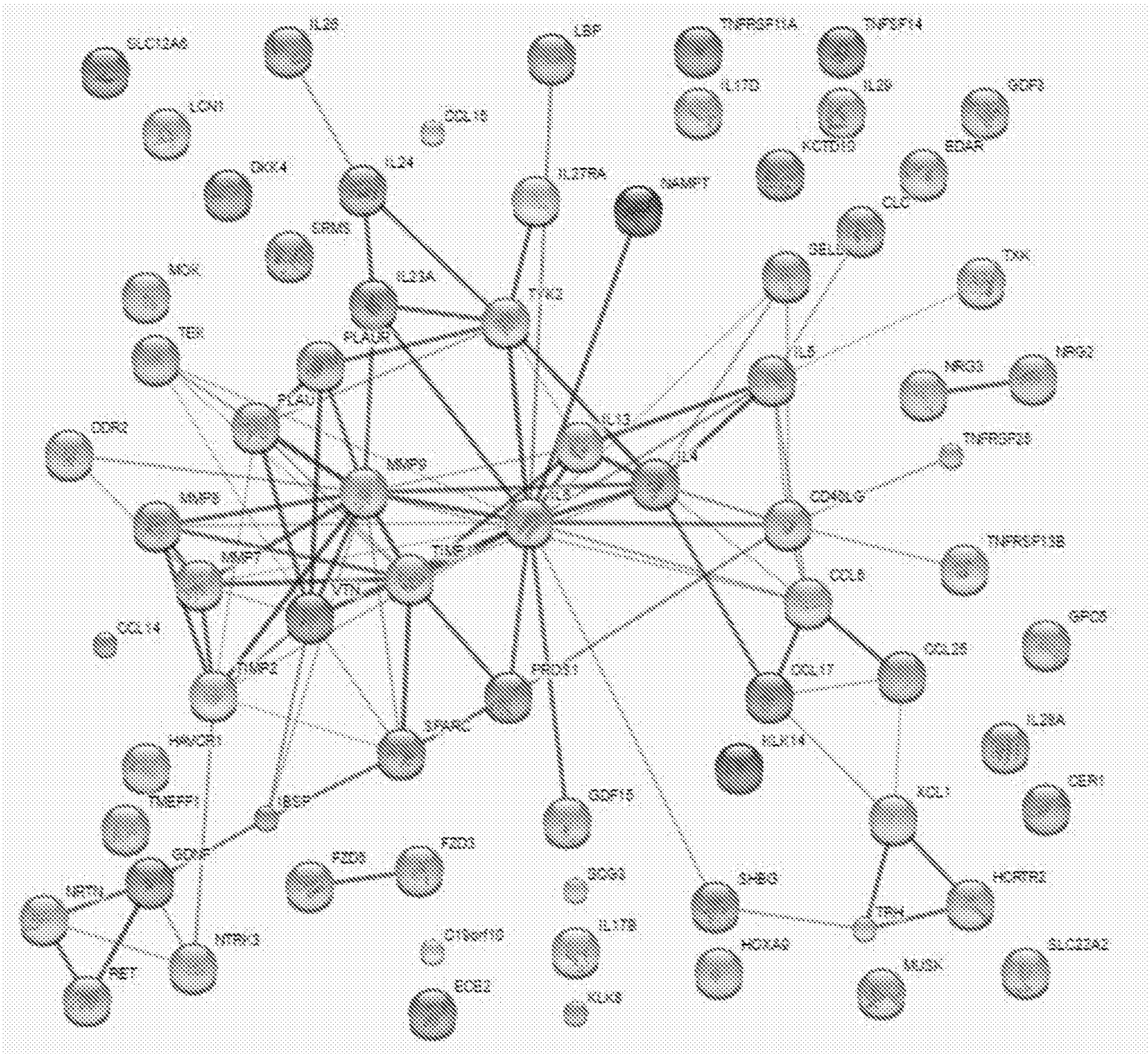

LBP
NAMPT
IL24
IL23A
IL27RA
IL5
IL13
IL4
PLAU
MMP9
MMP7
VTN
TIMP2
SPARC
CD40LG
TNFRSF13B
CCL8
CCL17
GDF15
NRG3
FZD3
IL17B
SHBG
HCRTR2
RET
NTRK3
MUSK

