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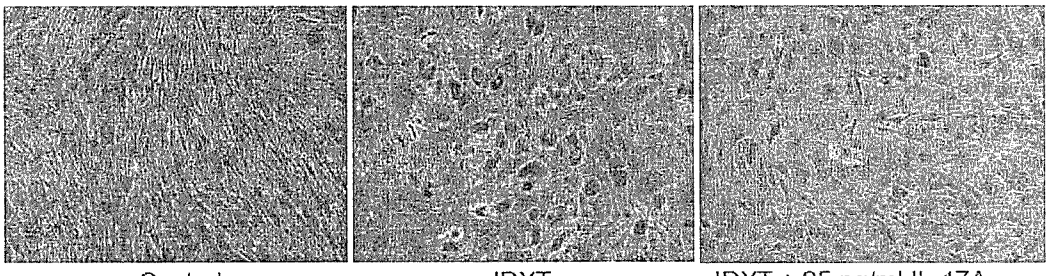
(54) Title: COMPOSITION FOR SLIMMING

[Figure 1]



(57) Abstract: A slimming composition containing inter leukin-17 (IL-17) as an effective ingredient is disclosed. The slimming composition may provide a superior slimming effect through the ability of the effective ingredient to inhibit the differentiation of adipocytes and reduce the level of lipid droplets in differentiated adipocytes.

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【DESCRIPTION】

【Invention Title】

Composition for Slimming

【Technical Field】

<1> This disclosure relates to a slimming composition, specifically to a slimming composition for inhibiting differentiation of adipocytes or reducing the level of lipid droplets in adipocytes.

【Background Art】

<2> Interleukin-17 (IL-17) is a kind of cytokine known as cytotoxic T-lymphocyte-associated serine esterase 8 (CTLA8).

<3> A variety of diseases including obesity and lipoma are known to be related with abnormal differentiation of adipocytes or abnormal level of lipid droplets in adipocytes. Researches are actively under way on the differentiation of adipocytes and the level of lipid droplets in adipocytes. Development of a factor or a substance capable of effectively controlling the differentiation of adipocytes or the level of lipid droplets in adipocytes is needed.

<4> The inventors have researched to find such factor or substance. As a result, they found out that interleukin-17 (IL-17) can effectively inhibit the differentiation of mesenchymal stem cells into adipocytes and reduce the level of lipid droplets in the differentiated adipocytes.

【Disclosure】

【Technical Problem】

<5> Therefore, the present invention has been made in view of the above problems, and it is an object of the present invention to solve the technical problems.

<6> Specifically, an object of the present invention is to provide a slimming composition comprising interleukin-17 (IL-17) inhibiting the differentiation of adipocytes as an effective ingredient.

<7> Another object of the present invention is to provide a slimming composition comprising interleukin-17 (IL-17) reducing the level of lipid

droplets in the differentiated adipocytes as an effective ingredient.

【Technical Solution】

<8> The present invention has been made in an effort to attain the aforesaid objects. In an aspect, the present invention provides a slimming composition comprising interleukin-17 (IL-17).

【Advantageous Effects】

<9> The inventors have identified that interleukin-17 (IL-17) can effectively inhibit the differentiation of mesenchymal stem cells into adipocytes and reduce the level of lipid droplets in the differentiated adipocytes, so that the present invention provides superior slimming effect by comprising interleukin-17 (IL-17) as an effective ingredient may provide a particularly.

【Description of Drawings】

<10> The above and other aspects, features and advantages of the disclosed exemplary embodiments will be more apparent from the following detailed description taken in conjunction with the accompanying drawings in which:

<11> Figs. 1 to 4 are micrographs and graphs showing the effect of inhibiting differentiation of adipocytes by interlukin-17A (IL-17A) or IL-17F;

<12> Figs. 5 to 10 are graphs showing the change of expression of IL-17RA and IL-17RC mRNAs by IL-17A or IL-17F and the change of expression of peroxisome proliferator activating receptor γ (PPARγ) mRNA, fatty acid binding protein 4 (FABP4) and adiponectin mRNAs in cells treated with IL-17A;

<13> Figs. 11 and 12 are graphs showing the effect of inhibiting differentiation of adipocytes by IL-17A observed with anti-IL-17A;

<14> Figs. 13 to 15 are micrographs and graphs showing the level of lipid droplets in adipocytes;

<15> Figs. 16 to 19 are graphs showing the control of IL-6 and IL-8 genes in differentiated adipocytes by IL-17A; and

<16> Fig. 20 shows the decrease of adipose tissue in obesity-induced C57BL/6 mice fed with a high fat diet for a month, 7 days after the injection of IL-

17A into right epididymal adipose tissue.

【Best Mode】

<17> Exemplary embodiments now will be described more fully hereinafter with reference to the accompanying drawings, in which exemplary embodiments are shown. This disclosure may, however, be embodied in many different forms and should not be construed as limited to the exemplary embodiments set forth therein. Rather, these exemplary embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of this disclosure to those skilled in the art. In the description, details of well-known features and techniques may be omitted to avoid unnecessarily obscuring the presented embodiments.

<18> The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of this disclosure. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, the use of the terms a, an, etc. does not denote a limitation of quantity, but rather denotes the presence of at least one of the referenced item. The use of the terms "first", "second", and the like does not imply any particular order, but they are included to identify individual elements. Moreover, the use of the terms first, second, etc. does not denote any order or importance, but rather the terms first, second, etc. are used to distinguish one element from another. It will be further understood that the terms "comprises" and/or "comprising", or "includes" and/or "including" when used in this specification, specify the presence of stated features, regions, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, regions, integers, steps, operations, elements, components, and/or groups thereof.

<19> Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one of ordinary skill in the art. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having

a meaning that is consistent with their meaning in the context of the relevant art and the present disclosure, and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

<20> In the drawings, like reference numerals in the drawings denote like elements. The shape, size and regions, and the like, of the drawing may be exaggerated for clarity.

<21> As used herein, the term "slimming" has a broad meaning, including, not only ameliorating or preventing obesity, but also preventing and treating of diseases related with the increase of adipose tissue, reducing body weight for cosmetic or beauty treatment, ameliorating or preventing decreased elasticity due to increase of adipose tissue, or maintaining charming body and smooth skin, and not specially limited unless contrary to the aforesaid purposes.

<22> The inventors have found out that a composition comprising interleukin-17 (IL-17), especially one or more selected from a group consisting of IL-17A and IL-17F, as an effective ingredient can inhibit differentiation of mesenchymal stem cells into adipocytes and reduce the level of lipid droplets in the differentiated adipocytes.

