Dokumenttyp: journal article

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Titel des Beitrags: Protease inhibitors prevent plasminogen-mediated, but not pemphigus vulgaris-induced, acantholysis in human epidermis.

Abstract: Pemphigus is an autoimmune blistering disease of the skin and mucous membranes. It is caused by autoantibodies directed against desmosomes, which are the principal adhesion structures between epidermal keratinocytes. Binding of autoantibodies leads to the destruction of desmosomes resulting in the loss of cell-cell adhesion (acantholysis) and epidermal blisters. The plasminogen activator system has been implicated as a proteolytic effector in pemphigus. We have tested inhibitors of the plasminogen activator system with regard to their potential to prevent pemphigus-induced cutaneous pathology. In a human split skin culture system, IgG preparations of sera from pemphigus vulgaris patients caused histopathologic changes (acantholysis) similar to those observed in the original pemphigus disease. All inhibitors that were tested (active site inhibitors directed against uPA, tPA, and/or plasmin; antibodies neutralizing the enzymatic activity of uPA or tPA; substances interfering with the binding of uPA to its specific cell surface receptor uPAR) failed to prevent pemphigus vulgaris IgG-mediated acantholysis. Plasminogen-mediated acantholysis, however, was effectively antagonized by the synthetic active site serine protease inhibitor WX-UK1 or by p-aminomethylbenzoic acid. Our data argue against applying
anti-plasminogen activator/anti-plasmin strategies in the management of pemphigus.