The Ageing Hair
Physiologic Hair Loss

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Ageing and Hair

- Follicular miniaturization
- Cellular senescence
- Loss of pigmentation (graying)
- Immunosenescence

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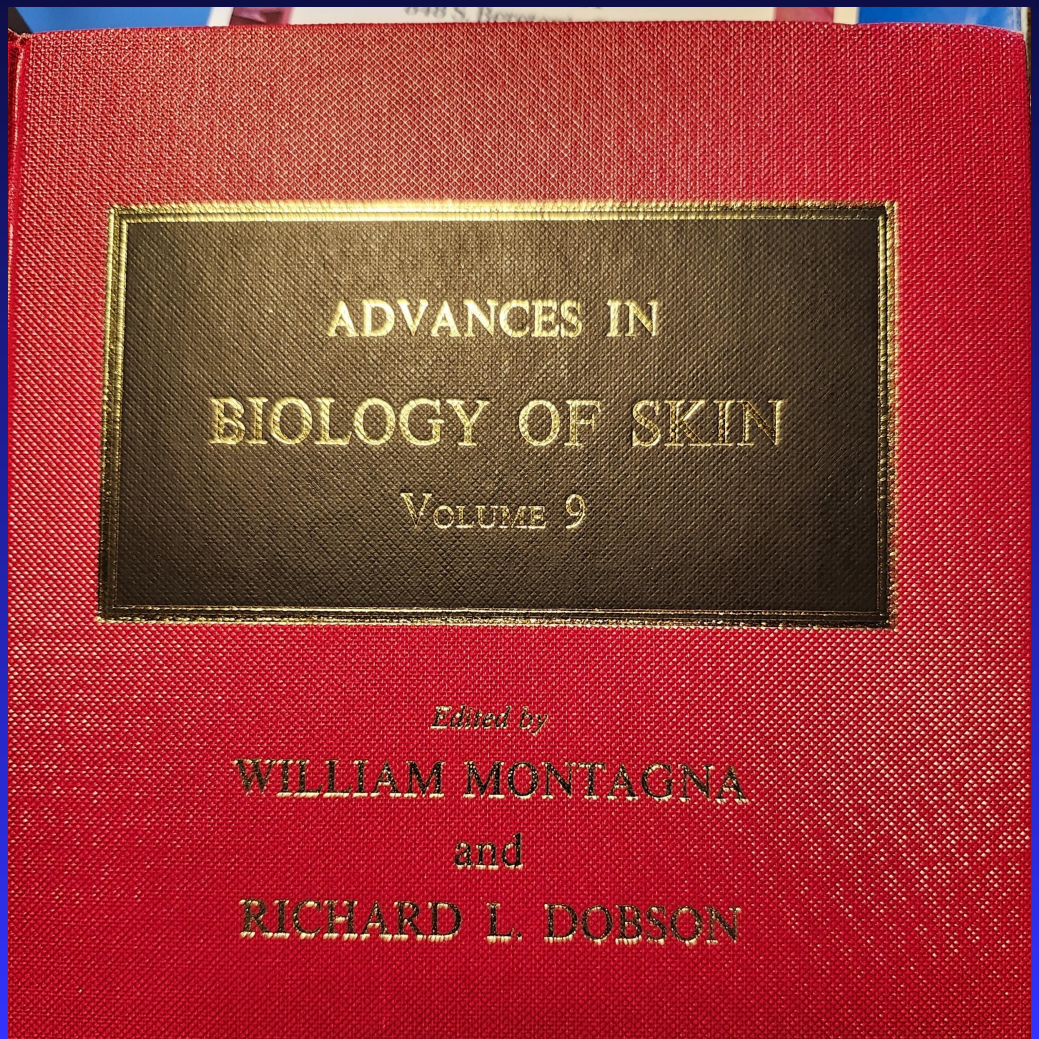
1967


ADVANCES IN
BIOLOGY OF SKIN
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Edited by
WILLIAM MONTAGNA
and
RICHARD L. DOBSON