<23> IL-17 is known to enhance the expression of the cytokines IL-6 and IL-8 and granulocyte colony stimulating factor (G-CSF), which are known to affect the differentiation of the hematopoietic system in human fibroblasts (Yao et al., Human IL-17: a novel cytokine derived from T cells. *J. Immun.* 155: 5483-5486, 1995). Further, IL-17 controls T-cell immune response which is related with allergic reactions. It was demonstrated from an experiment using IL-17-deficient mice (Nakae et al., Suppression of immune induction of collagen-induced arthritis in IL-17-deficient mice. *J. Immun.* 171: 6173-6177, 2003). Besides, considering that collagen-induced arthritis does not occur in IL-17-deficient mice, IL-17 presumably affects the onset of arthritis (Nakae et al., IL-17 production from activated T cells is required for the spontaneous development of destructive arthritis in mice deficient in IL-1 receptor antagonist. *Proc. Nat. Acad. Sci.* 100: 5986-5990, 2003). Especially,

considering that IL-17 is present in higher level in the synovial fluid of patients with rheumatoid arthritis than patients with osteoarthritis, IL-17 is presumably closely related with the onset of rheumatoid arthritis (Kotake et al., IL-17 in synovial fluids from patients with rheumatoid arthritis is a potent stimulator of osteoclastogenesis. *J. Clin. Invest.* 103: 1345-1352, 1999).

<24> Despite these researches, a superior slimming effect provided by a composition comprising IL-17 as an effective ingredient has never been reported.

<25> The IL-17 may include one or more selected from a group consisting of, for example, IL-17A, IL-17B, IL-17C, IL-17D, IL-17E and IL-17F. As demonstrated through experiments as will be described below, a composition comprising one or more selected from a group consisting of IL-17A and IL-17F, especially IL-17A, as an effective ingredient may provide a particularly superior slimming effect.

<26> In an embodiment, a composition comprising IL-17, especially IL-17A or IL-17F, as an effective ingredient may inhibit the differentiation of adipocytes. Thus, the composition may provide an effect of preventing or treating diseases related with hypertrophic adipose tissue, or reducing adipose tissue for cosmetic or beauty treatment. The diseases related with hypertrophic adipose tissue are not particularly restricted. For example, they may include obesity and lipoma.

<27> The effect of inhibiting the differentiation of adipocytes by IL-17A or IL-17F can also be confirmed from the fact that the expression level of one or more adipocytes-related gene(s) selected from a group consisting of peroxisome proliferator activating receptor γ (PPARγ) mRNA, fatty acid binding protein 4 (FABP4) mRNA and adiponectin mRNA decreases when adipocytes treated with IL-17A or IL-17F differentiate. This may mean that the differentiation of adipocytes can be effectively inhibited by IL-17A or IL-17F.

<28> The differentiation of adipocytes may refer to the differentiation of

preadipocyte cells or mesenchymal stem cells of an animal, particularly a mammal, into adipocytes. In particular, it may refer to the differentiation of human mesenchymal stem cells into adipocytes.

<29> Since the mesenchymal stem cells may be differentiated into adipocytes by a manner similar to that employed to differentiate preadipocyte cells taken from the subcutaneous tissue into complete adipocytes, they are widely used in the researches on the differentiation of adipocytes. The mesenchymal stem cells that can be differentiated into adipocytes are distributed in most of the body tissues. The mesenchymal stem cells, which are known to be able to differentiate into not only adipocytes but also other types of cells, including chondrocytes and osteocytes, have similar properties or characteristics in general, although there are some variations depending on what tissue they originate from. Specifically, the mesenchymal stem cells may be the mesenchymal stem cells derived from human bone marrow.

<30> In an embodiment, the composition may reduce the size and number of lipid droplets in differentiated adipocytes. As confirmed by the experiments that will be described below, measurement of the level of lipid droplets and the degree of lipid decomposition through glycerol concentration after treatment with IL-17, particularly IL-17A, exhibits that the size and number of lipid droplets decrease and that the lipid decomposition in adipocytes decrease remarkably.

<31> In an embodiment, the composition may be prepared into a cosmetic composition, a health food composition or a pharmaceutical composition.

<32> The cosmetic composition for slimming may be prepared into, for example, skin lotion, nourishing lotion, massage cream, nourishing cream, pack, gel, body lotion, body cream, body oil or body essence, but not limited thereto. Those skilled in the art will may include ingredients other than IL-17A or IL-17F in each form of cosmetic composition, depending on the particular preparation form or purpose of use, without difficulties.

<33> The health food composition for slimming may be prepared into for example, tablet, granule, drink, caramel, diet bar, or the like, but not

limited thereto. Those skilled in the art will may include ingredients other than IL-17A or IL-17F in each form of health food composition, depending on the particular preparation form or purpose of use, without difficulties. The addition of other ingredients may result in a synergic effect.

<34> The pharmaceutical composition for slimming may further include a pharmaceutic adjuvant such as antiseptic, stabilizer, hydration agent, emulsification promoter, salt and/or buffer for control of osmotic pressure, and the like, or other pharmaceutically and therapeutically useful substance. It may be prepared into a preparation form for oral or parenteral administration, according to common methods.

<35> Preparation forms for oral administration include, for example, tablet, pill, hard and soft capsule, liquid, suspension, emulsion, syrup, granule, and the like. These preparation forms may contain, in addition to the effective ingredient, a diluent (e.g., lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and glycine) or a lubricant (e.g., silica, talc, stearic acid, magnesium stearate, calcium stearate and polyethylene glycol). The tablet may contain a binder such as magnesium aluminum silicate, starch paste, gelatin, tragacanth, methyl cellulose, sodium carboxymethyl cellulose and polyvinylpyrrolidone. Depending on occasions, it may contain a pharmaceutic adjuvant such as a disintegrant, e.g., starch, agar, alginic acid or sodium alginate, an absorbent, a colorant, a flavor, a sweetener, or the like. The tablet may be prepared according to common mixing, granulation or coating methods.

<36> A typical preparation form for parenteral administration is an injection. Isotonic aqueous solution or suspension may be used. The preparation form for parenteral administration may be administered through a parenteral route or topically at an area rich in adipose tissue, with a dose of about 0.00001 to 0.01 mg/kg, particularly about 0.00001 to 0.001 mg/kg.

<37> The dose of the effective ingredient will be easily determined by those skilled in the art. A general dose is about 0.001 to 2,000 mg/kg/day, particularly about 0.5 to 2.5 mg/kg/day. However, the actual dose will be

determined considering various related factors, including severity of disease, selected administration route, age, sex, body weight and physical conditions of the subject, or the like. Thus, the aforesaid dose does not limit the scope of this disclosure in any means.

<38> The effective ingredient IL-17A or IL-17F may be included in an amount of 0.001-100 wt% based on the total weight of the composition. When the effective ingredient is included in an amount of 100 wt% based on the total weight of the composition, it means that the protein IL-17A or IL-17F itself may be used as the slimming composition as converted into a form adequate to provide a slimming effect.

<39> The IL-17 may be derived from a mammal, particularly from human, although not limited thereto. It may be either a recombinant IL-17 prepared through a recombinant technique or a purified natural IL-17. Particularly, it may be an IL-17 having i) an amino acid sequence of SEQ ID NO: 1; ii) a fragment of the amino acid sequence of SEQ ID NO: 1 with the same slimming activity as that of SEQ ID NO: 1; or iii) variant of the amino acid sequence of SEQ ID NO: 1 with an identity of at least 95% with the sequence of SEQ ID NO: 1 and the same slimming activity as that of SEQ ID NO: 1.

<40> As used herein, the term "fragment" refers to one having a slimming activity. Such fragments may be produced by known a restriction enzyme or recombinant technique.

