

# The sebaceous gland revisited: Friend and adversary

Peter M. Elias<sup>1</sup>, Joan Wakefield<sup>1</sup>

<sup>1</sup> Department of Dermatology, University of California, San Francisco and Veterans Affairs Health Care System, San Francisco, California, USA  
Corresponding author: Peter M. Elias ([joan.wakefield@va.gov](mailto:joan.wakefield@va.gov))

## Abstract

Historically, sebaceous glands (SG) have been viewed as troublesome provocateurs of seborrheic dermatitis and acne. Yet, recent studies have illuminated a suite of positive attributes of SG (Points 1–6, below), including lubrication of hair follicles to avert scarring alopecia. Because of their abundant lipase activity, secreted SG lipids deliver both glycerol (endogenous humectant) and antimicrobial free fatty acids onto the skin surface (Points 2&3). Though human epidermis makes substantial vitamin D3 (VD3), in furred mammals, VD precursors must first be delivered onto the surface prior to photo- and thermal conversion into VD3 (Point 4). Likewise, epidermis deploys several antioxidant enzymes, but vitamin E is delivered to the skin surface via SG secretions (Point 5). Finally, SG secrete volatile odorants (Point 6) and possibly pheromones.

**Key words:** Acne, glycerol, fatty acids, hair, sebaceous gland

## Introduction

Sebaceous glands (SG) are metabolically active, multi-lobular structures that are integrated into the hair follicles of mammals, forming the so-called pilosebaceous unit. As they differentiate, sebocytes undergo holocrine rupture, releasing their constituent lipids into the pilosebaceous canal. Because SG express the fatty acid transporter, FATP4, additional lipids could be added to sebum that derive from the circulation. Sebaceous lipids contribute around 90% of skin surface species in adolescent and adult humans, where they admix with epidermis-derived species, while exerting net negative effects on permeability function (a conclusion that has been disputed) [1]. Since SG remain quiescent from late infancy through early adolescence, their activity clearly is not required for skin development. But this observation should not be interpreted incorrectly – they certainly can impact skin function both positively and negatively later in life. Though in some ways problematic, SG secretions provide numerous benefits, detailed below. In addition, they signal a host of cutaneous innate and adaptive immune responses, which in turn regulate sebocyte differentiation and homeostasis [1].

## Friend or adversary?

The controversial, though influential dermatologist, Albert Kligman, M.D., Ph.D., once proclaimed that the only role of sebaceous glands (SG) was to provoke problems; i.e., seborrheic dermatitis and acne vulgaris [2]. Because SG need



Subject editor: Peter Wolf  
Received: 25 July 2025  
Accepted: 29 August 2025  
Published: 17 September 2025

Citation: Elias PM (2025) The sebaceous gland revisited: Friend and adversary. SKINdeep 1: e166714. <https://doi.org/10.1553/skindeep.2025.166714>

Copyright: © Peter M. Elias & Joan Wakefield.  
This is an open access article distributed under terms of the Creative Commons Attribution License (Attribution 4.0 International – CC BY-NC 4.0).

not supply important distal cholesterol metabolites, such as cholesterol itself and vitamin D3 in hairless humans (see below), the sterol biosynthetic pathway in human SG aborts at squalene (a form of metabolic conservation that diverts precious calories towards other critical functions, such as growth and/or lactation). Yet unfortunately for acne sufferers, squalene becomes highly inflammatory should it escape from SG into deeper layers of the skin.

Evolution long ago would have eliminated these metabolically expensive (and active) structures if they weren't bestowing critical benefits for mammals, including humans. Notably, sebaceous tissues respond to hormonal signals in a manner similar to adipose tissues. In both leptin-deficient and in ob/ob mice, SG glands hypertrophy in parallel with adipose tissues. Below, certain positive, and often critically important attributes of SG are enumerated.

## **Composition of epidermal vs. SG lipids**

Three key lipids generate the extracellular lamellar bilayers that both protect against external threats and minimize excessive transepidermal water loss: cholesterol, free fatty acids, and a family of ceramides. With the exception of cholesterol, each of these end products relies upon the prior synthesis of polar lipid precursors; i.e., phospholipids, which are hydrolyzed by a family of secretory phospholipases into a suite of non-essential free fatty acids [3, 4]; sphingomyelin, which is hydrolyzed into selected (two) ceramides by acidic sphingomyelinase [5]; and ceramides, which are generated from glucosylceramides by beta-glucocerebrosidase [6]. In addition, some cholesterol forms as cholesterol sulfate and is hydrolyzed during transit across the stratum corneum.

