Learning from eponyms: George F. Odland and Odland bodies

Rajiv Joshi

ABSTRACT
Odland bodies (lamellar) bodies are small sub-cellular structures of size 200-300 nm that are present in the upper spinous and granular cell layers of the epidermis. These act as processing and repository areas for lipids that contribute to the epidermal permeability barrier. They also contain proteases, cathepsin D, kallikrein and other proteins including corneo-desmosins. Recent information also credits them with a role in the local innate immune response as they contain beta 2 defensins, which are anti-microbial peptides with potent activity against Gram-negative bacteria and candida. Odland bodies are important for maintaining homeostasis of the epidermis and are involved in epidermal permeability barrier function, desquamation of keratinocytes, formation of the cornified envelope and in local anti-microbial immunity. This article reviews the structure and functions of these bodies with a brief biography of George F. Odland who first described these bodies in 1960 and whose name is eponymically associated with them.

Key words: Epidermal permeability barrier, George F. Odland, lamellar bodies, Odland bodies

INTRODUCTION
Odland (lamellar) bodies [Figure 1] were first described by Odland in 1960[1] as a distinctive submicroscopic granular component seen in the upper spinous and granular cell layers. He suggested that the small granules were probably attenuated mitochondria occurring due to fragmentation of the normal filamentous mitochondria. He noted that their role in keratinization was not known at that time. The same structure was noticed earlier by Selby[2] who interpreted it to be a small keratohyalin granule whereas Horstmann presumed them to be viral particles.[3]

Wolff and Holubar[4] studied Odland bodies of normal and keratin-stripped skin and made the following observations:
- Odland bodies are sub-microscopic membrane limited ovoid organelles, which contain a complex system of closely set lamellar structures. The individual lamellar units consist of three parallel membranes separated from each other by a gap of 55 angstroms
- Odland bodies are produced by keratinocytes of the upper spinous and intermediate (granular) layers and are extruded into the extracellular space
  - Rapid parakeratotic keratinization results in the retention of Odland bodies in the parakeratotic cells and these represent "polymorphic components" of Brody seen in psoriasis
  - Increased proliferation of epidermal cells and acceleration of the process of keratinization leads to increased production of Odland bodies by keratinocytes
- Odland bodies and their lamellated derivatives in the intercellular compartment contain acid phosphatase and therefore Odland bodies represent a special type of epidermal lysosomes
- Their behavior in conditions with increased epidermopoiesis is evidence for their role in epidermal keratinization.

STRUCTURE AND FUNCTION OF ODLAND BODIES
Odland (lamellar) bodies are ovoid in shape, 200-300 nm in size and are secretory organelles with a membrane bilayer. They do not occur in the basal cell layer of the epidermis and are seen
in keratinizing cells especially the keratinocytes of the upper spinous layers and in the stratum granulosum.

Permeability barrier homeostasis is dependent on the formation and secretion of Odland body contents into the extracellular milieu as well as processing of the contents into lamellar bilayers. Odland bodies contain phospholipids, glucosylceramides, sphingomyelin and cholesterol. Several enzymes, viz. lipid hydrolases such as beta glucocerebrosidase, acidic sphingomyelinase, secretory phospholipase A2 and neutral lipases and proteases such as kallikreins and cathepsins are present in Odland bodies. Recent studies have shown that anti-microbial peptides like human beta defensin 2 and cathelicidin LL-37 are also present in lamellar bodies and that they may play a role in local innate immune responses of the skin.[5]

The lipids stored in the lamellar bodies are precursors of the stratum corneum extracellular lipids and are secreted from Odland bodies along with enzymes that act on them in the extracellular spaces[6] forming ceramides from glucosylceramides and sphingomyelin, and glycerol and free fatty acids from phospholipids.[7] Dysfunction or deficiency of lipolytic enzymes leads to decreased conversion of lipid precursors to ceramides leading to impaired barrier function as is seen in Gaucher’s disease due to deficiency in beta glucocerebrosidase and in Niemann-Pick disease due to deficiency in acidic sphingomyelinase.[8]