FIG. 4

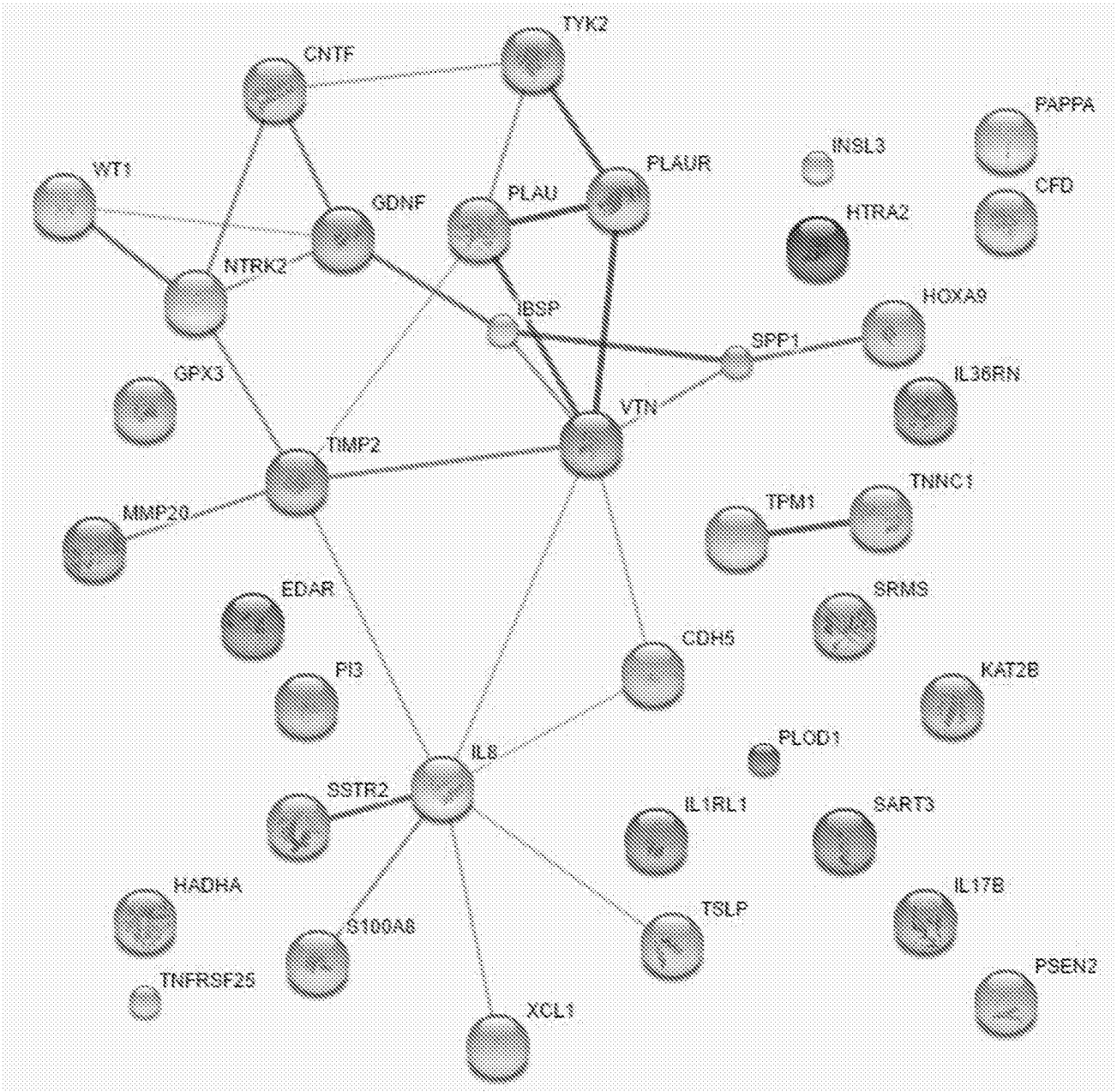

TYK2
CNTF
PAPPA
INSL3
WT1
PLAUR
CFD
PLAU
GDNF
HTRA2
NTRK2
HOXA9
IBSP
SPP1
GPX3
IL36RN
VTN
TIMP2
TNNC1
TPM1
MMP20
SRMS
EDAR
CDH5
KAT2B
PI3
PLOD1
IL8
SSTR2
IL1RL1
SART3
HADHA
IL17B
TSLP
S100A8
PSEN2
TNFRSF25
XCL1