After their synthesis, all these lipids are packaged within epidermal lamellar bodies, which then deliver their contents into the extracellular spaces at the junction of the stratum granulosum and stratum corneum (SC). By weight, ceramides comprise about 50% of SC lipids, though cholesterol, free fatty acids, and ceramides are present in an approximately 1:1:1 molar ratio that is required to form the extracellular lamellar bilayers.

In contrast, SG-derived lipids comprise a mixture of branched chain, unsaturated fatty acids of varying composition, depending upon the subject's age and gender. In a comprehensive review, Smith and Thiboudot document the key ingredients in human sebum, with glycerolipids and free fatty acids accounting for over 50% of the total, while wax esters (25%), squalene (12%), and cholesterol esters (2%) account for the remainder [7]. Yet, how administered topical agents (such as retinoids) and steroid hormones (such as testosterone and estradiol) influence this mixture is not well understood.

## **Enumeration of critical functions**

### **Hair follicle lubrication**

While studies in aseb2J (Scd1(ab2J)) mice [8] showed that sebaceous lipids are not required for permeability barrier function [9], others have documented several important roles for SG and SG secretions. Pertinently, barrier function remains intact in the hair follicle down to the entry point of the duct draining SG, while the hair follicle epithelium above that level can regenerate a fully

functional barrier [10]. Yet, function deteriorates immediately below that level, as demonstrated with electron dense tracers [9]. As noted above, reductions in SG secretions precipitate scarring alopecia in humans [11], indicating important lubricating properties that facilitate the outward migration of hair follicles.

### **1. Vitamin D delivery**

Several decades ago, researchers sought the origins of the skin's antirachitic properties in furred rodents [12]. While urine, feces, and other bodily secretions failed to reveal activity, testing of a greasy material, adherent to the animals' wire cages, exhibited the sought-after activity, providing the initial evidence that SG secretions could deliver vitamin D (VD3) to the surface of furred animals' skin. Though the fur of most mammals blocks incident UV-B from reaching the epidermis, VD3-laden, SG secretions can bypass this restriction. Accordingly, much of the 'social grooming' that occurs in furred animals includes licking of each other's skin surface, likely resulting in the ingestion of substantial VD3 (though not applicable to humans, here we record a second important function for SG – delivery of VD3 to the skin surface of hairy mammals, where it subsequently can be ingested).

In contrast, incident UV-B readily breaches the epidermis of sparsely haired, modern humans, quickly converting the distal cholesterol precursor, 7-dehydrocholesterol (7DHC) into pre-VD3 [13], followed by its thermal conversion to VD3. In geographic regions of northern Europe, where little UV-B irradiation penetrates the atmosphere, loss-of-function (LOF) mutations in the enzyme, 7-dehydrocholesterol reductase, become relatively common in affected humans, ensuring that 7DHC remains available for photoconversion [14, 15]. These northern-dwelling humans also frequently display LOF mutations in the gene encoding filaggrin, which after distal proteolysis and deimination yields trans-urocanic acid, the most potent UV-B photophore in human skin [16], further assuring that incident UV-B will penetrate deep into the nucleated layers of the epidermis (11), where VD3 is generated. Indeed, because we humans generate abundant vitamin D (VD3) in our epidermis, the cholesterol biosynthetic pathway in SG aborts distal to the formation of squalene in service to metabolic conservation.

### **2. Stratum corneum hydration**

Our studies in asebia mice yielded insights into yet another function of SG – hydration of the stratum corneum (SC). We found evidence of considerable lipase activity in SG, which if active, would hydrolyze sebum-derived tri- and diglycerides not only into free fatty acids [17], but also into glycerol, a potent endogenous humectant. This conjecture is consistent with the observation that SG-enriched skin sites, like the forehead and upper torso, exhibit elevated SC hydration [18]. This finding brings us up to three important functions of SG – prevention of scarring alopecia, VD3 delivery to the surface of hairy skin, and tissue hydration.

### **3. Antimicrobial activity**

Returning to the lipolysis of glycerolipids in SG, consider that not only glycerol, but also abundant free fatty acids (FFA) are formed, which join epidermis-derived FFA following the hydrolysis of phospholipids in epidermal terminal

differentiation [19]. These species are antimicrobial for several reasons, including their ability to destroy microbial pathogens in a chain-length dependent fashion, and their acidity, which is inimical to the growth of gram-positive pathogens. In contrast, that same low pH favors the colonization of human skin by its normal cutaneous flora. The addition of antimicrobial activity adds yet another (fourth) positive attribute of SG products.