<41> As used herein, the term "variant" refers to an amino acid with at least one of its complementarity changed. Those skilled in the art will understand that all the variants fabricated from the amino acids disclosed herein and confirmed to have a slimming activity by specifically binding to IL-17 having a slimming activity through tests are included in the scope of this disclosure.

<42> The variants include those in which the overall molecular structure of the amino acid sequence is conserved. Given informations on the properties of individual amino acids, those skilled in the art will recognize some reasonable substitutions. These conservative substitutions may be performed

based on, for example, polarity, charge, solubility, hydrophobicity, hydrophilicity and/or amphiphilicity of related residues. For example, amino acids may be classified into nonpolar (hydrophobic) amino acids, polar and neutral amino acids, positively charged (basic) amino acids, and negatively charged (acidic) amino acids, depending on polarity. Nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. Polar and neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine and glutamine. Positively charged (basic) amino acids include arginine, lysine and histidine. And, negatively charged (acidic) amino acids include aspartate and glutamate. Substitutions may be made in each group.

<43> As used herein, the term "sequence" may include not only the sequence of SEQ ID NO: 1 which encodes the amino acid disclosed herein but also its variant. The "variant" may have a sequence identity of at least 80%. Further, it may have a sequence identity of at least 90% or at least 95%. Of the variants having such identity, those that are hybridized under very strict conditions are included.

【Mode for Invention】

<44> The examples and experiments will now be described. The following examples and experiments are for illustrative purposes only and not intended to limit the scope of this disclosure.

<45> [Test Example 1] Effect of IL-17 on differentiation of mesenchymal stem cells from human bone marrow into adipocytes

<46> Human bone marrow mesenchymal stem cells (hBM-MSCs) purchased from Lonza, Inc. (Walkersville, MD, USA) are cultured following the company's instructions. More specifically, hBM-MSCs are cultured in a low-concentration glucose (1 g/L) culture medium (Dulbecco's modified Eagle's medium; DMEM) (Invitrogen, Carlsbad, CA, USA) containing 10% fetal bovine serum (FBS), 1% penicillin/streptomycin and 1% GlutaMAX. When the cell density in the culture dish reaches 100%, the condition under which differentiation into adipocytes proceeds is provided. 1 μg/mL insulin, 1 μM

dexamethasone (DEXA), 0.5 mM 3-isobutyl-1-methylxanthine (IBMX) and troglitazone (T) (hereinafter collectively referred to as "IDXT") are added to a hBM-MSCs culture medium [high-concentration glucose (4.5 g/L) culture medium], and hBM-MSCs are differentiated into adipocytes for 14 days.

<47> For a test group, 25 ng/mL IL-17A, IL-17F or IL-22 is further added to the medium in addition to IDXT when inducing differentiation of adipocytes. After 15 days' of treatment, the cell culture medium is removed, and the cells are washed with 10 mL of phosphate buffered saline (PBS) and fixed for 10 minutes using 10% formalin/PBS solution (0.2 mL/cm^2). The fixed cells are washed once with 60% isopropanol solution (0.5 mL/cm^2), and lipid droplets in the adipocytes are stained for 10 minutes using Oil Red O dissolved in 60% isopropanol (0.2 mL/cm^2). Subsequently, staining is carried out again using hematoxylin so that the cell nucleus can be distinguished easily. Observation is made using a microscope. The result is compared in Fig. 1 with that of the control group which is treated only with IDXT.

<48> Further, the degree of differentiation of adipocytes is determined as follows. After staining the adipocytes with Oil Red O, Oil Red O is removed using 100% isopropanol solution. Then, absorbance is measured at 500 nm. The result is shown in Fig. 2.

<49> Referring to Figs. 1 and 2, when compared with the control group which is treated only with IDXT, the group which is treated with IL-17A or IL-17F can inhibit the differentiation by about 77.6% and about 45.6%, respectively. The group treated with 25 ng/mL IL-22 does not show a statistically significant effect of inhibiting the differentiation of adipocytes.

<50> The effect of inhibiting the differentiation of adipocytes of different IL-17 cytokines is shown in Fig. 3.

<51> Referring to Fig. 3, differently from IL-17A and IL-17F, IL-17B, IL-17C, IL-17D or IL-17E does not show a significant effect of inhibiting differentiation as compared to the control group which is treated only with IDXT.

<52> Further, it is investigated whether IL-17A exhibits the effect of inhibiting differentiation in a concentration-dependent manner. The result is shown in Fig. 4.

<53> Referring to Fig. 4, treatment with IDXT and 25, 5 or 1 ng/mL IL-17A exhibits an inhibition effect of 81.9, 75.6 or 46.2%, respectively, as compared to the control group which is treated only with IDXT. This shows that IL-17A inhibits the differentiation of adipocytes in a concentration-dependent manner.

<54>

<55> [Test Example 2] Effect of IL-17A on transcription level of IL-17RC and IL-17RA

<56> hBM-MSCs are induced to differentiate into adipocytes in the same manner as Test Example 1. The cells are treated with 1 ng/mL IL-17 for 7 days, and RNAs are isolated from the cells using Trizol reagent (Invitrogen, Carlsbad, CA, USA). The isolated RNAs are further purified using Qiagen RNeasy kit (Qiagen, Valencia, CA), and the quality of the RNAs are investigated using Agilent 2100 BioAnalyzer (Agilent Technologies, Santa Clara, CA, USA). cDNAs are synthesized form the RNAs using Superscript Reverse Transcriptase (RT) II kit (Invitrogen, Carlsbad, CA), and are analyzed quantitatively through real-time reverse transcription polymerase chain reaction (Q-RT-PCR). It is investigated whether there is a change in the expression of IL-17RA and IL-17RC mRNAs, which are transmembrane receptor proteins induced by IL-17A at the early stage of differentiation of adipocytes and known to play an important role in IL-17A and IL-17F signaling, using TaqMan® gene expression assay kit (Applied Biosystems, Foster City, CA). The result is shown in Figs. 5 and 6.

<57> Referring to Fig. 5, the amount of both IL-17RA and IL-17RC mRNA expression increases in both the hBM-MSCs that did not differentiate into adipocytes and the hBM-MSCs that differentiated into adipocytes. However, 5 days after the inducement of differentiation, there is no significant difference in expression of IL-17RA mRNA among the control group in which the

hBM-MSCs did not differentiate, the group in which the hBM-MSCs are treated with IDXT and the group in which the cells are treated with IDXT and IL-17A.

<58> In contrast, referring to Fig. 6, expression of IL-17RC gene increases more than double in the cells treated with IDXT, as compared to the control group in which differentiation did not occur. Therefore, it is confirmed that the expression level of IL-17RC mRNA is significantly affected by the presence of IL-17A.

<59> Further, the effect of IL-17A on the expression pattern of adipocyte-related genes is investigated using TaqMan® gene expression assay kit (Applied Biosystems, Foster City, CA). The result is shown in Figs. 7 to 9. [leptin (Hs00174877_m1), leptin receptor (Hs00174497_m1), adiponectin (Hs00605917_m1), fatty acid binding protein 4 (FABP4: Hs00609791_m1), peroxisome proliferator activating receptor γ (PPARγ: Hs00233423_m1)]

<60> Referring to Figs. 7 to 9, 5 days after the commencement of differentiation of adipocytes, mRNA expression level of PPARγ, FABP4 and adiponectin decreases significantly in the cells treated with IDXT and IL-17A as compared to the IDXT control group.