Hideo Uno et al (1967)
Oregon National Primate Research Center

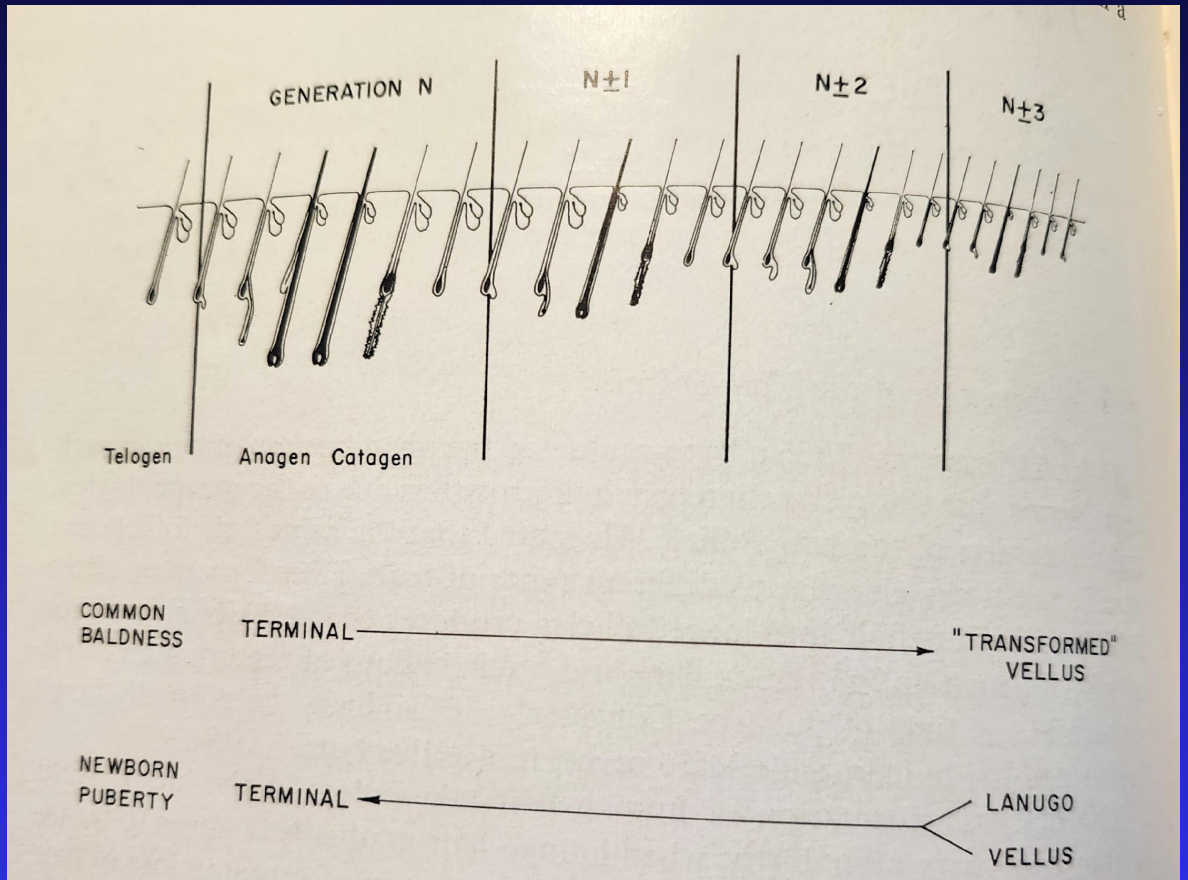
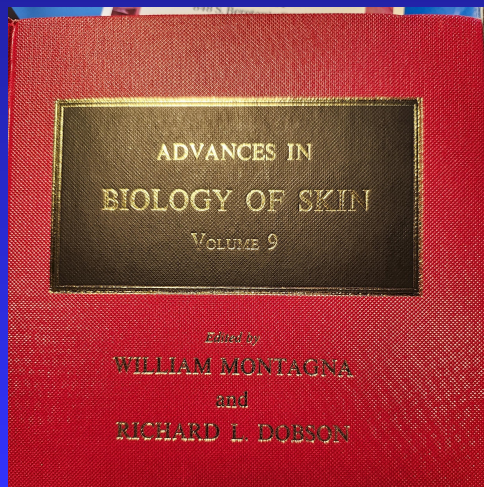


FIG. 6

Diagram representing the stepwise diminution or increasing size of the hair follicle through succeeding cyclic generations.

Follicular Ageing

- Sebaceous gland atrophy
- ‘Stranded’ arrector pili
- Rate of hair growth slows



Concept:
Is Androgenetic Alopecia (AGA) an unintended consequence of evolution

Evolution to hairlessness

Kamberov YT et al. Comparative evidence for the independent evolution of hair and sweat gland traits in primates. J Hum Evol 125:99-105, 2018.

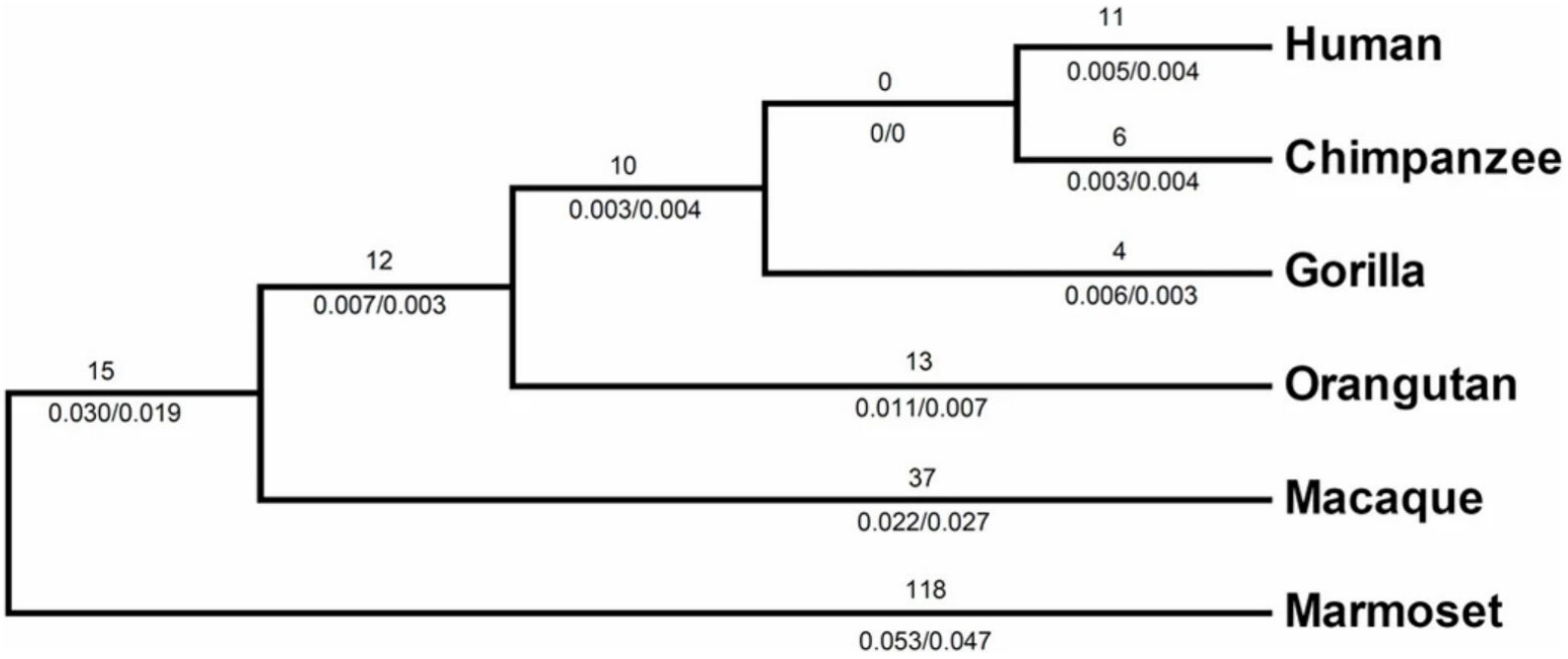
Why evolve to less hair cover?