#### **4. Vitamin E delivery**

In response to the many free radicles and pollutants in the environment, the epidermis (but not SG) generates a suite of antioxidant species, including glutathione reductase, thioredoxin reductase, superoxide dismutase, and catalase. Notably, this list does not include vitamin E (VitE), which instead is delivered to the skin surface via SG secretions. Once absorbed into the epidermis, VitE is metabolized by cytochrome p450 isoforms into a suite of additional tocopherols and tocotrienols, which in turn activate PPAR $\gamma$  [20]. The latter exhibits potent anti-inflammatory activity, accounting for the benefits of PPAR $\gamma$  analogues in the treatment of diverse inherited and acquired inflammatory disorders [21, 22]. Yet, whether VitE secretion is impacted by factors that regulate SG structure and secretion, such as androgens and their estrogen metabolites, or retinoids, remains unknown. Nonetheless, the delivery of VitE and other downstream, bioactive lipids to the skin surface illustrates yet another (fifth) important function of SG.

#### **5. Immunobiology of SG**

In a recent review article, Christos Zouboulis and his associates reviewed the negative impact of sebaceous lipids on perifollicular and dermal innate immune responses. The pathophysiological consequences, of course, include the provocation of acne, but extend to other inflammatory dermatoses, including seborrheic dermatitis and atopic dermatitis [1]. Hence, because of these apparently negative consequences of SG activity, we have chosen not to include these activities among the positive attributes of SG.

#### **6. Conjectural and disputed benefits**

From this point onward, cataloguing further benefits of SG secretions becomes more nebulous. Most controversial is the subject of pheromones in human biology. Pheromones are volatile, species-specific substances that have been implicated, though not yet proven to impact reproductive instincts in humans. Indeed, some authors doubt whether they play any role in human reproduction. Much more certain is a role for pheromones in earthworm reproduction [23]. Consider however that SG secretions, along with apocrine gland secretions, generate multiple volatile compounds that are odorants, including some that could function as pheromones [24]. Charles Darwin has been credited with the initial observation that when animals secrete odiferous secretions, they strongly signal reproductive responses [25]. Though our nasal passages display multiple odorant receptors, whether these structures also recognize and respond to pheromones remains unknown.

## Regulation of SG structure and function

Androgens and estrogens exert opposing influences on SG secretions. While androgens via the androgen receptor promote sebocyte growth and differentiation [26], estrogens and their plant-derived analogues oppose this activity, while also providing a host of other benefits for aging, glucose metabolism, and free radical defense [27–30].

B-lymphocyte-induced nuclear maturation protein 1 (BLIMP1) is an important marker of SG progenitor cells, where it suppresses sebocyte growth, as demonstrated by the dramatic expansion of SG following BLIMP1 deletion [31]. BLIMP-1 serves as a marker of differentiated compartments in both epidermis and SG. Thus, BLIMP1 appears to maintain steady-state homeostasis in SG and the epidermis, with a potentially positive impact on epidermal permeability homeostasis [32].

## Summary/conclusion

Though historically regarded as solely problematic, there is evidence for a host of positive attributes for SG, including key roles in preventing scarring alopecia, supporting both stratum corneum hydration and cutaneous antimicrobial defense, as well as the secretion of a key antioxidant species, vitamin E. Also cited here is historical evidence that SG secrete odorants that serve as sexual attractants, as well as potentially pheromones.

## Acknowledgements

The author much appreciates the editorial assistance of Ms. Joan Wakefield (No funding source involved). The contents of this manuscript do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

## Additional information

### Conflict of interest

The authors have declared that no competing interests exist.

### Ethical statements

The author declares no clinical trials were used in the present study.

The author declares that no experiments on humans or human tissues were performed for the present study.

The author declares that no informed consent was obtained from any humans, donors, or donors' representatives participating in the study.

The author declares that no experiments on animals were performed for the present study.

The author declares that no commercially available immortalized human and animal cell lines were used in the present study.

### Use of AI

No use of AI was reported.

## Funding

No funding was reported.

## Author contributions

PME reviewed literature and conceptualized and wrote the manuscript. JSW edited the manuscript.

## Author ORCIDs

Peter M. Elias  <https://orcid.org/0000-0001-7989-4032>

Joan Wakefield  <https://orcid.org/0000-0002-8802-2364>

## Data availability

All of the data that support the findings of this study are available in the main text.

