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Desquamation in the Stratum Corneum

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To maintain a constant thickness of the stratum corneum the desquamation rate and the de novo production of corneocytes is delicately balanced. Using a plantar stratum corneum model we have obtained evidence that proteolysis is a central event in the desquamation process. A number of regulatory mechanisms for desquamation have been postulated based on our findings.

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INTRODUCTION

The building blocks of the stratum corneum, the corneocytes, and their intercellular cohesive structures, constitute an important part of the barrier, and they form a backbone for the intercellular barrier lipids.

There is a continuous production of new stratum corneum. In order to maintain a constant stratum corneum thickness at a given body site superficial parts of the stratum corneum must be continuously shed in the process of desquamation at a rate which balances de novo production of corneocytes. Desquamation normally occurs invisibly with shedding of individual cells or small aggregates of cells. Disturbances in this process results in the accumulation on the skin surface of only partially detached cells with or without a concomitant thickening of the stratum corneum. The severity of the disturbance may vary from modest to very pronounced, from a barely visible scaling combined with a feeling of roughness and dryness of the skin surface, to the accumulation of thick brittle scales such as in psoriasis or in the various forms of ichthyosis.

The turnover time of the stratum corneum is normally two to four weeks. The mechanisms responsible for a well regulated desquamation may be assumed to be very complex. A central event in desquamation is elimination of corneocyte cohesion. If this took place in the barrier-forming parts of the stratum corneum it would be deleterious. Corneocytes are "dead" in the sense that they have no protein synthesis, which means that they have no active turnover of cell surface structures, and they can not respond to intercellular signalling. Thus, any process within the stratum corneum which leads to structural and functional changes will have to be inititated in one sense or the other by keratinocytes in the viable parts of the epidermis. At the time when the most superficial part of the the stratum granulosum is transformed to the deepest part of the stratum corneum there must be a "programming" of the tissue which allows individual cells to be strongly linked to each other for a certain period of time, after which cell cohesion should decrease to a point where cell shedding can occur.

In order to understand desquamation we will have to identify mechanisms of cell cohesion in the stratum corneum, the structures involved, and the changes these structures undergo as cell cohesion decreases. We must then identify the chemical reactions taking place, which would immediately give us information regarding the nature of the involved enzymes.

Using pieces of plantar stratum corneum we have developed a simple model system [1] in which some basic events in desquamation can be studied. In addition to information about the enzyme(-s) involved in stratum corneum cell dissociation, the system has provided information about the nature of the cohesive structures in the stratum corneum. An important finding was that corneocyte cohesion is mediated to a large extent by protein structures, i.e. the modified desmosomes of the stratum corneum [2, 3]. This implied that proteolysis may be a central event in desquamation. There is good evidence for the involvement of proteolytic enzymes in desquamation also in non-palmar-plantar stratum corneum [4, 5].

ENZYMES INVOLVED IN DESQUAMATION

The best characterised enzyme so far with a proposed function in desquamation is stratum corneum chymotryptic enzyme (SCCE) [6–9]. SCCE has several properties compatible with a role in desquamation in vivo, including pH profile of its catalytic activity, its inhibitor profile, and tissue location. SCCE is produced as an inactive precursor which can be converted to active enzyme by proteolytic modification by trypsin-like enzymes. The mechanisms of SCCE-activation in vivo remains to be elucidated.

Results of expression analyses suggest that SCCE may be skin-specific. It is expressed in high suprabasal keratinocytes in interfollicular epidermis [10]. In hair follicles and sebaceous glands it is expressed at sites with cornified epithelia [11, 12]. Ultrastructural studies have shown that SCCE is present in the stratum corneum extracellular space, to which it is transported during cornification [13]. In addition to SCCE there are also other proteases present in the stratum corneum. Of these a 30 kD serine protease with trypsin-like primary substrate specificity [8] may be of special interest. It has been postulated to have a complementary role to that of SCCE in desquamation [5], and it is a candidate for being responsible for the activation of the SCCE-precursor.

REGULATION OF DESQUAMATION

The mechanisms by which desquamation is regulated remain to be elucidated. Given the fact that proteolytic degradation of desmosomes may be a central event in desquamation, a number of possible regulatory mechanisms can be postulated. To these belong activation of enzyme precursors, protease inhibitors in the stratum corneum [14], changes in the lipid composition of the stratum corneum intercellular space [15],

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water content [16, 17] and pH of the stratum corneum [18], and the action of modifying enzymes such as various glycosidases [19].

CONCLUSION

A well regulated desquamation is a prerequisite for the barrier function of the stratum corneum and for a normal skin appearance. In recent years we have learnt some basic facts about stratum corneum cell cohesion and the role of proteolytic enzymes in desquamation. Our knowledge in this area is, however, still very limited. In the near future we may expect to discover a number of hitherto unknown enzymes and enzyme inhibitors involved. We may also expect to learn from studies on hereditary skin diseases with disturbances in the formation and turnover of the stratum corneum. And, of course, studies on the stratum corneum carried out by biophysicists will continue to provide crucial information, not only for the understanding of the barrier properties of the stratum corneum, but also for the understanding of desquamation.

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