- Temperature Regulation
  - Changing behavior
    - Hunting in the day—safer
  - Fire—temperature control better
  - Clothing
  - Infestation prevention (lice)

Human Hairless Gene

Figure 2

From: Molecular evolution of *HR*, a gene that regulates the postnatal cycle of the hair follicle



Molecular evolution of *HR* in primates.

Ka and *Ks* values were estimated for each branch of the *HR* tree with the reconstructed sequences at ancestral nodes. Number above the lineage indicates the minimum number of amino acid replacements to explain differences among reconstructed sequences. *Ka/Ks* ratios are shown below branches. Branch lengths are drawn arbitrarily and do not reflect evolutionary time.

Science. 1998 Jan 30;279(5351):720-4. doi: 10.1126/science.279.5351.720.

Alopecia universalis associated with a mutation in the human hairless gene

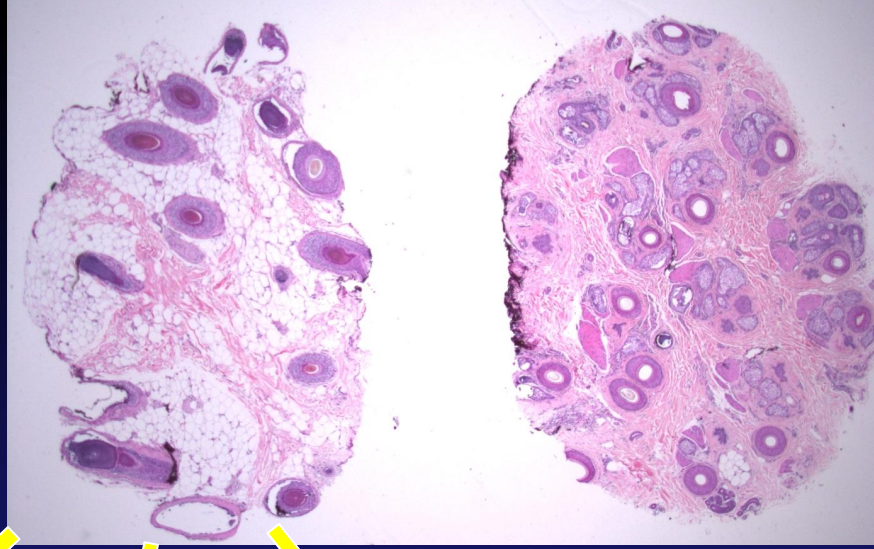
W Ahmad [1], M Faiyaz ul Haque, V Brancolini, H C Tsou, S ul Haque, H Lam, V M Aita, J Owen, M deBlaquiere, J Frank, P B Cserhalmi-Friedman, A Leask, J A McGrath, M Peacocke, M Ahmad, J Ott, A M Christiano

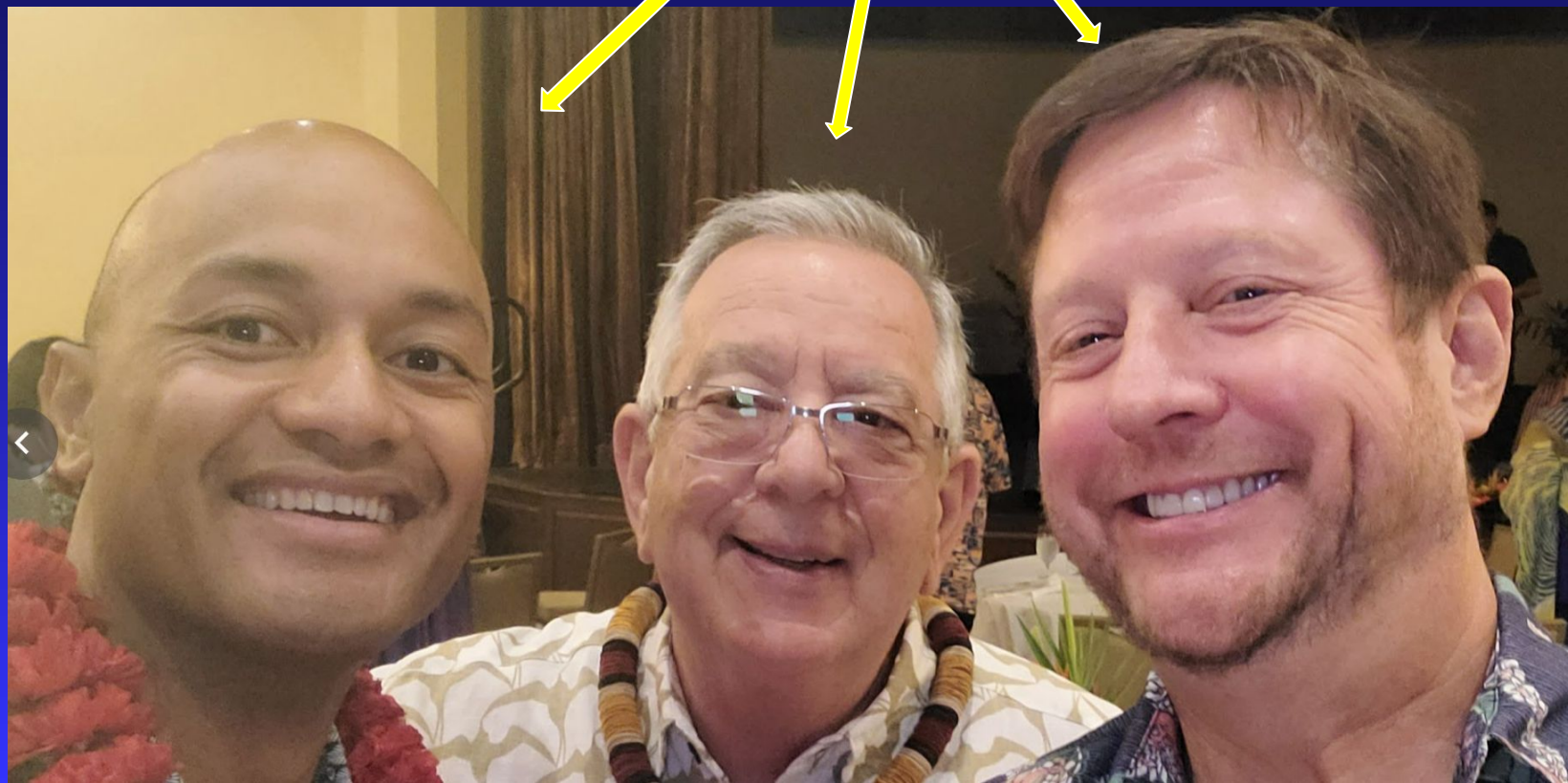
http://www.dermweb.com/hairnailsmucousmembranes/sideviewbaldmanpage.htm

