If someone asked you what is the largest organ in the body, one that serves multiple protective functions, one that is a barometer of disease elsewhere, and one that is indispensable to human existence, what would you answer? If you said ‘skin’, you would be right on target. But what if someone also asked whether more healthcare dollars are spent on skin disease than high blood pressure, whether certain skin cancers may be lethal when no more than the size of a grain or rice, or whether skin may hold the secret to tissue regeneration, aging, and cancer…if you answered true to all of these, you would again be correct.

These are among the key clinical and societal issues that relate to skin health and disease. They also address why the mission of the Harvard Stem Cell Institute’s Skin Program is so essential. This is because healthy skin is critically linked to stem cells that ‘reside’ in niches in order to maintain normal equilibrium and functions that span from temperature regulation to protection from the cancer-causing effects of sunlight to immune surveillance against infection to providing the tactile stimuli that mediate our very interface with the external environment.

The Harvard Stem Cell Institute’s Skin Program has been designed to specifically target disorders that most impact on global skin health. These include understanding of how stem cells may be harnessed to not only hasten effective healing of wounds and chronic ulcers, but also of how skin can provide the essential...
clues required for true regenerative healing. And because skin is actually a remarkably complex organ, our ability to regenerate skin should inform many other organ systems where tissue regeneration remains a premier goal in clinical medicine. We also seek to learn why skin stem cells become depleted and less effective as we age, knowing that the ability to thwart this phenomenon could hold the key to rejuvenation. Finally, skin cancers are driven by cancer stem cells, and the ability to target and destroy them will allow us to therapeutically ‘go for the jugular’ of the most aggressive tumors, like advanced forms of malignant melanoma.

Already well on the way

Based on the breakthrough discovery of HSCI clinician scientist Dennis Orgill, Ioannis Yannas, and their collaborators, we already have developed a biodegradable scaffold that when placed on a deep skin wound promotes partial skin regenerative healing. Now with our ability to isolate and manipulate different populations of skin stem cells and combine them with the scaffold approach, our trajectory for perfecting skin regeneration has increased dramatically. In addition, the availability of “3-D bioprinting” technology and expertise now allows us to precisely ‘plant’ stem cells within cutaneous bioprostheses in a spatially precise manner that should further enhance the regenerative potential of human skin.

Our studies focused on stem cell therapies for wound healing and skin regeneration have already advanced in the direction of the bedside. An Advanced Therapy Medicinal Product (ATMP) consisting of in vitro-produced ABCB5-positive dermal mesenchymal stem cells pioneered by HSCI investigator and Skin Program co-leader, Markus Frank, is currently being evaluated for safety and efficacy in the healing of chronic venous ulcers in an interventional phase I/IIa human clinical trial sponsored by industry collaborator and Harvard technology licensee Rheacell GmbH & Co. KG, conducted in collaboration with University Hospital Würzburg (ClinicalTrials.gov Identifier: NCT02742844).

Targeting melanoma stem cells

HSCI Skin Program investigators have identified and experimentally targeted stem cells in human malignant melanoma, showing that this approach significantly inhibits the genesis and progression of this potentially deadly form of cancer. This advance was awarded Pfizer Center for Therapeutic Innovation recognition, facilitating current further preclinical development with biopharmaceutical collaboration of fully human monoclonal antibodies as novel anti-melanoma stem cell immunotherapeutics.

Beyond diseased skin

One of the advantages of a Program designed to catalyze interdisciplinary and interinstitutional research alliances is the diversity of scientific input and output that accrues. As a consequence, major programmatic initiatives and accomplishments have been achieved in the following areas:

- Corneal restoration through deployment of limbal stem cells
- Advancements in understanding of hair follicle stem cell niches
- Insights into the fundamental role of epigenetic regulation of stem cell behavior
- Understanding of how mucosal and skin epithelial surfaces regenerate

Harvard Stem Cell Institute
Bauer Building, Admin Suite
7 Divinity Ave
Cambridge, MA 02138, USA
617-496-4050
hscl@hscl.harvard.edu
www.hscl.harvard.edu