


Reply

To the Editor:

Through the use of out-of-context scientific observations, irrelevant findings, misinterpretations of various studies (including our own), and isolated reports of what may be exceptional patients, the letter by Grande et al obfuscates the major bulk of the evidence that points to antidesmoglein antibodies as pathogenic in pemphigus. Grande et al do not understand the simple scientific principle that in any complex biologic system, findings will not be 100% the same, all the time, and there may be exceptions to the general rule.

Firstly, these exceptions do not validate an alternative theory for which there is no, or minimal, evidence. The evidence must be viewed as a whole, and that whole shows overwhelming support for desmoglein inactivation as the cause for pemphigus.
Possible Role for Non-Desmoglein Antigen in Pemphigus

To the Editor:
The editorial “Pemphigus: is there another half of the story?”, by Stanley et al (2001), signals a healthy controversy regarding the pathogenesis of pemphigus vulgaris. Despite the solid evidence that antidesmoglein (Dsg) antibodies have the central role in pemphigus vulgaris (PV) and foliaceous (PF), recent data raise questions that need to be addressed (Kalish, 2000). Data supporting a role for non-Dsg autoantigens in pemphigus include the following (Nguyen et al, 2000):

1. PV sera devoid of anti-Dsg1 activity produce blisters in Dsg3(−/−) mice. Dsg3(−/−) mice develop few spontaneous erosions, but with injection of this PV sera develop massive bullae, similar to those in Dsg3(+/+) mice. This confirms the importance of inactivating Dsg3 to produce PV-like blisters, but also indicates that anti-Dsg are not the sole pathogenic antibodies in PV sera.

2. PV sera immunoprecipitates multiple non-Dsg antigens from both normal and Dsg3(−/−) keratinocytes, including a antigen (not Dsg3) that migrates at 130 kDa.

3. Absorption of PV sera with Dsg3-Ig fusion protein removes pathogenicity; however, antibodies eluted from this column react with multiple antigens from both Dsg3(−/−) and normal keratinocytes. This was clearly demonstrated with western blots using eluted antibodies.

The only discrepancy between the data of Nguyen et al (2000) and that of John Stanley (Mahoney et al, 1999) relates to the site of blister formation in desmoglein (−/−) mice that receive PF sera. The solution is to repeat these experiments with shared reagents.

The above data suggest that PV is mediated by additional autoantibodies acting in concert with anti-Dsg. It is theorized that antibodies to keratinocyte cholinergic receptors may be the missing component (Nguyen et al, 2000). This last point is not proven, but is based on data, and should not be lightly dismissed. I have very high regard for all the investigators involved, and eagerly await additional scientific developments.

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REFERENCES
Kalish RS: Pemphigus, the other half of the story. J Clin Invest 106:1433−1435, 2000

Expression of Basal-Cell Adhesion Molecule (B-CAM) is Associated with Immature States of Human Keratinocytes

To the Editor:
We thank Dr. Boehncke for his interest and comments regarding our work. Unfortunately, his group’s publication (Bernemann et al, 2000) was not yet available to us at the time our manuscript was prepared and submitted. While we found B-CAM reactivity preferentially within the basal epidermal layer in inflammatory disorders or epithelial skin tumors (Schön et al, 2000), Dr. Boehncke proposed B-CAM as a marker for terminal differentiation of human keratinocytes based upon suprabasal antibody binding in a subset of normal human skin biopsies (Bernemann et al, 2000). Another study reports “weak and variable” B-CAM expression in the upper layers of the epidermis without specifying number or origin of the specimens tested (Garin-Chesa et al, 1994). The same study reports polarized basal expression of B-CAM in other stratified epithelia, such as esophagus or uterine cervix. The latter and...