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Development of orbital adipose-derived stem cells as a model for studying the formation of baggy lower eyelids

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ABSTRACT

In old population, there is often a protrusion of the orbital fat pad underlying the skin in the lower eyelids, giving an aspect of palpable pouches. It is generally thought that orbital fat hyperplasia is the main contributing factor to the formation of baggy lower eyelids, and resection of excessive orbital fat pad is routinely performed during the eyelid cosmetic surgery. In our clinical study, however, it was revealed that the adipocytes in orbital fat tissue from older people became smaller compared to those from the young individuals. Based on this finding, we hypothesize that the orbital fat size may not increase, but decrease with age, and the declined fat depot volume is related to the reduced fat cell size and impaired differentiation of preadipocytes into fat cells. Adipose-derived stem cells (ASCs) are a population of postnatal stem cells residing in the fat tissue, capable of differentiating into preadipocytes and subsequently into mature fat cells throughout the lifespan. As preadipocytes are a substantial component of fat tissue and can greatly influence the fat composition and function, we speculate that orbital adipose-derived stem cells can be used as an excellent model to determine effects of aging on orbital fat. By evaluating the age-related changes in preadipocyte number, replication, and differentiation, we can reveal alterations in orbital fat cellularity and function with age, and investigate the relationship between orbital fat volume and the of baggy lower eyelid formation.

Background

The orbital fat (OF) prominence in the lower eyelids that causes an under-eye bagging appearance is very common after middle or early old age and has been a frequent complaint prompting old people to seek ophthalmic cosmetic surgeries [1,2]. Although the exact causes for the prominent lower eyelids still remain controversial, progressive OF hyperplasia/hypertrophy with aging is traditionally considered as the main contributing factor [3–9]. A generally accepted concept is that the fat depot volume is not dependent on the fat cell number but on the adipocyte size, since new fat cells continue to be formed and the cell number remains constant throughout the lifespan [10]. Therefore, the OF cells are postulated to become larger in older individuals. Interestingly, we found it was not the case in our clinical work. As resection of partial OF pad was routinely performed during the cosmetic surgery for the prominent eyelids, some samples obtained from healthy patients, who had been excluded from obesity, orbital diseases or endocrine diseases, were processed for histomorphological evaluation using HE staining. Unexpectedly, the adipocytes from older patients with prominent lower eyelids were found smaller than those from the young donors, indicating declines in fat cell capacity for lipid accumulation.

Assessing the age-related changes of OF volume and expansion in the eyelids is of great significance. If the OF size dose reduce with age, measures should be taken in operation to prevent removing too much fat tissue and to strengthen the weakened supporting tissues of the eyelid instead. However, the extent of OF prolapse in the eyelids is not very big (only about 5–6 mm in length) [3,11]. So it is difficult to calculate OF volume changes accurately. For example, some studies using CT and MRI approaches to evaluate the pathophysiology of the expanded OF [3,12,13]. The imaging resolution (slice thickness) is usually set as 1 or 2 mm, and their measurement errors or subjective biases are uncertain. Regarding the anatomic research on autopsies, non-preserved fresh human cadavers are not always available. Thus the fat shrinkage and lipolysis are inevitable.

Adipose-derived stem cells

Adipose-derived stem cells (ASCs) are a population of postnatal adult stem cells existing abundantly in the fat tissue [14,15], which can undergo definite self-renewal and differentiate into multilin-