Pathologic Miniaturization

Zhou, C., Li, X., Wang, C. *et al.* Alopecia Areata: an Update on Etiopathogenesis, Diagnosis, and Management. *Clinic Rev Allerg Immunol* **61**, 403–423 (2021). https://doi.org/10.1007/s12016-021-08883-0

Miniaturization
?Pathologic?





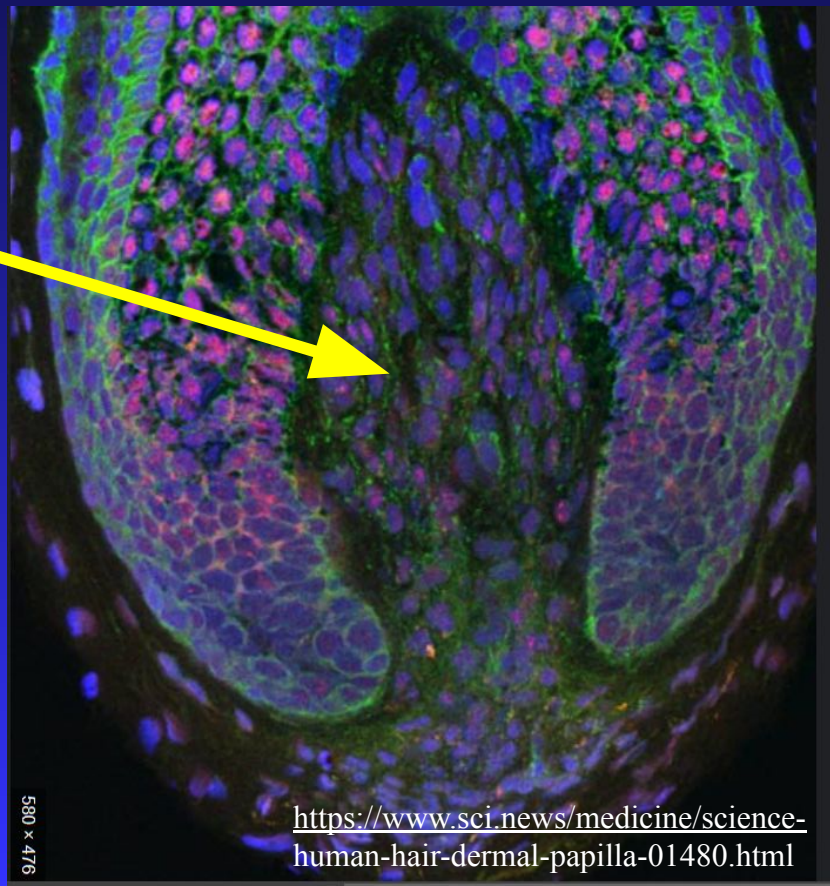
Unintended consequence of evolution?

Ageing and Hair

- Follicular miniaturization
- Cellular senescence
- Loss of pigmentation (graying)
- Immunosenescence (aka Immuno-ageing)

Hair follicle and Ageing

Dermal Papilla Cells (DPCs)



https://www.sci.news/medicine/science-human-hair-dermal-papilla-01480.html

Dermal Papilla Cells (DPCs)

- Hair growth stimulating factors
  - Vascular endothelial growth factor
  - Insulin-like growth factor 1
  - Inhibitory factors
    - Transforming growth factor-beta 2 (TGFβ2)
    - Dickkopf 1 (DKK-1)

DPCs are different in AGA

- Lose ability to induce new hair follicles
- Promote epidermal differentiation while inhibiting follicular differentiation.
- Produce more interleukin IL-6
  - Inhibits follicular epithelium proliferation
  - Blocks telogen to anagen transition.

