1. INTRODUCTION

While the important role of lipids in relation to cellular signaling is firmly established and in general well reviewed (Exton, 1994; Barrett, 1992), several novel aspects of the subject have only recently come to light, which involve peroxisomal function, and which appear deserving of further commentary.

Part of this reassessment of the significance of peroxisomal input to cellular signaling relates to the parallel reassessment of the metabolic role of the peroxisome in recent years. Far from the early perception that this organelle's activities were limited to minor substrates (De Duve and Baudhuin, 1966), it is now recognized that the peroxisome is a vital organelle implicated in a broad spectrum of metabolic activities and especially prominent in the area of lipid metabolism (Masters, 1996a; Masters and Crane, 1996). Again, it is now recognized that the peroxisome possesses a number of unique signaling characteristics which exert a significant influence on regulatory signaling, within and without the area of direct peroxi-
somal metabolism and at subcellular, intracellular, and intraorganellar levels (Masters, 1996b).

At a dietary level, too, it may be recalled that while historically, linoleic acid (ω-6) was long considered the main essential fatty acid (EFA), more recently, the ω-3 polyunsaturated fatty acids derived from α-linolenic acid have become the focus for much biomedical research because of their wide-ranging clinical significance (Hansen, 1994; Budowski, 1988), and the distinctive role of the peroxisome in the regulation of metabolism in this area has become recognized (Masters, 1996a).

This review is concerned with recent advances in lipidic signaling in all of the above areas.

2. LIPID METABOLISM AND THE PEROXISOME

The first of the recent developments that needs to be covered in this chapter is the extent of peroxisomal involvement in cellular lipid metabolism.

It has been known for some time, for example, that the β-oxidation of the common long-chain fatty acids may take place in the peroxisomes as well as in mitochondria (De Duve, 1983). There are several points of difference between the mechanisms of β-oxidation in peroxisomes and mitochondria, and for the details of these differences, the reader is referred to more specialized texts (Masters and Crane, 1995a). For the purposes of this chapter, it is necessary to highlight the fact that in the peroxisome the fatty acid is dehydrogenated to an enoyl CoA by an FAD-requiring fatty acyl-CoA oxidase with the concomitant production of hydrogen peroxide:

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\text{Fatty Acyl-CoA + O}_2 \rightarrow \Delta^2\text{-Enoyl-Acyl-CoA + H}_2\text{O}_2
\]

Other differences in the mechanisms which are of significance in the present context relate to the fact that peroxisomal β-oxidation is capable of acting on a much wider range of substrates than mitochondrial β-oxidation, and generally does not proceed to completion. Rather, peroxisomal β-oxidation is mainly concerned with the chain shortening of long-chain fatty acids (Masters and Crane, 1995a, 1984). These differences hold substantial implications in relation to signaling and the regulation of lipid metabolism.

As regards the aspect of substrate specificity, it may be noted that the peroxisome generally shows a marked preference for long-chain fatty acids, with short-chain fatty acids being oxidized little if at all. There is also a