<61> Referring to Fig. 10, secretion of the protein adiponectin decreases significantly when the same cell culture medium used for the Q-RT-PCR analysis is treated with IL-17A, as compared to the control group treated only with IDXT.

<62>

<63> [Test Example 3] whether the effect of IL-17A on hBM-MSCs neutralized by anti-IL-17A or not

<64> It is investigated whether anti-IL-17A can neutralize the effect of inhibiting the differentiation of hBM-MSCs by IL-17A. The result is shown in Figs. 11 and 12.

<65> Referring to Fig. 11, 250 ng/mL anti-IL-17A cancels the inhibition of the differentiation of adipocytes by IL-17A. To confirm the result, adiponectin level in hBM-MSCs cultured under different adipose formation conditions is determined by ELISA. The result is shown in Fig. 12.

<66> Referring to Fig. 12, the effect of inhibiting the secretion of adiponectin by IL-17A is remarkably decreased by the anti-IL-17A antibody. Therefore, it is confirmed that IL-17A plays an important role in inhibiting the differentiation of adipocytes in hBM-MSCs.

<67>

<68> [Test Example 4] Effect of IL-17A on level of lipid droplets in differentiated adipocytes

<69> hBM-MSCs are cultured, induced to differentiate into adipocytes and treated with 25 ng/mL IL-17A in the same manner as Test Example 1. The hBM-MSCs are induced to differentiate into adipocytes for 15 days. When 50% or more of the cells differentiate into adipocytes, treatment is made with IL-17A for 7 days.

<70> For quantitative determination of the level of lipid droplets in differentiated adipocytes and observation with a microscope, staining with Oil Red O, re-staining with hematoxylin and absorbance measurement are carried out. The result is shown in Figs. 13 to 15.

<71> Referring to Figs. 13 and 14, IL-17A decreases the size and number of lipid droplets in differentiated adipocytes. In order to determine the degree of lipolysis, the concentration of glycerol in the supernatant obtained from the culture medium of the differentiated adipocytes is measured. The result is shown in Fig. 15.

<72> Referring to Fig. 15, IL-17A remarkably increases lipolysis in adipocytes. Therefore, it is confirmed that IL-17A can regulate the metabolic state of differentiated adipocytes by controlling lipolysis in the differentiated adipocytes.

<73>

<74> [Test Example 5] Effect of IL-17A on production of IL-6 and IL-8

<75> It is investigated whether IL-17A affects the production of the pro-inflammatory cytokines IL-6 and IL-8, which express the receptors acting on IL-17A signaling in non-immune cells such as keratinocytes and synoviocytes.

<76> It is investigated whether IL-17A regulates the expression of IL-6 and

IL-8 genes in differentiated adipocytes. After inducement of differentiation of adipocytes for 15 days, the level of IL-6 mRNA is determined. The result is shown in Figs. 16 and 17.

<77> Referring to Fig. 16, when compared with untreated hBM-MSCs, transcription of IL-6 is down-regulated in the condition of differentiation in the presence of IDXT. In the differentiated adipocytes treated with IDXT and 25 ng/mL IL-17A, the level of IL-6 mRNA increases remarkably. In addition, referring to Fig. 17, the transcription level of IL-8 increases remarkably as differentiation of adipocytes proceeds, as compared to the IDXT control group.

<78> Further, the increase in the production of IL-6 and IL-8 protein during the differentiation of adipocytes in hBM-MSCs is confirmed by ELISA. The result is shown in Fig. 18. Referring to Fig. 18, treatment with 25 ng/mL IL-17A results in increased expression of IL-6 and IL-8 in adipocytes in protein level.

<79> Referring to Fig. 19, treatment with IL-17F leads to up-regulation of the IL-6 mRNA level. But, the difference between the untreated cells and the cells treated with IL-17F is not significant. IL-8 shows similar pattern in both protein secretion and gene expression when treated with IL-17A and IL-17F.

<80> Accordingly, it is confirmed that IL-17A regulates the production of IL-6 and IL-8 in differentiated adipocytes derived from hBM-MSCs.

<81>

<82> [Test Example 6] Effect of IL-17A on mass of adipose tissue

<83> Obesity is induced by feeding 4-week-old C57BL/6 mice with a high fat diet [AIN-93G 40%, Feedlab Korea (www.feedlab.co.kr), composition (grams per 1 kg): casein 200, shortening 330, soybean oil 70, sucrose 100, dextrose 132, cornstarch 48.7, cellulose 50, l-cystine 3, TBHQ 0.014, choline bitartrate 2, mineral complex 50, vitamin complex 14.3] for a month. Mice weighing about 35 g are selected. The selected mice are divided into two test groups, 6 or 7 each group. IL-17A is prepared for injection by

dissolving 1 μg of IL-17A in 1 mL of PBS followed by sterilization. The mice in one test group are anesthetized using ketamine, and 0.1 mL of the prepared IL-17A solution is injected at the epididymal adipose tissue (epididymal fat pad) of the anesthetized mice, using a 26-guage syringe. Only PBS is injected to the C57BL/6 mice in the control group using the same procedure. After the injection of IL-17A, mice are fed with the high fat diet for 7 more days. The mice are sacrificed after weighing body weight. Epididymal adipose tissue is taken from the sacrificed mice and its mass is weighed. The result is shown in Fig. 20. As seen from Fig. 20, the mice of the test group to which IL-17A was injected shows a smaller mass of epididymal adipose tissue than the mice of the control group to which only PBS was injected.

<84> The formulation examples will now be described. The following formulation examples are for illustrative purposes only and not intended to limit the scope of this disclosure.

<85>

<86> [Formulation Example 1] Lotion

<87> Lotion is prepared according to the following composition.

<88> IL-17A or IL-17F	30.00 (%)
<89> 1-Ascorbic acid-2-magnesium phosphate	1.00
<90> Water-soluble collagen (1% aqueous solution)	1.00
<91> sodium citrate	0.10
<92> citric acid	0.05
<93> Licorice root extract	0.20
<94> 1,3-Butylene Glycol	3.00
<95> Fat and oil	2.00
<96> Serine	1.00
<97> Purified water	to make 100

<98>

<99> [Formulation Example 2] Cream

<100> Cream is prepared according to the following composition.