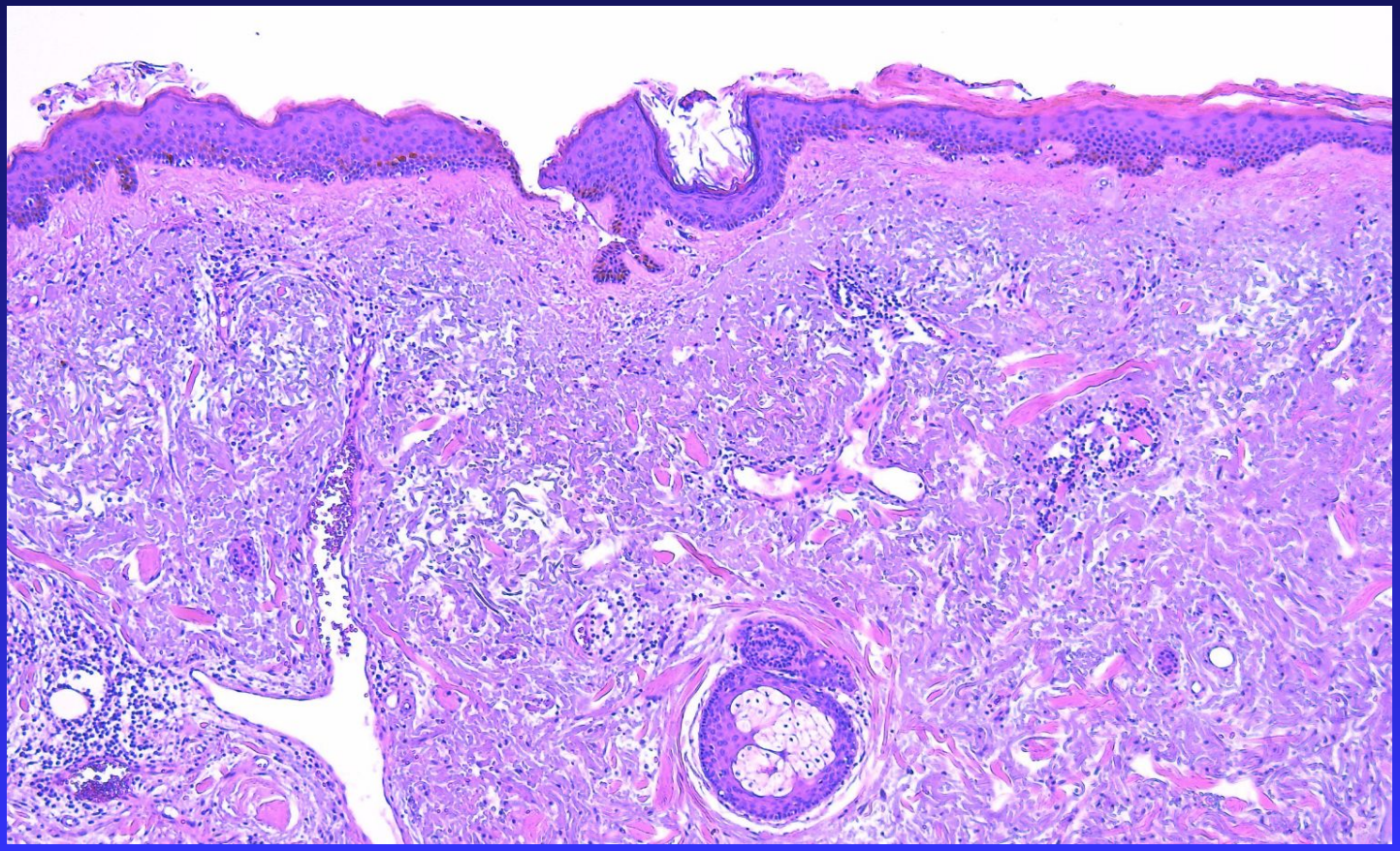
Androgenetic Alopecia (AGA)

- Androgen receptor overexpression by the dermal papilla cells
  - Senescent phenotype
  - High p16INK4α/pRb protein

iérard-Franchimont C, Piérard GE. Teloptosis, a turning point in hair shedding biorhythms. Dermatology. 2001;203(2):115–7. 23 Bahta AW, Farjo N, Farjo B, Philpott MP. Premature senescence of balding dermal papilla cells in vitro is associated with p16(INK4a) expression. J Invest Dermatol. 2008;128(5):1088–94.

