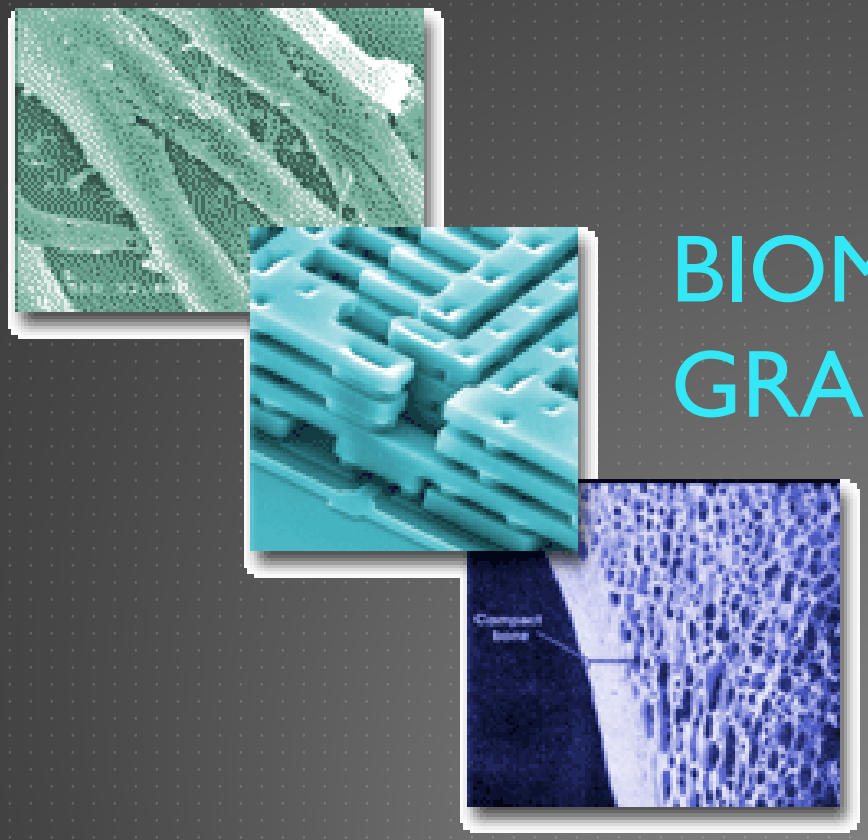
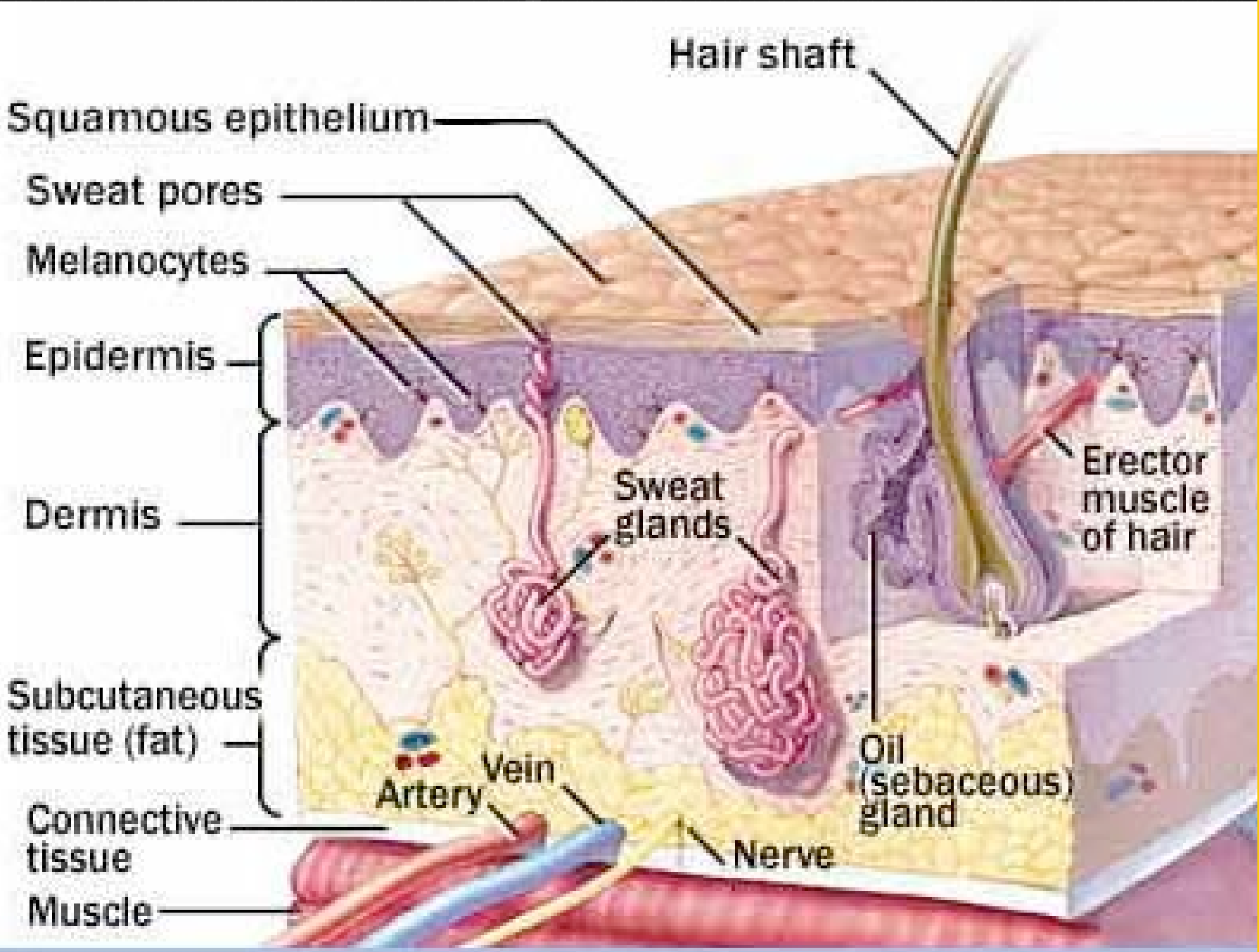


BIOMATERIALS FOR SKIN GRAFTING

Heba Osman

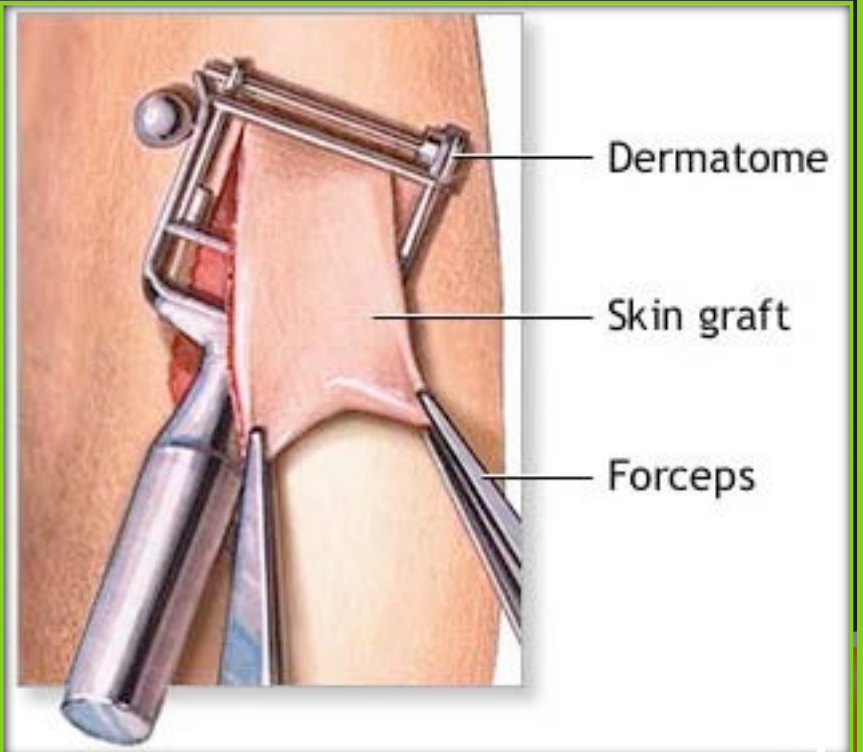
THE SKIN[4]

- Skin has its functions:
  - Serves as a protective barrier that helps prevent internal tissues from critical situations
  - Regulates the temperature of the body
  - Controls fluid loss
- Consists of layers:
  - Epidermis
  - Dermis
  - Hypodermis



WHAT IS SKIN GRAFTING?[1]

- It is the transplanting of the skin
- Used to permanently replace damage or missing skin or provide a temporary wound covering
- Necessary because:
  - It protects the body from fluid loss
  - Aids in temperature regulation
  - Helps disease causing bacteria or viruses from entering the body