## References

1. Zouboulis CC, Coenye T, He L, Kabashima K, Kobayashi T, Niemann C, et al. Sebaceous immunobiology - skin homeostasis, pathophysiology, coordination of innate immunity and inflammatory response and disease associations. *Front Immunol.* 2022;13:1029818. <https://doi.org/10.3389/fimmu.2022.1029818>
2. Kligman AM. Pathogenesis of acne vulgaris. *Mod Probl Paediatr.* 1975;17:153–73.
3. Ilic D, Bollinger JM, Gelb M, Mauro TM. sPLA2 and the epidermal barrier. *Biochim Biophys Acta.* 2014;1841(3):416–21. <https://doi.org/10.1016/j.bbali.2013.11.002>
4. Chan A, Mauro T. Acidification in the epidermis and the role of secretory phospholipases. *Dermatoendocrinol.* 2011;3(2):84–90. <https://doi.org/10.4161/derm.3.2.15140>
5. Uchida Y, Hara M, Nishio H, Sidransky E, Inoue S, Otsuka F, et al. Epidermal sphingomyelins are precursors for selected stratum corneum ceramides. *J Lipid Res.* 2000;41(12):2071–82. [https://doi.org/10.1016/S0022-2275\(20\)32369-5](https://doi.org/10.1016/S0022-2275(20)32369-5)
6. Holleran WM, Takagi Y, Imokawa G, Jackson S, Lee JM, Elias PM. beta-Glucocebreosidase activity in murine epidermis: characterization and localization in relation to differentiation. *J Lipid Res.* 1992;33(8):1201–9. [https://doi.org/10.1016/S0022-2275\(20\)40772-2](https://doi.org/10.1016/S0022-2275(20)40772-2)
7. Smith KR, Thiboutot DM. Thematic review series: skin lipids. Sebaceous gland lipids: friend or foe? *J Lipid Res.* 2008;49(2):271–81. <https://doi.org/10.1194/jlr.R700015-JLR200>
8. Sundberg JP, Boggess D, Sundberg BA, Eilertsen K, Parimoo S, Filippi M, et al. Asebia-2J (Scd1(ab2J)): a new allele and a model for scarring alopecia. *Am J Pathol.* 2000;156(6):2067–75. [https://doi.org/10.1016/S0002-9440\(10\)65078-X](https://doi.org/10.1016/S0002-9440(10)65078-X)
9. Fluhr JW, Man MQ, Brown BE, Wertz PW, Crumrine D, Sundberg JP, et al. Glycerol regulates stratum corneum hydration in sebaceous gland deficient (asebia) mice. *J Invest Dermatol.* 2003;120(5):728–37. <https://doi.org/10.1046/j.1523-1747.2003.12134.x>
10. Ford NC, Benedeck RE, Mattoon MT, Peterson JK, Mesler AL, Veniaminova NA, et al. Hair follicles modulate skin barrier function. *Cell Rep.* 2024;43(7):114347. <https://doi.org/10.1016/j.celrep.2024.114347>
11. Gruber R, Sugarman JL, Crumrine D, Hupe M, Mauro TM, Mauldin EA, et al. Sebaceous gland, hair shaft, and epidermal barrier abnormalities in keratosis pilaris with and without filaggrin deficiency. *Am J Pathol.* 2015;185(4):1012–21. <https://doi.org/10.1016/j.ajpath.2014.12.012>