<101> IL-17A or IL-17F	10.00 (%)

<102> Polyethyleneglycolmonostearate 2.00
<103> Self-emulsifiable glycerin monostearate 5.00
<104> Cetyl Alcohol 4.00
<105> Squalene 6.00
<106> Glyceryl tri- 2-ethylhexanoate 6.00
<107> Sphingoglycolipid 1.00
<108> 1.3-butyleneglycol 7.00
<109> Vitamin C 1.00
<110> Purified water to make 100
<111>
<112> [Formulation Example 3] Cosmetic essence
<113> Cosmetic essence is prepared according to the following composition.
<114> IL-17A or IL-17F 20.00 (%)
<115> Hydroxyethylenecellulose(2% aqueous solution) 12.00
<116> Xanthan gum (2% aqueous solution) 2.00
<117> 1.3-butyleneglycol 6.00
<118> Concentrated glycerin 4.00
<119> Sodium hyaluronate (1% aqueous solution) 5.00
<120> Fat and oil 2.00
<121> Serine 1.00
<122> Vitamin C 1.00
<123> Purified water to make 100
<124>
<125> [Formulation Example 4] Powder
<126> Powder is prepared by mixing the following ingredients and filling them in an airtight pouch.
<127> IL-17A or IL-17F 100 mg
<128> Lactose 100 mg
<129> Talc 10 mg
<130> Fat and oil 5 mg
<131>

<132> [Formulation Example 5] Tablet

<133> Tablet is prepared by mixing the following ingredients and following a common tablet making procedure.

<134>	IL-17A or IL-17F	50 mg
<135>	Cornstarch	100 mg
<136>	Lactose	100 mg
<137>	Magnesium stearate	2 mg
<138>	Vitamin C	50 mg

<139>

<140> [Formulation Example 6] Capsule

<141> Capsule is prepared by filling the following ingredient in a gelatin capsule.

<142>	IL-17A or IL-17F	50 mg
<143>	Cornstarch	100 mg
<144>	Lactose	100 mg
<145>	Magnesium stearate	2 mg
<146>	Vitamin C	50 mg
<147>	Serine	50 mg

<148>

<149> [Formulation Example 7] Injection

<150> Injection is prepared according to a common method, with a composition of an ampule (2 mL) as follows:

<151>	IL-17A or IL-17F	50 mg
<152>	Sterile water for injection	adequate
<153>	pH adjuster	adequate

<154>

<155> [Formulation Example 8] Liquid

<156> Liquid is prepared according to a common method. The following ingredients are dissolved in purified water and an adequate amount of lemon flavor is added. After mixing, purified water is added to make a final volume of 100 mL. The prepared liquid is filled in a brown bottle and

sterilized.

<157> IL-17A or IL-17F 100 mg
<158> Isomerized glucose 10 g
<159> Mannitol 5 g
<160> Vitamin C 50 mg
<161> Serine 50 mg
<162> Fat and oil adequate
<163> Purified water adequate
<164>
<165> [Formulation Example 9] Health food
<166> Health food is prepared according to the following composition. Changes may be made on the contents of vitamins and minerals. The following ingredients are mixed according to a common method to prepare granules.

<167> IL-17A or IL-17F 1,000 mg
<168> Vitamin Mixture
<169> Vitamin A acetate 70 μg
<170> Vitamin E 1.0 mg
<171> Vitamin B1 0.13 mg
<172> Vitamin B2 0.15 mg
<173> Vitamin B6 0.5 mg
<174> Vitamin B12 0.2 μg
<175> Vitamin C 10 mg
<176> Biotin 10 μg
<177> Nicotinamide 1.7 mg
<178> Folic acid 50 μg
<179> Calcium pantothenate 0.5 mg
<180> Mineral complex
<181> Ferrous sulate 1.75 mg
<182> Zinc oxide 0.82 mg
<183> Magnesium carbonate 25.3 mg
<184> Potassium phosphate monobasic 15 mg

<185> Calcium phosphate dibasic 55 mg

<186> Potassium citrate 90 mg

<187> Calcium carbonate 100 mg

<188> Magnesium chloride 24.8 mg

<189>

<190> [Formulation Example 10] Health drink

<191> Health drink is prepared according to a common method. The following ingredients are mixed and heated at 85 ℃ for about 1 hour while stirring. The resultant solution is filtered and filled in a sterilized 2 L container. After sealing and sterilizing, the solution is stored in a refrigerator before being used to prepare a health drink. The composition may be changed considering geological or ethnical tastes, such as the age group of consumers, country, purpose of use, or the like.

<192> IL-17A or IL-17F 1,000 mg

<193> Citric acid 1,000 mg

<194> Oligosaccharide 100 g

<195> Plum extract 2 g

<196> Taurine 1 g

<197> Purified water to make 900 mL

<198>

<199> While the exemplary embodiments have been shown and described, it will be understood by those skilled in the art that various changes in form and details may be made thereto without departing from the spirit and scope of this disclosure as defined by the appended claims.

<200> In addition, many modifications can be made to adapt a particular situation or material to the teachings of this disclosure without departing from the essential scope thereof. Therefore, it is intended that this disclosure not be limited to the particular exemplary embodiments disclosed as the best mode contemplated for carrying out this disclosure, but that this disclosure will include all embodiments falling within the scope of the appended claims.

【CLAIMS】

【Claim 1】

<202> A slimming composition comprising interleukin-17 (IL-17) as an effective ingredient.

【Claim 2】

<203> The slimming composition according to claim 1, wherein the IL-17 is one or more selected from a group consisting of IL-17A and IL-17F.

【Claim 3】

<204> The slimming composition according to claim 2, wherein the IL-17 is IL-17A.

【Claim 4】

<205> The slimming composition according to claim 1, which inhibits the differentiation of adipocytes.

【Claim 5】

<206> The slimming composition according to claim 4, wherein the differentiation of adipocytes is a differentiation of mesenchymal stem cells into adipocytes.

【Claim 6】

<207> The slimming composition according to claim 5, wherein the differentiation of adipocytes is a differentiation of mesenchymal stem cells of bone marrow into adipocytes.

【Claim 7】

<208> The slimming composition according to claim 1, which reduces the number or size of lipid droplets in adipocytes.

【Claim 8】

<209> The slimming composition according to claim 1, which is a pharmaceutical composition.

【Claim 9】

<210> The slimming composition according to claim 1, which is a cosmetic composition.

【Claim 10】

<211> The slimming composition according to claim 1, which is a health food composition.

【Claim 11】

<212> The slimming composition according to claim 1, wherein the effective ingredient is included in an amount of 0.001-100 wt% based on the total weight of the composition.

【Claim 12】

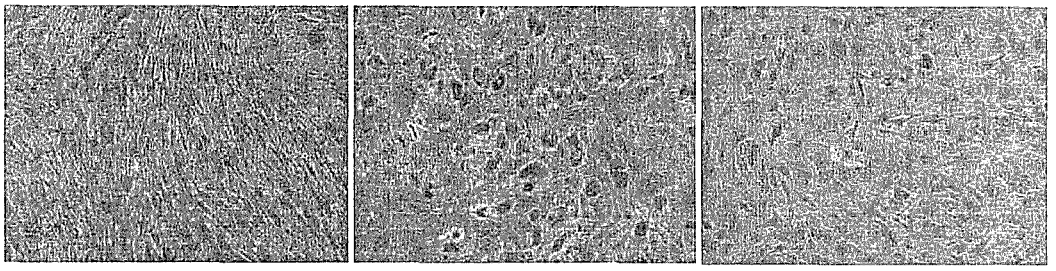
<213> The slimming composition according to claim 12, wherein the IL-17 is a recombinant IL-17 or a purified natural IL-17.