TYPES OF SKIN GRAFTS[3]

- Autograph
  - Use of one's own skin as the source area
  - If there's not enough skin on the body, skin can be harvested from outside sources
- Allograft – Skin taken from another human source (eg. Cadaver)
- Xenograft – skin taken from an animal source
- Synthetic tissue

QUESTION

- Which of the following would be permanent solutions and which would be temporary?
  - Autograft
  - Allograft
  - Xenograft
  - Synthetic tissue

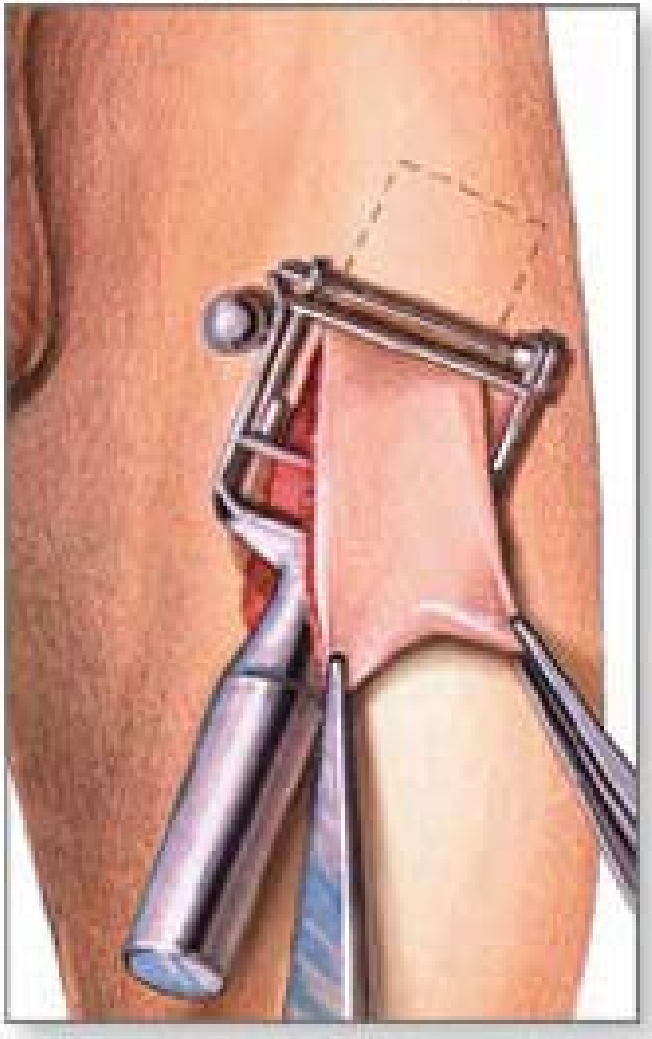
ANSWER[17]

- Allograft, Xenograft and synthetic tissue are all temporary because none of them come directly from the patients own skin. Therefore they're rejected by the patient's immune system with 5-10 days.
- They help heal the partial thickness burn or wound
- And close the excised wound till skin is available

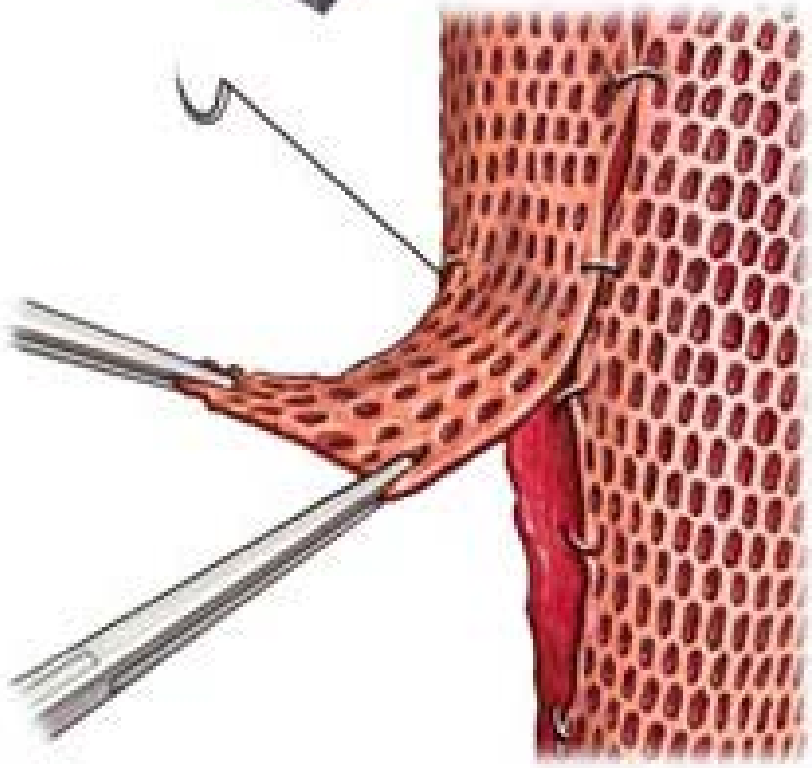
The pigskin dermis adheres to cleaned partial thickness burn

SKIN GRAFT

Graft taken from patient's healthy skin



Skin is meshed to cover a large wound



ADAM.

SKIN GRAFTS TECHNIQUES [2]

- Split-thickness grafts
  - For the shallowest wounds (only affect the epidermis and part of the dermis)
- Full-thickness grafts
  - Requires all 3 skin layers; epidermis, dermis and hypodermis to be removed from the donor site.
- Composite grafts
  - For wounds that include bone, tendon, cartilage or the loss of muscle

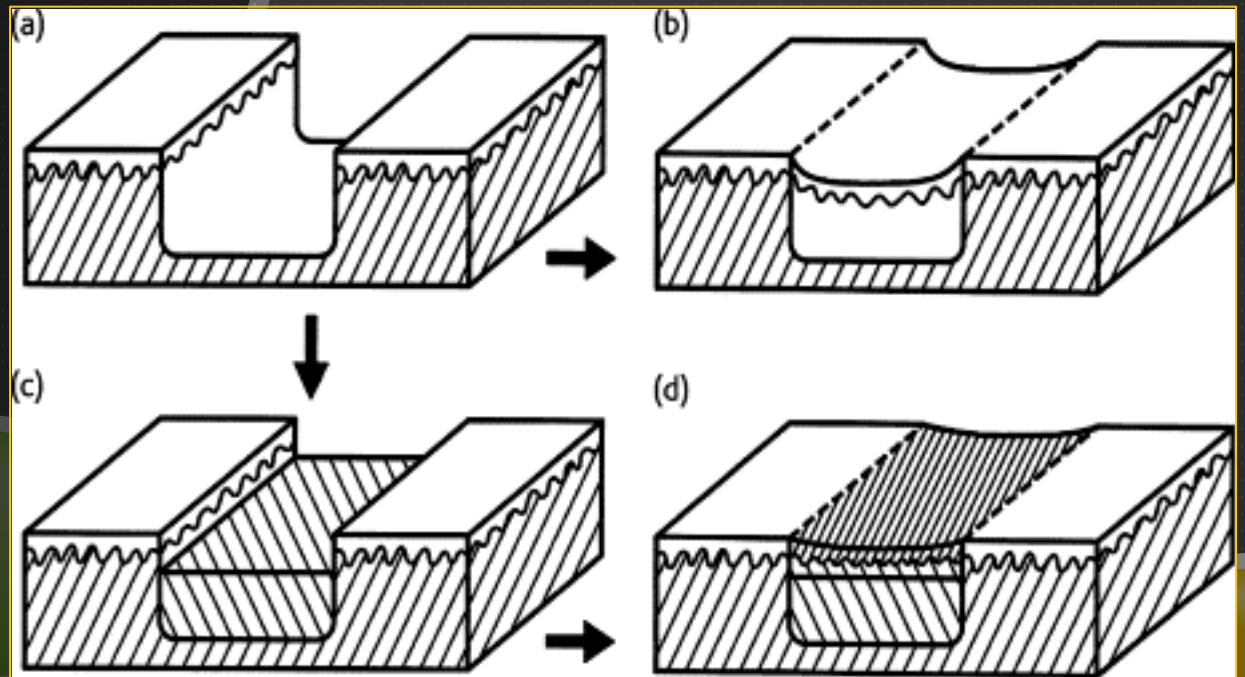
SPLIT SKIN GRAFT[14]

After 5 days

Healed skin graft

Full thickness burn injuries: In most cases,

- (a) a full thickness skin defect is treated with
- (b) a split thickness skin graft taken from elsewhere on the body. Where skin grafts are not available, then they're repaired in two stages using
- (c) a dermal substitute, which is then covered by
- (d) an epidermal material, usually a thin split thickness skin graft.

