

**Table 2.6** Evidence That Barrier Function (Water Loss) Regulates Epidermal Lipogenesis

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Dietary or solvent-induced barrier disruption stimulates epidermal lipogenesis.

Extent of lipid biosynthetic rates parallels severity of barrier defect.

Normalization of lipid biosynthetic rates parallels barrier recovery.

Occlusion with impermeable, but not vapor-permeable membranes after barrier disruption blocks acceleration of lipid biosynthesis.

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modulations in cutaneous sterogenesis in response to either vitamin D deficiency or excess, despite the known importance of the cutaneous free sterol, 7-dehydrocholesterol, for vitamin D synthesis (43).

In more recent studies, the role of the water molecule itself as the regulatory signal has been explored in greater detail (41; Table 6). Whereas occlusive membranes blunted the expected burst in lipid biosynthesis that follows barrier disruption, application of semi-permeable membranes did not block synthesis, retard the rate of return of normal barrier function, nor impede the return of stainable lipid in the stratum corneum. These studies lend strong support to the concept that the rate of water loss itself may be the regulatory signal for epidermal lipogenesis.

Although the foregoing body of evidence demonstrates the capacity of the epidermis to synthesize lipids in response to barrier requirements, they leave unanswered the sites of synthesis in the epidermis and the relative importance of specific SC lipids for barrier function. The rapid rate of return of barrier function to normal [i.e., by 15–20 hr, even after exhaustive delipidization accompanied by transepidermal water loss (TEWL) rates  $> 1000$  ppm/(cm<sup>2</sup>/hr (39,40)] suggests that lipid synthesis may not be limited to the basal layer but may extend to, or even be accelerated in, the outer layers of the viable epidermis. Indeed, in both in vivo and in organ culture, the rates of epidermal lipogenesis in the SG of neonatal mouse epidermis approach those in the subjacent basal/spinous layers, even under basal conditions (44; Fig. 4), that is, in the absence of barrier perturbation. The importance of this observation is underscored further by the simultaneous, precipitous decrease in protein, DNA, and CO<sub>2</sub> generation in the same layer (44). Whether the SG is the site of accelerated synthesis after barrier perturbation is currently under investigation.

Certainly, the foregoing studies establish that nonsaponifiable lipids (i.e., sterols and possibly hydrocarbons) are important for