Apart from providing lipids for the formation of the lipid membranes and permeability barrier function the extracellular breakdown of Odland body lipids releases several substances that play important roles in several stratum corneum functions such as:

- Glycerol is formed from phospholipids and serves as a water holding substrate keeping the horny layer well hydrated.
- Free fatty acids formed during phospholipid breakdown help in maintaining the pH in the acidic range of about 5.5,[9] which helps regulate the activity of several enzymes in the stratum corneum. Formation of ceramides is optimal at pH 5.5, whereas the increase in pH to higher than 7 results in a decrease in ceramide production with resulting impairment of barrier function. Higher pH also leads to increased desquamation of the stratum corneum due to increased protease activity.

The structural proteins that Odland bodies are made up of have not yet been identified but their function is regulated by acute disruption in the permeability barrier by physical events, either experimental or in daily life situations e.g., sequential tape stripping, use of strong solvents like acetone or strong detergents.

Damage to the permeability barrier induces rapid secretion of the contents of the Odland bodies in the outer stratum granulosum cells resulting in a marked decrease in the number of Odland bodies (50-80%).[10] Soon thereafter newly formed lamellar bodies appear in the stratum granulosum cells until permeability barrier function is restored.[10] Odland body synthesis is regulated by the ambient calcium gradient in the upper epidermis in the granular cell layer.[11] Disruption of the barrier results in decreased calcium surrounding the stratum granulosum cells and change in calcium concentration appears to be the primary signal inducing Odland body secretion and regeneration. Potassium and other ions may also play a part as also cytokines such as interleukin-1 alpha, which is released in the epidermis following barrier disruption.[12]

Studies have shown that ABCA 12, a member of the ABC family of transport molecules is necessary for Odland body formation and mutations in ABCA 12 lead to failure to form normal Odland bodies and extracellular lipid membranes. Harlequin fetus is associated with severe ABCA 12 mutations leading to almost complete loss of Odland bodies while milder partial dysfunction of the gene leads to lamellar ichthyosis.[13,14]

X linked ichthyosis is a good model to study the interaction of lipids from Odland bodies and enzymatic processes that regulate orderly desquamation of the stratum corneum corneocytes. In normal skin, cholesterol sulfate is stored and secreted by Odland bodies. The enzyme steroid sulfatase ensures continuous degradation of cholesterol sulfate leading to reduction of cohesive forces of corneocytes allowing desquamation. Absence of the enzyme in X linked ichthyosis causes cholesterol sulfate to build up in the outer layers of the skin and interferes with desquamation of corneocytes leading to visible scaling characteristic of that disease.[15]
Premature Odland body secretion and foci of electron-dense material in the intercellular spaces of the stratum corneum may be considered as markers for the Netherton syndrome,[16] which clinically presents with erythroderma similar to psoriasis and non-bullous congenital ichthyosiform erythroderma.

In hyperproliferative conditions like psoriasis although many lamellar body containing cells are present, the secretion of Odland bodies is impeded and most of them remain intracellular within the cornified cells and do not release their lipids and other stored components.

George F. Odland (August 27, 1922-November 21, 1997): ![Figure 2](image) was born to Henry and Alice Odland in St. Paul, Minnesota, USA on August 27, 1922. The family moved shortly thereafter to Seattle in 1925, where he attended the Lakeside School for boys (the school attended by Bill Gates of Microsoft Fame). He joined Princeton, where he majored in biology and joined Harvard Medical School, graduating in 1946. He interned at the Massachusetts General Hospital and later spent 2 years in the Navy as medical officer before returning to Harvard to complete a residency in dermatology in 1954.