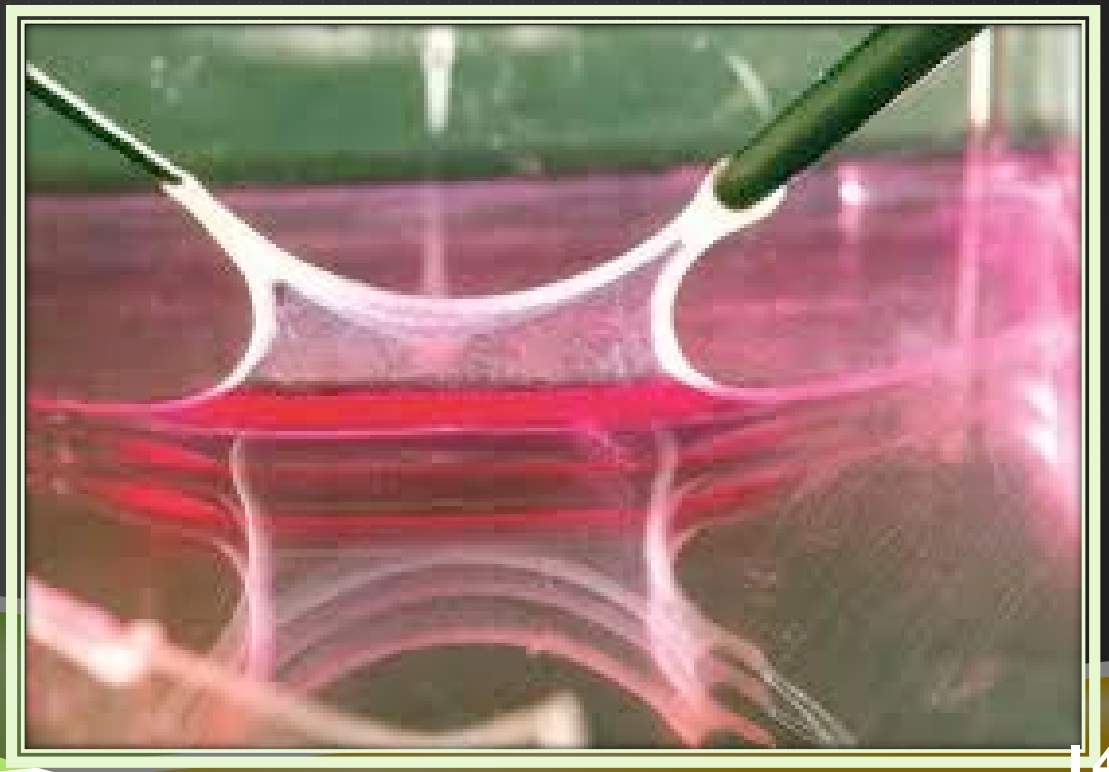


ENGINEERING SKIN

- Tissue engineered skin needs to:
  a) Provide a barrier layer of keratinocytes
  b) Be securely attached to the underlying dermis
  c) Well vascularized
  d) Provide an elastic structural support for skin

BIOMATERIAL[5]

- Definition: "Material used to construct artificial organs, rehabilitation devices, or prostheses and replace natural body tissues."

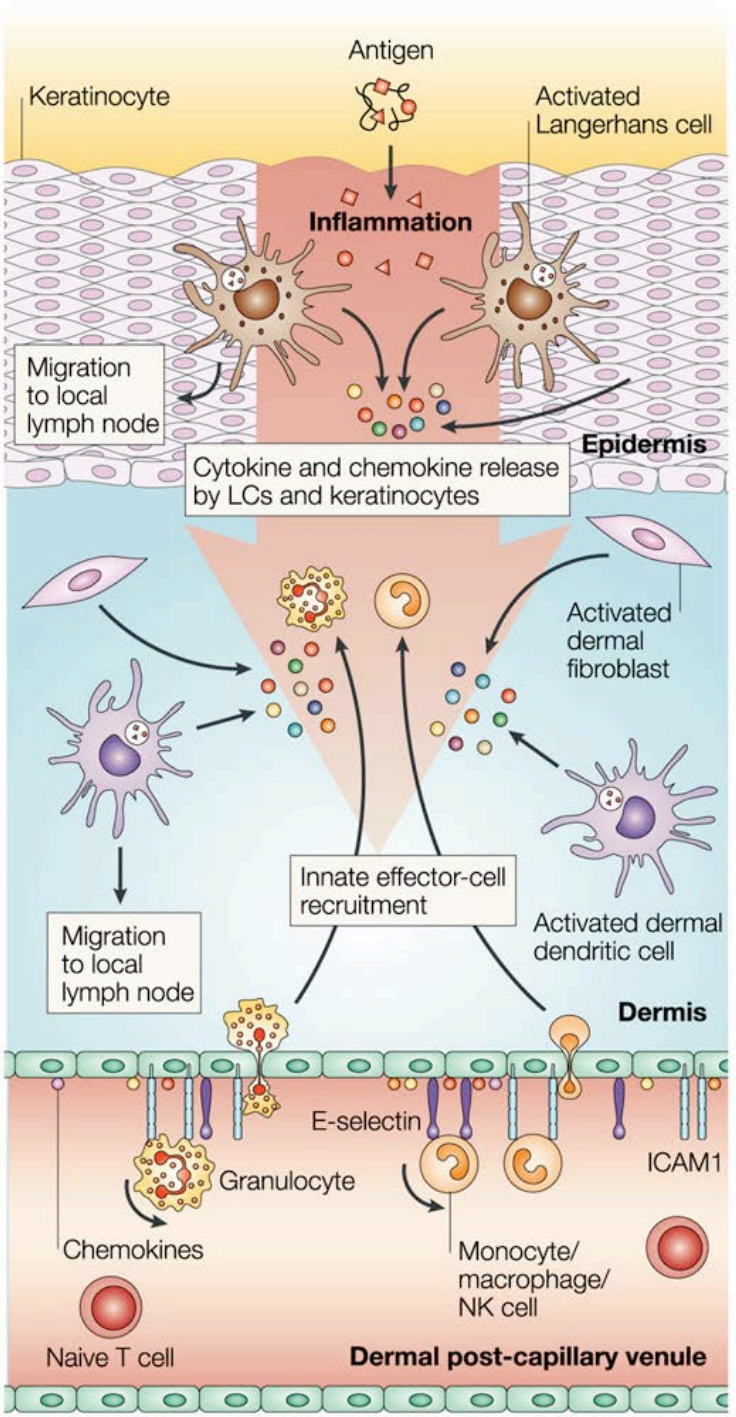


QUESTION

- What are some components of the skin that you think might be necessary for the engineered skin to contain?

