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Lipid metabolism in the epidermis

Kenneth R. Feingold

Metabolism Section and Dermatology Service; Department of Veterans Affairs Medical Center; University of California, San Francisco; San Francisco, CA USA

The major function of the epidermis is to provide a barrier to the movement of water and electrolytes. Without this permeability barrier life would not be possible. This point is clearly illustrated when severe disruptions of the permeability induced by cutaneous burns or premature birth lead to profound problems in fluid balance and abnormal electrolytes, which can result in death. This cutaneous permeability barrier resides in the extracellular domains of the stratum corneum and consists of lipid enriched lamellar membranes that contain predominantly ceramides, free fatty acids and cholesterol. The cells in the stratum corneum i.e. the corneocytes, are surrounded by a cornified lipid envelop that consists of omega acylceramides that are covalently bound to the proteins that comprise the cornified envelope. The cornified lipid envelope plays an important role in linking the lipid enriched lamellar membranes to the cornified envelope that provides a scaffold that is required for normal permeability barrier function. Thus, while all cells require lipids as both structural and signaling molecules, keratinocytes have an additional need for lipids to form the extracellular lipid membranes and the cornified lipid envelope to provide for a fully functional permeability barrier.

In 2007 I wrote a detailed review on lipid metabolism in the epidermis and its role in the formation of the permeability barrier (see ref. 1). Since that time there have been additional studies that have further enhanced our understanding of the regulation and role of lipid metabolism in the epidermis. In the series of articles in this issue this new information is discussed in detail.

First, several articles focus on fatty acid metabolism. Fatty acids are the building blocks required for the formation of ceramides, phospholipids, and triglycerides and the fatty acids in the epidermis need to be elongated and undergo desaturation. The role of fatty acid transporters in regulating the entry of fatty acids into keratinocytes is discussed by Khnykin and colleagues. Uchida discusses the enzymes required for the elongation of fatty acids while Sampath and Ntambi discuss the enzymes required for fatty acid desaturation. Finally, Rizzo discusses the key role of fatty aldehyde dehydrogenase and how mutations in this enzyme lead to defective barrier function and ichthyosis.

Second, the utilization of fatty acids in the synthesis of phospholipids and triglycerides and the catabolism of these compounds is discussed. Jiang and I review the enzymes in the epidermis that mediate triglyceride and phospholipid synthesis and the factors that regulate the activity of these enzymes. Radner and colleagues discuss the enzymes and co-activators that mediate the lipolysis of triglycerides and the importance of this pathway in permability barrier formation. Chan and Mauro discuss the breakdown of phospholipids by phospholipases and the importance of this step in both the formation of the permeability barrier and the acidification of the stratum corneum.

Third, an update on the role of ceramides is presented. Akiyama discusses the key role of ABCA12 in mediating the transport of glucosylceramides into lamellar bodies.

Fourth, Elias and colleagues discuss the effect of mutations in the distal enzymes of the cholesterol synthetic pathway on epidermal structure and function.

Finally, I discuss how the lipids required for the formation of the permeability barrier may in addition to playing a structural role also act as signaling molecules to induce keratinocyte differentiation and stimulate permeability barrier formation.

It is hoped that this series of articles will not only be informative for both dermatologists and lipidologists but will also stimulate further research to further elucidate the role and regulation of lipids metabolism in the epidermis.

References

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Correspondence to: Kenneth R. Feingold; Email: kenneth.feingold@ucsf.edu
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