PHARMACEUTICAL COMPOSITION FOR DERMATOLOGY AND USES THEREOF

FIELD OF THE INVENTION

[0001] The present invention relates to the fields of development, cell biology, molecular biology and genetics. More particularly, the invention relates to a method of deriving a conditioned media from mesenchymal stem cells obtained from a mammal pertaining to the genus *canis* and uses of such media for the treatment of skin inflammatory disorders such as psoriasis or atopic dermatitis.

BACKGROUND OF THE INVENTION

[0002] The skin, once thought to be immunologically sequestered from the body, is now deemed to be an integral part of a multisystem inflammatory axis.

[0003] Atopic dermatitis (AD) and psoriasis, especially in their most severe forms, have been linked to a variety of systemic inflammatory disorders and comorbidities. These comorbidities highlight that inflammatory skin diseases of childhood are serious chronic multisystem illnesses and not merely cosmetic conditions.

[0004] Atopic dermatitis comorbidities vary by age and length of illness. Some of the most common comorbidities are included in the gold-standard AD diagnostic criteria by Hanifin and Rajka (*Acta Derm Venereol Suppl* (Stockh) 1980; 92:44-47). These criteria include pruritus, chronic or recurrent dermatitis, specific distribution by age (e.g., flexural disease of childhood) and personal and/or family history of atopy, i.e., food allergies, asthma and allergic rhinoconjunctivitis. Minor features include more than a dozen comorbid conditions, including ichthyosis vulgaris; bacterial and viral infections; allergic predisposition with positive immunoglobulin E and skin prick testing; eye findings such as cataracts; and excessive skin reactivity to touching foods, pressure and environmental triggers. These major and minor criteria actually have been staring us in the face for almost 40 years with the concept of comorbidities being part and parcel of the definition of atopic dermatitis and the atopic diathesis.

[0005] Recently, both pediatric psoriasis and atopic dermatitis have been linked to cutaneous infections and psychosocial disorders such as anxiety, depression and hyperactivity for the children involved and their parents. Linkage to cutaneous autoimmunity, including vitiligo and alopecia areata, may be noted in both sets of diseases.

[0006] The most important and well-described series of comorbidities shared by these two diseases is the association with obesity and the metabolic syndrome—a cluster of conditions characterized by increased risk of heart disease, stroke and diabetes. Early childhood obesity has been associated with atopic dermatitis development and severity. In psoriasis, increased abdominal girth and obesity may precede disease by a few years, suggesting their role as triggers in disease. One interesting feature of psoriatic disease is promising data from adults who had weight loss surgery and experienced psoriatic disease improvement.

[0007] Despite many common comorbidities, paediatric atopic dermatitis and paediatric psoriasis have many distinctive features.

[0008] In atopic dermatitis, the skin barrier is both weak and weakened by inflammation, allowing a series of unusual allergic features, i.e., the atopic march and infectious complications. Alternatively, in psoriasis the skin is triggered to thicken, and the joints may become inflamed.

[0009] Further divergence is seen in the clinical manifestations. In psoriasis, arthritis is the leading comorbidity, sometimes triggered by streptococcal disease. There also is a far more definitive association with metabolic syndrome features such as hypertension, hyperlipidemia and insulin resistance. Despite the common nature of psoriasis and the frequency of disease, atopic dermatitis has developed a more extensive laundry list of comorbidities, including infantile seborrheic dermatitis, *Malassezia* sensitization, dust allergy, asthma, food allergy, environmental allergens, contact dermatitis (e.g., lanolin, fragrance), prurigo, sleep disturbance, upper respiratory infections, warts, coxsackie generalization (e.g., eczema coxsackium) and cataracts.

[0010] At any rate, the development of screening tools and effective pharmacological interventions for patients of any age with inflammatory skin disease such as psoriasis or atopic dermatitis is a work in progress and it has become a crucial need nowadays. In this sense, the present invention provides for the use of conditioned media in which MSCs (mesenchymal stem cells) derived from a mammal pertaining to the genus *canis* are cultured in order to obtain such conditioned media suitable for the treatment of skin inflammatory disorders such as psoriasis or atopic dermatitis. It is particularly important to highlight, that the composition disclosed in the present invention is particularly effective in the xenogeneic treatment of human atopic dermatitis even though there is a high phylogenetic divergence between humans and dogs (see FIGS. **7** to **9**).

[0011] In this regard, WO2008155659 discloses compositions for preventing or treating skin defects comprising conditioned cell medium from mesenchymal stem cells (MSC). In addition, this document indicates that MSCs can be obtained from humans, pigs, dogs, cats, mice, horses and other mammals. However, this document fails to specifically refer to "atopic dermatitis" or "psoriasis" and much less that these diseases can be treated with compositions comprising a conditioned cell medium from mesenchymal stem cells (MSC) obtained from dogs. In this sense, example 2 of the present invention indicates that MSCs from different origins provide different conditioned media under a qualitative and quantitative point of view. In fact, as illustrated in the figures (FIG. **2** in comparison to FIGS. **1**, **3** and **4**), a conditioned culture media from dog adipose MSCs is considerably different from a conditioned culture media obtained from human, cat or horse adipose tissue. Again, WO2008155659 provides no indication that a conditioned culture media specifically obtained from dog adipose MSCs is particularly useful for an effective treatment of dermatitis such as atopic dermatitis and psoriaris in human beings.

[0012] In addition, the fact that the present invention is preferably focus in the xenogeneic treatment of human atopic dermatitis, is certainly counterintuitive in light of documents such as WO2017041133 wherein the following statements can be found: "Adipose tissue may be human adipose tissue or mammalian animal adipose tissue, such as canine, equine or feline. Typically the source of the adipose tissue will be of the same species as the intended recipient of the MSCs . . . ."

[0013] Furthermore, although Mohd Matin Ansari "Therapeutic potential of canine bone marrow derived mesenchymal stem cells and its conditioned media in diabetic rat wound healing", Journal of stem cell research & therapy,