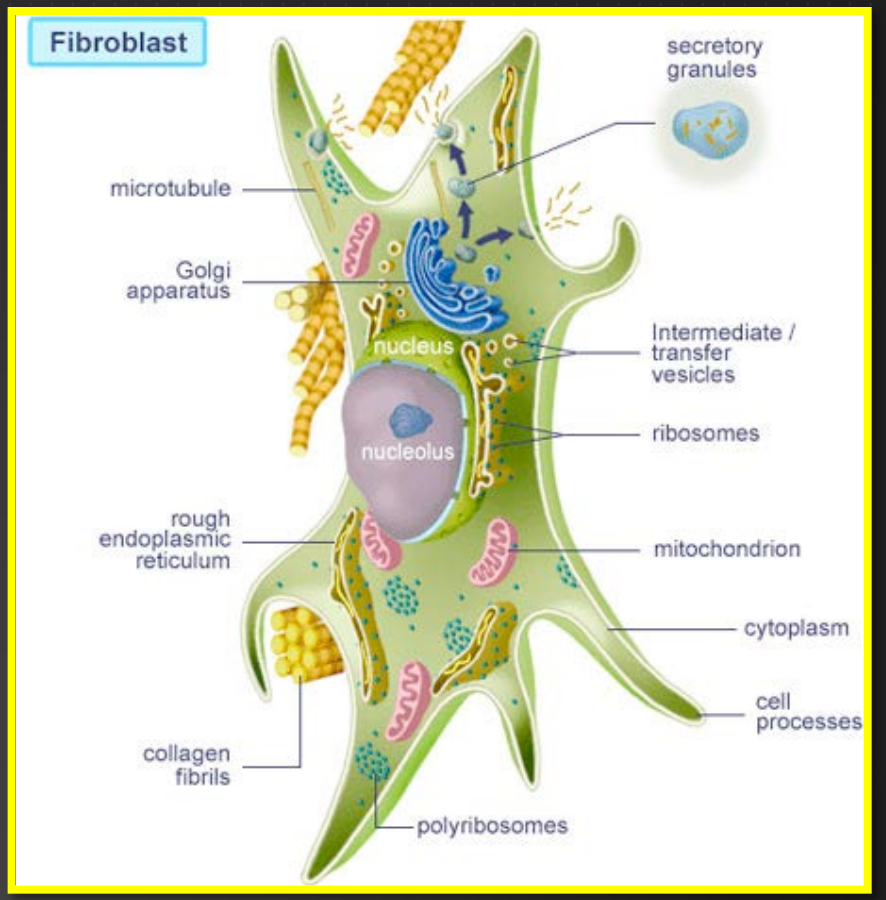
ANSWER

- Fibroblast
- Collagen
- Keratinocytes



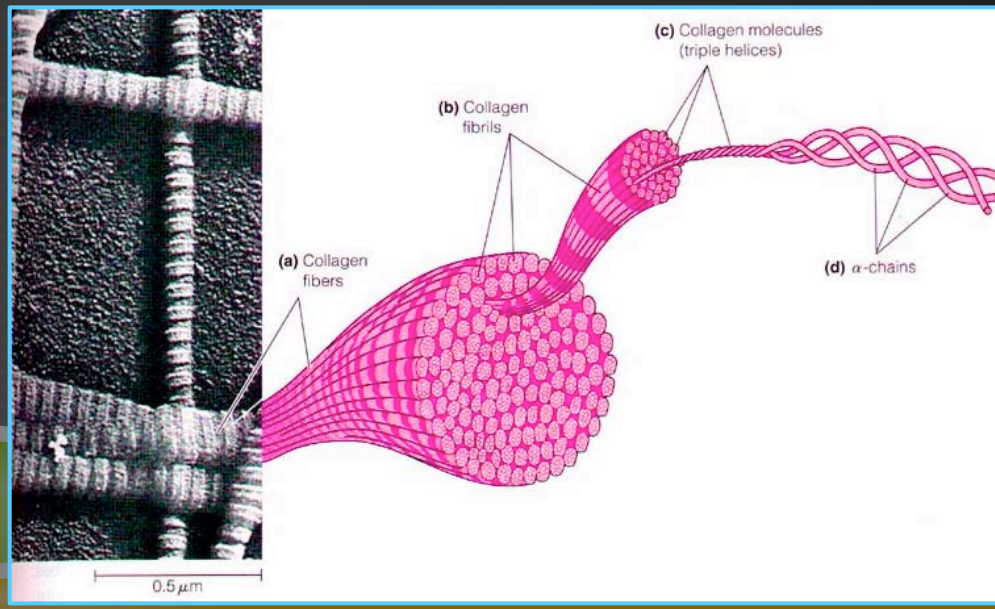
FIBROBLASTS[22]

- Synthesizes the extracellular matrix and collagen, the structural framework for animal tissues
- Plays a critical role in wound healing.
- Following tissue injury, fibroblasts migrate to the site of damage, where they deposit collagen and facilitate the healing process.



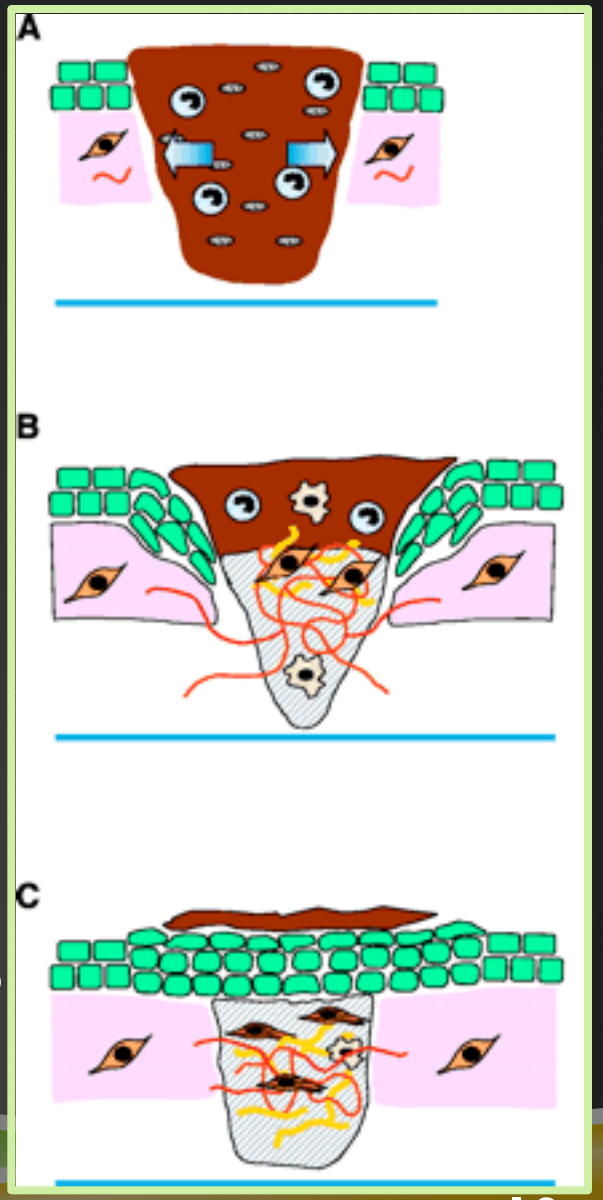
COLLAGEN[23]

- Strong, fibrous, insoluble in water
- Winds itself into a fiber mesh to add structural stability
- Helps support skin and give it its elastic nature
- Collagen sponge - surgical sponge made of collagen; used to fill surgical space.
- Not absorbable but has enormous fluid absorption capacity.



KERATINOCYTES[24]

- Most common type of skin cell and makes keratin
- Knitted tightly together to form seams between the nerves of the skin and the underlying tissues.
- Forms a protective barrier that prevents the entry of foreign substances through the skin
- Responsible for the repair of the wound
- To form the protective layer, the newly formed cells from the basal skin layer begin to migrate from the wound edges to form a sheet across the site



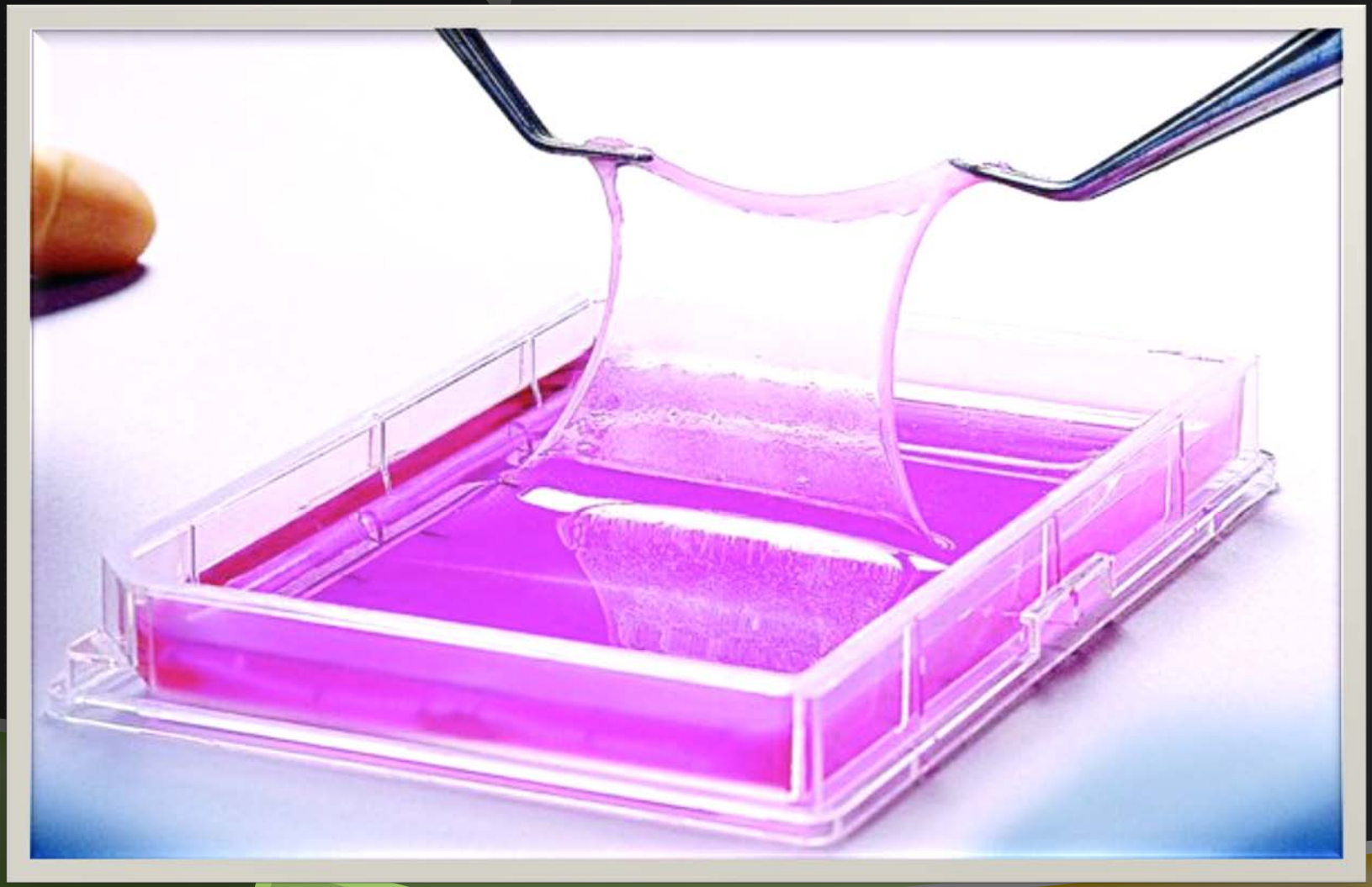
BIOMATERIALS IN USE[6]