FIG. 5

FIG. 6

FIG. 7

FIG. 8

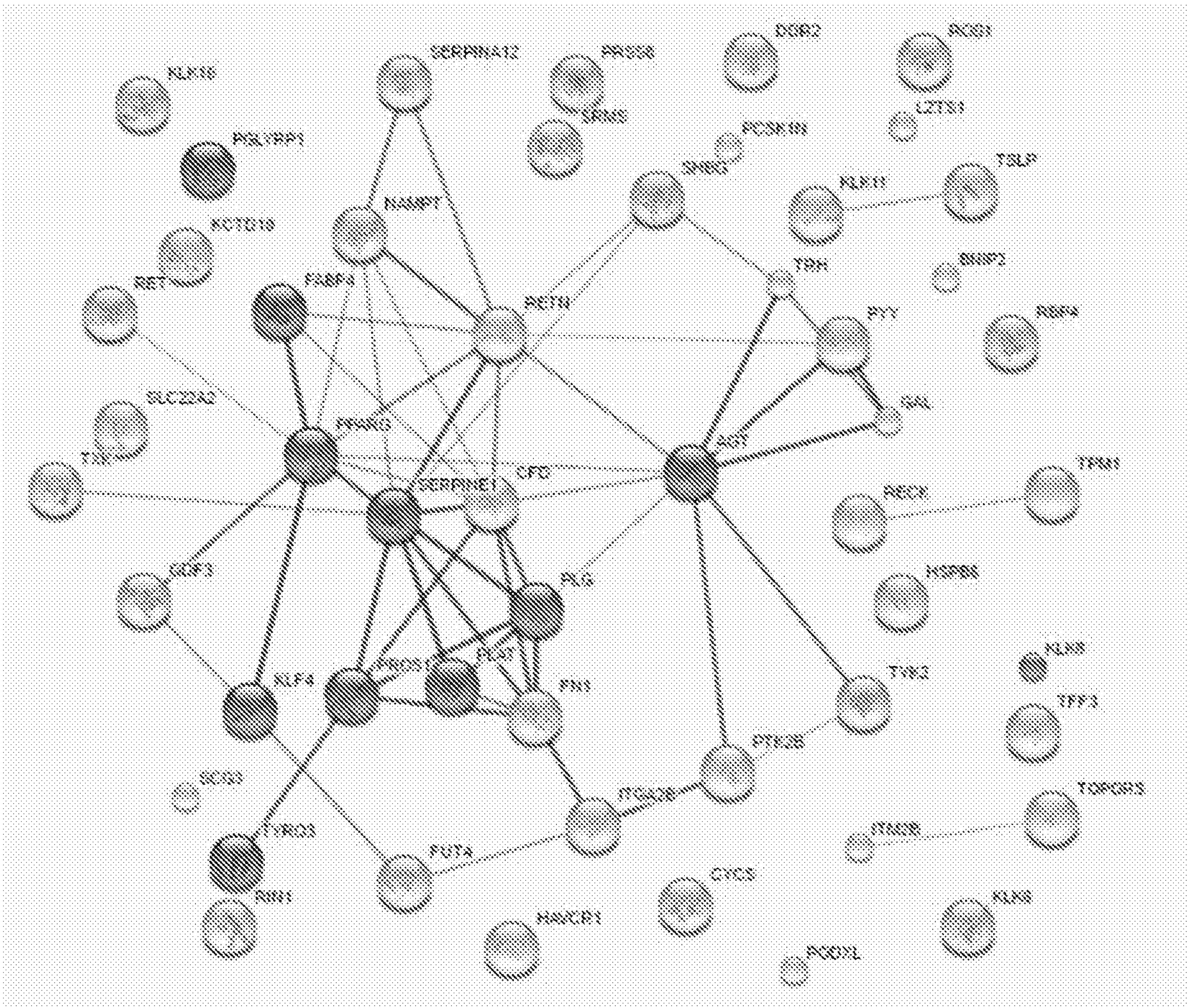

SERPINA12
PRSS8
DGR2
PGLYRP1
LZTS1
PCSK1N
SHBG
TSLP
NAMPT
FABP4
RET
TRH
RETN
PYY
RBP4
SLC22A2
PPARG
GAL
AGT
SERPINE1
CFD
TPM1
RECK
GDF3
PLG
TFF3
KLF4
PROS1
PLAT
FN1
TYK2
PTK2B
TYRO3
ITGA2B
TOPORS
FUT4
CYCS
HAVCR1
PODXL

