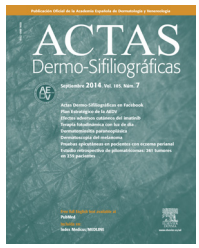
Actas Dermosifiliogr. 2015;106(9):725–732

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org



REVIEW

Skin Stem Cells: At the Frontier Between the Laboratory and Clinical Practice. Part 1: Epidermal Stem Cells☆

I. Pastushenko,[a,*] L. Prieto-Torres,[b] Y. Gilaberte,[c,d] C. Blanpain[a,e]

[a] *Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire (IRIBHM), Université Libre de Bruxelles (ULB), Bruselas, Bélgica*
[b] *Servicio de Dermatología, Hospital Clínico Lozano Blesa, Zaragoza, Spain*
[c] *Servicio de Dermatología, Hospital San Jorge, Huesca, Spain*
[d] *Instituto Aragonés de Ciencias de la Salud, Zaragoza, Spain*
[e] *Walloon Excellence in Life Sciences and Biotechnology (WELBIO), Université Libre de Bruxelles (ULB), Bruselas, Bélgica*

Received 1 May 2015; accepted 27 May 2015

KEYWORDS
Adult stem cells;
Epidermal stem cells;
Review;
Dermatology;
Therapeutic applications

Abstract Stem cells are characterized by their ability to self-renew and differentiate into the different cell lineages of their tissue of origin. The discovery of stem cells in adult tissues, together with the description of specific markers for their isolation, has opened up new lines of investigation, expanding the horizons of biomedical research and raising new hope in the treatment of many diseases.

In this article, we review in detail the main characteristics of the stem cells that produce the specialized cells of the skin (epidermal, mesenchymal, and melanocyte stem cells) and their potential implications and applications in diseases affecting the skin.

Part I deals with the principal characteristics and potential applications of epidermal stem cells in dermatology.

PALABRAS CLAVE
Células madre del adulto;
Células madre epidérmicas;

Células madre de la piel: en la frontera entre el laboratorio y la clínica. Parte I: células madre epidérmicas

Resumen Las células madre son células que se caracterizan por su capacidad para autorrenovarse y diferenciarse hacia células de todos los linajes que constituyen su tejido de origen. El descubrimiento de las células madre en un organismo adulto, y la descripción de los marcadores

☆ Please cite this article as: Pastushenko I, Prieto-Torres L, Gilaberte Y, Blanpain C. Células madre de la piel: en la frontera entre el laboratorio y la clínica. Parte I: células madre epidérmicas. Actas Dermosifiliogr. 2015;106:725–732.

* Corresponding author.
E-mail address: jane.pastushenko@gmail.com (I. Pastushenko).

1578-2190/

Revisión;
Dermatología;
Aplicaciones terapéuticas

que han permitido aislar de forma específica estas células, han abierto nuevas perspectivas y nuevos horizontes en la investigación biomédica y también nuevas esperanzas en el tratamiento de muchas enfermedades. En este artículo se revisan de forma detallada las principales características de las células madre que dan origen a las distintas células de la piel humana, incluyendo las células madre epidérmicas, mesenquimales y melanocíticas, y sus potenciales implicaciones y aplicaciones en las enfermedades cutáneas. La primera parte de este artículo revisa las células madre epidérmicas, con sus principales características y sus potenciales aplicaciones en dermatología.

Introduction

Stem cells are defined by 2 fundamental characteristics: their capacity for self-renewal and for differentiation into all cell lines within their tissue of origin.[1]

In adults, stem cells have been identified in different organs, including the skin, intestine, muscle, hematopoietic system, and even the human brain.[2] These cells are responsible for maintaining tissue homeostasis where they reside and also for repairing damage when it occurs.

The discovery of stem cells in adult organisms and characterization of their markers to enable isolation of specific cells have opened up new perspectives and new horizons in biomedical research, with new hopes for treatment in an range of diseases. Epidermal stem cells are of particular interest as they are relatively numerous and also accessible, making them easy to obtain. In the first part of this review, we have aimed to summarize the main findings of basic research in the field of epidermal stem cells. We then discuss their potential applications in clinical dermatology.

Different Stem Cell Populations in the Epidermis

Two types of progenitor cell are present in the basal layer of the interfollicular epidermis: $\alpha6^{+}CD34^{-}$ stem cells, characterized by slow division rates (4-6 times a year) and a long lifespan, and basal layer $K14^{+}Inv^{+}$ progenitor cells,[3] as well as possibly $Axin2^{+}$ cells,[4] characterized by faster division rates (once a week) and shorter lifespan. After a certain number of divisions these cells undergo terminal differentiation into differentiated keratinocytes, thereby losing their capacity for division. Table 1 summarizes the main characteristics of the markers.

The hair follicle has 3 phases: anagen or growth phase (lasting on average 3 years), catagen or involuting phase (which lasts several weeks), and telogen or resting phase (which lasts several months). The stem cells responsible for hair follicle regeneration during anagen reside in the bulge (the lower part of the permanent portion of the hair follicle) and are characterized by expression of the markers CD34, Lgr5, and K15. The cells are multipotent,[5] as they can differentiate into all cell lines present in the hair follicle unit. During anagen, the stem cells in the bulge give rise to transit-amplifying cells, which reside in the hair follicle. These rapidly and transiently proliferate before embarking on 7 differentiation programs which finally give rise to the mature hair follicle. When the matrix cells have exhausted their proliferative capacity, hair growth stops and the follicle enters catagen,[6] leading to degeneration of the lower two-thirds of the follicle while the bulge region remains intact.

The hair bulb is found in the lower part of the hair follicle. This structure, which rests on the dermal papilla, is made up of differentiated progeny of stem cells from the bulge. The dermal papilla contains specialized dermal fibroblasts, nerve fibers, and a capillary loop. It plays a fundamental role in the development of the hair follicle and control of the hair cycle in adults.[7] Cells in the dermal papilla can differentiate into neuronal and mesodermal cell lines.[8,9] In a recent study, Rahmani et al.[10] eliminated stem cells from the dermal papilla and observed a delay in the regeneration of the hair follicle, along with change in hair type, suggesting that the dermal papilla plays a fundamental role in restoring hair growth after damage, disease, or aging.

At least 3 types of epithelial stem cells have been identified recently: these types reside in the sebaceous glands, the infundibulum, and sweat glands. The sebaceous glands are maintained by unipotent $Lgr6^{+}$ stem cells, which originate from $Blimp1^{+}$ progenitor cells.[11] In addition, stem cells from the isthmus express the MTS234 marker,[12] and if transplanted to an immunodeficient mouse, are surprisingly able to give rise to epidermal, follicular, and sebaceous cell lines, suggesting that these might be multipotent cells.[13] The stem cells in the infundibulum are characterized by expression of the Lrig1 marker and their multipotent capacity.[14] It is also thought that they may contribute to the homeostasis of the sebaceous glands.[15] Finally, although sweat glands have traditionally be considered as quiescent in adults, a study published recently suggests 4 different types of progenitor cells are present in the epithelium of these structures.[16] Figure 1 shows a microphotograph of the hair follicle (Fig. 1A) and a schematic of the different compartments in the epithelium of the skin and where the stem cells reside, as well as a summary of their markers (Fig. 1B).

Self-Renewal of Stem Cells

As mentioned earlier, stem cells can give rise to differentiated cells, but they also propagate to maintain a constant pool of stem cells, and can divide symmetrically or asymmetrically. During the process of asymmetric division, a stem