Objective	Approach	Examples
Epidermal Cover	Delivers keratinocytes so that they "take" on the wound bed & form a new epidermal layer	- Cultured epidermal sheets – Epicell - Cultured epidermal sheets from plucked hair follicles – Epidex - Subconfluent cells on a synthetic carrier – Myskin - Cells delivered in a fibrin spray
Dermal replacement	Provides a dermal alternative to promote wound healing	- Donor skin - Permacol - Dermagraft - TransCyte - Integra
Epidermal/Dermal replacement	Acts as an alternative to a split-skin graft	- Apligraf - Permaderm - Orcel

EPICEL CULTURED EPIDERMAL AUTOGRAFT[7]

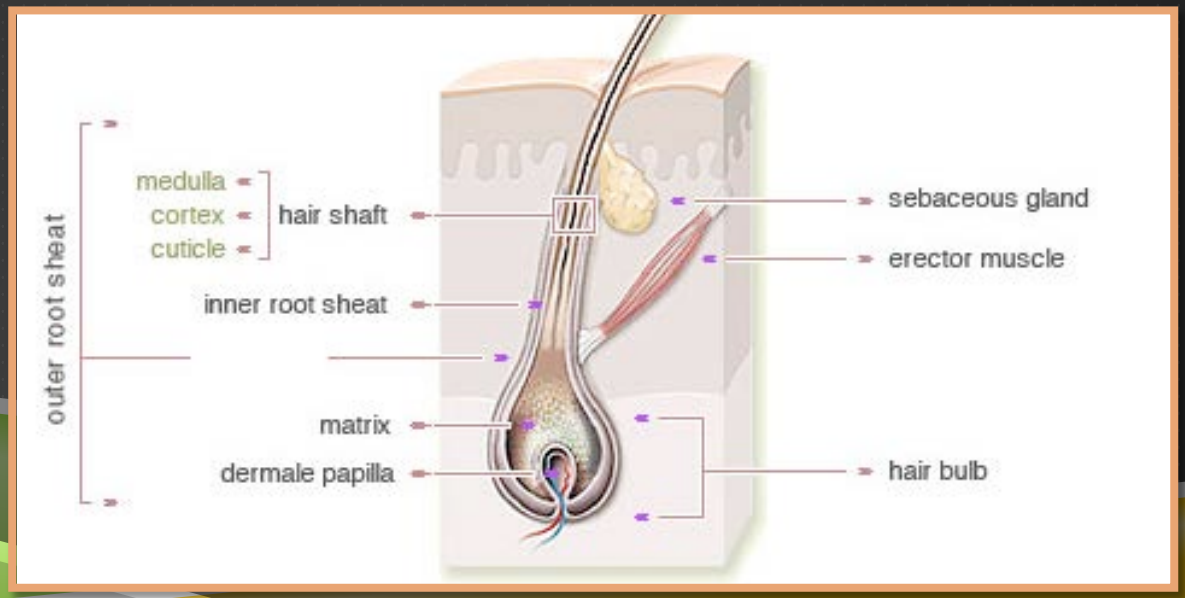
- Sheets of keratinocytes used to replace the epidermal
- Required to close or heal the wound
- The patient's own skin cells are grown from a sample of their own skin
- Used in patients who have deep dermal or full thickness burns comprising a surface area greater than 30%

- May be used with split-thickness autografts, or alone
- Permanent



EPIDEX[13]

- To cultivate an equivalent to the epidermal layer, the necessary cells are extracted by plucking the patient's head hairs
- The outer root sheath of isolated hair follicles contains precursor cells for epidermal keratinocytes.
- The keratinocytes start to grow in the primary culture after a few days.



- After 2-3 weeks, the propagation of cells is finished

New skin occurs

- Under organotypic culture conditions the keratinocytes then develop into tissue in a second complex process within 2 weeks
- This tissue corresponds to the multilayered structure of the human epidermis.

DERMAGRAFT [10]

- **A** cryopreserved human fibroblast-derived dermal substitute
- It is composed of fibroblasts, extracellular matrix, and a bioresorbable scaffold.
- Manufactured from human fibroblast cells derived from newborn foreskin tissue
- Does not contain macrophages, lymphocytes, blood vessels, or hair follicles.

Dermagraft
Active Living Cells

Applying Dermagraft

1. 

Your doctor will remove the dead or unhealthy skin around the wound – this is called debridement. Then, the doctor will clean your wound with a sterile saline solution. This is necessary to make sure there is a clean surface for application of Dermagraft.

2. 

The Dermagraft product will be thawed, rinsed, and cut to the size of your wound.

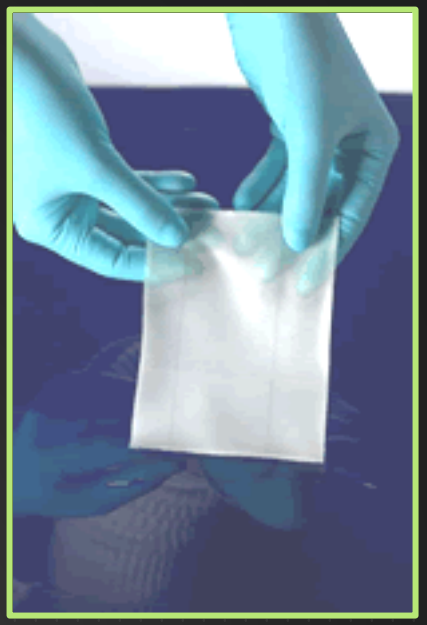
3. 

Dermagraft will be placed on your wound and covered with another dressing to keep it clean and protected.

4. 

Once Dermagraft and the protective dressing are in place, you will be instructed how to care for your wound, including how to change the dressings when appropriate and how to keep pressure off your wound so it can heal quickly.

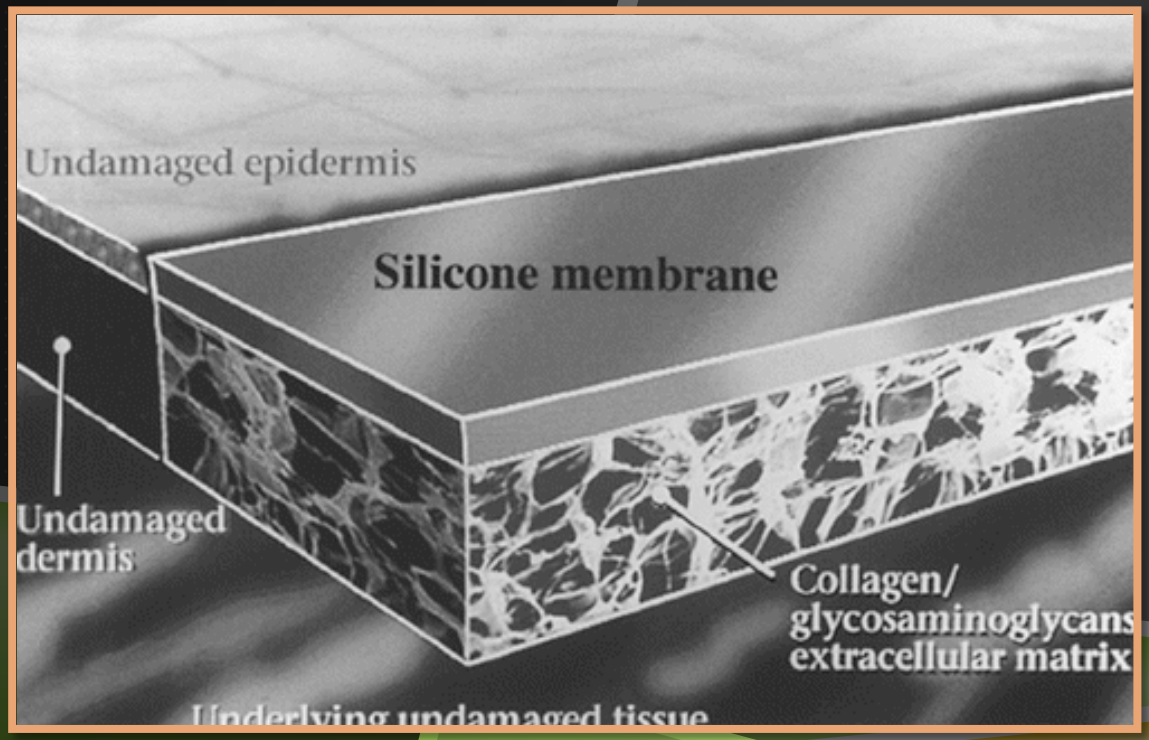
INTEGRA[8]