FIG. 9

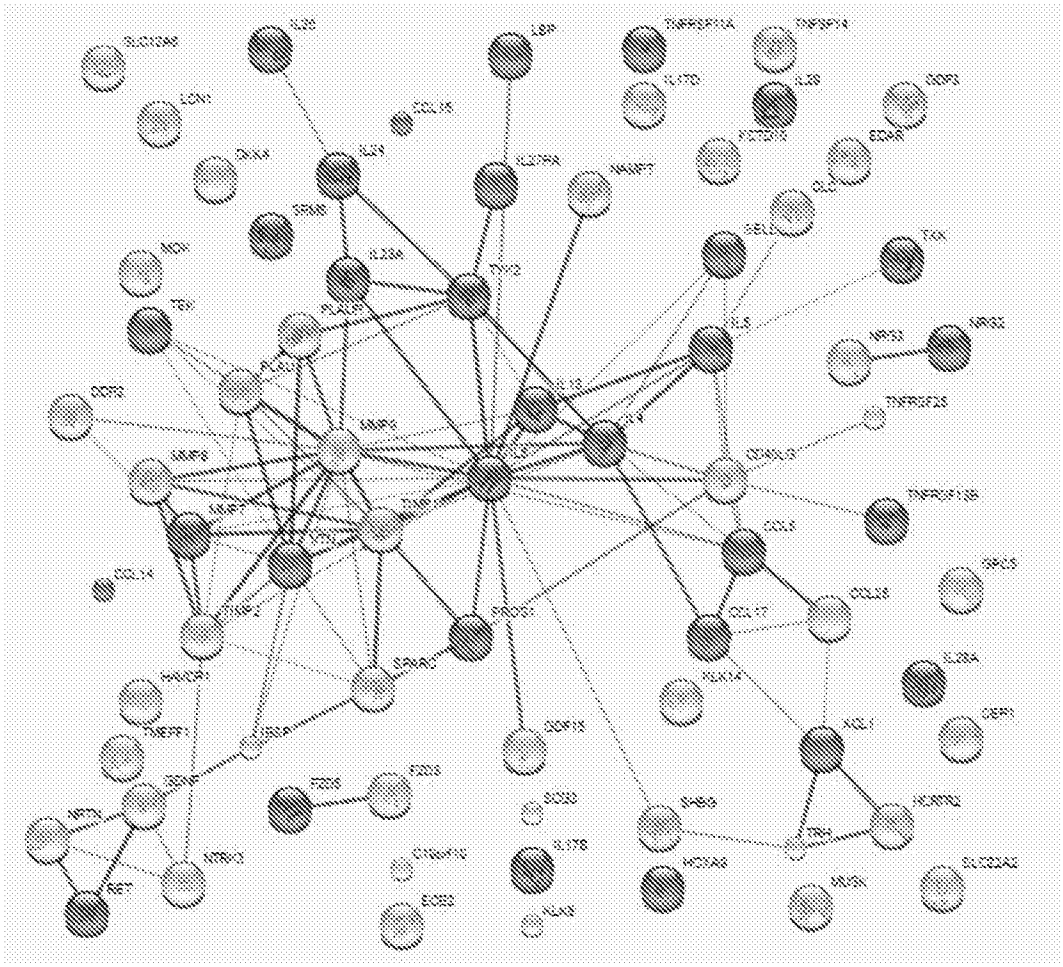
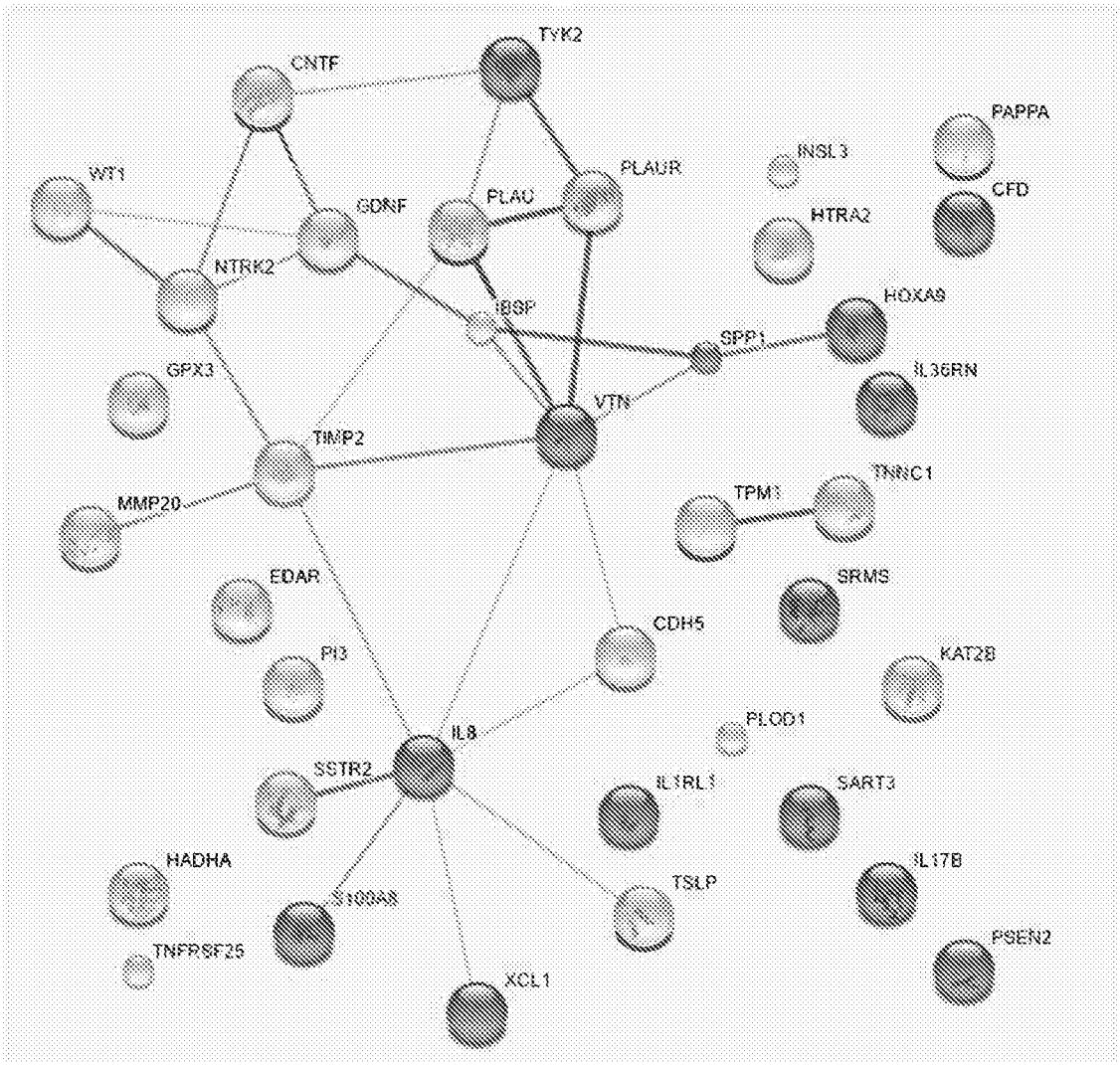