12. Carpenter KJ, Zhao L. Forgotten mysteries in the early history of vitamin D. *J Nutr*. 1999;129(5):923–7. <https://doi.org/10.1093/jn/129.5.923>
13. Holick MF, MaLaughlin JA, Clark MB, Holick SA, Potts JT, Jr., Anderson RR, et al. Photosynthesis of previtamin D3 in human skin and the physiologic consequences. *Science*. 1980;210(4466):203–5. <https://doi.org/10.1126/science.6251551>
14. Kuan V, Martineau AR, Griffiths CJ, Hypponen E, Walton R. DHCR7 mutations linked to higher vitamin D status allowed early human migration to northern latitudes. *BMC evolutionary biology*. 2013;13:144. <https://doi.org/10.1186/1471-2148-13-144>
15. Prabhu AV, Luu W, Sharpe LJ, Brown AJ. Cholesterol-mediated Degradation of 7-Dehydrocholesterol Reductase Switches the Balance from Cholesterol to Vitamin D Synthesis. *J Biol Chem*. 2016;291(16):8363–73. <https://doi.org/10.1074/jbc.M115.699546>
16. Thyssen JP, Bikle DD, Elias PM. Evidence that loss-of-function *filaggrin* gene mutations evolved in northern europeans to favor intracutaneous vitamin D3 production. *Evol Biol*. 2014;41(3):388–96. <https://doi.org/10.1007/s11692-014-9282-7>
17. Menon GK, Grayson S, Elias PM. Cytochemical and biochemical localization of lipase and sphingomyelinase activity in mammalian epidermis. *J Invest Dermatol*. 1986;86(5):591–7. <https://doi.org/10.1111/1523-1747.ep12355263>
18. Man MQ, Xin SJ, Song SP, Cho SY, Zhang XJ, Tu CX, et al. Variation of skin surface pH, sebum content and stratum corneum hydration with age and gender in a large Chinese population. *Skin Pharmacol Physiol*. 2009;22(4):190–9. <https://doi.org/10.1159/000231524>
19. Man MQ, Jain M, Feingold KR, Elias PM. Secretory phospholipase A2 activity is required for permeability barrier homeostasis. *J Invest Dermatol*. 1996;106(1):57–63. <https://doi.org/10.1111/1523-1747.ep12327246>
20. Jiang Q. Metabolism of natural forms of vitamin E and biological actions of vitamin E metabolites. *Free radical biology & medicine*. 2022;179:375–87. <https://doi.org/10.1016/j.freeradbiomed.2021.11.012>
21. Tóth BI, Géczy T, Griger Z, Dózsa A, Seltmann H, Kovács L, et al. Transient receptor potential vanilloid-1 signaling as a regulator of human sebocyte biology. *J Invest Dermatol*. 2009;129(2):329–39. <https://doi.org/10.1038/jid.2008.258>
22. Dózsa A, Dezso B, Tóth BI, Bacsí A, Poliska S, Camera E, et al. PPARgamma-mediated and arachidonic acid-dependent signaling is involved in differentiation and lipid production of human sebocytes. *J Invest Dermatol*. 2014;134(4):910–20. <https://doi.org/10.1038/jid.2013.413>
23. Zirbes L, Mescher M, Vrancken V, Wathelet JP, Verheggen FJ, Thonart P, et al. Earthworms use odor cues to locate and feed on microorganisms in soil. *PLoS One*. 2011;6(7):e21927. <https://doi.org/10.1371/journal.pone.0021927>
24. Wyatt TD. The search for human pheromones: the lost decades and the necessity of returning to first principles. *Proc Biol Sci / The Royal Society*. 2015;282(1804):20142994. <https://doi.org/10.1098/rspb.2014.2994>
25. Darwin C. *The descent of man and selection in relation to sex*. London: John Murray; 1871. <https://doi.org/10.5962/bhl.title.24784>
26. Lai JJ, Chang P, Lai KP, Chen L, Chang C. The role of androgen and androgen receptor in skin-related disorders. *Arch Dermatol Res*. 2012;304(7):499–510. <https://doi.org/10.1007/s00403-012-1265-x>
27. Sanchis D, Balada F, del Mar Grasa M, Virgili J, Peinado J, Monserrat C, et al. Oleoyl-estrone induces the loss of body fat in rats. *Int J Obes Relat Metab Disord*. 1996;20(6):588–94.

28. Bórras C, Gambini J, López-Gruoso R, Pallardó FV, Viña J. Direct antioxidant and protective effect of estradiol on isolated mitochondria. *Biochim Biophys Acta*. 2010;1802(1):205–11. <https://doi.org/10.1016/j.bbadis.2009.09.007>
29. Mauvais-Jarvis F, Clegg DJ, Hevener AL. The role of estrogens in control of energy balance and glucose homeostasis. *Endocr Rev*. 2013;34(3):309–38. <https://doi.org/10.1210/er.2012-1055>
30. Liu T, Li N, Yan YQ, Liu Y, Xiong K, Liu Y, et al. Recent advances in the anti-aging effects of phytoestrogens on collagen, water content, and oxidative stress. *Phytother Res : PTR*. 2020;34(3):435–47. <https://doi.org/10.1002/ptr.6538>
31. Kretzschmar K, Cottle DL, Donati G, Chiang MF, Quist SR, Gollnick HP, et al. BLIMP1 is required for postnatal epidermal homeostasis but does not define a sebaceous gland progenitor under steady-state conditions. *Stem Cell Reports*. 2014;3(4):620–33. <https://doi.org/10.1016/j.stemcr.2014.08.007>
32. Sellheyer K, Krahl D. Blimp-1: a marker of terminal differentiation but not of sebocytic progenitor cells. *J Cutan Pathol*. 2010;37(3):362–70. <https://doi.org/10.1111/j.1600-0560.2009.01434.x>