the antimicrobial action of fatty acids, lipids, and the hostile pH of the skin surface. Human β-defensin-2 mRNA can also be induced in SZ95 sebocytes by *P. acnes* (Nagy *et al.*, 2006), and psoriasin adds to the mixture. We show here that combining only two antimicrobials (LL-37 and psoriasin) produced a synergistic effect against *P. acnes* and greatly increased the potency of cathelicidin. The actual concentration of β-defensins, psoriasin, or other potential antimicrobial peptides in the sebaceous gland remains unknown, but the current findings support the conclusion that the sebaceous gland contributes to epithelial defense by the release of multiple antimicrobial molecules to the skin surface. LL-37 may contribute more to inflammation surrounding the sebaceous gland than in antimicrobial defense (Yamasaki *et al.*, 2007).

CONFLICT OF INTEREST

The authors state no conflict of interest.

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Illuminating Role of CYP1A1 in Skin Function

Journal of Investigative Dermatology (2008) **128,** 1866–1868; doi:10.1038/sj.jid.5701236; published online 10 January 2008

TO THE EDITOR

Acne remains both a distressing and sometime serious skin condition with both environmental and hereditary factors playing an important role in this disease. An example of the former is the association of chloracne with dioxin exposure, so much so that chloracne is considered a clinical sign of dioxin exposure (Pelclova *et al.*, 2006); an example of the latter is correlative association between polymorphism in the cytochrome P450 1A1 (CYP1A1) gene and acne (Paraskevaidis *et al.*, 1998). CYP1A1 catabolises the metabolism of xenobiotics, including the oxygenation of polycyclic aromatic hydrocarbons, with the most potent known inducer of CYP1A1 being 2,3,7,8-tetrachlorodibenzo-p-dioxin (Nohara *et al.*, 2006).

We have generated transgenic mice that indicate basal CYP1A1 gene activity is restricted to the sebaceous gland in mice. The transgene differs from that described previously (Campbell *et al.*, 1996) in that the CYP1A1 gene promoter drives the expression of enhanced green fluorescent protein (EGFP), a red-shift variant of wild-type green fluorescent protein. EGFP is excitable using blue light of wavelength 488 nm and is detected by monitoring light of wavelength 509 nm. The transgenic mice were generated using standard pronuclear microinjection on a mixed C57/BL6 × CBA background. Activation of EGFP can be studied in animals without the use of sophisticated image

Abbreviations: CYP1A1, cytochrome P450 1A1; EGFP, enhanced green fluorescent protein