Concept

Ageing = A chemopreventative mechanism



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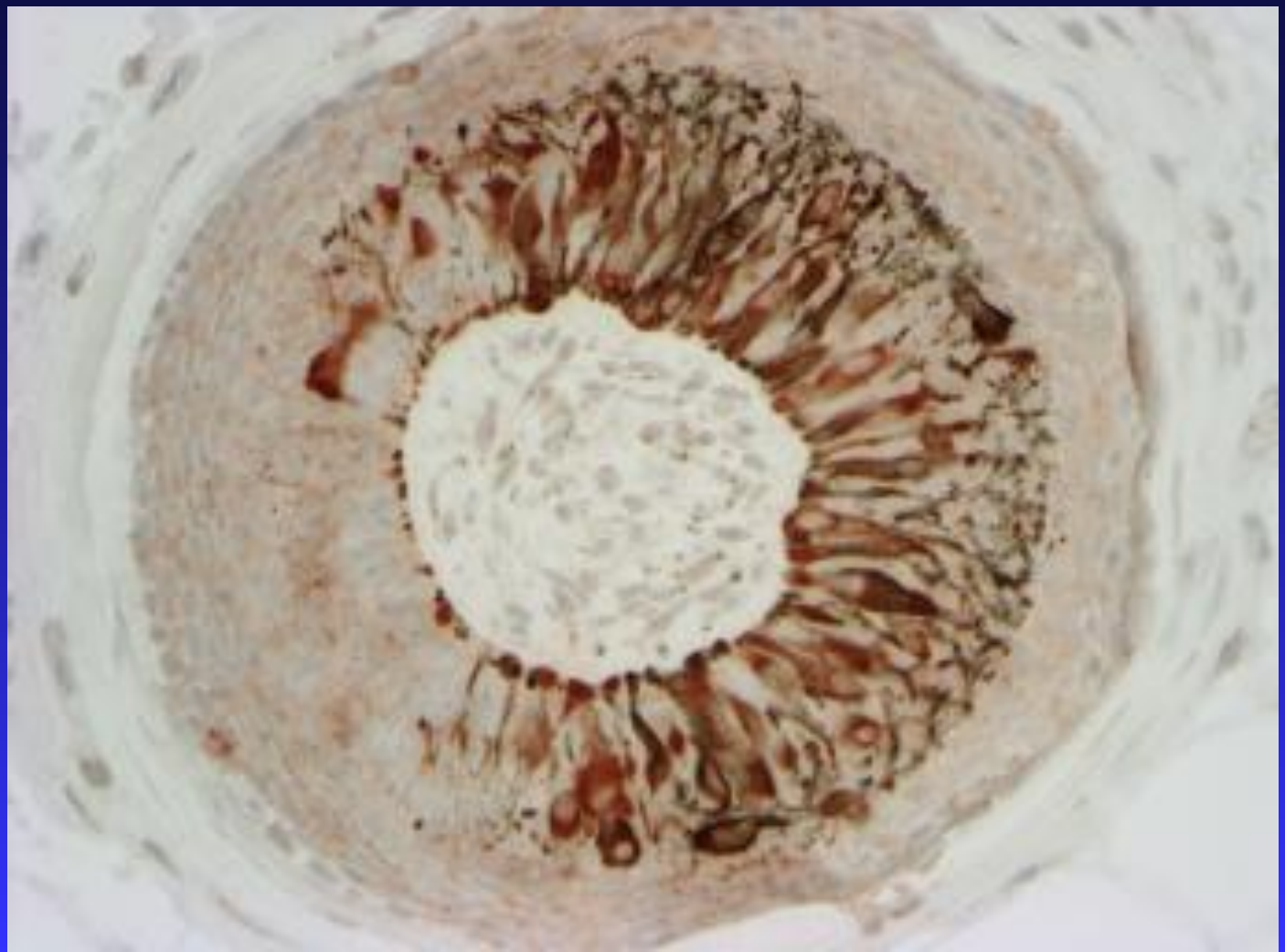
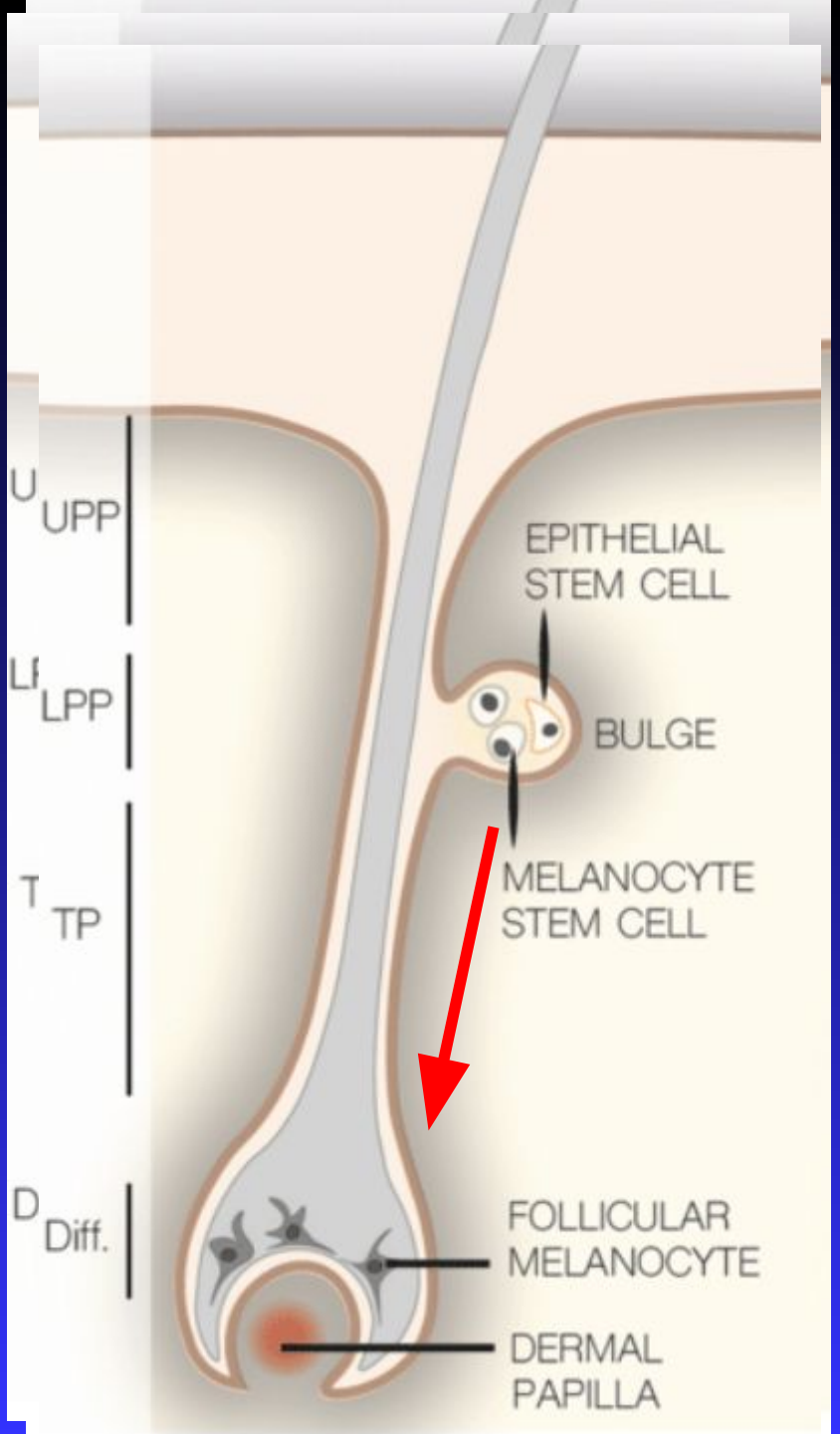
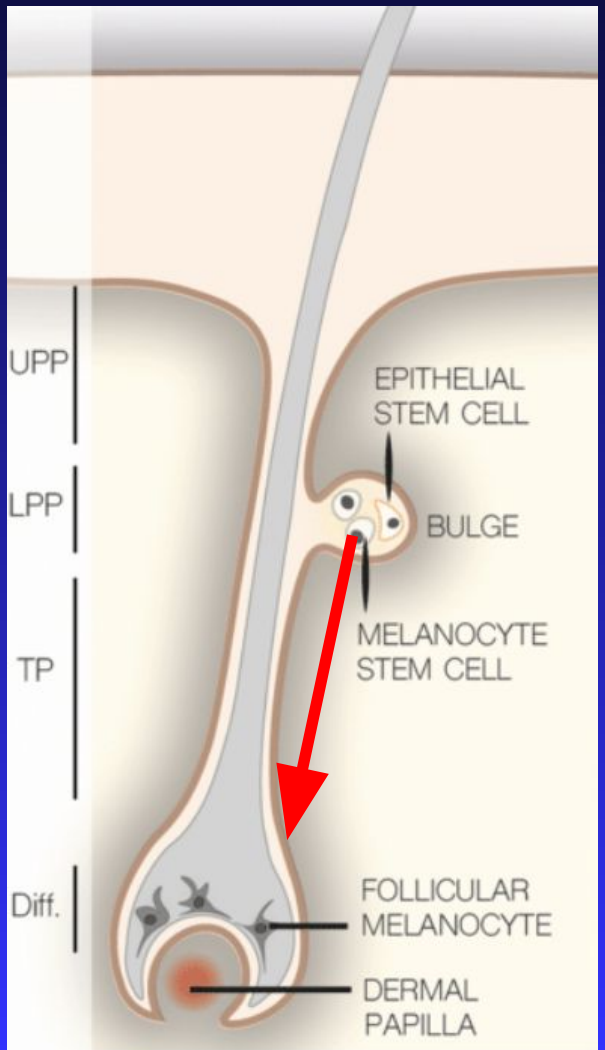
Matrical melanocytes come from follicular melanocytes stem cells in bulge