At Harvard, he was in the same department as Walter Lever, the famous Dermatopathologist, who was a personal friend and who encouraged his interest in histology of the skin and especially his love for electron microscopic study of the skin. Being a tall man, he had a habit of using big tomes to prop up the microscope to avoid bending forwards and this used to bemuse Dr. Lever who was not known for his height. While at Harvard, he had also been a research fellow in anatomy and pioneered several histochemical techniques and developed great expertise in the use of the electron microscope to diagnose skin diseases.

He returned to Seattle in 1955 and started private practice along with his father Dr. Henry Odland who had been one of the first Dermatologists in that city. He joined the University of Washington Medical School as a member of the clinical faculty in anatomy and dermatology and continued research in anatomy which he would do in the mornings and join his father to practice dermatology in the afternoons. He was keen on academics and joined the anatomy department so as to have access to his passion, the electron microscope.

Following the untimely death of Dr. Jim Case, he was in 1962 appointed as head of the newly formed Division of Dermatology, a position that he served until his retirement in June 1988.

Dr. Odland was a pioneer in the use of the electron microscope, developing an international reputation based on his research and made discoveries that bear his name, namely the Odland body, a sub-cellular component in the skin associated with the epidermal permeability barrier. He served on a peer-review panel for the National Institutes of Health and was a world expert in skin research. At the University of Washington, he developed a dermatology program that is internationally recognized for its contribution to investigation of cutaneous anatomy and biology.

He was a great Dermatologist, a respected researcher, a marvelous teacher and an effective leader. As Chief of Dermatology he trained many young dermatologists who went on to provide outstanding service in the community, many went on to serve as faculty at institutions around the country and also in other countries around the world. He was a humble man who was effective in motivating those lucky to work with him and he was liked and admired not only by his physician colleagues, but also by all staff and his patients alike.

After his retirement, The George F. Odland Endowed Chair in Dermatology was established in 1989, by various friends and colleagues and the Carl J. Herzog Foundation, in recognition of his outstanding contribution as an inspirational teacher, skin biologist and physician. The Odland Scholars program was established in the Division of Dermatology by support of the Herzog Foundation to encourage academic careers in dermatology and cutaneous biology.

George Odland was a good athlete in his younger years and was part of the Princeton University Rowing club crew. He was very fond of fishing and his father Dr. Henry Odland had a small fishing cabin where the family would spend several weeks every summer. His son Dr. Peter Odland (personal communication) has many fond memories of the summer camping trips where they would go out into the wilderness, learning many lessons about pitching tents, building fires, trout fishing, canoeing and swimming. George Odland was also a good tennis player and had a regular weekly game at the local tennis club. He was a great family man, had a wonderful relationship with his wife and raised his three sons with lots of love [Figures 3-5].
George Odland died in Seattle, November 21, 1997, from complications of a stroke at the age of 75.

His son Dr. Peter Odland is also a dermatologist and a dermatosurgeon and is a third generation Odland practicing dermatology in Seattle.

ACKNOWLEDGMENTS

Many thanks to Dr. Peter Odland, MD and John Odland for details and photographs of Dr. George Odland.

REFERENCES

1. Odland GF. A submicroscopic granular component in human epidermis. J Invest Dermatol 1960;34:11-5.
2. Selby CC. An electron microscope study of thin sections of human skin. II. Superficial cell layers of footpad epidermis. J Invest Dermatol 1957;29:131-49.
3. Horstmann E, Knoop A. Electron microscopic studies on the epidermis. I. Rat paw. Z Zellforsch Mikrosk Anat 1958;47:348-62.
4. Wolff K, Holubar K. Odland bodies (membrane coating granules, keratinosomes) as epidermal lysosomes. An electron microscopic-cytochemical contribution on the cornification process of the skin. Arch Klin Exp Dermatol 1967;231:1-19.
5. Elias P, Feingold K, Fartasch M. Epidermal lamellar body as a multifunctional secretory organelle. In: Elias P, Feingold K, editors. Skin Barrier. New York: Taylor and Francis; 2006. p. 262-72.
6. Freinkel RK, Traczyk TN. Lipid composition and acid hydrolase content of lamellar granules of fetal rat epidermis. J Invest Dermatol 1985;85:295-8.
7. Mao-Quang M, Jain M, Feingold KR, Elias PM. Secretory phospholipase A2 activity is required for permeability barrier homeostasis. J Invest Dermatol 1996;106:57-63.