【Claim 13】

<214> The slimming composition according to claim 12, wherein the IL-17 is an IL-17 having i) an amino acid sequence of SEQ ID NO: 1; ii) a fragment of the amino acid sequence of SEQ ID NO: 1 with the same slimming activity as that of SEQ ID NO: 1; or iii) variant of the amino acid sequence of SEQ ID NO: 1 with an identity of at least 95% with the sequence of SEQ ID NO: 1 and the same slimming activity as that of SEQ ID NO: 1.

【DRAWINGS】

【Figure 1】



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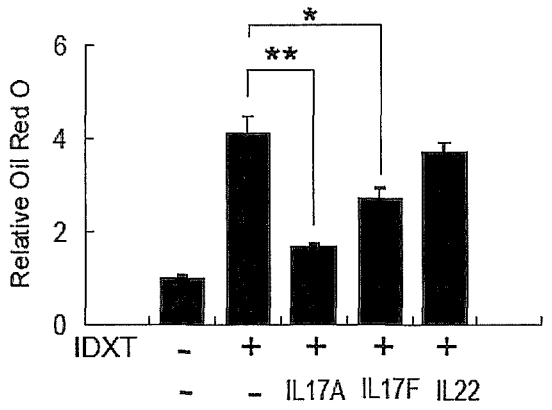
【Figure 2】



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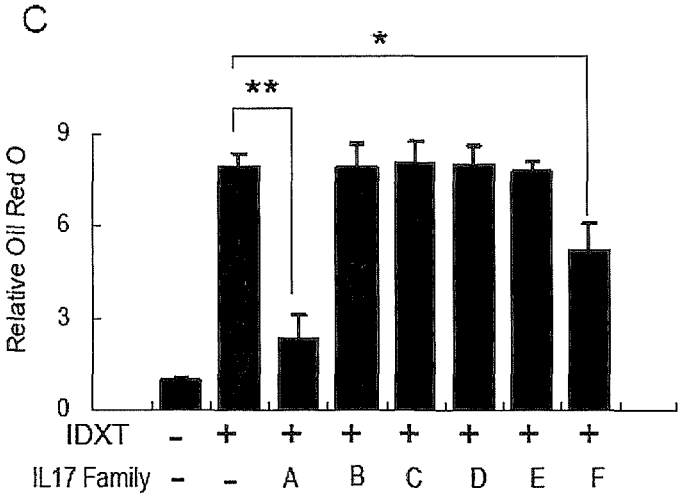

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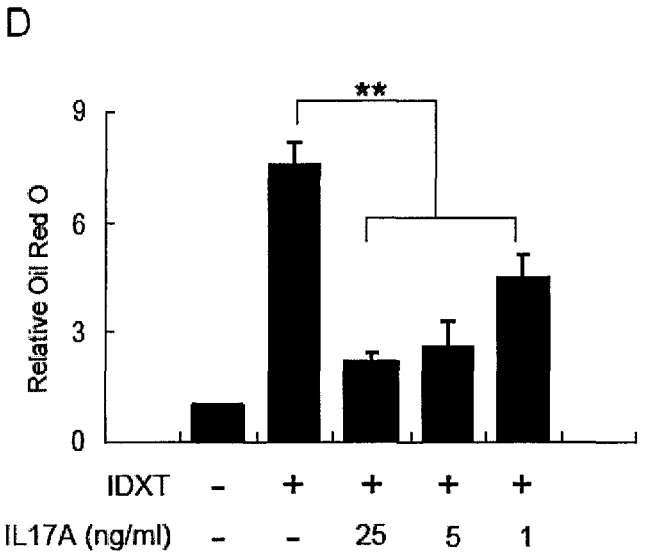

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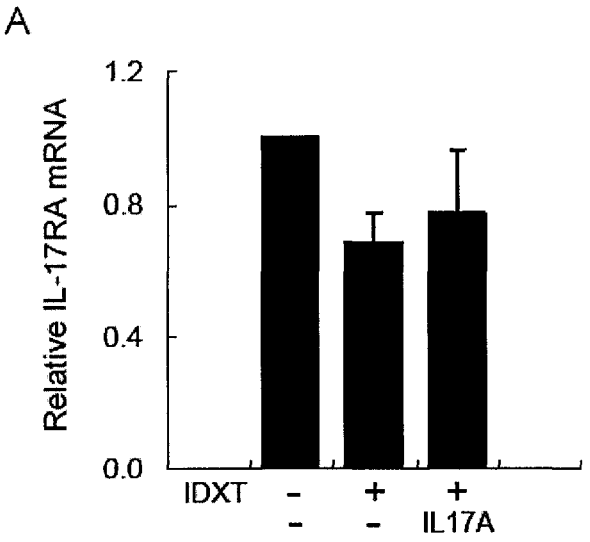

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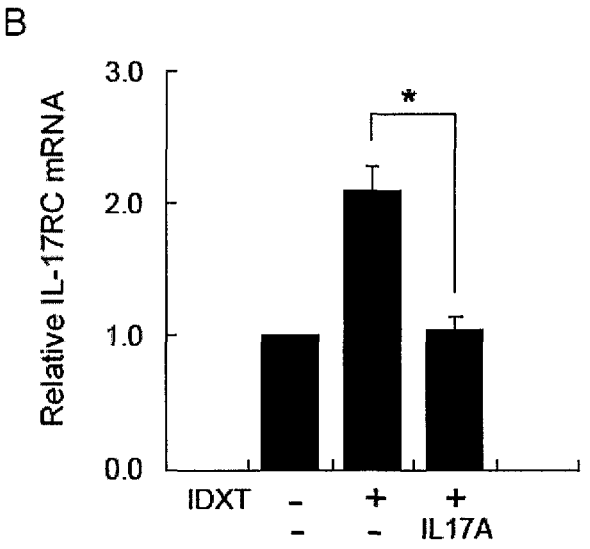

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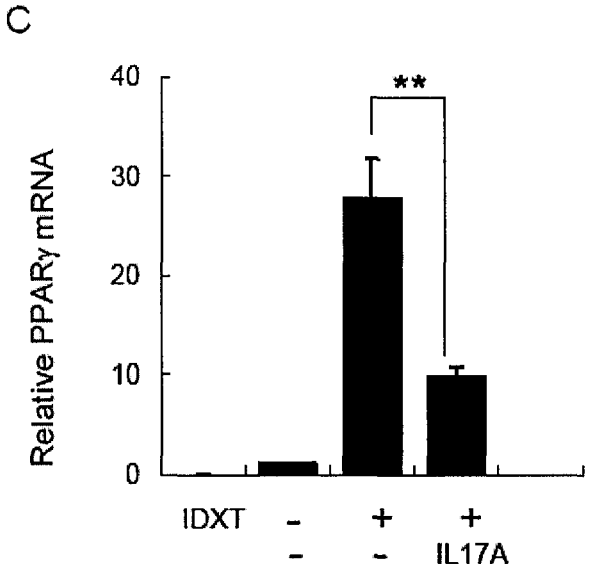