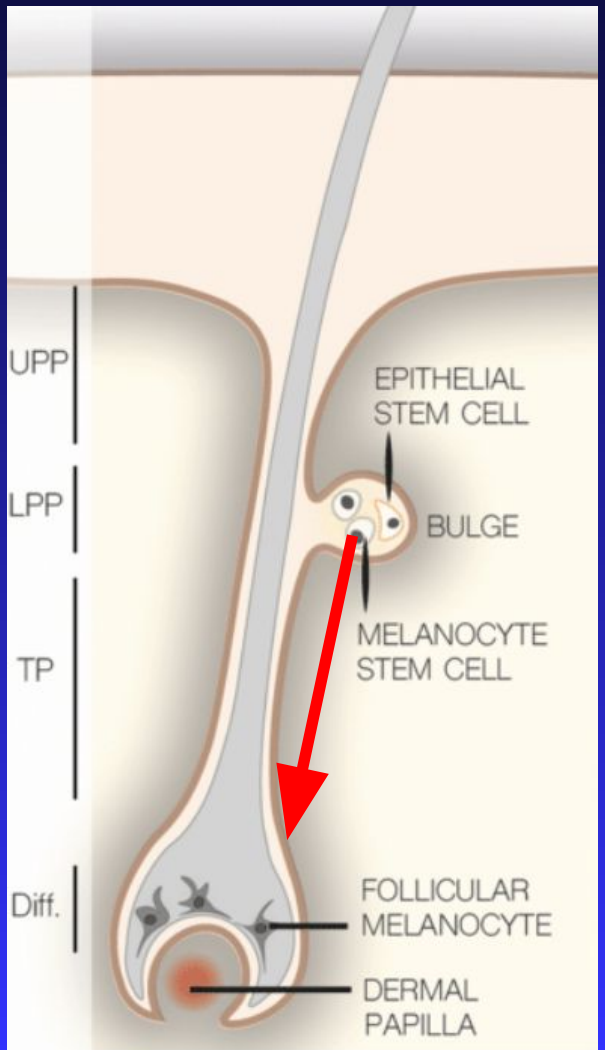
Vandamme N, Berx G. From neural crest cells to melanocytes: cellular plasticity during development and beyond. Cell Mol Life Sci. 2019 May;76(10):1919-1934

Gray hair after melanocyte stem cells fails to divide



Vandamme N, Berx G. From neural crest cells to melanocytes: cellular plasticity during developme and beyond. Cell Mol Life Sci. 2019 May;76(10):1919-1934.

Is loss of melanocyte stem cell chemopreventative?