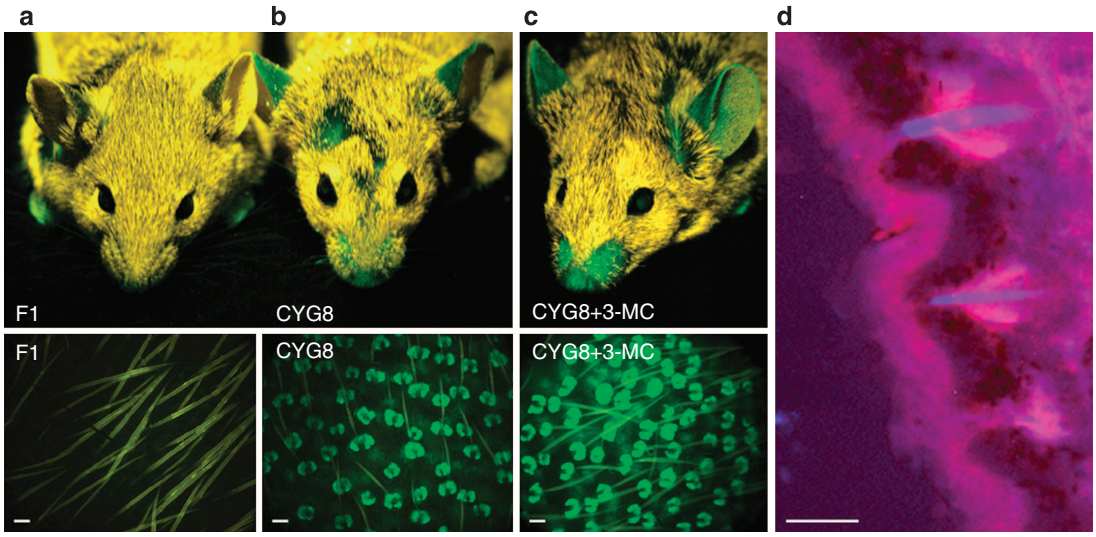

Figure 1. CYP1A1 gene activity in sebaceous gland of mice. (**a**) Wild-type and (**b**, **c**) transgenic CYP1A1–EGFP live mouse and ear punch illuminated with blue light of wavelength 488 nm and detected by monitoring light of wavelength 509 nm. Examples of basal transgene activity (**b**) or transgene activity induced by intraperitoneal injection of 3-methylchlorathene suspension in corn oil by at 40 mg g^{-1} body weight are shown. (**d**) Immunostained ear section of mouse shown in (**b**) confirming predominant CYP1A1 (pink) location to the sebaceous gland surrounding the hair shaft (blue). Bar = 1 mm.

analysis systems. These studies were approved by the Animal Ethics Committee of the Roslin Institute.

While utilising these mice in liver toxicity studies, we observed that adult transgenic mice were easily identifiable by their ''green'' ears (Figure 1a). Low-resolution imaging of ear punches indicated that green fluorescent protein activity rather than generalised transgene activity dispersed throughout the epithelium was largely restricted to define three-dimensional structures within the skin (Figure 1b). Immunostaining indicated that basal CYP1A1-driven EGFP activity in the skin was predominantly detected in the sebaceous gland (Figure 1d). Animals showed expression predominantly in the sebaceous gland, with reduced expression elsewhere in the skin, including the epidermis. Both epidermal and sebaceous expression were elevated with 3-methylchlorathene, with the majority of activity occurring in the sebaceous gland (Figure 1c).

Sebaceous glands are small, sacculated, glandular organs found associated with hair follicles in the epidermis. They secrete sebum in a holocrine manner, contributing to the integrity of the skin barrier (Zouboulis, 2004). CYP1A1 activity has been reported in skin and is induced upon topical drug treatment (Smith *et al.*, 2006); however, we have limited understanding of the non-induced function of CYP1A1 in tissue. The sebaceous gland contributes to skin barrier function. Given the association of CYP1A1 and acne (Paraskevaidis *et al.*, 1998), it is tempting to speculate that the observed strong CYP1A1 expression in the sebaceous gland relates to inflammation. However, there is evidence that sebum (Katsuta *et al.*, 2005), and more particularly cytochrome P450, activity is involved in the permeability barrier (Behne *et al.*, 2000), whereas CYP1A1 is also involved in combating xenobiotics (Zouboulis, 2004). Without experimental study we are unable to associate the high CYP1A1 expression in the sebaceous gland with specific barrier function.

Sebaceous gland and epidermis both show 3-methylchlorathene induction of CYP1A1 activity. The level of activity in the epidermis was always considerably lower than that in the sebaceous gland. This suggests that the sebaceous gland may have the predominant role in elimination of toxins and that barrier lipid production is influenced by xenobiotics. We suggest that CYP1A1 has a role in normal skin barrier function and that its role in acne, in particular neonatal acne, which is characterised by high sebum excretion rate, warrants further investigation.

CONFLICT OF INTEREST

The authors state no conflict of interest.

ACKNOWLEDGMENTS

This work was supported by sponsorship from AstraZeneca, Cyclacel Ltd, Glaxo SmithKline, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Schering-Plough and Wyeth, with further support from the Biotechnology and Biological Sciences Research Council.

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