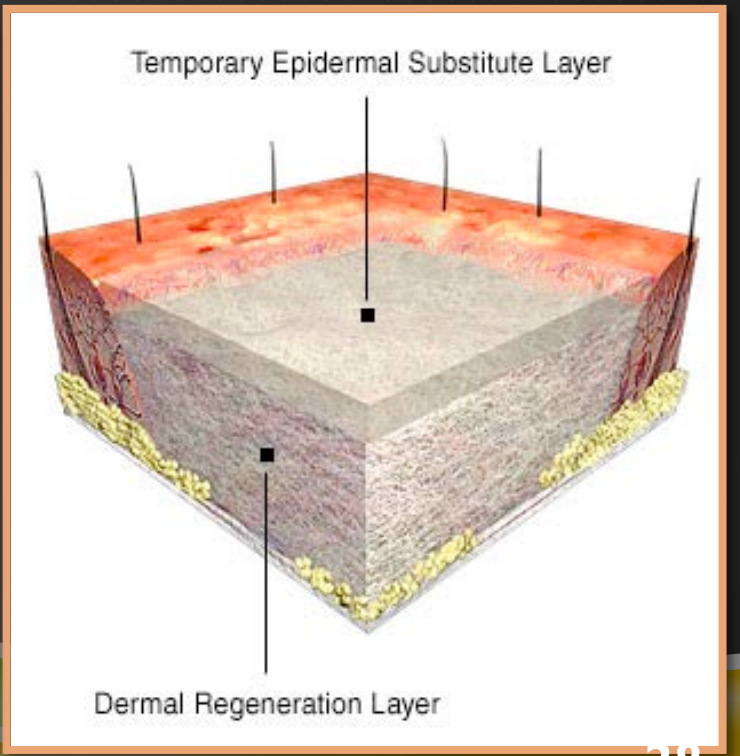


- The bottom layer is made of collagen from cows.
- The top layer is made of silicone.
- Placed on a wound, it allows blood vessels and other cells to grow a new layer of skin while the collagen is absorbed.
- The silicone layer helps close the wound and prevent fluid loss. It is then removed, and a very thin graft of the patient's own skin is applied.
- Used on patients with severe burns or too ill to have more wound sites created

[9]

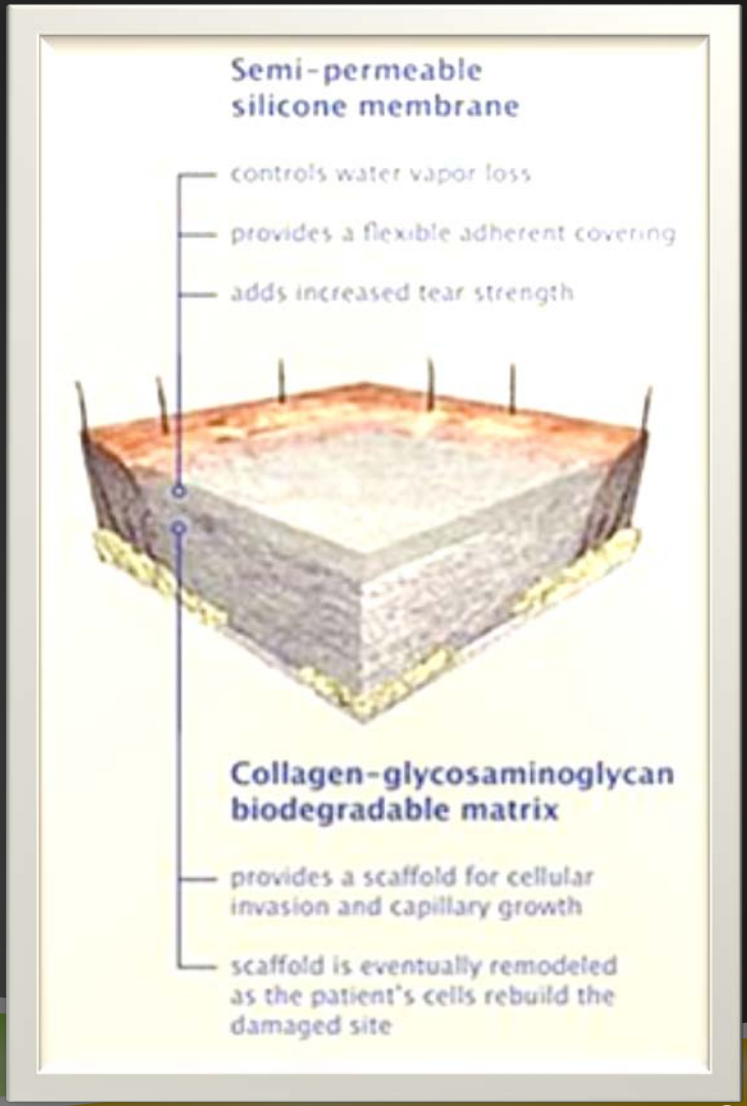
- Dermal Replacement Layer is made from collagen and glycosaminoglycan.
- Temporary Epidermal Layer (silicone)



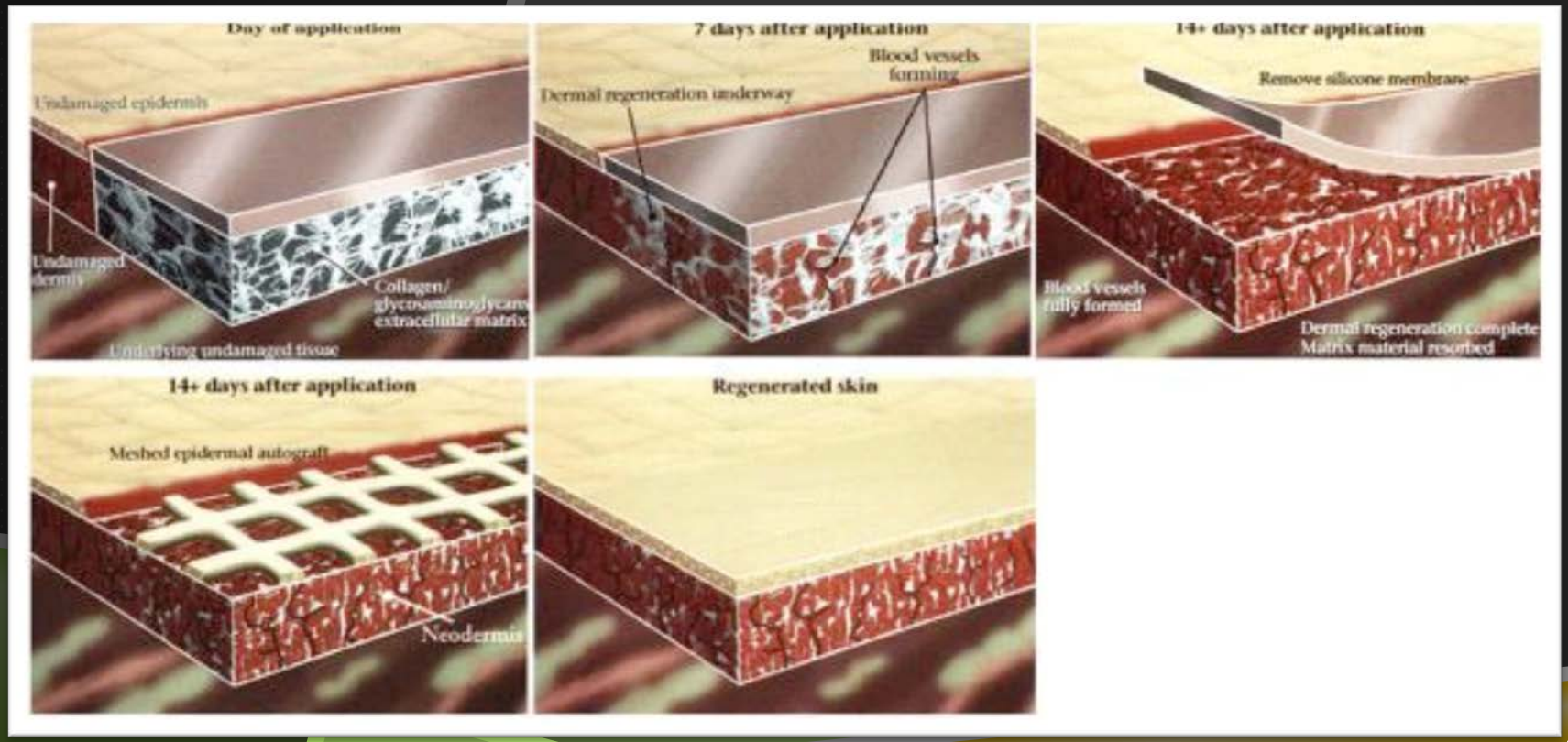


APPLICATION OF INTEGRA

- After obtaining both **fibroblasts and keratinocytes** from a particular patient, they populate a collagen sponge with fibroblasts, allow it to mature, and then introduce keratinocytes expanded in culture.



