shown in Figure 5 of the report this is not the case. These results raise an important and unanswered question regarding the IFN-γ-dependent mechanism(s) that restrict the temporal infiltration of neutrophils into the allograft to mediate this extreme histopathology. This continues to be a focus of our studies to fully understand and minimize this attack.

Tarek El-Sawy
Robert L. Fairchild

The Cleveland Clinic
Cleveland, Ohio

Explaining Decreased Nitric Oxide Production in Psoriatic Lesions: Arginase 1 Overexpression versus Calcitonin Gene-Related Peptide

To the Editor-in-Chief:

I read with great interest the paper written by Bvuch-Gerharz et al, in the January 2003 issue of The American Journal of Pathology. In this paper, the authors have explained the reason for the low NO concentration in the psoriatic plaques, in the face of high expression of inducible NO synthase (iNOS) mRNA and protein, by showing that arginase 1, which substantially regulates iNOS activity by competing for the common substrate L-arginine, is highly overexpressed in the psoriatic epidermis.

This is a feasible explanation, but not the only one. As a complement to the explanation for the low NO concentration in psoriatic plaques, I would like to mention the effects of calcitonin gene-related peptide (CGRP) on nitric oxide generation. The pathogenesis of psoriatic plaque lesions is closely related to the overexpression of CGRP and it has been shown that CGRP-containing nerve fibers are more dense in the psoriatic epidermis. Taylor and co-workers have shown that CGRP suppresses the production of NO most probably through inhibition of iNOS enzymatic activity.

Therefore, it could be concluded that in addition to the overexpression of arginase 1, overexpression of CGRP in the psoriatic lesions could decrease the production of NO, thereby preventing the NO concentration to reach the keratinocytotic levels.

Mohammad Reza Namazi
Shiraz University of Medical Sciences
Shiraz, Iran

References


Author’s Reply:

In the letter by M. R. Namazi, the interesting idea is put forward that in addition to our demonstration of arginase 1 overexpression, calcitonin gene-related peptide (CGRP) might contribute to depressing the iNOS activity in psoriatic plaques. His suggestion is based on two observations: a known overexpression of CGRP in psoriasis and a previous publication on the suppressive activity of ocular aqueous humor on NO synthesis being due to the presence of CGRP.

We were well aware of these findings, however, as relates to a CGRP-mediated inhibition of iNOS activity, there are controversial data in the literature. In a series of carefully controlled experiments it has also been shown that CGRP actually enhances iNOS expression and activity with doses of CGRP that were both lower and higher as in the first study. Moreover, in ocular aqueous humor the presence of several other factors with known and confirmed depressive action on iNOS activity had been characterized subsequently by the same group. It thus appears that depending on the presence of additional factors, CGRP may do both, either further enhance or additionally depress NO formation. And in this respect there is no way to currently estimate whether a hypothetically increased presence of this peptide in the epidermal layer might contribute to suppression of NO formation.
In contrast, there is general agreement on the influence of arginase 1 on the substrate availability for NO formation via the iNOS, and we had shown in our study that such an interaction does indeed apply for keratinocytes also. Thus, for the time being our finding serves a good and sufficient explanation for low NO formation despite iNOS expression and whether other factors hypothetically contribute (to a lesser degree) will not alter the major conclusions to be drawn, especially as concerns future therapeutic strategies.

Victoria Kolb-Bachofen
Heinrich-Heine-University
Duesseldorf, Germany

References