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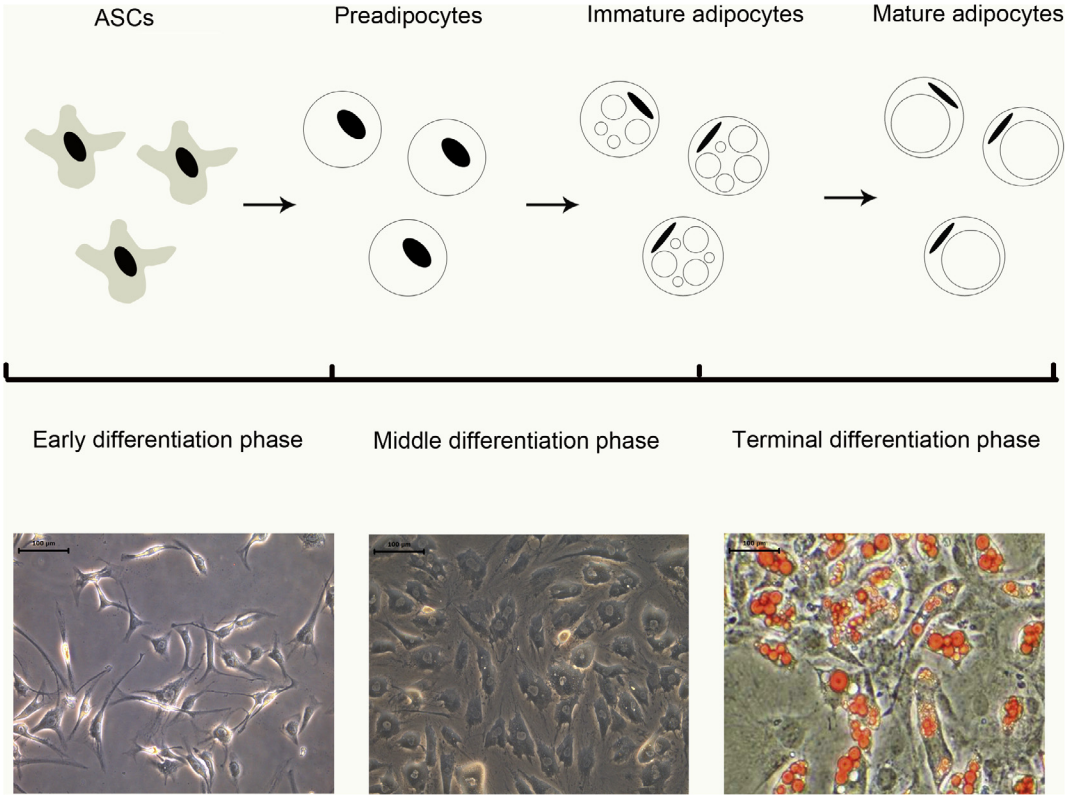

Fig. 1. Illustration of ASCs as a model for studying adipogenesis *in vitro*. ASCs can differentiate through a three-phase process into the mature adipocytes. The adipogenic differentiation is initiated by exposure of ASCs to conditioned culture medium and results in changes of cell morphology, indicating loss of capacity to replicate and acquisition of the ability to accumulate lipid droplets, which are demonstrated by positive Oil Red O staining in the lower right figure (×200). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

eage cell fates *in vitro*, including adipogenic, neurogenic, chondrogenic, myogenic and osteogenic differentiation [15,16]. ASCs are progenitor cells present in fat depots throughout the lifespan that can differentiate into preadipocytes and subsequently into lipid-containing mature fat cells (Fig. 1. 1). Since fat cells do not divide in *in vitro* cultivation, making it difficult to study the intrinsic factors affecting fat mass directly, preadipocytes derived from ASCs have become as an excellent model to determine effects of aging on fat cellularity and function [17–19]. As a substantial component of fat tissue, preadipocytes are able to strongly affect the growth and biological function of adipose tissue in their own right [20,21]. Changes with differing propensities for preadipocyte proliferation, apoptosis, differentiation and lipid metabolism can contribute significantly to the alterations in fat cell number, size and function, which would in turn influence the fat depot size.

Hypothesis

We hypothesize that OF volume may decrease with age and the OF hypertrophy is not the major contributing factor to the palpable pouches in lower eyelids. Aging can definitely cause alterations in OF cellularity and function, and these changes, we speculate, are linked to the effects of age on preadipocyte dynamics. If the OF size declines in the older individuals with baggy eyelids, decreased preadipocyte capacity to differentiate into fat cells with age will be predicted.

Evaluation of the hypothesis

Our hypothesis is supported by the following facts: (1) Subcutaneous fat (SF) mass experiences substantial volume changes between young and old ages [21]. For example, triceps skinfold thickness decreases dramatically in old age, indicating significant loss of the SF depots. The decline of SF mass common in older humans may also occur in the OF depots. (2) OF samples are easy to harvest during eyelid aesthetic surgeries. This makes it feasible to culture ASCs isolated from donors of various ages *in vitro* [22–24]. (3) ASC-derived preadipocytes can remain stable over long-term culture. Their viability changes little with different donor age, and the dynamic changes during adipogenic differentiation can be studied under carefully controlled conditions *in vitro* [20,21].

In summary, the use of orbital ASC-derived preadipocytes is a good approach for determining effects of aging on OF cellularity and function, and investigating the relationship between OF volume changes and the formation of baggy lower eyelids.

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Conflict of interest

None.

References

[1] Rohrich RJ, Ahmad J, Hamawy AH, Pessa JE. Is intraorbital fat extraorbital? Results of cross-sectional anatomy of the lower eyelid fat pads. Aesthet Surg J 2009;29(3):189–93.
[2] Yu B, Kang SY, Akthakul A, et al. An elastic second skin. Nat Mater 2016;15(8):911–8.