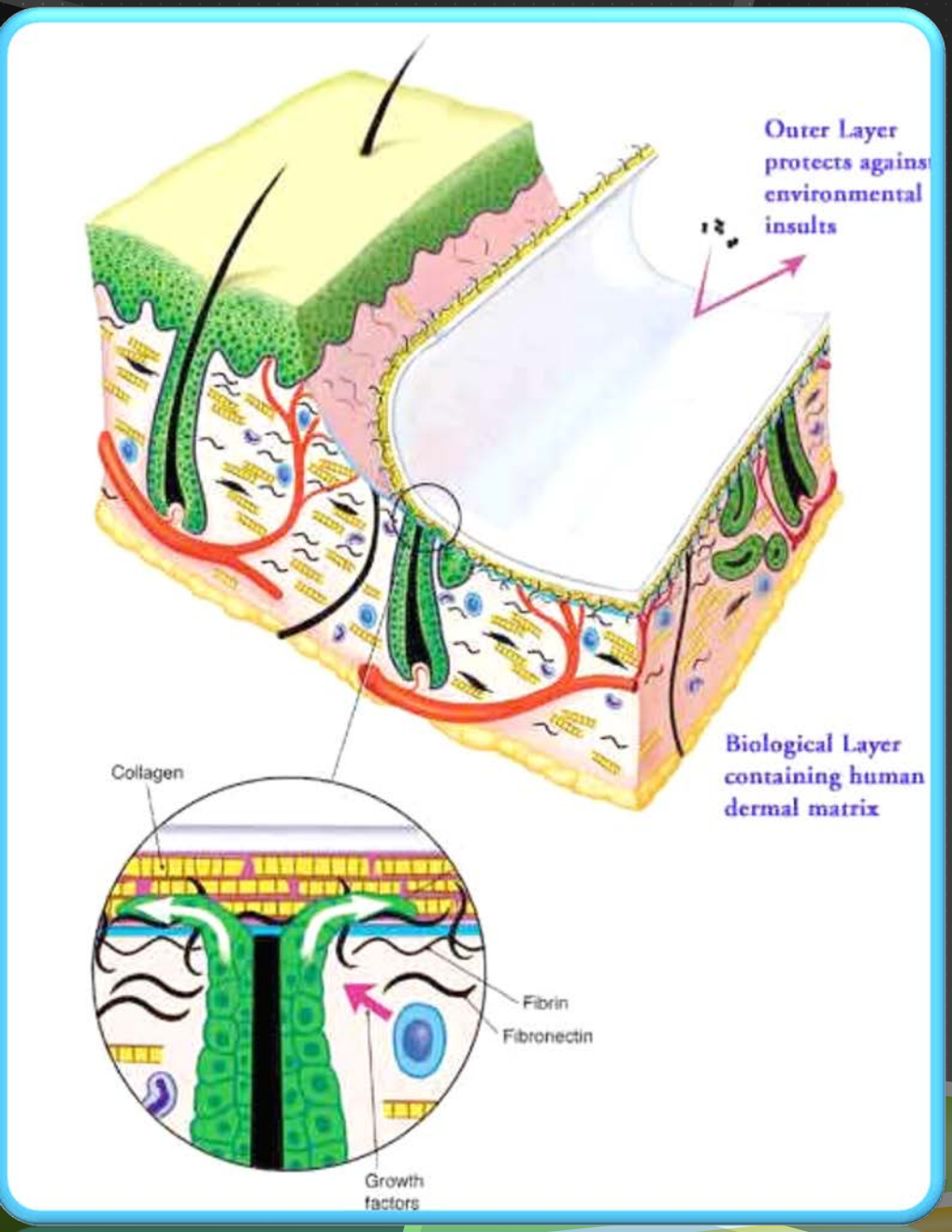
- Next, they culture the product & expose the epidermal layer to air.
- This produces a bilayered, engineered skin replacement, which they then graft on the mature Integra neodermis.
- Result: durable skin with no evidence of scar at 6 months post grafting.



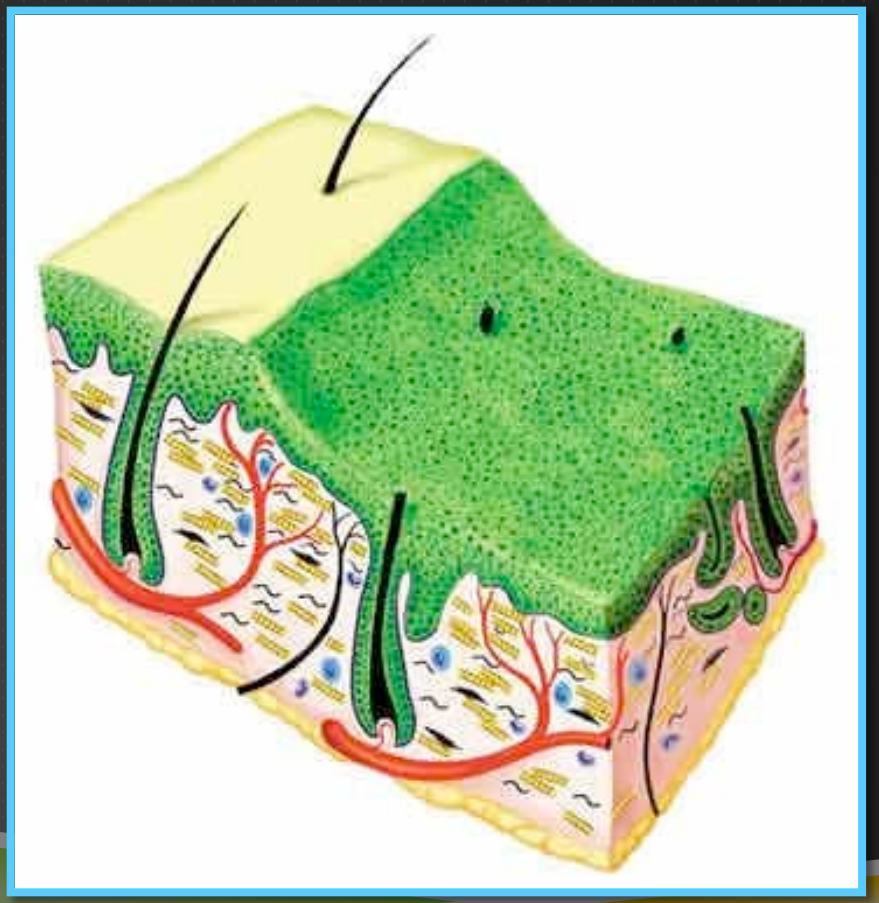
TRANSCYTE[12]

- A human fibroblast-derived **temporary** skin substitute consisting of a polymer membrane & neonatal human fibroblast
- Prior to cell growth, this nylon mesh is coated with collagen and bonded to a polymer membrane (silicone).
- Provides a transparent synthetic epidermis when applied.
- As fibroblasts multiply within the nylon mesh, they secrete human collagen and growth factors.

