Stem Cells in Dermatology and Anti-aging Care of the Skin

Amy Forman Taub, MD[a,b,c,*], Kim Pham[d,1]

KEYWORDS

• Stem cells • Homeostasis • Dysregulation • Basal cells

KEY POINTS

- The activity of stem cells is stimulated by the start of tissue dysfunction.
- One important application of stem cell biology is how these cells can be used in the context of aging and age-related dysfunctions.
- A key hallmark to aging is the exhaustion or dysregulation of the endogenous stem cell population, which aids in maintaining tissue homeostasis and repair of injured tissues.

INTRODUCTION

Since the discovery of multipotent stem cells by Till and McCulloch in 1961,[1] further elucidation of stem cells' functions have been identified as both facilitating development of new cells and maintaining homeostasis of current normal cells. The activity of stem cells is stimulated by the start of tissue dysfunction. Several applications using these functions have been implemented in medicine already: reestablishing the hematopoietic lineage via bone marrow transplantation,[2] development of stem-cell based therapy for type 1 diabetes[3,4] and retinitis pigmentosa,[5] and using stem cells to advance the cure for spinal cord injury.[6] One important application of stem cell biology is how these cells can be used in the context of aging and age-related dysfunctions. During aging, DNA accumulates damage, impairing protein homeostasis, cell function and communication, as well as normal organ physiology.[7] Another key hallmark to aging is the exhaustion or dysregulation of the endogenous stem cell population, which aids in maintaining tissue homeostasis and repair of injured tissues. Because aging is so intimately tied to stem cell integrity, one of the major goals of stem cell biology and regenerative medicine is how one can use these cells to reverse aging and the associated dysfunctions that come with it.

Stem cells are undifferentiated or partially differentiated cells that are capable of dividing and generating differentiated and proliferative cells (**Fig. 1**). Stem cells range from pluripotent cells that are found in the inner cell mass of preimplantation blastocysts or isolated from other sources to unipotent progenitors such as fetal tissues, birth-associated tissues, or adult tissues. Several advances have been made to apply the unique traits of this variety of stem cell types. These include establishment of an

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[a] Department of Dermatology, Northwestern University, Medical School, Chicago, IL, USA; [b] Advanced Dermatology, 275 Parkway Drive, Suite 521, Lincolnshire, IL 60069, USA; [c] Advanced Dermatology, Glencoe, IL, USA; [d] University of Wisconsin, School of Medicine and Public Health, Madison, WI, USA
[1] Present address: 2355 University Avenue Apartment 2015, Madison, WI 53726.
* Corresponding author. 275 Parkway Drive, Suite 521, Lincolnshire, IL 60069.
E-mail address: drtaub@advdermatology.com

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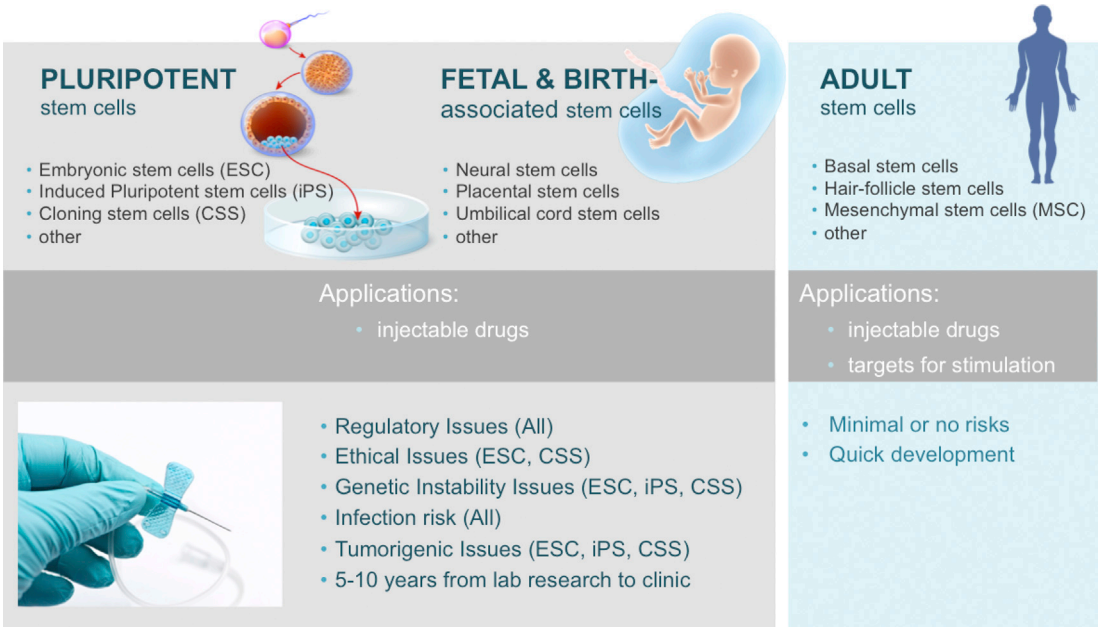

Fig. 1. Types of human stem cells.

embryonic stem cell line via in vitro fertilization, the reprogramming of differentiated adult cells to induced pluripotent stem cells (iPSC), and the generation of cloning stem cells (somatic nuclear transfer stem cells). Other strategies include the creation of parthenogenetic stem cells, isolation of stem cells from fetal tissues (including neural stem cells or retinal progenitor cells), and separation of birth-associated stem cell populations including cord blood stem cells or placental stem cells. Although these different modes of pluripotent and fetal stem cells provide great potential for treating aging and age-related diseases, there are several associated disadvantages. Pluripotent and fetal stem cells may be tumorigenic,[8] possess genetic instability,[9] and are often tied to ethical and regulatory debate.[10] Even though iPSCs bypass the ethical issues of embryonic stem cells, they still possess the same mutations and damage that the donor cells had, which can decrease its ability to proliferate and respond to its respective niche.[11] Stem cells isolated from birth-associated tissues have limited ability to proliferate and limited directions of differentiation, and therefore therapeutic potential of areas of their applications is rudimental.[12] An alternative method that is being explored is the use of pharmaceuticals to modulate endogenous stem cell populations to leverage their respective mechanism of cell signaling and communication. One such example is the use of CBP/Catenin antagonist, ICG-001, that acts more selectively than retinol by shifting the balance of cell division to asymmetric division and thus more differentiation.[13,14] With more alternative methods emerging in regenerative medicine, several other advances that target the individual's stem cells could provide the means for dealing with age-related dysfunctions such as skin aging.

DERMATOLOGIC STEM CELLS

There has been great interest in understanding the regulation and coordination of the stem cells found within the skin in order to repair aged skin (**Fig. 2**). Through wound healing and genetic knock out experiments, several stem cell populations have been elucidated in the skin that have applications to regenerative medicine.[15,16] Within the epidermis lay basal epidermal stem cells that proliferate and maintain epidermal turnover and homeostasis.[15] Other stem cells that are involved in transient repair of skin wounds (although they do not contribute skin's homeostasis on a daily basis) are hair follicle stem cells.[16] These follicular-based stem cells include *Lrig1*+ stem cells (residing in the junctional zone of the hair follicle and contributing to the infundibulum), *Gli1*+ stem cells (maintaining sebaceous glands), and *Lgr6*+ stem cells (acting as skin's master stem cells).[15,17]