FIG. 10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CNTF
PAPPA
INSL3
WT1
PLAUR
CFD
GDNF
PLAU
HTRA2
NTRK2
IBSP
HOXA9
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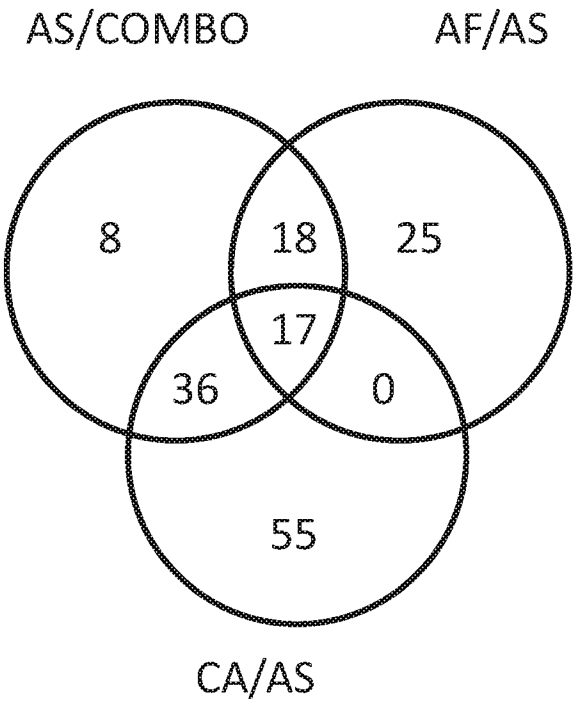
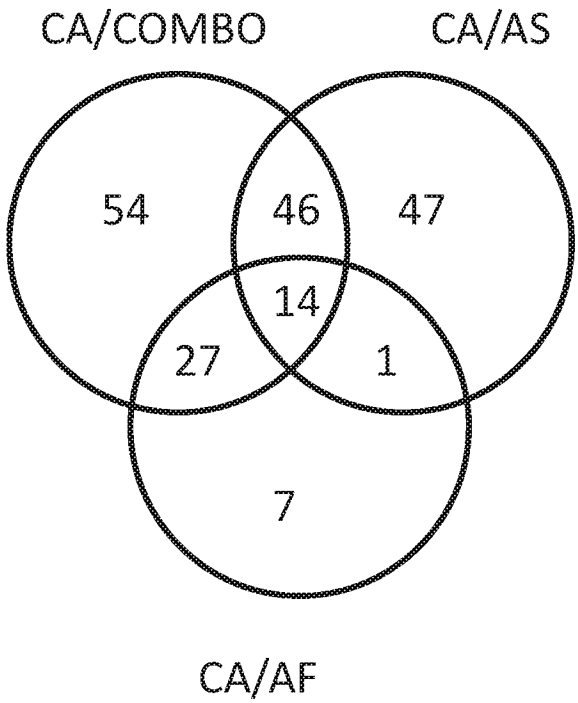
GPX3
IL36RN
VTN
TIMP2
TNNC1
MMP20
TPM3
EDAR
SRMS
CDH5
PI3
KAT2B
PLOD1
IL8
SSTR2
IL3RL1
SART3
HADHA
IL17B
TSLP
S100A8
PSEN2
TNFRSF25
XCL1

