As the first line of defense against invading organisms, the skin uses a multiplicity of processes to ensure host survival, including physical, immunological, and innate systems of defense. The innate immune system, which defends skin in a nonspecific fashion, includes the cathelicidins and the single currently known human cathelicidin, hCAP18. This 8-kDa cationic antimicrobial protein is produced by leukocytes as well as epithelial and mucosal cells (Agerberth et al., 1995) as part of a broader defense system. The active region is its cationic C-terminal 37-amino-acid domain, LL-37, which mediates broad antimicrobial activity (Dorschner et al., 2001) by disruption of the microbial cell membrane (Oren et al., 1999). Beyond this function, LL-37 defends the organism by stimulating inflammation (Koczulla et al., 2003) and speeding wound healing (Dorschner et al., 2001). LL-37’s effect on host cells appears to be concentration dependent, but its specific effect on keratinocytes has not been previously studied.

Chammorro et al. (2009, this issue) studied whether LL-37 induced or suppressed apoptosis in keratinocytes and by which mechanisms this occurred (Chammorro et al., 2009). Through the use of camptothecin (CAM, a widely used experimental apoptosis-inducing agent) and the study of capsase-3 (a protein in the apoptotic pathway), cyclooxygenase-2, and other genes involved in regulating apoptosis, these investigators were able to better understand the role of LL-37 in keratinocyte apoptosis. LL-37 appears to protect keratinocytes from apoptosis by inhibiting CAM-induced capsase-3 activation. This is thought to occur by upregulation of several antiapoptotic genes, including cyclooxygenase-2 and inhibitor apoptosis protein-2. This action is mediated, at least in part, via prostaglandin E-2; LL-37 ensures keratinocyte survival while its antimicrobial action takes place.

Through the following questions, we examine this paper in greater detail. For brief answers, please refer to http://network.nature.com/group/jidclub.

REFERENCES

QUESTIONS
1. What are the roles of the epidermis in immunity?
2. What is LL-37, and what is the authors’ rationale for studying it?
3. What methods can be employed to study apoptosis?
4. What were the major findings of the study?
5. What may be the clinical implications of the study?
6. What further studies could be performed to confirm or further the observations?

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