TransCyte

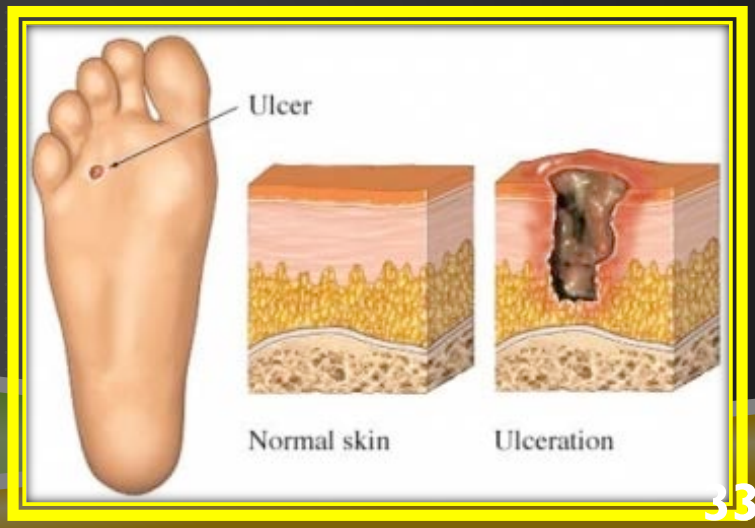


After removal of TransCyte



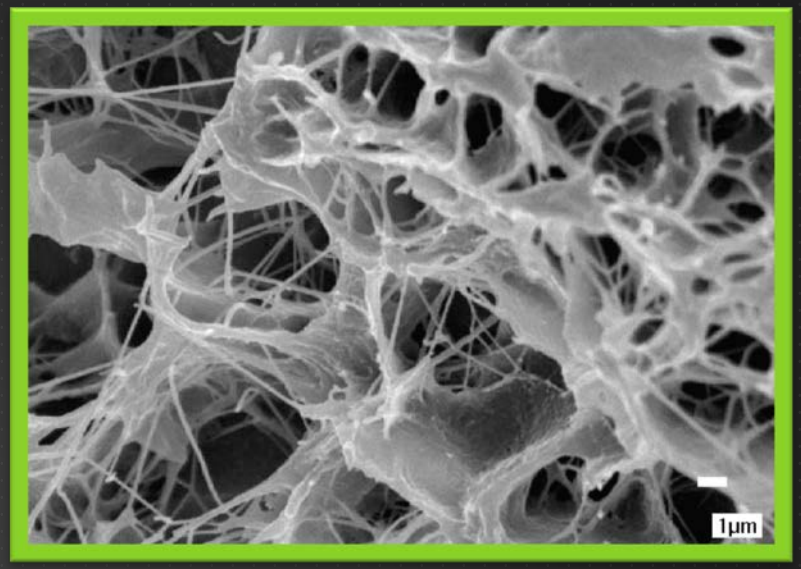
APLIGRAF[11]

- An advanced treatment for healing venous leg and diabetic foot ulcers.
- Created from healthy human skin cells.
- Contains two types of cells:
  - An outer layer of protective skin cells,
  - and an inner layer of cells contained within collagen.
- Constructed by culturing human foreskin-derived neonatal fibroblasts in a collagen matrix over which human foreskin-derived neonatal epidermal keratinocytes are then cultured and allowed to stratify.



USE OF COLLAGEN[19][20]

- Due to its excellent biocompatibility and safety, the use of collagen in biomedical application has been rapidly growing.
- Characteristics that make it the primary resource:
  - Biodegradable
  - weak antigenicity (ability to react with an antibody)
  - Mechanical strength
- Suitable since only a small amount of people possess humoral immunity against it
- Can form fibers with extra strength and stability through cross-linking.



LATEST BREAKTHROUGHS[18]

- Scientists have been able to combine lab-grown flesh with nanoscale wires.
- Ability to graft skin onto people with injuries that killed their nerve endings, while also giving them back their sense of touch.
- Researchers laid out a mesh of organic polymer around nanoscale wires, which serve as the sensing elements.
- Nanoscale electrodes were built within the mesh to enable nanowire transistors to measure the activity in cells.
- Once completed, the substrate was dissolved, leaving a netlike mesh, that can be folded into a variety of 3D shapes.

HarvardScience
SCIENCE AND ENGINEERING AT HARVARD UNIVERSITY

REFERENCES

- 1. Grande, Donald, and Dirk Elston. "Skin Grafting." *Medscape*. N.p., 15 Aug. 2011. Web. 20 Sept. 2012. <http://emedicine.medscape.com/article/1129479-overview>.
- 2. Roos, Dave. "Skin Grafts." *Discovery*. N.p., n.d. Web. 21 Sept. 2012. <health.howstuffworks.com/skin-care/information/anatomy/skin-graft2.htm >.
- 3. Zeltser, Ross. "Skin Graft." *Lifescript*. N.p., 4 Nov. 2009. Web. 19 Sept. 2012. <www.lifescript.com/health/a-z/treatments_a-z/procedures/s/skin_graft.aspx>.
- 4. Bonilla , Carlos, Angel Massanet, and Natacha Almodóvar. "Mechanics of Biomaterials: Skin repair and grafts ." *Applications of Engineering Mechanics in Medicine* 1 (2005): n. pag. Web. 21 Sept. 2012.
- 5. "Biomaterial." *Dictionary*. N.p., n.d. Web. 16 Sept. 2012. <medical-dictionary.thefreedictionary.com/biomaterial >.
- 6. MacNeil, Sheila. "Biomaterials for tissue engineering of skin." *Materials Today* 11.5 (2008): Pages 26-35. *SciVerse*. Web. 19 Sept. 2012.
- 7. "Medical Devices." *FDA*. N.p., 30 May 2009. Web. 17 Sept. 2012. <www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm074878.htm >.
- 8. "Integra." *FDA*. N.p., 29 May 2009. Web. 17 Sept. 2012. <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm083520.htm >.
- 9. "Product Makeup." *Integra*. N.p., n.d. Web. 16 Sept. 2012. <www.ilstraining.com/idrt/idrt/brs_it_03.html >.
- 10. "Dermagraft." *Dermagraft*. N.p., n.d. Web. 19 Sept. 2012. <www.dermagraft.com/about/overview/ >.
- 11. "What is Apligraf." *Apligraf*. N.p., n.d. Web. 20 Sept. 2012. www.apligraf.com/patient/what_is_apligraf/what_is_apligraf.html .

REFERENCES

- 12. "TransCyte ." *Human fibroblast-derived temporary skin substitute* . N.p., n.d. Web. 24 Sept. 2012. http://www.transcyte.com
- 13. "EpiDex ." *Euroderm-Biotech AG*. N.p., n.d. Web. 24 Sept. 2012. <http://www.euroderm-biotech.ch/epidex&lang=en&lang=en.phtml>. .
- 14. "General data about burns." *Burn Centre Care*. N.p., n.d. Web. 24 Sept. 2012. <http://burncentrecare.co.uk/burn_wounds_surgery.htm>.
- 15. Haberzeth, Sophie, Thomas Biedermann, Luca Pontiggia, Erik Braziulis, Clemens Schiestl, Bart Hendriks, Daniel Widmer, Martin Meuli, and Ernst Reichmann. "Human Eccrine Sweat Gland Cells Turn into Melanin-Uptaking Keratinocytes in Dermo-Epidermal Skin Substitutes." *Journal of Investigative Dermatology* 13 (2012): n. pag. *Nature.com*. Web. 24 Sept. 2012.
- 16. J. F. Burke, J. T. Schulz and R. G. Tompkins, "Artificial SKin." *Annual Review of Medicine* 51 (2000): n. pag. *Annual Reviews*. Web. 24 Sept. 2012.
- 17. Demling , Rober, Leslie Desanti, and Dennis Orgrill. "Use of Skin Subtitutes." *Burn Surgery*. N.p., n.d. Web. 27 Sept. 2012. <www.burnsurgery.com/Modules/skinsubstitutes/sec3.htm >.
- 18. Reuell, Peter. "Merging the biological, electronic." *Harvard Gazette*. N.p., 26 Aug. 2012. Web. 28 Sept. 2012. <news.harvard.edu/gazette/story/2012/08/merging-the-biological-electronic/ >.

REFERENCES

- 19. Lee, Chi, Anuj Singla, and Yugyung Lee. "Biomedical applications of Collagen." *International Journal of Pharmaceutics* 1.22 (2001): n. pag. *Elsevier*. Web. 28 Sept. 2012.
- 20. Gauvin, Robert, Franois Berthod, and Remi Bareil. "Collagen-Based Biomaterials for Tissue Engineering Applications." *materials* 3 (2010): n. pag. *MPDI.com*. Web. 28 Sept. 2012.
- 21. Zaulyanov , Larissa, and Robert Kirsner. "A review of a bi-layered living cell treatment (Apligraf ®) in the treatment of venous leg ulcers and diabetic foot ulcers." *National Center for Biotechnology Information*. N.p., 21 Mar. 2007. Web. 30 Sept. 2012. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2684073/>.
- 22. "Fibroblasts ." *THe Medical News*. N.p., n.d. Web. 29 Sept. 2012. <http://www.news-medical.net/health/Fibroblasts-What-are-Fibroblasts.aspx>.
- 23. Andrews, Erik. "What Do Collagen Fibers Do? ." *Livestrong.xon*. N.p., 14 June 2011. Web. 28 Sept. 2012. <http://www.livestrong.com/article/227884-what-do-collagen-fibers-do/>.
- 24. DiChiara, Timothy. "Keratinocyte ." *About.com*. N.p., 10 Feb. 2009. Web. 30 Sept. 2012. <http://skincancer.about.com/od/glossary/g/keratinocyte.htm>.