FIG. 11


AS/COMBO
AF/AS
8
18
25
17
36
0
55
CA/AS


CA/COMBO
CA/AS
54
46
47
14
27
1
7
CA/AF

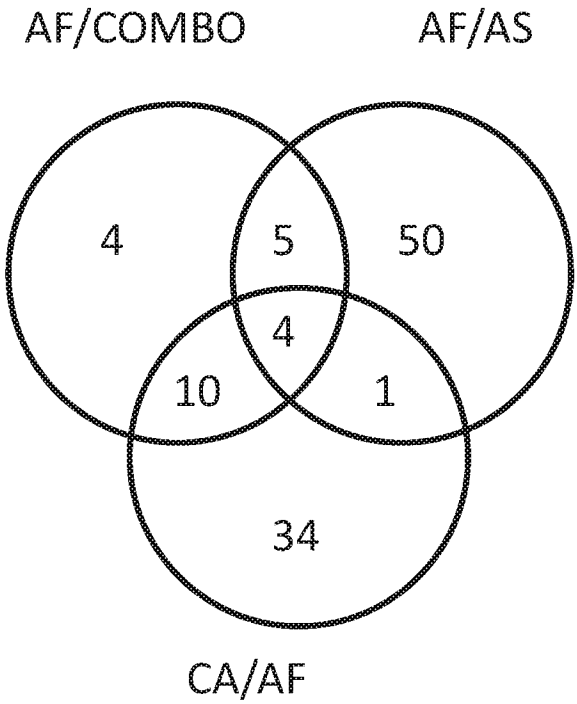

AF/COMBO
AF/AS
4
5
50
4
10
1
34
CA/AF

FIG. 12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/64158

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 38/00, A61K 8/00, A61K 8/72, A61K 8/67 (2017.01)
CPC - A61K 8/676, A61K 8/64, A61K 8/671, A61K 8/678, A61Q 19/08
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)
IPC(8) - A61K 38/00, A61K 8/00, A61K 8/72, A61K 8/67 (2017.01)
CPC - A61K 8/676, A61K 8/64, A61K 8/671, A61K 8/678, A61Q 19/08

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)
PatBase, Google Scholar; Search terms: topical skin composition formulated blend proteins skin benefit topical skin composition homogenous donor delivery vehicle proteins

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/0132267 A1 (Shacknai et al.) 14 May 2015 (14.05.2015); para[0018], para[0020], para[0022], para[0025], para[0026], para[0032], para[0033], para[0041], para[0043]	1-20
A	US 2009/0016994 A1 (Gibbs et al.) 15 January 2009 (15.01.2009); entire document	1-20
A	US 2003/0147830 A1 (Phillips et al.) 07 August 2003 (07.08.2003); entire document	1-20
A	US 2004/0265268 A1 (Jain) 30 December 2004 (30.12.2004); entire document	1-20
A	US 2007/0077232 A1 (Naughton et al.) 05 April 2007 (05.04.2007); entire document	1-20

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
19 January 2017	17 FEB 2017
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)