Table 1: Disorders associated with abnormalities of Odland bodies

| Disease               | Abnormality                          | Clinical presentation |
|-----------------------|--------------------------------------|-----------------------|
| X linked ichthyosis   | Steroid sulfatase deficiency         | Ichthyosis            |
| Netherton syndrome    | Premature Odland body secretion      | Erythroderma          |
| Harlequin fetus       | ABCA 12 mutations with complete loss of Odland bodies | Armour like plates with deep fissures, ectropion |
| Lamellar ichthyosis   | ABCA 12 dysfunction with loss of function of Odland bodies | Ichthyosis |
| Gaucher’s disease type 2 | Beta glucocerebrosidase deficiency with decreased ceramide formation | Ichthyosis |
| Niemann-Pick disease  | Sphingomyelinase deficiency          | Xanthomatous changes in skin |

ABCA 12: ATP-binding cassette sub-family A member 12

COMMENT

The sub-microscopic structure that Dr. Odland described in 1960 has over the years been shown to be a vital multi-functional constituent of the epidermis. Odland bodies are important for maintaining homeostasis of the epidermis by maintaining the epidermal permeability barrier. They also play a role in desquamation of keratinocytes, formation of the cornified envelope and in local anti-microbial immunity against Gram-negative bacteria and yeasts. Several diseases presenting with abnormal keratinization have been associated with absence or altered functions of Odland bodies [Table 1].
8. Schmuth M, Man MQ, Weber F, Gao W, Feingold KR, Fritsch P, et al. Permeability barrier disorder in Niemann-Pick disease: Sphingomyelin-ceramide processing required for normal barrier homeostasis. J Invest Dermatol 2000;115:459-66.

9. Fluhr JW, Kao J, Jain M, Ahn SK, Feingold KR, Elias PM. Generation of free fatty acids from phospholipids regulates stratum corneum acidification and integrity. J Invest Dermatol 2001;117:44-51.

10. Menon GK, Feingold KR, Mao-Qiang M, Schaude M, Elias PM. Structural basis for the barrier abnormality following inhibition of HMG CoA reductase in murine epidermis. J Invest Dermatol 1992;98:209-19.

11. Lee SH, Elias PM, Proksch E, Menon GK, Mao-Quiang M, Feingold KR. Calcium and potassium are important regulators of barrier homeostasis in murine epidermis. J Clin Invest 1992;89:530-8.

12. Wood LC, Elias PM, Calhouan C, Tsai JC, Grunfeld C, Feingold KR. Barrier disruption stimulates interleukin-1 alpha expression and release from a pre-formed pool in murine epidermis. J Invest Dermatol 1996;106:397-403.

13. Thomas AC, Cullup T, Norgett EE, Hill T, Barton S, Dale BA, et al. ABCA12 is the major harlequin ichthyosis gene. J Invest Dermatol 2006;126:2408-13.

14. Lefèvre C, Audebert S, Jobard F, Bouadjar B, Lakhdar H, Boughdene-Stambouli O, et al. Mutations in the transporter ABCA12 are associated with lamellar ichthyosis type 2. Hum Mol Genet 2003;12:2369-78.

15. Elias PM, Williams ML, Maloney ME, Bonifas JA, Brown BE, Grayson S, et al. Stratum corneum lipids in disorders of cornification. Steroid sulfatase and cholesterol sulfate in normal desquamation and the pathogenesis of recessive X-linked ichthyosis. J Clin Invest 1984;74:1414-21.

16. Fartasch M, Williams ML, Elias PM. Altered lamellar body secretion and stratum corneum membrane structure in Netherton syndrome: Differentiation from other infantile erythrodermas and pathogenic implications. Arch Dermatol 1999;135:823-32.