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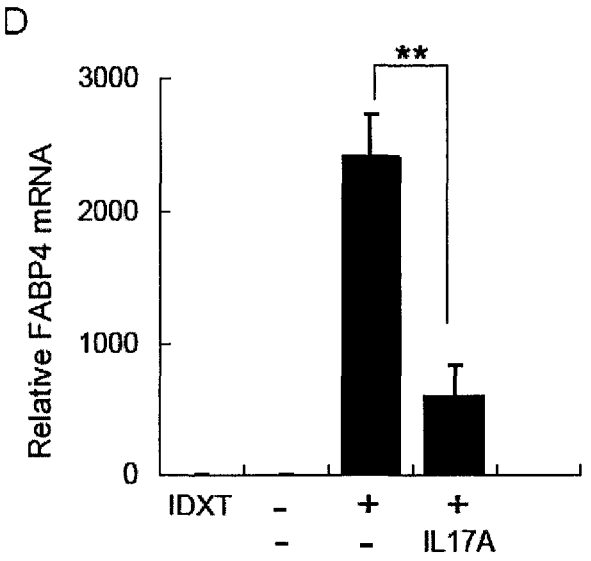

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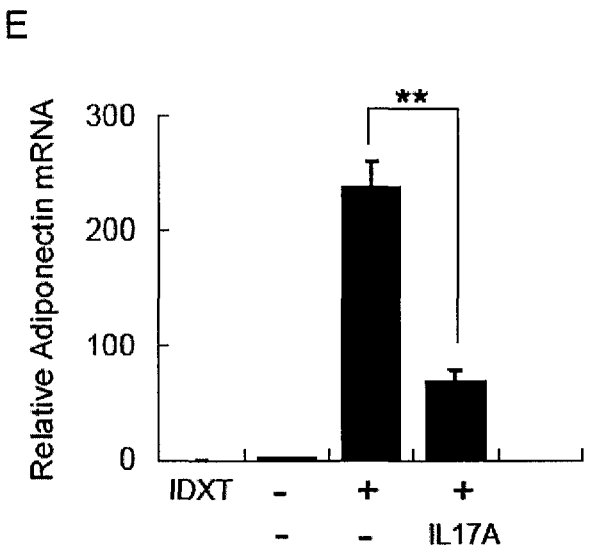

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【Figure 10】

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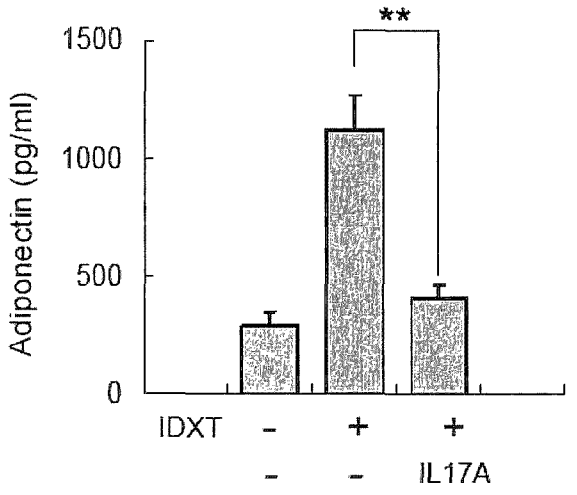

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【Figure 11】

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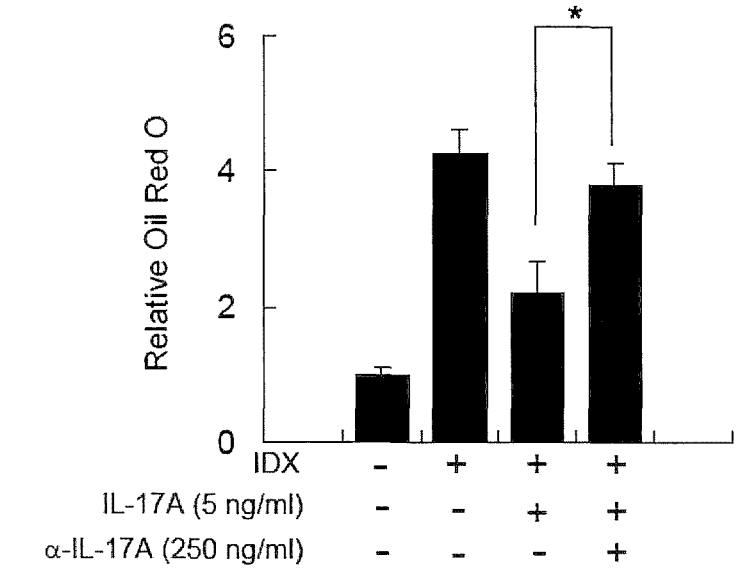

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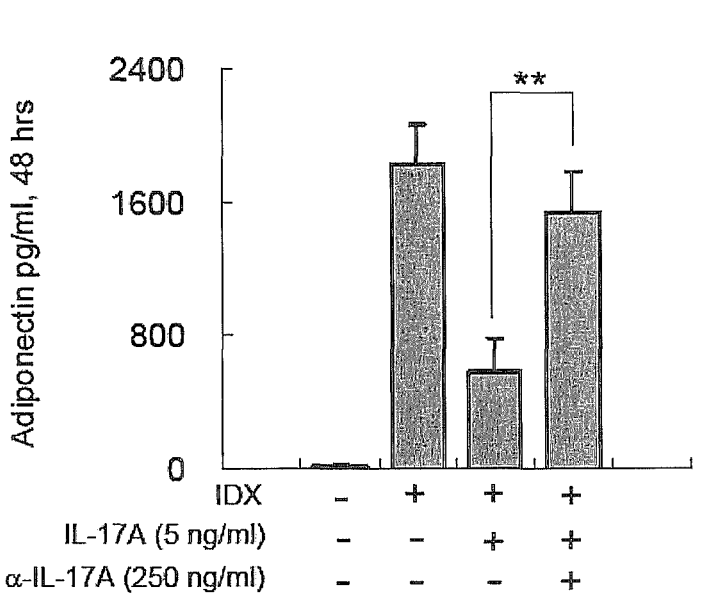

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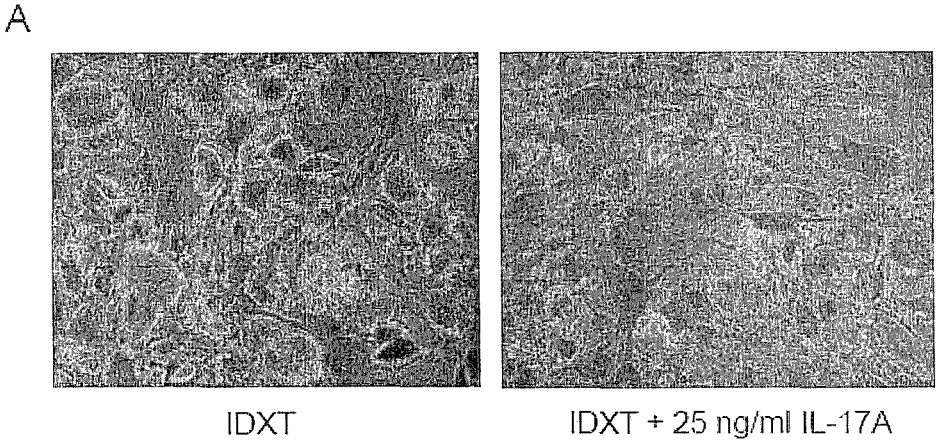

