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Philip W. Wertz is a Professor Emeritus from the University of Iowa. He earned his A.B. in biochemistry at Rutgers University in 1971 and his Ph.D in biochemistry at the University of Wisconsin in 1976. After post-doctoral training at McArdle Laboratory for Cancer Research, he moved to the University of Iowa in 1981. He was initially an Assistant Research Scientist in the Department of Dermatology, but in 1990 he became an Associate Professor in the Department of Oral Pathology, Radiology and Medicine with an appointment in the Dows Institute. He was promoted to the rank of Professor in 1993. His research interests have included the structures and functions of lipids in the permeability and antimicrobial barriers of skin and oral mucosa. He has published many research articles, reviews and book chapters. He is currently on the editorial boards of Skin Pharmacology and Physiology, the International Journal of Cosmetic Science, the Journal of Lipids and Antibiotics.

Abstract:

"Biochemical events in formation of the cornified lipid envelope"

Acylglucosylceramides synthesized in the viable epidermis and associated with lamellar granules is the precursor of the corneocyte lipid envelope (CLE). This consists of ω-hydroxyceramide molecules ester-linked through the ω-hydroxyl group to acidic side chain groups on the outer surface of the cornified envelope. A series of fatty acyl-CoA elongases (ELOV6, ELOV3, ELOV1 and ELOV4) convert palmitoyl-CoA into 30- 34-carbon fatty acyl-CoA species. Although saturated species predominate, there are some monoenoic and dienoic entities. Then, a thioesterase cleaves the thioester linkage to release the free ω-hydroxyacid, which is ω-hydroxylated by a P450 (CYP4F22). Then the ω-hydroxyacid is converted back to a CoA thioester (FATP4). This entity serves as a substrate for ceramide synthase 3 to produce a ceramide in which the long ω-hydroxyacid is amide linked to a dihydrosphingosine. The long chain base can then be trans desaturated between carbons 4 and 5 to produce a sphingosine-containing ceramide. or it can be hydroxylated on carbon 4 to produce a phytosphingosine-containing ceramide. The sphingosine-containing ceramide can be hydroxylated at carbon 6 to yield a 6-hydroxysphingosine-containing ceramide. Next, linoleate is transferred (PNPLA1) from a triglyceride, or possibly a phosphoglyceride, to the ω-hydroxylgroup to produce acylceramide. This is glycosylated in the Golgi apparatus to produce acylglucosylceramide. Acylglucosylceramide in the bounding membrane of the lamellar granule is introduced to the corneocyte surface when the bounding membrane of the granule fuses into the cell plasma membrane. There are two lipoxygenase (12R-LOX & eLOX3) attacks on the linoleate chain to produce an epoxy alcohol. At this time, the glucose is removed by a β-glucocerebrosidase and the oxidized linoleate is removed through the action of a yet to be identified esterase. Transglutaminase then attaches the ω-hydroxyceramide to the outer surface of the cornified envelope. Recently, a dehydrogenase (SDR9C7) has been identified that converts a hydroxyl group the oxidized linoleate into a ketone that can chemically react with amino groups at the surface of the cornified envelope to attach the lipid to the protein.