inhibit proliferation and induce differentiation (62). PPARγ activity abrogates the induction of macrophage inflammatory mediators (198). As mentioned before, various eicosanoids, but also fatty acids bind to PPARs. Arachidonic, linolenic and linoleic acids are all PPARs ligands. The synthetic AA analogue and LOX inhibitor 5,8,11,14-eicosatetraynoic acid (ETYA) is another PPAR ligand. Of the eicosanoids, 8(S)-HETE and 15-HETE can also serve as PPAR ligands (62). The prostaglandin J_2 metabolites 15d-$\Delta^{12,\ 14}$-PGJ_2 and LTB_4 are specific PPARγ and PPARα ligands respectively (68, 69, 70, 71). It is interesting that MK886, a FLAP inhibitor, inhibits PPARs. MK886 induces apoptosis and blocks PPARα-induced differentiation (72). Fatty acids such AA, LA, docosahexaenoic (DHA) and eicosapentanoic acid (EPA), which activate PPARs, may have anticancer effects (68).

2. AIM OF THE STUDY

Since all LOX isoforms are expressed in the skin, a wide spectrum of associated skin disorders have been investigated. The involvement of eicosanoids in dermatology has been concentrated to the fields of inflammatory diseases and skin cancers. Psoriasis and atopic dermatitis are major chronic skin diseases, in which LTs may be involved. Many studies investigated the presence of LOXs in keratinocytes, since psoriasis is characterized by keratinocyte hyperproliferation.

In contrast, the involvement of LOXs in acne, another chronic inflammatory skin disease, and consequently in the sebaceous gland has not been evaluated. In acne, neutrophil infiltration plays a significant role and LTB_4-mediated inflammation is believed to participate in this process. Few studies are available about 5-LOX or other LOXs expression in the pilosebaceous unit. In our study we tried to determine:

1) the expression of 5-LOX, 15-LOX and LTA_4 hydrolase in human SZ95 sebocytes in vitro, at protein and mRNA levels, as well as by immunocytochemistry,
2) the activity of 5-LOX, defined as LTB_4 formation and associated release of pro-inflammatory cytokines,
3) the effect of 5-LOX on sebaceous lipid synthesis,
4) the potential effects of 5-LOX specific inhibitors, in vitro. This was particularly interesting since a current in vivo study performed in our department detected an anti-acne effect of zileuton, an oral 5-LOX inhibitor.