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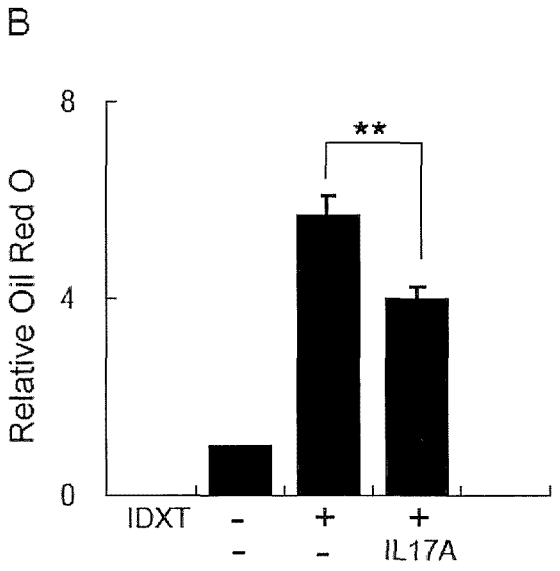

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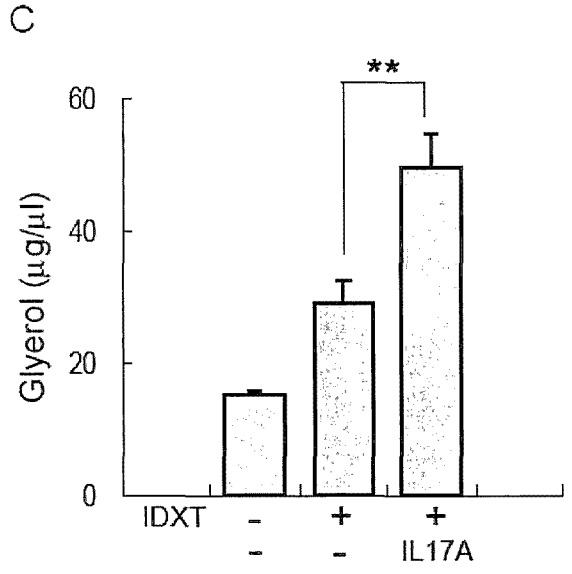

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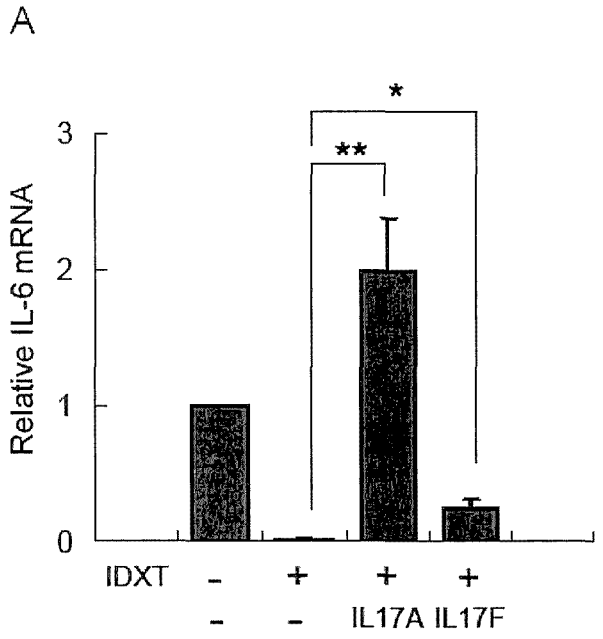

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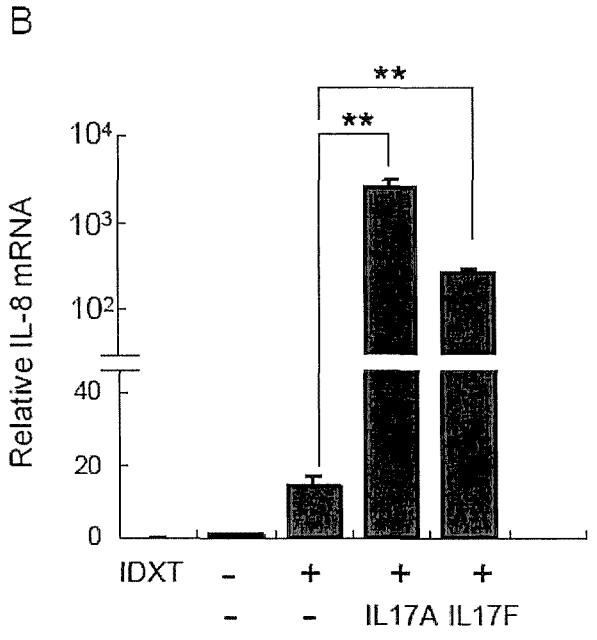

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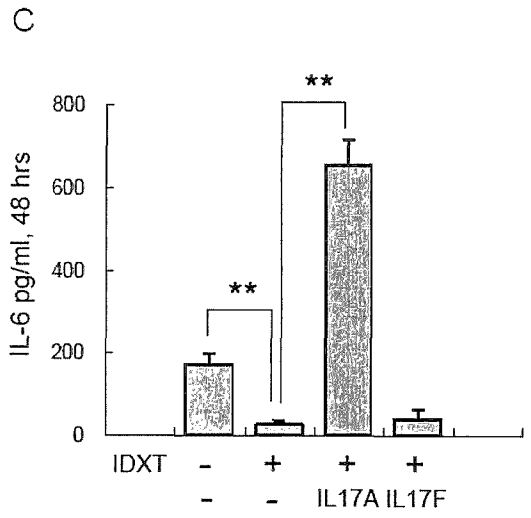

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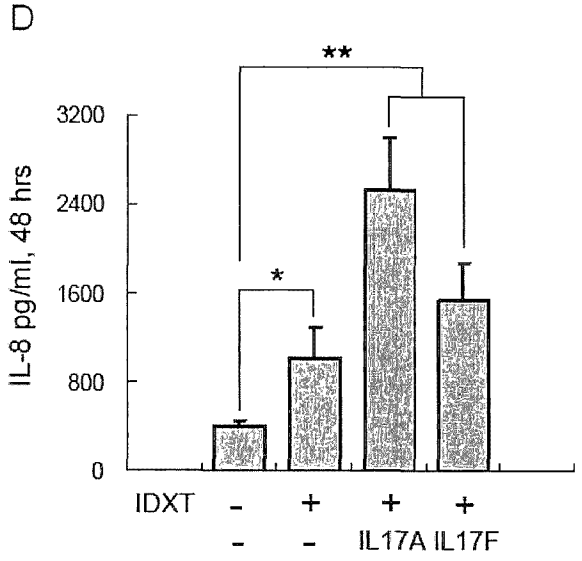

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【Figure 20】

Change in mass of epididymal adipose tissue of C57BL/6 mice after injection of IL-17A

	Control group	IL-17A treated group	
Average body weight before treatment (g)	34.5±0.1	34.8±0.8	
Average body weight 7 days after treatment (g)	37.2±0.1	36.3±1.4	
Mass of epididymal adipose tissue (mg)	874.5±52.0	651.7±97.2	$p < 0.01$

<237>