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  - Immuno-ageing
  - Inflammo-ageing

Inflamm-aging

- Chronic low-level innate immune activation leading to increased oxidative stress.
- Reactive oxygen species are believed to be the driving force

ITCHING DISORDERS

- Alterations of the barrier function of the stratum corneum
- ↓ activity of the sebaceous and sweat glands
- ↓ levels of ceramides
- ↓Aquaporin 3 production
- ↑pH alkaline

↓

↑Activity of serine proteases in the skin

↓

↑Activation of PAR receptors

↓

Pruritus

PSORIASIS

↑ High senescent T cells

↑CD57 expression on CD8+ cellsin nonlesional skin

↑ Keratinocites hyperproliferation

↓

Psoriatic plaque

SKIN IMMUNOSENESCENCE

ATOPIC DERMATITIS

- environmental and genetic factors
- immunosenescence phenomena
- age-related epidermal barrier dysfunctions
- cutaneous dysbiosis
- functional impairment of sweat production
- external stimuli

→

- epithelial-derived cytokines releasing(IL-25,IL-18,IL-33, TSLP)
- ILC2s activation
- Th2-mediated production of IL-13,IL5,IL.4

- ↑Th17 levels → IL-17, IL-19
- ↑Th1 levels → IFN-γ
- ↑Th22 levels → IL-22

} Epidermal thickness
Spongiosis
Barrier dysfunction

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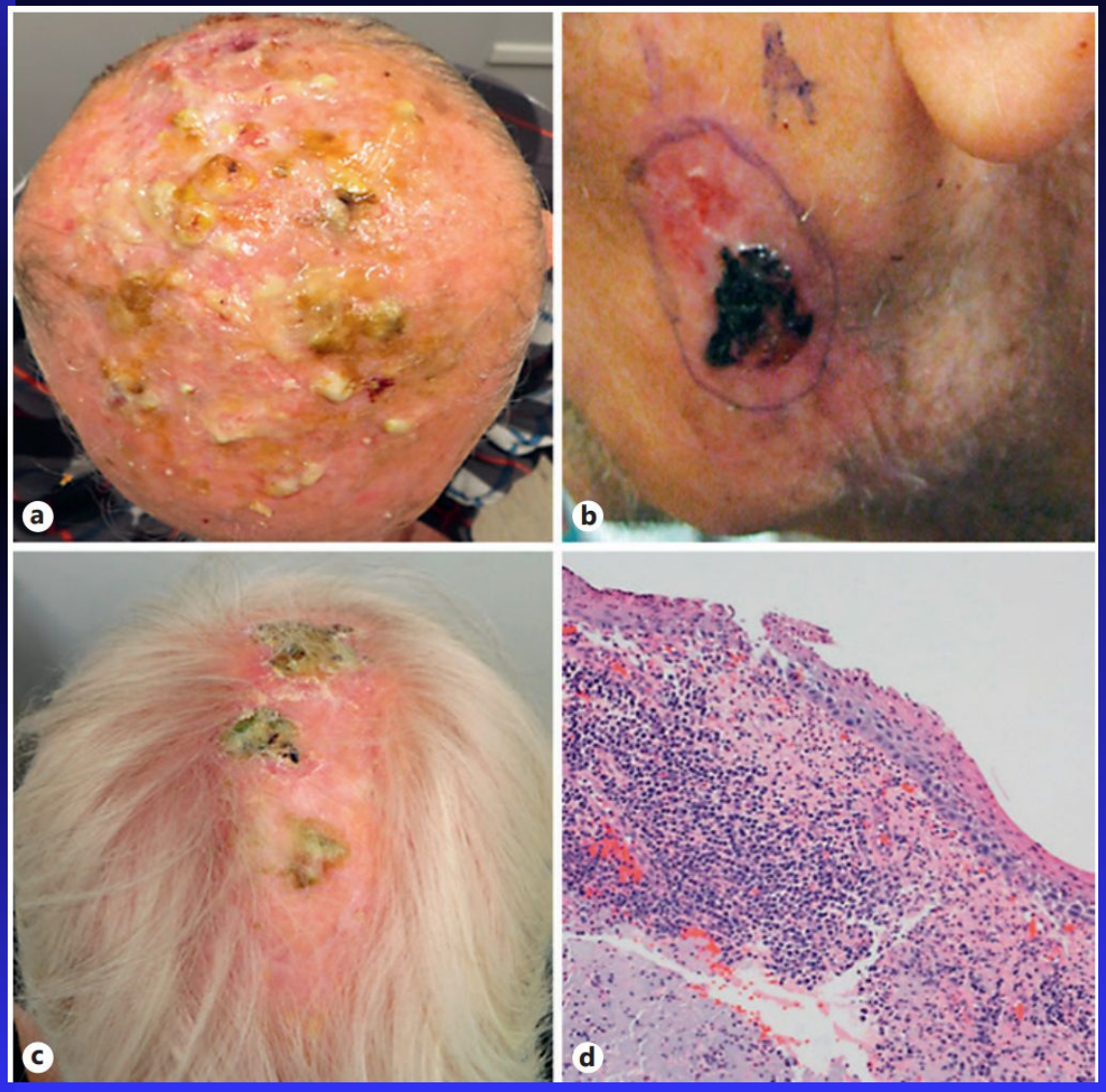
SKIN IMMUNOSENESCENCE

Erosive Pustular Dermatosis



Thurasingam and Mirmiani, Skin Appendage Disord 2018;4:180–186

Erosive Pustular Dermatosis

- Solar elastosis
- Poor maintenance of epithelialization
- Immunosenescence
  - Often colonized/infected with bacteria (Staphylococcus)

Erosive Pustular Dermatosis

- Hypothesis: Aberrant release of neutrophil-stimulating cytokines and chemokines results in neutrophilic hyperactivation

Molle, M.F.; Burroni, A.G.; Herzum, A.; Parodi, A. Erosive Pustular Dermatosis of the Scalp and Multiple Sclerosis: Just a Coincidence? Dermatol. Rep. 2022, 14, 9445

Summary—The Ageing Hair

- Unintended consequences of evolution (follicular miniaturization)
- Chemoprevention
  - Fibroblasts—Sarcoma
  - Melanocyte stem cells—melanoma

Summary—The Ageing Hair

- Immunosenescence
  - Lose cancer surveillance
  - Overexpression of cytokines, etc (neutrophil activation)
  - Loss of barrier protection

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Mahalo!

Thanks!

¡ Gracias!